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Original Research Article

Indian Journal of Anesthesia and Analgesia
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Comparative Evaluation of Efficacy and Safety of Intravenous Propofol and Dexmedetomidine for Intraoperative Sedation during Subarachnoid block: A Prospective Study

Manas Ranjan Panigrahi[1], Bhabananda Mukhopadhyay[2]

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Abstract

Aims: **C**omparing Propofol and Dexmedetomidine to assess the relative safety and efficacy in achieving adequate intraoperative sedation (Ramsay Sedation Score of 3–4) and cardiorespiratory safety in patients undergoing abdominal hysterectomy under subarachnoid block. *Setting and Design:* Department of Anesthesiology pain & Palliative Medicine, ESI PGISMR and Hospital, Manicktala (Tertiary Care Government Hospital located in Kolkata, WB, India) Operation theatres, Postanesthesia Care Unit, Gynecology & Maternity Ward. *Study Design*: Uni-centric prospective double blinded comparative *Statistical analysis used*: With Shapiro-Wilk test and Chi-square test *Materials and Methods:* Forty female participants between 18 and 65 years of age were divided into two groups *via* systematic random sampling. After administering subarachnoid block with 15 milligrams of 0.5% hyperbaric bupivacaine, bolus IV Dexmedetomidine (Group D, n = 20) or Propofol (Group P, n = 20) was started. All patients were monitored. Dexmedetomidine and Propofol infusions were discontinued at the end of surgery and the patients were transferred to the Postanesthasia Care Unit (PACU). The modified Aldrete scoring system was used to assess the readiness for shifting the patients to the postsurgical wards. *Results:* Both the groups had comparable demographics and basal values of heart rate, blood pressure, respiratory rate, ASA physical status, duration of infusion, depth of sedation, incidence of hypotension, bradycardia, over-sedation, but Group P had higher incidence of transient respiratory depression which were easily manageable.

Keywords: Propofol; Dexmedetomidine; Intraoperative Sedation; Procedural Sedation; Spinal Anesthesia.

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Introduction

Subarachnoid block (spinal anesthesia) is one of the commonest anesthetic techniques worldwide owing to its simplicity and predictability. It is established that underlying stress, anxiety, unfamiliar environment of the operating room and more importantly intraoperative awareness can lead to short-term and long-term undesirable consequences.[1] Despite, procedural sedation being recognized to have paramount importance while a patient is operated under regional anesthesia, it is less frequently used by anesthesiologists

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during subarachnoid block, probably because of a valid concern regarding patient safety.[2] The key deterring factor seems to arise from the potential cardiorespiratory compromise that might occur with the use of conventional procedural sedatives above and over subarachnoid block which bears its own set of overlapping physiological changes.[3] The concern seems to be even more profound if the center is under equipped or remotely located. Propofol is by far the most commonly used agent for procedural sedation in India, the routine usage during subarachnoid block seems to be limited in more equipped centers.[4] This study was designed to investigate the cardiorespiratory safety of conventionally used agents in procedural sedation *viz*. Propofol and comparing its effects with relatively a novel agent Dexmedetomidine, which is considered to have a better cardiorespiratory safety profile.[5–7] For this study to be reproducible in remote locations, the primary outcome was measured on easily noticeable clinical parameters and basic hemodynamic monitoring. Although, Bispectral Index (BIS) was used during this study to objectively assess the depth of sedation in parallel with clinical scales (Ramsay Sedation Scale, RSS), has not been accounted to be the primary determinant of therapeutic target.[8,9] The goal of this study was to assess safety, choosing the right agent and estimating the mandatory duration of postoperative observation with procedural sedation during subarachnoid block. *The principle objectives were*: (a) to investigate if intraoperative sedation during subarachnoid block could be safe in ASA I and ASA II patients with Propofol and Dexmedetomidine; and (b) to compare the efficacy, safety and advantages of one agent over the other.

Materials and Methods

This study planned in accordance with the principles of Helsinki declaration. After obtaining the approval from the Institutional Ethical Committee on 11.1.2014, forty patients admitted for elective abdominal hysterectomy were divided into Two Groups Group "P" and Group "D" *via* computer-generated systematic randomization. This study was performed with all safety measures, equipment and backup systems ready. Informed consent by the participants in own language was taken, and they could opt out anytime. Group P was designed to receive Propofol and Group D with Dexmedetomidine for the purpose of procedural sedation.

Study area: Department of Anesthesiology pain & Palliative Medicine, Name of the Institute ESI PGISMR and Hospital, Manicktala (Tertiary Care Government Hospital located in Kolkata, WB, India) Operation theatres, Postanesthesia Care Unit, Gynecology & Maternity Ward.

Study population: Women undergoing abdominal hysterectomy under Subarachnoid block.

Age group: 18–65 years of age.

Study design: Uni-centric prospective double blinded comparative study.

Method of randomization: Computer-generated Systematic Random Sampling.

A windows-based random number generator program called "Random Number Generator 1.3" (under Freeware license by 2×D Soft) was used to randomly arrange a set of 40 discrete serials numbers. Correspondingly 40 closed paper vouchers of identical size was created with those numbers. From the resultant roster, odd ones in the sequence were labelled "Group P"; and even ones as "Group D". Group P (n = 20) were to receive Propofol and Group D (n = 20) received Dexmedetomidine for intraoperative procedural sedation.

Inclusion criteria

1. Patients of between 18 and 65 years old,
2. Patients with ASA I–II,
3. Patients undergoing Abdominal Hysterectomy under subarachnoid block.

Exclusion criteria

1. Patients with Hemodynamic Instability,
2. Known Hypersensitivity Reactions to the Drugs,
3. Contraindications to Subarachnoid Block,
4. Obstetric Patients,
5. Uncontrolled Hypertension/Diabetes,
6. Substance Abuse/Addiction (Opium Products/Alcohol),
7. Patients on Sedative Medications,
8. Diagnosed Neurological/Psychiatric Illness, Electrolyte Imbalance, Documented Metabolic, Cardiac, Renal, Hepatic illness.

The depth of sedation was monitored by the Ramsay Sedation Score (RSS) along with monitoring of vital signs:

Ramsay Sedation Scale (Score):

1. Patient anxious, agitated, or restless,
2. Patient cooperative, oriented, and tranquil alert,
3. Patient responds to commands,
4. Asleep, but with brisk response to light glabellar tap or loud auditory stimulus,
5. Asleep, sluggish response to light glabellar tap or loud auditory stimulus,
6. Asleep, no response.

The final preanesthetic checkup was done one day before operation. Information that were recorded for each cases were age, gender (all female, in our case), height and weight of the patients, presence of concomitant diseases, history for drug use and smoking and ASA classification. If she was found fully eligible for the study, an informed consent was taken. The patient was also educated on how to respond for assessment of RSS Scoring. The patients were kept on preoperative fasting as per ASA guidelines.[10] Premedication was given in form of 5 mg Midazolam tablets 60 minutes before the schedule in the preoperative area. An intravenous cannulation was done with 18G cannula on the nondominant forearm. As per institutional protocol, intravenous hydration with 10 ml/kg/hr Ringer's lactate was started 30 min before performing subarachnoid block. The study serial number was retrieved by randomly opening a voucher previously generated and the patient was tagged. The corresponding grouping information for that serial was retrieved from the Roster by the personnel who would be administering the drugs. The grouping information was kept strictly confidential from both the patient and the assessor. The patients were not labelled with any grouping information. The infusion pump was kept facing against the assessor and was controlled by the drug administrator only. Patients were monitored with noninvasive arterial blood pressure, electrocardiogram, heart rate, pulse oximetry and bispectral index.

After local infiltration, subarachnoid block was performed in sitting position, *via* L4-L5 interspace using a 25-gauge Quincke's needle (B. Braun Medical, Melsungen, Germany) while maintaining strict aseptic techniques with 12.5 milligrams of 0.5% hyperbaric bupivacaine (ANAWIN HEAVY 0.5%, NEON Inc, Mumbai, India). The patients were finally positioned supine. After confirming the onset of subarachnoid block bilaterally to the T4 level, bolus IV Dexmedetomidine for Group D and Propofol for Group P was started.

Patients in Group P received Propofol (NEOROF®, NEON Inc., Mumbai, India) at a dose of 1 mg/kg as the loading dose over 1 minute and then infusion was started at a rate of 50 mcg/kg/min and continued till the end of surgery. Group D received Dexmedetomidine (DEXTOMED®, NEON Inc., Mumbai, India) infusion at a dose of 1 µg/kg for the first 10 min and 0.5 µg/kg/h throughout the surgery. Both groups simultaneously received Ringer's Lactate at a rate of 10 mL/kg/h for the first hour and continued at a rate of 5 mL/kg/h. The time at which the RSS score comes between 3 and 4 was considered the time of start of sedation. BIS was noted as a secondary objective measurement. Patients were given with IV midazolam 0.5 mg as 'rescue sedation'; doses repeated until the patient exhibited a RSS score ≥ 3. The infusions were temporarily paused if there were RSS Score of 6 or BIS < 40 at any point of time, until RSS is ≤ 5 or BIS > 40. The systolic mean blood pressure, heart rate, peripheral oxygen saturation, respiratory rate and level of sedation were recorded every 5 min intervals after Dexmedetomidine or Propofol infusion being started, and also at the Postanesthesia Care Unit (PACU). Dexmedetomidine and Propofol infusions were discontinued at the end of surgery and the patients were transferred to the PACU. The modified Aldrete scoring system was used to assess recovery from anesthesia (score ≥ 9).[11] Patients were discharged from PACU to the respective Gynecology wards, after two hours of continuous uneventful observation. Stay in the PACU were extended if significant distress was experienced by the patient, in form of nausea, vomiting, respiratory distress, rebound sedation, headache etc. or the observed parameters indicate inadequate recovery, shown as in (Table 1).

Table 1: Time from Start of Infusion to Start of Sedation

	Group	N	Mean	Std. Deviation	Std. Error Mean	
Time of Onset of Sedation	D	20	11.5000	2.85620	.63867	$p < 0.001$
	P	20	6.7500	2.93571	.65645	

Working Definitions: Hypotension was defined as systolic blood pressure of less than 90 mm Hg or decrease of 30% from baseline and were treated with a bolus administration 6 mg of intravenous Mephentermine.[12] Bradycardia was defined as heart rate < 50 beats/min and treated with 0.6 mg of intravenous atropine.[13] Respiratory depression was defined, as respiratory rate < 8/min, or peripheral oxygen saturation declining below 90%.[14] The patients were managed by a quick evaluation to detect tongue fall back, or lack of respiratory drive and managed either by airway manipulation like jaw thrust or bag-mask ventilation. Emergency airway cart and standby ventilators were kept ready for all cases. Over sedation was defined as RSS Score of 6 or BIS < 40.

Data Analysis: All data were expressed as mean ± standard deviation. Parametric demographic data were analyzed using one-way analysis of variance (ANOVA). Sphericity of data was assessed with Shapiro-Wilk test. Nonparametric data were compared using Chi-square test. The study groups were compared by independent sample (unpaired sample) '*t*' test (with Bonferroni correction) for arterial blood pressure, heart rate, respiratory rate and peripheral oxygen saturation. RSS Score was compared using Friedman's test. *p* - values of < 0.05 considered significant. Statistical analysis has been performed using SPSS software (version 23.0; IBM Inc., Chicago, IL, USA, 2015). Results were cross-checked with GraphPad Prism version 6.01 for Windows OS (GraphPad Software Inc., California, USA.

Results

Sample characteristics, in terms of age in years (P: 54.1 ± 4.78; D: 55.55 ± 3.09), ASA classification, BMI (P: 25.44 ± 4.45; D: 25.17 ± 4.03) were found similar. Basal values of SBP in mm Hg (P: 134.05 ± 9.62; D: 136.95 ± 9.07), Respiratory Rate: (P: 22.3 ± 3.47; D: 23.4 ± 2.68) were also similar. There was an observed difference in the time of onset of sedation: (P: 6.75 ± 2.94; D: 11.5 ± 2.86). There was an early incision time in Group P (P: 8.95 ± 3.24; D: 13.3 ± 2.13; *p* - value 0.032). Shown in Table 2, duration of infusion in both groups were similar (P: 59.55 ± 8.27; D: 56.95 ± 7.09), and difference in the duration of sedation were nonsignificant (P:62.25 ± 8.19; D:59 ± 8.68). None needed rescue sedation, shown in Table 3. There was a statistically significant difference in the duration of sedation after stopping infusion at the end of surgery,shown as in Table 4. Time to reach Modified Aldrete Score of 9, were comparable in both groups. Hypotension was observed in 10 [P: 6 (60%) D: 4 (40%)], bradycardia was observed in 4 [1 (25%) in Group P and 3 (75%) in Group D]. Over sedation & Respiratory Depression were noted in 2 ($p = 0.147$) and 4 ($p = 0.035$) cases respectively, all belonged to Group P. Out of them, 3 were managed with Jaw thrust and bag-mask ventilation, 1 patients needed LMA insertion. Incidence of Postoperative Nausea and Vomiting (PoNV) observed in 6 with 3 cases in each group. Change in mean BP following the initial bolus doses in both group were not significant. RSS Scores had no significant difference in first 90 minutes, except there was a difference in first 10 minutes of infusion, with Group P having a lower rank.

Discussion

This study was unique in terms of comparing both the agents in patients undergoing operations of equivalent operative-stress (abdominal hysterectomy) under subarachnoid block to eliminate an important confounding factor of variable levels of the surgical stimuli, gender predisposition (the study population consisted exclusively female), age.

The depth of sedation was comparable in both the groups. But, the time of onset of sedation was significantly shorter in Group P, which is probably attributable pharmacokinetics of Propofol and the initial rate of infusion to induce sedation (1 minute in Propofol, whereas 10 minutes in Dexmedetomidine). Possibly, because of the same reasons, Group P showed an initial spike in RSS at 5–10 minutes postinitiation, compared to Group D, who experienced a spike in RSS score at 25–30 minutes postinitiation. Consequently, there was a scope for early incision time in Group P, saving costly resources.

The incidence of hypotension and bradycardia was comparable in both groups. The incidence of respiratory depression was more in Group P, which tend to occur immediately after the bolus infusion. But, no incidence of apnea during maintenance dose of Propofol was observed, more importantly, they were fewer in comparison than that was being perceived from earlier case reports.[15] Postoperatively, subjects in Group D experienced lower heart rate and BP, possibly because of waning spinal, supplemented by residual analgesic effects of Dexmedetomidine, or may be attributed to early elimination of Propofol.

Procedural sedation during subarachnoid block with either of the agent in the studied dosage was

safe, when continuous monitoring was done. Early detection of adverse situations like hypotension and bradycardia needed careful vigilance, but were manageable with commonly available drugs like Atropine and Mephentermine. Respiratory depression, observed with Propofol were managed with simple airway manipulations/interventions. Over sedation was found to be a relatively rare occurrence with either of the agent at the studied dosage, and Ramsay Sedation Scale (RSS) was sufficient to diagnose over sedation in absence of monitors like BIS. In both cases of over sedation, RSS was found to be comparatively early predictor to detect over sedation than BIS (BIS reading was above 40 in both cases). Postoperative monitoring in PACU for a period of two hours was found sufficient in all of the study subjects, before shifting to ward.

Conclusion

Choosing the right agent for procedural sedation should be guided by patient's profile. No agent could be found superior over the other in the context of quality of sedation, at the studied dosages sedation during subarachnoid block can be generally safe, with careful clinical vigilance, and

Table 2: Duration of Infusion

Parameters	Group	N	Mean	Std. Deviation	Std. Error	Mean
Duration of Infusion	D	20	56.9500	7.08947	1.58525	$p = 0.292$
	P	20	59.5500	8.26836	1.84886	

Table 3: Duration of Sedation after Stopping Infusion

Parameters	Group	N	Mean	Std. Deviation	Std. Error	Mean
Duration of Sedation after Stopping Infusion	D	20	13.5500	3.39466	0.75907	$p = 0.001$
	P	20	9.4500	3.60519	0.80614	

Table 4: Time for Modified Alderete Score of 9 after Stopping Infusion

Parameters	Group	N	Mean	Std. Deviation	Std. Error	Mean
Time for Modified Alderete Score of 9 after Stopping Infusion	D	20	11.5000	3.28473	0.73449	$p = 0.218$
	P	20	12.7500	3.02403	0.67619	

Table 5: Friedman Test: RSS Score

Ranks					
Group	**Time Mean**	**Rank Time**	**Group**	**Mean Rank**	***p* Value (from ANOVA)**
D	0	0	P	3.08	
	5	5		8.73	0.004
	10	10		13.00	0.001
	15	15		13.88	0.531
	20	20		11.65	0.345
	25	25		11.93	0.268
	30	30		11.90	0.076
	35	35		12.45	0.886
	40	40		13.18	0.048
	45	45		11.33	0.020
	50	50		12.13	0.406
	55	55		9.70	0.679
	60	60		7.55	0.347
	100	100		3.23	0.813
	110	110		3.10	0.757
	115	115		3.10	0.316
	120	120		3.10	0.561

basic hemodynamic monitoring. To draw a definite conclusion on the feasibility of its application in remote and underprivileged areas, wider population-based multicentric study is necessary.

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Comparison of the Efficacy of Neuraxial Blockade Analgesic Effect between Intrathecal Clonidine and Tramadol as An Adjuvant with 0.5% Bupivacaine

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Abstract

Background: A number of adjuvants in the form of opioids analgesics were routinely used intrathecally to prolong the analgesia effect both in the intraoperative and postoperative period. Clonidine and tramadol were the common agents used intrathecally along with bupivacaine for increasing the duration of analgesia. *Aim:* To assess and compare the neuraxial blockade analgesic effect between intrathecal clonidine and intrathecal tramadol along with 0.5% hyperbaric bupivacaine for lower limb surgeries. *Methodology:* A prospective double blinded randomized study was conducted for a period of one year at Dhanalakshmi Srinivasan Medical College and Hospital. A total of 100 patients who had been posted for elective lower limb surgery were included in our study and they were randomized into two groups of 50 each. Group A patients received clonidine hydrochloride 37.5 mcg (0.25 ml) and Group B patients received tramadol 25 mg (0.5 ml) and both the groups received 0.5% hyperbaric bupivacaine hydrochloride (3 ml) along with normal saline. Assessment of pain score was done using VAS scale and the motor blockade was assessed using Bromage motor blockade score and the vital parameters were also assessed along with it. *Results:* The onset of sensory analgesia was found to be much faster and the duration of sensory analgesia was found to be more prolonged among the group which received clonidine and the pain score which was measured using VAS was higher among the patients who received tramadol and the difference was found to be statistically significant ($p < .05$). The duration of motor function recovery was almost similar in both the groups and no significant side effects reported between the two groups. *Conclusion:* Both the groups were effective in producing adequate surgical anesthesia with hemodynamic stability without causing serious adverse events but clonidine group was found to have a faster onset of action with prolonged duration of analgesia.

Keywords: Clonidine; Tramadol; Intrathecal; Analgesia.

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Introduction

Local anesthetic agents are the common drugs used for spinal anesthesia and because of its early onset and short duration of action additional requirement of analgesia is needed much earlier during the postoperative period. A number of adjuvants in the form of opioids analgesics were routinely used intrathecally to prolong the analgesia effect both in the intraoperative and postoperative period. Use

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of opioids as intrathecal analgesia has a prolong analgesic effect which extends throughout the postoperative period without significant motor or autonomic blockade. However, few side effects such as pruritus, nausea, vomiting, urinary retention, respiratory depression has prompted future research towards nonopioid analgesics which would cause less serious adverse events.[1–3]

Clonidine being a selective alpha (α) 2 agonist agent, commonly used as a premedication agent when the patient is given general anesthesia, as it has the advantage of reducing the additional usage of analgesics and anesthetic drugs intraoperatively. Clonidine when used intrathecally it produces analgesic activity by indirectly inhibiting the activity of Wide Dynamic Range (WDR) neurons.[4] Other than intrathecal route clonidine can also be used orally, epidural, spinal or parenteral route for obtaining analgesic effect in the postoperative period.[5] The dosage of clonidine used in the previous studies ranged between 15–150 mcg without producing any significant side effects.[6]

Tramadol is a synthetic opioid introduced initially in mid -1970s. It has opioid agonist activity for all types of opioid receptors with more selectivity for mu (μ)-receptors. Tramadol, a synthetic 4-phenyl-piperidine analog of codeine, is a racemic mixture of two enantiomers, with synergistic antinociceptive interaction. The (+) enantiomer has moderate affinity for the opioids μ-receptor and inhibits serotonin uptake, and the (−) enantiomer is a potent norepinephrine synaptic release inhibitor and through this receptor it provides an effective analgesic property when given intrathecally. Moreover tramadol is very much cost-effective.[7]

Previous studies done earlier had compared clonidine with other sedatives or hypnotics like fentanyl or midazolam to assess the difference in hemodynamic response as well as the analgesic property, not much studies done previously had compared the analgesic property between clonidine and tramadol and so, the present study was undertaken to assess the effect of these two drugs in providing analgesia postoperatively and hemodynamic response.[8–10]

Aim

To assess and compare the neuraxial blockade analgesic effect between intrathecal clonidine and intrathecal tramadol along with 0.5% hyperbaric bupivacaine for lower limb surgeries.

Materials and Methods

A prospective double blinded randomized study was conducted for a period of one year at Dhanalakshmi Srinivasan Medical College and Hospital in the Department of anesthesiology. The study was started after obtaining clearance from the institutional ethical committee and informed consent was obtained from all the study subjects involved in the study. All patients in the age group of 18 to 60 years with ASA grading of I or II and have been posted for elective lower limb surgeries under spinal anesthesia were included as our study subjects. A total of 100 patients were included in our study and they were randomized into two groups of 50 each. Randomization was done through lot system and double blinding technique was followed where both the patient and the anesthetist is not aware of the which patient belong to which group. Group a patients received clonidine hydrochloride 37.5 mcg (0.25 ml) and Group B patients received tramadol 25 mg (0.5 ml) and both the groups received 0.5% hyperbaric bupivacaine hydrochloride (3 ml) along with normal saline. A complete preanesthetic evaluation was performed on all patients before the start of the procedure. Preanesthetic medication IV midazolam was given to all the patients. Under strict aseptic precautions midline lumbar puncture was performed using a 25 G quincke needle with patient in lateral decubitus position and the anesthetic drugs were given based on the group the patient belong to. Patients was then placed in supine position, the time when the intrathecal injection was given was considered as 0 mins and from then the patients were monitored every 5 mins for the first 15 mins and then onwards they were monitored for every half an hour till 180 mins. During this time the vital parameters such as heart rate, systolic and diastolic BP, respirator rate and SpO_2 were monitored and recorded along with the time duration for sensory blockade, motor blockade, duration of analgesia and sedation. Assessment of pain score was done using VAS scale and the motor blockade was assessed using Bromage motor blockade score and these two parameters were assessed upto 360 mins. Apart from the above mentioned drugs when the patients complained more pain a rescue analgesic injection of diclofenac 75 mg was given. Duration of effective analgesia was defined as the time interval between the onset of subarachnoid block and the time to reach VAS ≥ 4. Patient was kept in the recovery room till complete recovery had occurred from motor blockade and later shifted to the postoperative room. In the postoperative room patient was monitored for the occurrence of any side effects like vomiting, dry mouth or pruritus for 24 hours.

All the data were entered and analyzed using SPSS version 22. Student *t*-test and Chi-square test was used to derive the statistical inference by comparing the parametric and nonparametric variables that were measured among the two groups, considering $p < 0.05$ as statistical significance.

Results

The mean age group between the two groups was between 40 and 42 and in both the groups females outnumbered males. Other demographic variables like height, weight and BMI did not show statistical significant difference between the two groups. Most of the surgeries performed did not extend more than 2 hours in both the groups and the duration of the surgery did not show statistical significant difference between the two groups shows as in Table 1. The mean onset of sensory analgesia was found to be much quicker in the group that received clonidine (151.4 mins *vs* 172.4 mins) and similarly the mean duration of sensory analgesia was prolonged among the patients who received clonidine compared to the patients who received tramadol (319.6 mins *vs* 295.8 mins) and the difference in the time duration between the two groups was found to be statistically significant. The maximum sensory blockade among both the groups was achieved between T6 and T8 levels and there was no difference in the levels of achievement of sensory blockade and similarly the mean duration of full motor recovery was slightly more in the clonidine (286.7 mins) group compared to tramadol group (282.9 mins) but the difference was not statistically significant shows in Table 2.

Pain score was assessed using the visual analog scale and the motor functional activity was assessed using the Bromage scale score in our study subjects. The VAS score for the first 120 mins was zero among both the groups and a statistical significant difference was seen in VAS score from 180 mins to 300 mins, in which the mean VAS score among the tramadol group was higher than the mean VAS score among the clonidine group.

Table 1: Comparison of the demographic variables and the duration of surgery between the two groups

Variables	Group A (clonidine hydrochloride group)	Group B (tramadol group)	*p* - value
Age	40.25 ± 9.76	41.92 ± 10.26	0.891
Gender (M/F)	12/38	10/40	0.585
Height (in cms)	165.26 ± 6.21	163.45 ± 7.59	0.717
Duration of surgery (in mins)	104.6 ± 8.94	99.4 ± 7.48	0.285

Table 2: Comparison of sensory and motor blockade functions between the two groups

Variables		Group A (clonidine hydrochloride group)	Group B (tramadol group)	*p* - value
Mean onset of sensory analgesia (in secs)		151.4 ± 25.5	172.4 ± 32.8	0.0167
Maximum sensory blockade	T6	23	24	0.798
	T8	25	25	
	T10	2	1	
Mean duration of sensory analgesia (mins)		319.6 ± 27.5	295.8 ± 28.8	0.0108
Mean duration of full motor recovery (in mins)		286.7 ± 21.9	282.9 ± 15.8	0.329

Table 3: Comparison of VAS score and Bromage score between the two groups at various time intervals

Time (mins)	VAS score (mean ± SD)			Bromage score (mean ± SD)		
	Group A	Group B	*p* - value	Group A	Group B	*p* - value
0	0	0	1.00	0	0	1.00
15	0	0	1.00	3	3	1.00
30	0	0	1.00	3	3	1.00
60	0	0	1.00	3	3	1.00
120	0	0	1.00	3 ± 0.36	2.65 ± 0.31	0.0031
180	1.12 ± 0.12	1.72 ± 0.18	0.0028	2.45 ± 0.28	2.39 ± 0.29	0.0851
240	2.16 ± 0.35	3.01 ± 0.41	0.0019	2.21 ± 0.45	2.18 ± 0.25	0.761
300	2.85 ± 0.43	3.45 ± 0.56	0.0197	1.08 ± 0.29	0.55 ± 0.13	0.0017
360	5.65 ± 0.76	6.05 ± 0.81	0.0866	0	0	1.00

The Bromage motor functional score for the first 60 mins was similar among both the groups but a statistical significant difference was seen in the bromage score from 120 to 180 mins, where the mean bromage score was high among the clonidine group compared to tramadol group and a similar pattern was observed at 300th min shows in Table 3.

Very few side effects were reported among the study subjects in both the groups such as

Table 4: Incidence of side effects between the two groups

Side effects	Group A (clonidine hydrochloride group)	Group B (tramadol group)	*p* - value
Hypotension	4 (8%)	2 (4%)	0.0816
Bradycardia	2 (4%)	2 (4%)	1.000
Vomiting	1 (2%)	3 (6%)	0.219
Dryness of mouth	1 (2%)	0	0.384

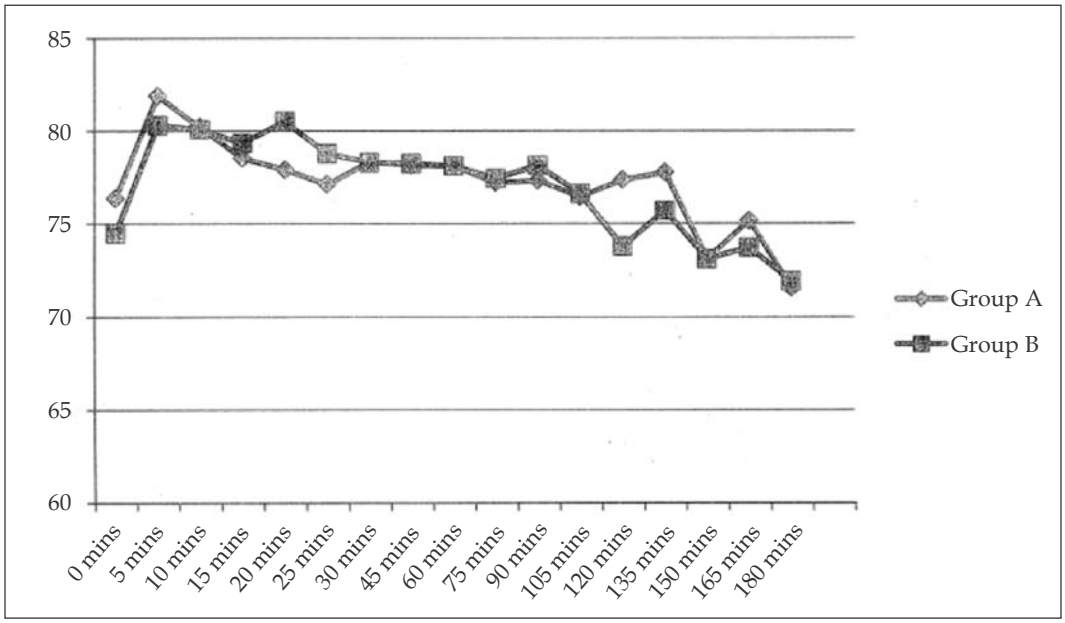

Fig. 1: Heart rate comparison between the two groups over a period of time

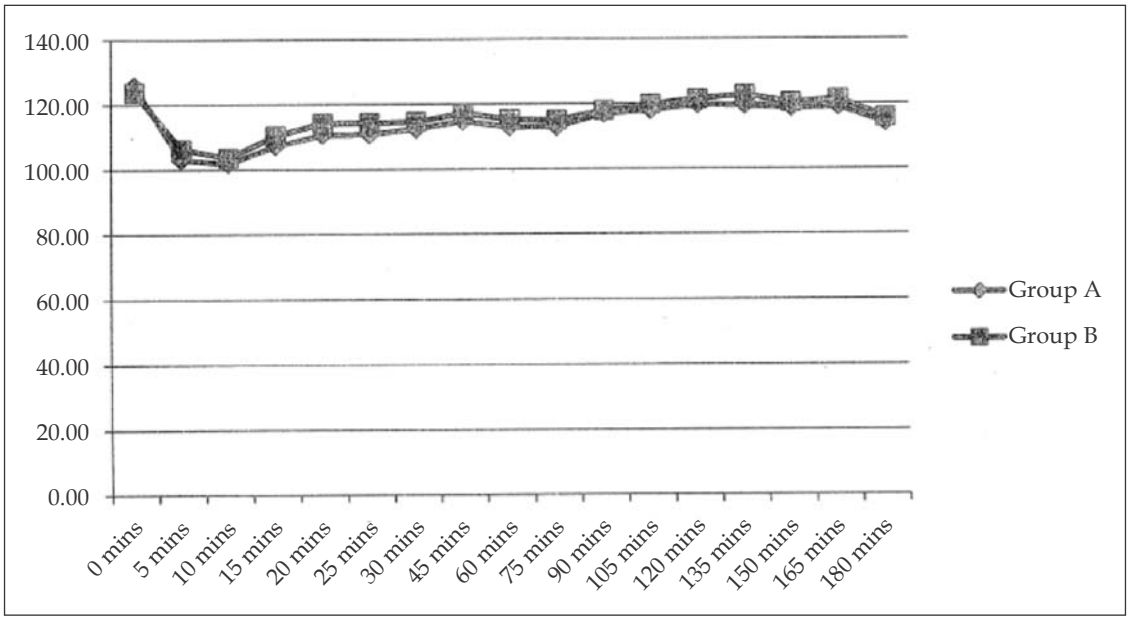

Fig. 2: Systolic blood pressure comparison between the two groups over a period of time

hypotension, bradycardia, vomiting and dryness of mouth and the distribution of these side effects were very minimal among the patients in both the groups and none of the side effect had shown a statistical significant difference between the two groups shows in Table 4. The vital parameters measured in the study subjects were heart rate, systolic and diastolic blood pressure and SpO_2. All these vitals were measured from the time of infusion of the anesthetic drug upto 180 minutes and the readings between the two groups were almost similar no statistical significant difference was observed between them at any point of time. It is represented shows in Figs. 1–4.

Discussion

Clonidne, being an alpha-2 agonist when added to local anesthetics had shown an excellent surgical anesthesia. It increases the sensory and motor block of the local anesthesia. Studies had shown that intrathecal administration of opioid provides effective postoperative analgesia but with a risk of causing respiratory depression.[6] In contrast to the opioid analgesics tramadol is a drug which shows less affinity towards μ-receptors and so, causing a minimal effect on respiratory depression. Added to this tramadol also inhibits the reuptake of serotonin

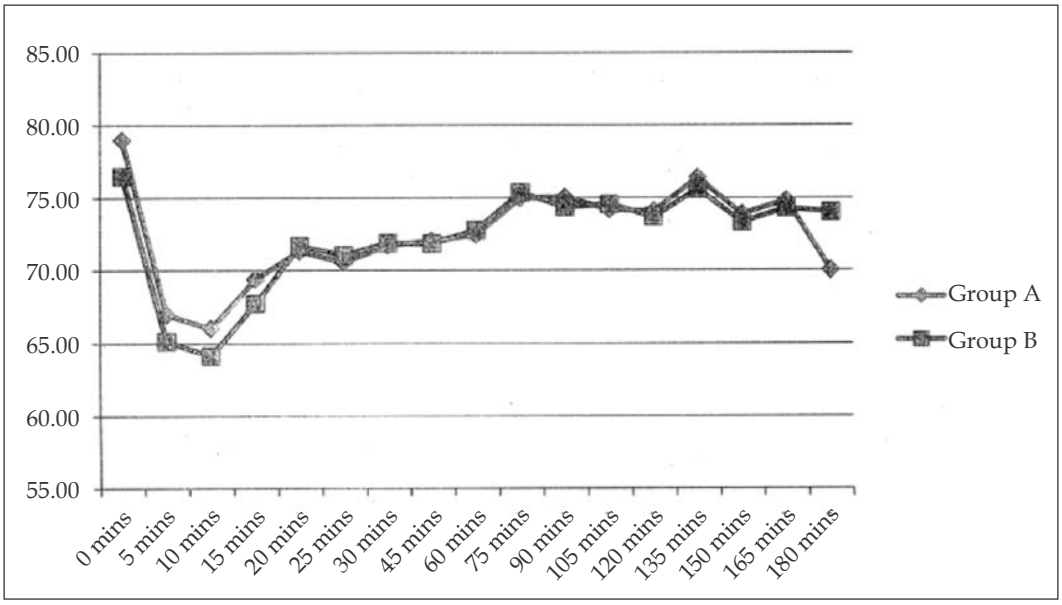

Fig. 3: Diastolic blood pressure comparison between the two groups over a period of time

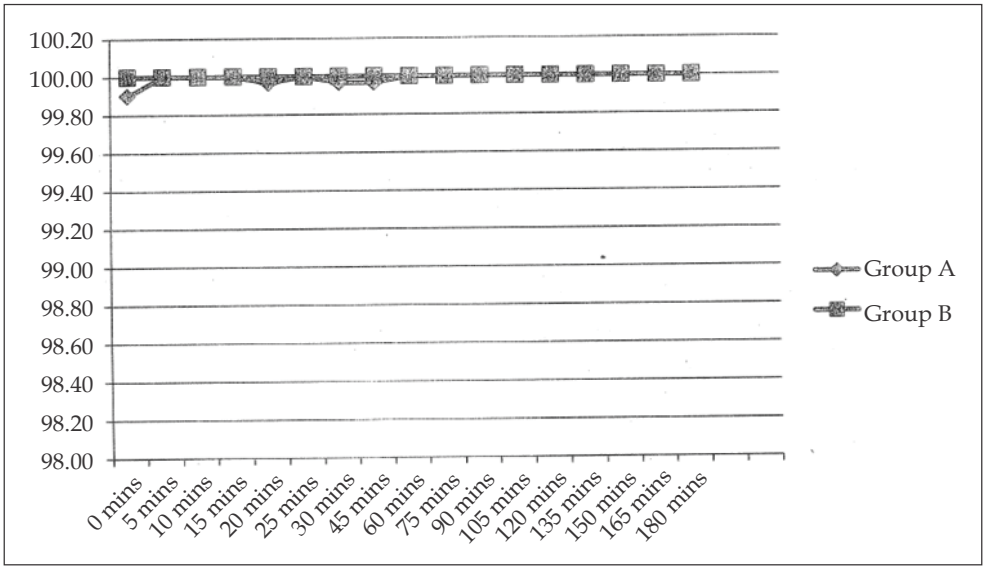

Fig. 4: SpO_2 comparison between the two groups over a period of time

and norepinephrine in the spinal cord and so, no neural toxicity was reported.[11]

In the present study, we compared the analgesic effects of clonidine and tramadol when given intrathecally along with the routine spinal anesthesia for patients undergoing lower limb surgeries. It was done through randomization technique by dividing the entire study subjects into two groups and one group received tramadol and the other group received clonidine by following a double blinded technique. The demographic variables and the types of surgeries along with the duration of surgery were found to be almost similar in both the groups without any significant variations between the two groups.

In our study, we found that the mean time of onset of sensory analgesia among the group that has received clonidine drug was 151.4 mins compared to the group that received tramadol which was 172.4 mins and the difference was found to be statistically significant. It is similar to the previous studies done by Khezri et al. and Bajwa et al. where they had shown that the onset of sensory analgesia was much earlier in the group which received clonidine, these two studies compared clonidine with either bupivacaine or fentanyl and proved clonidine was much superior in achieving the onset of sensory analgesia.[10,12] In the current study, the maximum level of sensory block that was achieved in both the groups was T6 and T8 where no statistical significant difference was observed between them and a similar type of results was also seen in a study done by Nishikawa et al., in his study he compared fentanyl with tramadol and proved that the maximum level of sensory blockade achieved in both the groups was at T6 level and another study done by Singh et al., comparing clonidine and tramadol and shown that the maximum number of patients had achieved the level of blockade at T8 level.[13,14] The duration of sensory analgesia lasted for 320 mins among the patients received clonidine whereas it was 296 mins among the group that received tramadol and the difference was found to be statistically significant. As most of the studies done earlier had compared the analgesic effect between clonidine and fentayl or fentayl with tramadol or clonidine with bupivacaine, not many studies done comparing clonidine with tramadol.[15–17] So, as per the results of the previous studies it was found that clonidine was much superior to fentanyl and fentanyl was superior to tramadol in achieving the maximum duration of sensory block.

In our study, we didn't find a statistically significant difference in full motor recovery between the two groups whereas studies which had compared clonidine with bupivacaine had showed that the group that received clonidine showed more time for complete motor recovery and the studies done comparing fentanyl with tramadol did not show any significant time difference in full motor recovery and similarly studies comparing clonidine with fentanyl showed no difference in motor recovery time.[17–19]

In the present study, the analgesic effect was assessed by using visual analog scale and through that we found a statistical significant difference was seen in VAS score from 180 mins to 300 mins, in which the mean VAS score among the tramadol group was higher than the mean VAS score among the clonidine group and a similar type of result was observed in the study done by Pratapa Reddy et al. in a tertiary hospital at Hyderabad.[20] In a study, done by Benhamou comparing addition of clonidine to bupivacaine *versus* bupivacaine alone among patients undergoing cesarean section had showed that adding a small dose of Intrathecal Clonidine to Bupivacaine had increased the duration of intraoperative analgesia and the patients were free from pain postoperatively for a longer period and the study further proved that adding fentanyl to clonidine further improves analgesia.[21] Filoskriton in their study, intrathecal Clonidine was used as a solo analgesic for pain relief after cesarean section and they found that the pain scores were lower in Clonidine group patients.[22] A study done by Sanjul Dandona et al. in Uttarkand in comparing between tramadol and fentanyl had found that profound analgesia was seen in fentanyl group rather than tramadol group and similar type of results was seen in studies done by Singh et al., Biswas et al. and Dahlgren et al.[14,23–25] Later after 5 hrs the pain score showed no difference between the clonidine and tramadol group in our study.

In the current study, the mean bromage score was high among the clonidine group compared to tramadol group between 120 and 180 mins which can be explained because of the high sedation effect produced by clonidine compared to tramadol. These results were comparable to the study done by Pratappa Reddy et al. and the results of Dobrydnjov et al. who reported excellent or good operating conditions in patients receiving 15 and 30 mcg clonidine with Bupivacaine.[20,26] In another study, done by Klimscha et al. 12 showed that intrathecal Clonidine 150 mcg added to 0.5% bupivacaine significantly increased the intensity of motor block when compared to 0.5% of bupivacaine

given alone.[27] A study done by Sanjul Dandona et al. showed that the motor block was more prolonged among the group that received fentanyl compared to the group received tramadol.[23] There was no significant difference in the intraoperative heart rate between the two groups. A small dose of intrathecal clonidine is not usually associated with side effects such as bradycardia, hypotension or sedation. Accordingly studies using very low-doses of intrathecal clonidine 15 to 30 mcg. found no hemodynamic instability.[6,9] A similar type of results was also observed with systolic and diastolic blood pressure. Most of the studies using 37.5 mcg to 150 mcg[28] reported significant hypotension and bradycardia while with higher doses of 300 and 450 mcg, relative hemodynamic stability is observed, suggesting a pressor effect on peripheral sites as shown by Goudas Leonidas et al. and H Saxena et al. found in their study that 30% of patients who received 37.5 mcg Clonidine had a significant fall in mean arterial pressure and heart rate and 90% patients were sedated.[29,30] Another study done by Alsheshmi JA et al. 17 in 2003 found that intrathecal tramadol did not seem to influence the intraoperative hemodynamic profile as it acts only on the μ-receptors sparing the alpha or beta (β)-receptors which predominate the cardiovascular system.[31] In our study, the dose of clonidine used was 37.5 mcg but the hemodynamic stability was well-maintained as that of the tramadol group.

The incidence of side effects such as hypotension, bradycardia, nausea, vomiting and dryness of mouth was found to occur in very minimal number of patients in both the groups and it is similar to the results derived by Chiari Astrid et al. and Filoskritonetal and in both these studies clonidine was compared with fentanyl and the incidence of the above mentioned side effects was very minimal among these groups. Another study Seah YS et al. which used clonidine dose of 75 mcg and found the incidence of hypotension was slightly higher but well-managed with ephedrine and atropine.[22,32,33]

Conclusion

Bupivacaine when combined with clonidine or tramadol it provides acceptable subarachnoid block for performing lower limb surgeries. Both the groups were effective in producing adequate surgical anesthesia with hemodynamic stability without causing serious adverse events but clonidine group was found to have a faster onset of action with prolonged duration of analgesia without any prolongation in the time for full motor recovery.

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Original Research Article

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Comparitive Evaluation of Dexamtheasone and Tramadol as An Adjuvant to 0.5% Ropivacaine in Supraclavicular Brachial Plexus Block

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Abstract

Aims and Objectives: The aim of the study is to compare and study the efficacy of dexamethasone *versus* tramadol when added as adjuvant to 0.5% ropivacaine in supraclavicular brachial plexus block for upper extremity surgeries. To compare the duration of postoperative analgesia with dexamethasone and tramadol added as an adjuvant to 0.5% Ropivacaine in supraclavicular brachial plexus block. To observe the side effects of the above two groups. *Materials and Methods:* All the patients were randomly allocated into two groups so that, each group consists of 30 patients of either sex in a given age range posted for elective upper extremity surgeries after obtaining consent from each of them. Group - RD: Injection Ropivacaine 0.5% (29 ml) + Injection dexamethasone 8 mg (2 ml) Group - RT: Injection Ropivacaine 0.5% (29 ml) + Injection tramadol 2 mg/kg. Hemodynamic variables and Visual Analog Scale (VAS) score was significantly were noted at regular intervals until the end of the surgery. *Results:* Onset of motor block was earlier in Group RD: (21.8 ± 1.57 min) as compared to Group RT: (25.1 ± 2.41 min). Onset of sensory block was earlier in Group RD: (16.63 ± 0.88 min) as compared to Group RT (17.43 ± 0.97 min). Total Duration of sensory block was lesser in Group RT (475.99 ± 31.24 mins) as compared to Group RD (580.00 ± 40.42 mins) *p* - value < 0.001. Total duration of motor block was lesser in Group RT(415.99 ± 31.24 mins) as compared to Group D (520.00 ± 40.42 mins) *p* - value < 0.001. Time to rescue analgesia was earlier in Group RT (580 mins) than in Group RD (816 mins). Duration of analgesia was longer in Group RD, as compared to Group RT. *Conclusion:* We observed that Group RD (Inj. 0.5% Ropivacaine + Inj. Dexamethasone 8 mg) has faster onset of sensory and motor blockade than RT (Inj. 0.5% Ropivacaine + Inj. Tramadol 2 mg/kg) when used in supraclavicular block in upper extremity surgeries. Duration of analgesia was greater with Dexamethasone when added as an adjuvant as compared to Tramadol and also Dexamethasone reduces the requirement of postoperative analgesia.

Keywords: Supraclavicular brachial plexus block; Dexamethasone; Tramadol.

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Introduction

The supraclavicular block is also called as the "spinal anesthesia of the upper extremity" because of its universal application for upper extremity surgery. This block can be given at the level of distal trunks which is limited to the smallest area of brachial plexus.[1] Temporary block of the sensation and movements of the upper extremity are achieved by injecting local anesthetics in close proximity to the brachial plexus.

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Brachial plexus block is less invasive and affects fewer organ systems than general anesthesia. Nerve stimulator or ultrasound guided blocks are superior than blind technique as they are accurate and several complications can be avoided that arise due to the blind technique.[2] Lignocaine and bupivacaine combinations or bupivacaine alone have been the commonly used drugs in brachial plexus block.[3] Ropivacaine is a long acting amide local anesthetic agent and first produced as a pure S enantiomer. Due to less lipophilic nature and steroeselectivity, ropivacaine has less cardiotoxicity and neurotoxicity than bupivicaine.

Dexamethasone is a derivative of synthetic glucocorticoid, which is a potent anti inflammatory, analgesic and immunosuppressive agent. It directly blocks the transmission in nociceptive C fibers by reducing the release of inflammatory mediators and up regulating the potassium channels. Perineural glucocorticoid is eventually absorbed and exerts systemic effects[4] and also influences postoperative analgesia.

Tramadol is an analgesic with μ mixed opioid and nonopioid activity. It acts by inhibiting the reuptake of both Norepinephrine (NE) and serotonin from the nerve endings and enhances the effect of local anesthetics when used together in peripheral regional nerve block. It has less respiratory depressant effect due to weak μ-receptor affinity.[5] Hence, the present study was to compare the efficacy of sensory and motor onset of dexamethasone *versus* tramadol as an adjuvant to 0.5% ropivacaine in supraclavicular brachial plexus block. The duration and quality of sensory and motor blockade and postoperative analgesia was studied and any associated complications and side effects were noted.

Materials and Methods

Institute Ethics committee (ICS) clearance was obtained prior to commencement of study. 60 patients undergoing elective upper limb surgeries under supraclavicular block were selected randomly after applying the already mentioned stringent inclusion and exclusion criteria.

All the patients were divided into 2 Groups, Group RD and RT. An informed consent was taken for every case selected for the study. Using computer generated random allocation chart, patients were randomly allocated to one of the Two Groups according to the drug to be used.

Place of study was at DY Patil, Medical College, Hospital and Research Centre. Pimpri, Pune 411018.

Brachial plexus block was carried out on patients undergoing elective upper limb surgery. 60 patients were divided into 2 groups of 30 each, group RD (ropivacaine with dexamethasone) and Group RT (Ropivacaine with tramadol). Each Group was given their respective drug as per to a double blind method. The drug was prepared by an anesthesiologist who was not involved in the administration of anesthesia, patient care or data collection.

Group RD - Injection Ropivacaine (0.5) 28 ml + Injection Dexamethasone 8 mg;

Group RT - Injection Ropivacaine (0.5%) 28 ml + Injection Tramadol 2 mg/kg.

All the patients were subjected to thorough preoperative evaluation and relevant laboratory investigations. All patients were kept fasting 8 hours prior to surgery. On arrival to the operating room NBM status and consent was checked. Basic monitoring equipment (pulse oximeter, NIBP, ECG monitor) was connected. Baseline vital parameters were recorded. An intravenous line was secured using 20G IV cannula in the arm not being operated. All patients were made to lie supine. Head was rotated to the other side. Ipsilateral arm was extended and shoulder depressed. A small bolster was placed between the shoulder blades to make the plexus taut. Supraclavicular brachial plexus block was performed under all aseptic precautions. A nerve stimulator with 22G, 5 cm insulated needle will be used for precise location of brachial plexus.

A skin wheal raised in the supraclavicular region, 1 cm above the medial two third and the lateral one third of the clavicle. Subclavian artery is usually palpated on this site. Nerve stimulator frequency was set at 2 Hz and intensity of stimulating current was initially set to deliver 1 mA for 0.1 ms. Insulated needle was inserted through the skin wheal in a posterior, caudal and medial direction until a distal motor response is elicited. As the nerve was approached, movement of the wrist or fingers was identified and the current was gradually reduced to 0.5 mA. Position of needle is considered acceptable when an output current 0.5 mA elicits a distal motor response. At this point after negative aspiration for blood, a mixture of local anesthetic, Inj. Ropivacaine 0.5% and adjuvant either with Inj. Dexamethasone 8 mg or Inj. Tramadol 2 mg/kg as per the group allotted were given in incremental doses.

Completion of injection will be considered as T0. Sensory and motor blockade evaluation should was calculated every 2 min until complete sensory or motor block or till 30 min whichever was earlier.

Assessment of sensory block: Onset of sensory block was evaluated by pin prick sensation. Dull sensation on pin prick which was compared with the other arm, was taken as the time of onset of sensory blockade.

Assessment of motor block: the motor block was assessed with the help of modified bromage scale.

Onset of motor blockade, was considered from the injection of drug upto the time when patient felt heaviness on abduction of arm, at shoulder or on achieving bromage scale where:

0- Able to raise the extended arm to 90 degree for a full 30 seconds;

1- Able flex the elbow and move the fingers but unable to raise the extended arm;

2- Unable to flex the elbow but able to move the fingers;

3- Unable to move the arm, elbow or fingers.

Duration of analgesia: Was taken from the time of administration of drug to the time of giving first rescue analgesia. Postoperative rescue analgesia with Inj. Diclofenac sodium 75 mg IM was given if the complaints of moderate pain (VAS > 4). The patients were taught to assess the intensity of pain using visual analog scale (VAS) for postoperative pain assesement.

All patients were educated regarding the use of VAS (Visual Analog Scale), in which 0 means no pain and 10 means worst pain.

Following recordings were made:

T0 : Time of administration of drug;

T1: Time of onset of sensory response;

T2 : Time of onset of motor response;

T3 : Total duration of sensory block - return of pin prick sensation (minutes);

T4 : Total duration of motor block-return of motor effect (minutes);

T5 : Duration of analgesia is time of first rescue analgesia (minutes).

Side effects: Like nausea, vomiting, bradycardia, hypotension, and complications of supraclavicular block like respiratory distress due to pneumothroax, etc. were noted in the intraoperaitve and postoperative period and treated accordingly.

Data was collected within the stipulated period of time. The statistical analysis was done using parametric test and final interpretation will be based on "Z test" (standard normal variant) with 95% level of significance. Qualitative data was analyzed by Chi-square test, for establishing any association between the parameters under study.

Results

The demographic variables such as age, weight, gender and ASA grading were comparable in both the groups.

In this study, Onset of sensory block was earlier in Group RD: (16.63 $\pm$ 0.88 min) as compared to Group RT (17.43 $\pm$ 0.97 min). Onset of motor block was earlier in Group RD: (21.8 $\pm$ 1.57 min) as compared to Group RT: (25.1 $\pm$ 2.41 min) (Table 1).

Total Duration of sensory block was lesser in Group RT (475.99 $\pm$ 31.24 mins) as compared to Group RD (580.00 $\pm$ 40.42 mins) p - value < 0.001. Total duration of motor block was lesser in Group RT (415.99 $\pm$ 31.24 mins) as compared to Group RD (520.00 $\pm$ 40.42 mins) p - value < 0.001 (Table 2).

Time to rescue analgesia was earlier in Group RT (580 mins) than in Group RD (816 mins). Duration of analgesia was longer in Group RD, as compared to Group RT (Tables 3–6 and Fig. 1).

Table 1: Comparison of T1 and T2 in study groups

Onset of Block in mins	Group	Mean	SD	*t* - Test Value	*p* - Value
T1 (Sensory onset)	RT	17.4333	0.97143	3.32	0.02
	RD	16.6333	0.88992		
T2 (Motor onset)	RT	25.1	2.41	3	< 0.0001
	RD	21.8	1.57		

Table 2: Comparison of T3 and T4

Total duration of Block in mins minutes	Group	Mean	SD	*t* - Test Value	*p* - Value
Motor	RT	415.998	31.2498	-11.43	< 0.001
	RD	520.002	40.4286		
Sensory	RT	475.998	31.2498	-11.34	< 0.001
	RD	580.002	40.4286		

Table 3: Time for Rescue analgesia (T5)

Group	*n*	Mean	SD	*t* - Test Value	*p* - Value
RT	30	580.002	53.0454	-15.25	< 0.001
RD	30	816	66.1032		

Table 4: Heart rate wise distribution between RT group and the RD group

Heart Rate	Group	Mean	SD	*t* - Test Value	*p* - Value
Baseline	RT	78.5333	2.40306	-1.43	0.16
	RD	79.4667	2.72578		
Giving drug	RT	78.0000	2.40689	-2.256	0.10
	RD	79.4667	2.72578		
After 5 mins	RT	77.6667	2.10637	-0.865	0.39
	RD	78.2000	2.64445		
After 15 mins	RT	77.6667	2.10637	-0.834	0.10
	RD	78.2000	2.64445		
After 30 mins	RT	77.7000	2.81805	-1.34	0.33
	RD	78.6667	2.74595		
After 60 mins	RT	77.1667	3.58236	-1.23	0.18
	RD	78.7333	2.85190		
After end of surgery mins	RT	78.5000	2.52914	-1.45	0.12
	RD	79.2667	2.8031		

Table 5: MAP wise distribution between Tramadol group and the Dexamethasone group

Mean Arterial Blood Pressure	Group	Mean	SD	*t* - Test	*p* - Value
Baseline	RT	126.4667	4.46408	0.85	0.38
	RD	125.4667	4.46408		
Giving drug	RT	97.0889	3.58577	1.124	0.11
	RD	95.5889	3.58577		
After 5 mins	RT	96.6444	2.40359	2.42	0.09
	RD	95.1444	2.40359		
After 15 mins	RT	86.7333	3.12866	1.234	0.22
	RD	85.7333	3.12866		
After 30 mins	RT	81.7111	3.31574	1.453	0.16
	RD	80.5111	3.31574		
After 60 mins	RT	97.1556	3.23739	1.564	0.12
	RD	95.8556	3.23739		
After end of surgery mins	RT	115.545	3.2345	0.784	0.15
	RD	114.545	3.2335		

Table 6: SpO_2 wise distribution between Tramadol group and the Dexamethasone group

SpO_2	Group	Mean	SD	*t* – Test Value	*p* - Value
Baseline	RT	99.43	.898	701	.486
	RD	99.27	.944		
Giving drug	RT	99.77	.568	0.00	1.000
	RD	99.27	.504		
After 5 mins	RT	99.73	.583	-.482	.632
	RD	99.80	.484		
After 15 mins	RT	99.57	.774	-.979	.332
	RD	99.73	.521		
After 30 mins	RT	99.63	.809	-1.008	.317
	RD	99.80	.407		
After 60 mins	RT	99.77	.568	-.823	.414
	RD	99.47	.346		
After end of surgery mins	RT	99.97	.568	-.245	.808
	RD	99.80	.484		

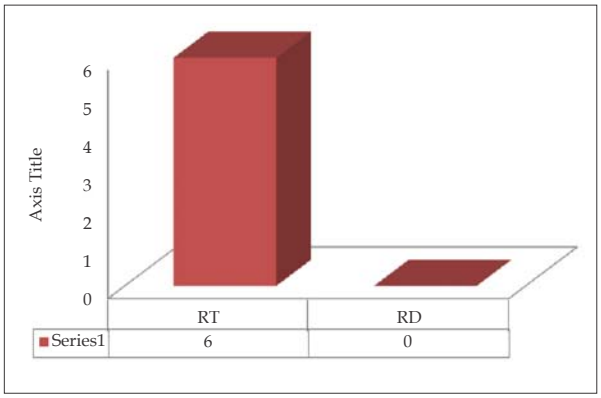

Fig. 1: Comparison of incidence of side effects in both the groups

Discussion

The supraclavicular approach to the brachial plexus characteristically is associated with a brisk onset of anesthesia and is highly successful. It is ideal for procedures of the arm, forearm and hand. The brachial plexus is most concise at the level of C5-T1 nerve roots and therefore blockade at this level is of utmost importance.

Supraclavicular nerve block with local anesthetics can provide superior anesthesia of the upper extremities. Advantages of supraclavicular nerve block:

- Technically easy to perform;
- Complete block is achieved without sparing of nerves;
- Outstanding regional anesthesia and muscle

relaxation for surgery and for providing long-term postoperative analgesia;

- Maintains hemodynamics;
- Good for patients who are at high-risk for general anesthesia, or not adequately nil by mouth;
- Early ambulation in postoperative period is possible.

The extent and duration of the block can be customized to meet the needs required by the type of surgery and the patient´s condition, by selecting, the Local Anesthetic (LA), and the use of either a single shot or a continuous technique.

The ability to administer this block with precision has become possible with the advent of ultrasound, peripheral nerve stimulator, echogenic needles and depth coded needles. Historically, peripheral nerve blocks were administered using a technique that elicited paresthesia on needle contact with a nerve. Nerve stimulation is appreciated for its objectivity and the fact that there is no need for patient reporting of paresthesia. Using this technique, it becomes easy to precisely locate peripheral nerves based on nerve twitch response. Now-a-days, ultrasound guidance for peripheral nerve blockade is gaining popularity, due to greater success rates and fewer complications.

In the current study, identical volumes and concentrations were used. In Group RD, Inj. Ropivacaine 29 ml (0.5%) with dexamethasone 8 mg (2 ml) was used and in Group RT, Inj. Ropivacaine 29 ml (0.5%) with Tramadol 2 mg/kg was used. Recommended dose of Ropivacaine in supraclavicular brachial plexus block is 3 mg/kg body weight. The maximum allowable toxic dose of Ropivacaine in an adult is 300 mg.

Studies contrasting intense danger of ropivacaine with bupivacaine found that ropivacaine was at least 25% less lethal than bupivacaine. In numerous examinations, greatest portion of ropivacaine up to 5 mg/kg was accounted for to be sheltered with no dangerous impact.

Be that as it may, Geiger and associates[6] detailed safe utilization of 1% ropivacaine up to 500 mg.

Hickey et al.[7], did a comparative study with 0.25% ropivacaine and 0.25% bupivacaine for supraclavicular block and evaluated that the 0.25% concentration for brachial plexus block is not sufficient to achieve surgical anesthesia because of a slow onset and a high-rate of inadequate block.

Onset of sensory block was evaluated by pin prick sensation. Dull sensation on pin prick, which was compared with the other arm, was taken as the time of onset of sensory blockade. Onset of sensory block was earlier in patients given Group RD (16.6 ± 0.88 mins) than in Group RT (17.4 ± 0.97 mins). On comparing the onset time of sensory block in the Two Groups, the *p* - value was 0.02 which was statistically highly significant (*p* - < 0.001).

In 2015, Jigisha Prahladrai[8], Rashida M et al., conducted a randomized double blinded study in patients posted for upper limb orthopedic surgery who underwent Supraclavicular brachial plexus block. Their study compared equal volumes (30 ml) of 0.5% bupivacaine and 0.5% ropivacaine. 0.5% ropivacaine provided significant earlier onset of sensory block 9.5 ± 2 min as compared to 0.5 % bupivacaine 7.46 ± 2.54 min.

In 2007, Shrestha[9] et al. compared tramadol and dexamethasone as an adjuvant to bupivacaine for supraclavicular brachial plexus block using surface landmark technique and showed the mean onset time for sensory blockade in Tramadol Group were 18.47 min and for Dexamethasone Group was 16.76 min.

Onset of motor blockade, was considered from the injection of drug upto the time when patient felt heaviness on abduction of arm, at shoulder or on achieving bromage scale 1. The onset of motor block was earlier with Group RD (21.8 ± 1.57 mins) than with RT (25.1 ± 2.41 mins). On comparing the onset time of motor block among the Two Groups, the *p* - value < 0.001, which was statistically significant, (*p* < 0.05).

In 2015, Prerana P Mankad[10], Jayendra C Makwana, did a comparative study of 0.5% ropivacaine and 0.5% levobupivacaine in supraclavicular brachial plexus block. The motor onset was considerably quicker with 0.5% ropivacaine (9.50 ± 2.403 min) when compared with 0.5% levobupivacaine (12.33 ± 2.537 min; *p* < 0.05).

In 2019, Kataria AP, Mohan B, Singh L[11] did a study to evaluate and compare tramadol and dexamethasone as an adjuvant to levobupivacaine in supraclavicular block and found out that the onset of motor block was earlier in study group of dexamethasone having the mean value of (7.93 ± 0.73 min) and in comparison, the control group had a mean value of (9.00 ± 1.33 min), which is statistically significant (*p* > 0.05).

Total duration of sensory block was taken as the time interval between sensory block and re appearance of pin prick response. The patients either started feeling either touch sensation on pin prick or slight pain.

Duration of sensory blockade is considerably less in RT (475.99 ± 31.24 mins) compared to RD (580.00 ± 40.42 mins). The data between the two groups was compared and found to be highly significant (p - value < 0.001).

In 2013, Prashant A Biradar[12], Padmanabha Kaimar, and Kannappady Gopalakrishna performed a prospective, randomized, double-blind study to evaluate the effect of dexamethasone added to lidocaine (1.5%) *versus* lignocaine (1.5%) and adrenaline (1:2,00,000) and concluded that addition of dexamethasone 8 mg in supraclavicular brachial plexus block prolongs the duration of sensory block (326 ± 58.6 *vs* 159 ± 20.1) as in compared to the control group. (p = 0.001).

The Total duration of motor block was calculated as the time from the onset of motor block to complete recovery of movement of the hand.

Duration of motor blockade was lesser in Group RT (475.99 ± 31.24 mins) than in Group RD (580.002 ± 40.42 mins). Duration of motor blockade (mins) of the two groups was analyzed statistically (p < 0.001) and found to be significant (p < 0.05).

In 2017, Raj SA[13], Singh DR, Charles SA, et al. evaluated the efficacy of tramadol or dexamethasone as an adjuvant to levobupivacaine in ultrasoundguided supraclavicular brachial plexus block in terms of complete duration of motor blockade. In Group T was 764.63 min and for Group D was 1150.27 min which was statistically significant (p < 0.05). Therefore, most of the studies suggested that time taken for motor blockade was lesser in groups receiving Tramadol when compared to Dexamethasone as adjuvants.

Duration of analgesia was taken from the time of administration of drug to the time of giving first rescue analgesia. Rescue analgesia was given when VAS score was 4 or more.

The results of this study, demonstrated that a supraclavicular nerve block in Group RD provides longer postoperative analgesia (816 ± 66 minutes) than in Group RT (580 ± 53 mins).

In 2018, Chandrashekar[14] did a comparative study between tramadol and dexamethasone with bupivacaine when added as an adjuvant in supraclavicular brachial plexus block and concluded that the mean duration of postoperative analgesia was prolonged with dexamethasone group (1023.87 ± 161.01 mins) compared to that with tramadol group (454.47 ± 44.29 mins).

There was no significant fall or rise in Mean arterial pressure and heart rate within groups after administration of drug, or after 5, 10, 15 and 30 minutes, 1 hour and at the end of the surgery. Incidence of side effects like nausea an pronounced in 6 patients in the Group RT and were minimum with Group RD, there was no incidence of significant complications (intraoperative and postoperative) such as pneumothorax, intravascular injection of the drug, cardiotoxicity, or neurotoxicity in either group.

There were certain limitations in this study also. The sample size was small for the study, so, further studies have to be carried out. There was no ultrasound machine availability and recent studies show that accuracy of the block is improved on using an ultrasound combined nerve stimulation technique for nerve location. The patients who had a failed block or inadequate block were given general anesthesia and were excluded from the study.

Conclusion

To conclude the study, we observed that Group RD (Inj. 0.5% Ropivacaine + Inj. Dexamethasone 8 mg) has faster onset of sensory and motor blockade than RT (Inj. 0.5% Ropivacaine + Inj. Tramadol 2 mg/kg) when used in supraclavicular block in upper extremity surgeries.

Duration of analgesia was greater with Dexamethasone when added as an adjuvant as compared to Tramadol and also Dexamethasone reduces the requirement of postoperative analgesia.

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Original Research Article

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An Observational Study to Compare Supraglottic Airway Device I-Gel with Classic LMA for Short Surgical Procedures

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Abstract

Introduction: Major responsibility of anesthesiologist is to provide adequate ventilation to the patient. Supraglottic airway device is a novel device that fills the gap in airway management between tracheal intubation and the use of face mask. In this study, we aim to compare supraglottic airway devices I-Gel with Classic LMA in relation to time for insertion, success rate of insertion in first attempt, hemodynamic changes and complications. *Materials and Methods:* The present study, was a prospective, randomized and comparative study, which included 50 patients of age between 18 and 55 years, belonging to ASA I and II, scheduled for elective short surgical procedures under general anesthesia. Patients were divided into Two Groups: Group I (I-Gel) and Group II (Classic LMA). After induction of anesthesia, proper sized supraglottic airway was inserted according to weight of the patient. *Results:* The success rate of insertion in first attempt in Group I and Group II was 96% and 88% respectively, meantime taken for insertion in Group I and Group II was 12.92 ± 1.41 sec and 18.56 ± 1.23 sec respectively, sore throat seen in Group I and Group II was in 1 (4%) and 3 (12%) patients respectively. *Conclusion:* I-Gel have higher success rate of insertion in first attempt and shorter time of insertion in comparison to Classic LMA. Lower incidence of blood staining of device and postoperative sore throat was seen in I-Gel as compared to Classic LMA. Hence, I-Gel is a better alternative to existing Classic LMA.

Keywords: Supraglottic; I-Gel; Classic LMA.

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Introduction

The major responsibility of the anesthesiologist is to provide adequate ventilation to the patient. Management of the airway has come a long way since, the development of endotracheal intubation by Macewen in 1880 to the present day usage of sophisticated devices.[1] The wide variety of airway devices available today may broadly be classified as intraglottic and extraglottic airway devices.

The supraglottic airway device is a novel device that fills the gap in airway management between tracheal intubation and the use of a face mask. Archie Brain, a British anesthesiologist, for the first time introduced the laryngeal mask airway designed to be positioned around the laryngeal inlet that could overcome the complications associated with endotracheal intubation, and yet, be simple and atraumatic to insert. The first successful supraglottic airway device – Laryngeal Mask Airway (LMA)

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classic, an inflatable supraglottic airway device became available in 1981. Insertion of supraglottic airway devices do not require laryngoscopy, therefore, pressor response is attenuated.[2,3] The Laryngeal Mask Airway (LMA) is tolerated atlighter levels of anesthesia than an endotracheal tube.[4] I-Gel is designed to create a noninflatable anatomical seal of the pharyngeal, laryngeal and perilaryngeal structures. I-Gel has several advantages including it is cheaper, easier insertion, minimal risk of tissue compression and stability after insertion.[5] The incidence of postoperative sore throat is significantly lesser in patients receiving LMA as compared to endotracheal tube.[6,7] In this study, our aim was to compare supraglottic airway devices I-Gel with Classic LMA in relation to time for insertion, success rate of insertion in the first attempt, hemodynamic changes and complications if any in anesthetized, nonparalyzed adult patients posted for surgeries under general anesthesia.

Materials and Methods

The present study, was a prospective, randomized and comparative study, which included 50 patients of age between 18 and 55 years, belonging to ASA Grade I and II scheduled for elective short surgical procedures under general anesthesia at Choithram Hospital and Research Center Indore from January 2016 to November 2016.

Approval from the Ethics Committee and Scientific Review Committee and a written informed consent for participation in the study was taken. Patients were selected and assigned to the two groups randomly with the help of computer generated random numbers. In each group 25 patients were taken.

Group I (I-Gel): All the patients in whom I-Gel was inserted;

Group II (Classic LMA): All the patients in whom Classic LMA was inserted.

Patients with history of difficult intubation, mallampatti score 3 and 4, mouth opening less than 3 cm, Thyromental distance less than 6 cm, known airway problems like anatomic abnormalities of oropharynx, glottis or subglottic airway obstruction, and increased risk of aspiration as in pregnancy, GERD, neuromuscular dysfunction were excluded from the study.

After obtaining the voluntary written informed consent, a preanesthetic checkup, detailed history was taken and physical examination was done and advised nil by mouth for 6 hours prior to surgery.

Intravenous access was established in the preoperative holding area and premedicated with Injection Glycopyrrolate 0.004 mg/kg IV, Injection Ondansetron 0.1 mg/kg IV and Injection Midazolam 0.02 mg/kgIV half an hour prior to induction of anesthesia.

On arrival to the operation theatre, patients were reassured and left undisturbed for ten minutes and baseline readings of following parameters were recorded: Heart Rate (HR), Systolic Blood Pressure (SBP), Diastolic Blood Pressure (DBP), Mean Arterial Pressure (MBP), SpO_2 monitoring was carried out in all patients.

Preoxygenation for 3 minutes was done. After preoxygenation all patients received Injection Fentanyl in the dosage of 2 mcg/kg. Anesthesia was induced with Injection Propofol which was titrated till loss of verbal contact, loss of eye lash reflex and relaxation of jawof patients. After confirming the possibility of bag and mask ventilation, the proper size supraglottic airway according to weight of patient, I-Gel (Group I) or Classic LMA (Group II) was inserted. Classic LMA was inflated with adequate volume of air. After inflating, the device was connected to the breathing circuit. Confirmation of adequate placement was done by observing adequate chest rise on squeezing reservoir bag and by seeing wave pattern on $EtCO_2$.

Maintenance was done by oxygen, nitrous oxide and isoflurane. Intraoperatively any occurrence of aspiration, regurgitation or bronchospasm was noted.

After completion of procedure the supraglottic device was removed in the deeper plane of anesthesia with the patient on spontaneous ventilation. After removal of device any occurrence of coughing, bronchospasm or blood staining of device was noted.

Patients were observed with bag and mask till they became fully awake and following commands. Patients were shifted to recovery after vocalizing.

Patients were interviewed about any soreness, or any discomfort in the throat after 1 hour and then after 24 hours.

The following parameters were recorded:

Time for insertion (the time from grasp of device till the confirmation of adequate placement) was recorded. The number of attempts were noted. More than 3 attempts wasconsidered as failure. Any complication while inserting the device like coughing, gagging or vomiting were looked for and noted. Hemodynamic parameters such as heart

rate, mean arterial pressure, SpO_2 and end-tidal CO_2 of the patient were recorded at 1, 3, 5 and 10 minutes after insertion.

The data thus, obtained from the Two Groups was compared using paired'*t*' test. *p* - value < 0.05 was taken as significant and *p* - value < 0.01 was taken as highly significant.

Results

In the present study, total 50 patients aged between 18 and 55 years were included and as per study design, they were consecutively divided into 2 groups. Mean age and weight were compared among 2 groups. No statistically significant difference was found among two groups as *p* - value was > 0.05 shows in Table 1.

Success rate of insertion in the first attempt between both the groups was compared. In Classic LMA group, in 22 (88%) patients device was inserted in one attempt, while in 3 (12%) patients two attempts of insertion were required. In the I-Gel Group, in 24 (96%) patients device was inserted in one attempt, while in only 1 (4%) patient, two attempts of insertion were required. Success rate (one attempt) was comparable in both the groups ($p > 0.05$), shows in Table 2.

Time taken for insertion of the Classic LMA and I-Gel between both the groups was compared. The meantime taken for insertion in Classic LMA Group was 18.56 ± 1.23 sec and that in I-Gel Group was 12.92 ± 1.41 sec. The difference was found to be statistically significant ($p < 0.05$), with a lower time of insertion in I-Gel Group as compared to Classic LMA Group, shows in Table 3.

Mean heart rate (bpm) between Classic LMA and I-Gel Groups at different time intervals was compared. In the Classic LMA Group, there was a constant fall in mean heart rate from the preoperative value till 10 min, similar trend was seen in I-Gel Group also.

The difference in mean heart rate at all the time intervals was found to be statistically not significant ($p > 0.05$), showing that mean heart rate was comparable between the two groups across all the time intervals, shows in Table 4.

Mean MAP (mm Hg) between Classic LMA and I-Gel Groups at different time intervals was compared. In the Classic LMA Group, there was a constant fall in mean MAP from the preoperative value till 10 min, similar trend was seen in I-Gel Group also.

The difference in mean MAP at all the time intervals was found to be statistically not significant ($p > 0.05$), showing that mean MAP is comparable between the two groups across all the time intervals, shows in (Table 4).

Table 1: Sociodemographic details

Parameter	Classic LMA Group (*n* = 25) [Mean ± SD]	I-Gel Group (*n* = 25) [Mean ± SD]	*p* - Value
Age (years)	35.64 ± 8.46	36.84 ± 10.20	0.653, NS
Weight (kg)	59.76 ± 5.15	59.88 ± 5.53	0.937, NS

Table 2: Success rate of insertion in the first attempt

Number of Attempts of Insertion	Classic LMA Group		I-Gel Group		*p* - Value
	No.	%	No.	%	
One attempt	22	88.0	24	96.0	0.292. NS
Two attempts	3	12.0	1	4.0	
Total	25	100.0	25	100.0	

Table 3: Comparison of time taken for insertion between the two groups

Parameter	Classic LMA Group (*n* = 25) [Mean ± SD]	I-Gel Group (*n* = 25) [Mean ± SD]	*p* - Value
Time taken for insertion (sec)	18.56 ± 1.23	12.92 ± 1.41	0.000

Table 4: Comparison of mean heart rate and mean arterial pressure between the two groups at different time intervals

	Mean Heart rate			Mean MAP		
Time Interval	Classic LMA Group (*n* = 25) [Mean ± SD]	I-Gel Group (*n* = 25) [Mean ± SD]	*p* -Value	Classic LMA Group (*n* = 25) [Mean ± SD]	I-Gel Group (*n* = 25) [Mean ± SD]	*p* - Value
Preoperative	77.56 ± 6.78	77.08 ± 6.48	0.799, NS	91.24 ± 3.09	90.92 ± 3.57	0.736, NS
1 min	75.32 ± 6.14	74.12 ± 6.25	0.496, NS	89.24 ± 2.73	88.80 ± 3.37	0.614, NS
3 min	74.12 ± 5.62	72.84 ± 5.81	0.432, NS	87.64 ± 2.68	86.52 ± 3.42	0.203, NS
5 min	73.12 ± 5.49	72.44 ± 4.87	0.645, NS	87.00 ± 3.01	85.32 ± 3.05	0.056, NS
10 min	72.04 ± 4.93	72.16 ± 4.30	0.927, NS	86.44 ± 2.97	85.60 ± 3.14	0.336, NS

In the Classic LMA Group, sore throat was seen in 3 (12%) patients, while in the I-Gel Group it was seen in 1 (4%) patient. Sore throat incidence was more in Classic LMA Group in comparison to the I-Gel Group. But this difference in proportion was found to be statistically not significant ($p > 0.05$), (Table 5).

In our study, we found blood staining of the device as the only complication. In the Classic LMA group, blood stainingwas seen in 3 (12%) patients, while in the I-Gel group it was seen in 1 (4%) patient (Table 5).

In Classic LMA Group, there were more number of blood staining cases in comparison to I-Gel Group, but this difference in proportion was found to be statistically not significant ($p > 0.05$).

Table 5: Comparison of sore and complications throat between the two groups

Parameter	Classic LMA Group		I-Gel Group		*p* - Value
	No.	%	No.	%	
Sore throat	3	12.0	1	4.00	0.292, NS
Complications	3	12.0	1	4.00	0.292, NS

Discussion

Both groups were comparable and there was statistically no significant difference with regards to mean age and weight.

In our study, the meantime taken for insertion in Classic LMA Group was 18.56 ± 1.23 sec and that in I-Gel Group was 12.92 ± 1.41 sec. The difference was found to be statistically significant ($p < 0.05$), with a higher time of insertion in Classic LMA Group in comparison to I-Gel Group. Our study results are in corroboration with the studies done by Chandura et al. (2013),[8] Polat et al. (2015),[9] Saha et al. (2015),[10]. Kasturi et al. (2016),[11] they found that I-Gel required less time for insertionas compared to the Classic LMA.

The success rate of insertion in first attempt in Group I-Gel and Classic LMA is 96% and 88% respectively. The difference was found to be statistically not significant ($p > 0.05$). Our study results are comparable with studies done by Chandura et al. (2013),[8] Polat et al. (2015),[9] Gupta et al. (2015),[12] Revi et al. (2015),[13] Engineer et al. (2016),[14] Kasturi et al. (2016),[11] they found that less number of attempts were required in I-Gel Group in comparison to Classic LMA Group ($p < 0.05$).

In our study, comparison of mean heart rate and mean MAP was done preoperatively, at 1 min, at 3 min, at 5 min and at 10 min. The difference in mean heart rate and mean MAP at all the time intervals was found to be statistically not significant ($p > 0.05$), showing that mean heart rate and mean MAP was comparable between the two groups across all the time intervals. Our study results are comparable to the studies done by Saha et al. (2015),[10] Engineer et al. (2016),[14] Kasturi et al. (2016)[11] while studies done by Jindal et al. (2009),[15] Chandura et al. (2013),[8] found that I-Gel maintained better hemodynamic stability following insertion.

In our study, in the Classic LMA Group, sore throat was seen in 3 (12%) patients, while in the I-Gel Group it was seen in 1 (4%) patient. The difference in proportion was found to be statistically not significant ($p > 0.05$). Our study results are comparable with studies done by Chandura et al. (2013),[8] Polat et al. (2015),[9] Gupta et al. (2015),[12] while Kasturi et al. (2016),[11] found a higher incidence of sore throat in I-Gel Group in comparison to the Classic LMA Group.

In our study, only 1 case of blood staining was seen in I-Gel Group. There were 3 cases of blood staining in Classic LMA Group. The difference in proportion was found to be statistically not significant ($p > 0.05$). We didn't observe any other complications like coughing, gagging, vomiting, aspiration, regurgitation, bronchospasm in both the groups. Our study results are comparable with the studies done by Chandura et al. (2013),[8] Gupta et al. (2015)[12] Engineer et al. (2016)[14] found lower incidence of blood staining in I-Gel in comparison to the Classic LMA Group.

Conclusion

I-Gel is the newer supraglottic airway device with a higher success rate of insertion in the first attempt and a shorter time of insertion in comparison to Classic LMA. Lower incidence of blood staining of device was seen in I-Gel as compared to Classic LMA. The postoperative sore throat with I-Gel is also minimal, hence, I-Gel is a better alternative to the existing Classic LMA.

Abbreviations

IV - Intravascular

SBP - Systolic Blood Pressure

DBP - Diastolic Blood Pressure

MAP - Mean Arterial Pressure

HR - Heart Rate

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Comparative Evaluation of Clonidine and Nalbuphine for Control of Post-Spinal Anaesthesia Shivering

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Abstract

The aim of this study was to evaluate the efficacy, potency and side effects of clonidine and nalbuphine in postspinal anesthesia shivering. In this prospective double-blind randomized controlled clinical trial, 60 American Society of ASA Grade I and II patients aged between 18 and 60 years scheduled for various surgical procedures under spinal anesthesia, who developed shivering were selected. The patients were divided into Two Groups: Group C (n = 30) comprised of patients who received clonidine 1 mcg/kg intravenously (IV) and Group N patients who received nalbuphine 0.05 mg/kg IV. Grade of shivering, disappearance of shivering, hemodynamic and side effects were observed at scheduled intervals. Disappearance of shivering was significantly earlier in Group C (2.75 ± 1.35) than in Group N (3.58 ± 1.19) (p = 0.01704). Bradycardia is seen more in Group C than Group N (p = < 0.001). Whereas, sedation is seen in Group N after drug administration but patient remain hemodynamically stable in Group N. We conclude that both the drugs are effective but nalbuphine controls shivering with more hemodynamic stability.

Keywords: Spinalanesthesia; Shivering; Clonidine; Nalbuphine.

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Introduction

Spinal anesthesia is a safe technique indicated mainly in abdominal and lower limb surgeries in both emergency and elective settings. Shivering which is an involuntary muscular activity occurs approximately in 40–50% of patients after spinal anesthesia.[1,2] Shivering causes mismatch between oxygen demand and supply which can lead to side effects like hypoxemia, hypercarbia and lactic acidosis. It also causes rough recovery from anesthesia.[5] Shivering causes serious side effects in patients having less cardiac reserves and those having increased intracranial pressure and in elderly and apprehensive patients.[6,7]

Spinal anesthesia does not affect thermoregulation by hypothalamus but it causes decrease in core body temperature. Heat loss occurs due to inhibition of vasoconstriction leading to vasodilation. Rapid infusion of cold IV fluids, cold temperature of operative room, direct contact of skin surface with cold scrubbing solutions, all these factors play an important role in occurrence of hypothermia and shivering in patients after spinal anesthesia.[3,4] There are various nonpharmacological as well as pharmacological methods that could help in

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controlling shivering. Use of gamgi pads and blankets to wrap the exposed body of patients, use of warmer to increase the temperature, use of warm IV fluid, intravenous fluid warmers, keeping operative room temperature adequate are some of nonpharmacological methods that could help. Pharmacological method includes use of various drugs like tramadol, clonidine, dexmeditomedine, nalbuphine, pethidine, ketamine are some of them.[8]

Unfortunately, drugs administered for control of shivering have got many side effects associated with them.

Nalbuphine is a semisynthetic, mixed agonist antagonist opioid that has characteristics of μ-antagonist and κ agonist activities. It has a high affinity for opioid receptors in central nervous system.[9] A clinically important contribution of κ receptors for the treatment of shivering is supported by the observation that meperidine which is a μ and κ receptor agonist and reduces the intensity of the cold induced shivering even in moderate dose of naloxone. Naloxone blocks μ-receptor and have little effect on κ-receptor. Nalbuphine also has high affinity for κ-opioid receptors in the central nervous system.

Clonidine, a highly selective α_2 adrenoreceptor agonist. Its antishivering action is at level of hypothalamus, locus coeruleus and spinal cord.[10,11] It does not produce side effects like vomiting but it causes bradycardia and hypotension. Clonidine has high specificity towards the presynaptic alpha-2 receptors present in vasomotor center located in brainstem of our body. It decreases presynaptic calcium level and therefore, subsequent release of norepinephrine resulting in decrease in sympathetic tone and blood pressure.

Materials and Methods

Institutional Ethics Committee approval was obtained along with written informed consent from each patient, sixty patients of American Society of Anesthesiologists (ASA) physical status I to II of both genders, aged 18–60 years, scheduled for surgery under spinalanesthesia were selected for this prospective, randomized double-blind study. Patient who refused for the study or the procedure, or patients with clinically significant coagulopathy, infection at the injection site, allergy to local anesthetics or the study drugs, severe cardiovascular or pulmonary disease, renal or hepatic disorder, patients on any other opioids or any sedative medications in the week prior to the surgery were also excluded from the study.

A written and informed consent was obtained from each subject.

The patients were divided into 2 Equal Groups: Group C and Group N.

Group C - 30 cases (Injection Clonidine 1 mcg/kg IV);

Group N - 30 cases (Injection Nalbuphine 0.05 mg/kg IV).

The drug preparation was done by an anesthesiologist who was not involved in administration of anesthesia, patient care or data collection. Further, intervention and monitoring were done by an investigator blinded to the group allocation.

All patients were thoroughly reevaluated preoperatively. In the preoperative room, the patient's pulse, blood pressure and temperature were taken, with the patient lying comfortably in supine position.

All the patients were kept nil by mouth for at least 6 hours prior to surgery to avoid risk of aspiration and any other anesthesia related complications.

IV access was secured with 20-gauge cannula. Basic monitoring devices were attached (these included heart rate, pulse oximeter, ECG, noninvasive BP). Baseline vitals were recorded. All the patients were preloaded with 10 ml/kg Ringer's Lactate fluid and maintained on IV fluids throughout the surgery.

In the sitting position under all aseptic precautions spinal anesthesia was given. After painting and draping of lumbar area with 26G Quincke's spinal needle was introduced in L3-L4 intervertebral space. Free flow of CSF confirmed the subarachnoid space. 0.5% bupivacaine heavy (3/3.5 ml) given to achieve desired level of block according to surgical procedure. All operation theatres were maintained at an optimum temperature of around 22°C–24°C. Supplemental oxygen was administered with the Hudson's face mask to all the patients at the rate of 2 l/min and patients were covered with drapes but not actively warmed. IV fluids and drugs were administered at room temperature.

After induction of spinalanesthesia, patients were observed for the occurrence of shivering until the postoperative period. Shivering was graded according to the Wrench Grade of Shivering.[12] In which 0 is No shivering, 1 is One or more of the following: Piloerection, peripheral vasoconstriction, peripheral cyanosis, but without visible muscle activity, 2 is Visible muscle activity confined to one muscle group, 3 is Visible muscle activity in more

than 1 muscle group, 4 is Gross muscle activity involving the whole body.

Patients who develop either Grade 3 or 4 shivering will be included in the study. Injection Clonidine 1.0 mcg/kg or Injection Nalbuphine 0.05 mg/kg were diluted to a volume of 10 ml in a 10 ml syringe. And the syringe presented as coded syringes as per randomization list by an anesthesiologist who was unaware of the group allocation. This was then administered to the patient as a slow IV injection over a period of 10 minutes.[13]

The attending anesthesiologist recorded the time of onset of shivering in minutes at which shivering started after spinalanesthesia, time of administration of the test drug, and time to the cessation of shivering.

Shivering control was defined as 'complete' when posttreatment, the shivering score declined to 0; 'incomplete' when the scores decreased but did not abolish the shivering completely; and 'failed' if no change in scores was observed.

Heart rate, systolic blood pressure, diastolic blood pressure, mean arterial pressure, oxygen saturation, ECG, axillary temperature and Wrench's shivering grades were recorded at 0, 1, 2, 5, 10, 15 and 30 minutes after administering the test drug.

Duration of surgery was recorded and duration of spinalanesthesia was noted by assessing spontaneous recovery of sensory block using the pinprick method and observing spontaneous movements of limbs in the postoperative period. Recurrence of shivering was also noted.

In case there was recurrence of shivering, patients were treated with an additional dose of clonidine (1 μg/kg IV) or nalbuphine (0.05 mg/kg IV) in the respective groups and/or active warming measures using convection heaters or infusing moderately warm IV fluids.

Adverse effects such as nausea, vomiting, dizziness, sedation, bradycardia (heart rate < 50 beats/minute) and hypotension (fall in systolic blood pressure > 20% of baseline) were watched for and recorded.

Nausea and vomiting were treated with injection metoclopramide 10 mg IV as and when required. Bradycardia, if it occurred, was treated with a bolus dose of Inj. Atropine 0.6 mg intravenously. Whereas, hypotension was treated with intravenous Inj. Mephenteramine 6 mg increments.

Sedation was assessed as per the modified Ramsay Sedation Scale:[14]

In which 1 means Patient anxious or agitated or both, 2 is Patient cooperative, oriented and tranquil, 3 is Patient responses to commands only, 4 is A brisk response to light glabellar tap, 5 is A sluggish response to a light glabellar tap and 6 is No response. Sedation score > 3 was termed as sedation.

The coding was opened after completion of the study to compile results.

Statistical Analysis

All the cases, were completed in the stipulated time. Data was collected, compiled and tabulated. The statistical analysis was done using parametric test and the final interpretation was based on *Z*-test (standard normal variant) with 95% level of significance.

Quantitative data was analyzed by *Student 't'- test*.

Qualitative data was analyzed by *Chi-square test.*

Results

A total of 60 patients were enrolled in the present study and were randomized into two groups of 30 each, 40 of whom were male and 20 were female shows in Table 1. Both the groups were comparable with respect to age, sex, weight, duration of surgery, and the duration of spinal block. The mean age of the patients in Group C was 35.4 ± 9.27 years; and patients in Group N, 36.03 ± 8.64 years (p = .785).

Shivering disappeared in 22 (73.33%) patients who received clonidine and 22 (73.33%) who

Table 1: Demographic characteristics, ASA grade

			Group C	Group N	*p* - Value	
1	Age (yrs)		35.4 ± 9.27	36.03 ± 8.644	0.785	NS
2	Weight (kgs)		59.33 ± 10.21	58.766 ± 10.07	0.829	NS
3	Sex	Male	20	20		
		Female	10	10		
4	ASA I/II		19/11	18/12		

Table 2: Successful treatment of postspinal shivering

Control of shivering	Group N	Group C
Complete	22 (73.33%)	22 (73.33%)
Incomplete	6 (20%)	6 (20%)
Failed	2 (6.67%)	2 (6.67%)

Table 3: Time taken to control shivering and its significance

Time taken to control shivering	Group N	Group C
Mean	3.58929	2.75
Std dev	1.19454	1.35058
p - value	0.01704 (Significant)	
Inference	Shivering was controlled significantly earlier in Clonidine group	

received nalbuphine, shows in Table 2. Both the drugs were found to be effective in reducing shivering. Though, severity of shivering was not satisfactory in 6 (20%) patients of Group C and 6 (6%) patients of Group N and unchanged in 2 (6.67%) patient of Group C and 2 (6.67%) patients of Group N. No patient had any recurrence of shivering.

The time taken for control of shivering was 2.75 ± 1.35 min for Group C and 3.589 ± 1.19 for Group N ($p = 0.01704$), shows in Table 3. Time for onset of shivering and severity of shivering were not statistically significantly different between the two groups. However, shivering was controlled significantly earlier in Group C ($p = 0.01704$).

We also observed the change in the heart rate after giving study drug in both the group. Both Group C causes significant decrease in mean heart rate than Group N ($p = < 0.001$).

There was no statistically significant difference with respect to mean blood pressure, axillary temperature and oxygen saturation between the two groups.

Bradycardia mostly seen with clonidine whereas, nalbuphine causes sedation as an adverse effect.

Discussion

Spinal anesthesia is most common technique used for lower abdominal and lower limb surgeries. Its rapid onset of action and association with postoperative analgesia makes it a very popular technique. Shivering is an involuntary muscular activity experienced by almost 40–50% of patients undergoing surgeries under spinal anesthesia.[1,2] Shivering is a protective mechanism for hypothermia. Vigorous involuntary muscular activity generates the heat in the body in response to hypothermia. It is very discomforting sensation to a patient. In addition, shivering causes increase in oxygen demand up to six times the normal requirement.

Mechanism of shivering under regional anesthesia though not fully understood but it appears to be mediated by norepinephrine, dopamine, neuropeptides, 5-hydroxy tryptamine as a response to hypothermia. Hypothermia occurs after spinal anesthesia as a result of peripheral vasodilation of lower part of the body causing heat loss which is not compensated by metabolic heat production of the body.

Shivering can be controlled intraoperatively by various methods. Which includes pharmacological and nonpharmacological methods.

Nonpharmacological methods include covering the exposed part of the patient with cotton and warming blankets, using intravenous fluids warmers, maintaining optimum operating room temperature are some of these. Pharmacological method includes use of various drugs like tramadol, clonidine, dexmeditomedine, nalbuphine, pethidine, ketamine are some of them.[8] Unfortunately, all the drugs have some or the other side effect and perfect drug is yet to be known. And studies are being performed to find the best possible drug to control the shivering.

In the present study, we compared the efficacy of clonidine and nalbuphine for treatment of shivering after spinal anesthesia in patients undergoing various elective surgeries. Clonidine is a centrally acting selective α_2 agonist. Clonidine exerts its antishivering effects at three levels: Hypothalamus, locus coeruleus and spinal cord. At the hypothalamic level, it decreases thermoregulatory threshold for vasoconstriction and shivering, because hypothalamus has high density of α_2 adenoceptors and hence is effective in

treating the established postanesthetic shivering. It also reduces spontaneous firing in locus coeruleus - a proshivering center in pons. At the spinal cord level, it activates the α_2 adrenoreceptors and release of dynorphine, norepinephrine and acetylcholine. The depressor effects of these neurotransmitters at the dorsal horn modulate cutaneous thermal inputs. Clonidine is highly lipid-soluble and easily crosses the blood-brain barrier. Due to these merits, interaction at the α_2 adrenoreceptors at spinal and supraspinal sites occurs within the central nervous system.

Nalbuphine is a semisynthetic, mixed agonist antagonist opioid that has characteristics of μ-antagonist and κ(kappa)-agonist activities. It has a high affinity for opioid receptors in central nervous system. A clinically important contribution of κ receptors is supported by the observation that meperidine which is a μ and κ receptor agonist, reduces the intensity of cold induced shivering even in the presence of moderate doses of naloxone. It has less ability to depress respiratory function as compared to other opioids. Nalbuphine in the dose 0.05 mg/kg IV is selected for the study.

In our study, we found out that both clonidine 1 mcg/kg IV and nalbuphine 0.05 mg/kg IV were effective in treatment of postspinal shivering. Though time taken to control the shivering is less with clonidine (2.75 ± 1.35 min) than with nalbuphine (3.58 ± 1.194 min), (p = 0.017).

Bradycardia was significant after clonidine administration and sedation was more in nalbuphine group (p = < 0.001). But patients in Group N were more hemodynamically stable after the drug administration.

Conclusion

Both intravenous nalbuphine 0.05 mg/kg and clonidine 1 mcg/kg are effective in treating patients with postspinal shivering. Time taken to control shivering is lesser with clonidine than nalbuphine but clonidine causes bradycardia. We preferred Nalbuphine 0.05 mg/kg over clonidine 1mcg/kg as nalbuphine controls shivering with more hemodynamic stability.

Limitations

1. Smaller sample size as lesser number of people willing to give consent for the study.
2. Only ASA 1 and ASA 2 patients were considered in our study. We have to conduct studies in elderly and cardiac compromized patients for use of nalbuphine and clonidine in control of postspinal anesthesia shivering in high-risk patients.
3. We used 0.05 mg/kg of nalbuphine and 1 μg/kg of clonidine as a dose for control of postspinal anesthesia shivering. Different studies using different dose ranges must be conducted to get ideal dose for control of postspinal anesthesia shivering.

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Original Research Article

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Comparison of Caudal Block Using Ropivacaine with Clonidine and Ropivacaine with Fentanyl for Post Operative Analgesia

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Abstract

Aim: The aim of the study was to compare the postoperative analgesia provided by Clonidine and Fentanyl when given as additives with Ropivacaine for caudal block in children. *Methods:* After obtaining the approval of our Institutional Ethics Committee, the study was conducted in 60 pediatric patients undergoing elective infraumbilical surgeries. The patients were randomly divided into two study groups i.e. Group I and II. After inducing general anesthesia, patients in Group I received Ropivacaine 0.2% with Clonidine 2 mcg/kg whereas Group II received Ropivacaine 0.2% with Fentanyl 1 mcg/kg *via* caudal route. The parameters observed included heart rate, blood pressures, oxygen saturation, postoperative pain score, sedation score, motor blockade, time to rescue analgesia and adverse effects. Statistical analysis was done by applying Fishers exact test and unpaired *t*-test. *Results:* Demographic variables were comparable in both groups. Heart rate, blood pressures, peripheral capillary oxygen saturation values were significantly lower in the Clonidine group compared to the Fentanyl Group. The onset of pain and time to 1st dose of rescue analgesia was lesser in the Fentanyl Group (< 3 hours) when compared to Clonidine Group (3–5 hours) was statistically significant with *p* - value < 0.05. Sedation scores were significantly higher for the Clonidine Group. Motor blockade was not present in any patient. Adverse effects were comparable in both the groups. *Conclusion*: Addition of Clonidine to Ropivacaine in a single shot caudal block is more advantageous than Fentanyl for postoperative pain relief without increasing the incidence of adverse effects.

Keywords: Clonidine; Fentanyl; Ropivacaine.

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Introduction

Pain is an unpleasant subjective sensation and its emotional component is very pronounced in children.[1] Caudal epidural analgesia is one of the simplest and safest technique in pediatric anesthesia and also has a high success rate.[2] It is commonly used along with an adjuvant for both intraoperative and postoperative analgesia in children undergoing surgical procedures below the level of umbilicus.[3] Ropivacaine has less motor blockade and less cardio-toxic effects than Bupivacaine makes it a more suitable agent for caudal epidural analgesia, especially following day care surgeries.[4–8]

In this study, we assessed the efficacy of clonidine and fentanyl with Ropivacaine through caudal

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route with regard to the onset and duration of sensory and motor blockade and also to document any side effects .

Aims and Objectives

To compare the postoperative pain relief of Ropivacaine 0.2% with Clonidine (2 mcg/kg) *versus* Ropivacaine 0.2% with Fentanyl (1 mcg/kg) for pediatric patients undergoing infraumbilical surgeries.

Materials and Methods

Study Design

Prospective; Randomized: Double-blinded study.

Study Population

Total of 60 patients with 30 each in two study groups, all undergoing elective infraumbilical surgeries of age group 1–7 years of ASA I and II. Children with spine abnormalities, ASA more than III and those have contraindication for neuro axial block were excluded from the study.

Children were premedicated with oral Midazolam 0.4 mg/kg 20 minutes prior to shifting to the operating theatre and monitors such as electrocardiogram, pulse oximetry and noninvasive blood pressure were connected. Baseline heart rate, blood pressure and oxygen saturation were noted. Induction was done with stepwise inhalation of Sevoflurane 8% in 6L oxygen. After adequate depth of anesthesia, intravenous access was secured. Fentanyl of dose 2 mcg/kg was administered intravenously. Ventilation was controlled using a Jackson-Ree's modification of Ayre's T-piece and appropriately sized face mask. Anesthesia was maintained with 1–2% Sevoflurane and nitrous oxideoxygen mixture in a ratio of 1:1and inj. Atracurium 0.5 mg/kg for skeletal muscle relaxation. Intubated using an appropriate tracheal tube. Bilateral air entry was checked by auscultation and tube secured.

The patient was then placed in the left lateral decubitus position. The caudal space was identified and the assigned group drug was injected using a 23G beveled needle. The patients were selected to a particular group by computer generated randomization and prefilled syringes were provided containing the study drug combinations. Study drug was prepared by the third anesthetist who doesn't participate in the study. The patient was then turned back to supine position. Group I received 0.2% Ropivacaine with Clonidine 2 mcg/kg and Group II received 0.2% Ropivacaine with Fentanyl 1 mcg/kg. The volume of the drug was decided using the Armitage formula.[9] The vitals during caudal block were noted. The intraoperative hemodynamic parameters and oxygen saturation was monitored and documented every 5 minutes until awakening. The duration of surgery was noted. After closure of skin incision, nitrous oxide and Sevoflurane was discontinued. Neuromuscular blockade was reversed with intravenous Glycopyrolate 0.01 mg/kg with Neostigmine 0.05 mg/kg. Once the patient was awake and taking good respiratory efforts, thorough suctioning was done and trachea was extubated. Patient was then shifted to PACU for observation. The heart rate, blood pressure, oxygen saturation, pain score and sedation score was followed up for 24 hours. Pain score was assessed using Children's Hospital of Eastern Ontario Pain Scale and documented at 1, 2, 3, 4, 5, 6, 12, 24th hour postoperatively. Adverse effects were also noted, if any. The follow up in the PACU was done by the PACU anesthesiologist.

An increase or decrease in HR > 20% of baseline value was considered as tachycardia or bradycardia respectively.[10] Hypotension was defined as a MAP < 25% of baseline value. Desaturation was taken as a decrease in SpO_2 < 95%. A Cheops more than 6 warranted the 1st dose of rescue analgesia. Rescue analgesia was provided with 15 mg/kg of intravenous Paracetamol. The duration of postoperative analgesia was defined as the time interval between caudal anesthesia and the 1st dose of rescue analgesia. Assessment of sedation was also done at 1, 2, 3, 4, 5, 6, 12 and 24th hour postoperatively.

Spontaneous eye opening-3;

Eye opening to verbal command-2;

Eye opening physical shaking-1;

Not arousable-0.

Motor blockade was assessed using modified Bromage scale duration of motor blockade was documented by noting the time taken by the patient to have a modified Bromage score of 0.

Results

Data analysis

The patients were divided into two groups as Ropivacaine with Clonidine and Ropivacaine with Fentanyl. Descriptive statistics was done for all the data and were reported in terms of mean values and

percentages. Suitable statistical tests of comparison were done. Normality of the data was confirmed using Shapiro-wilk test. Continuous variables were analyzed with the unpaired *t*-test. Categorical variables were analyzed with Fisher Exact Test. Statistical significance was taken as p - value < 0.05. The data was analyzed using SPSS version 20 and Microsoft Excel.

Sample size calculation

Sample size was determined based on the study' Postoperative analgesia in children when using Clonidine or Fentanyl with Ropivacaine given caudally' authored by Usha Shukla, et al. and published in Journal of Anesthesiology Clinical Pharmacology. 2011 Apr–Jun; 27(2): 205–210. In this study, increased patient comfort with pain score significantly 18% higher in Group II (Fentanyl) than Group I (Clonidine) (p - < 0.05).

The confidence level is estimated at 95% with a *z*-value of 1.96 and the confidence interval or margin of error is estimated at ± 10.

Assuming $p = 18\%$ and $q = 82\%$, $n = p \times q \times [z/e]^2$

$N = 18 \times 22 \times [1.96/12]^2$

$N = 56.70$

Therefore, 57 is the minimum sample size required for the study.

A sample size of 60 has been taken in this study:

$N = 22$ in Ropivacaine + Clonidine Group;

$N = 38$ in Ropivacaine + Fentanyl Group;

Both the groups were similar with respect to the distribution of age, weight ASA physical status, gender distribution and duration of surgery, (Table 1).

The mean heart rate was considered to be statistically significant between 3–6 hours. In the patients belonging to Group I, the heart rate decreased with a p - value of 0.0243, 0.0035, 0.0008 and 0.0016 at 3rd, 4th, 5th, and 6th hour respectively, (Fig. 1). There was significant difference of 3% reduction in systolic blood pressure in Group I compared to Group II with a p - value of 0.0448 and 0.0114 for 5th and 6th hour respectively, (Fig. 2). Diastolic blood pressure showed significant fall during 4th 5th 6th hours in Group I than in Group II with a p - value of 0.0056, 0.0007 and 0.0002 for the 4th, 5th and 6th hour respectively, (Fig. 3). Though Group I patients had significant fall in saturation during the 50 minutes and 5 hrs no patient had clinically significant desturation requiring intervention. On analyzing the values for the pain score, we found that the values were significant for 3rd, 4th, 5th and 6th hour, (Table 2). In Group I, the Cheops Pain Score showed an average of 6.34 whereas it was 8.09 in Group II, (Fig. 4). Group I had an average sedation score of 1.70 (more sedated) than Group II with an average of 2.54, (Fig. 5). It was observed that none of the patients in Group I required any rescue analgesia in the 1st 3 hours whereas 16 patients in Group II (53.33%) required it. Majority of the patients in Group I required rescue analgesia only during 5–7 hours postcaudal block. All the patients in Group II required rescue analgesia within 1st 5 hours difference was significant with a p - value of 0.0000, (Fig. 6). Majority of the Group I patients had no adverse effects ($n = 26$, 86.67%) followed by nausea ($n = 3$, 10.00%). Adverse effects between the groups was not statistically significant, (Fig. 7).

Table 1: Demography

Parameters	Group I	Group II	p - value
Mean Age in years	3.88 2 1.82	4.32 2.07	0.3409
Mean weight in Kgs	15.57 4.03	16.37 4.66	0.4924
Duration of surgery in minutes	38.83 16	38.33 18.35	0.9109
ASA			
I	29	29	> 0.999
II	1	1	
Gender			
Male	25	26	0.4178
Female	5	4	

Table 2: Cheops Pain score

Cheops Pain Score		PS 1 hr	PS 2 hr	PS 3 hr	PS 4 hr	PS 5 hr	PS 6 hr	PS 12 hr	PS 24 hr
Group I	N	30	30	30	30	30	30	30	30
	Mean	6.00	6.00	6.00	6.10	6.20	7.07	8.10	8.90
	SD	0.00	0.00	0.00	0.31	0.41	0.74	0.76	1.09
Group II	N	30	30	30	30	30	30	30	30
	Mean	6.00	6.00	6.70	8.07	9.03	8.57	8.47	8.10
	SD	0.00	0.00	0.79	0.74	1.16	1.33	1.22	1.16
p - value	Unpaired t-Test	> 0.9999	>0.9999	0.0000	0.0000	0.0000	0.0000	0.1696	0.1379

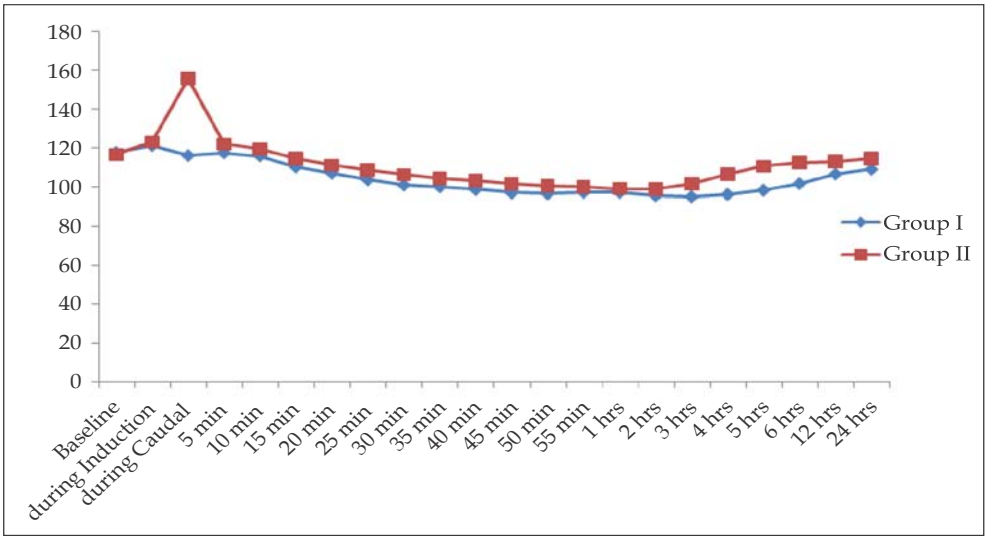

Fig. 1: Mean Heart rate

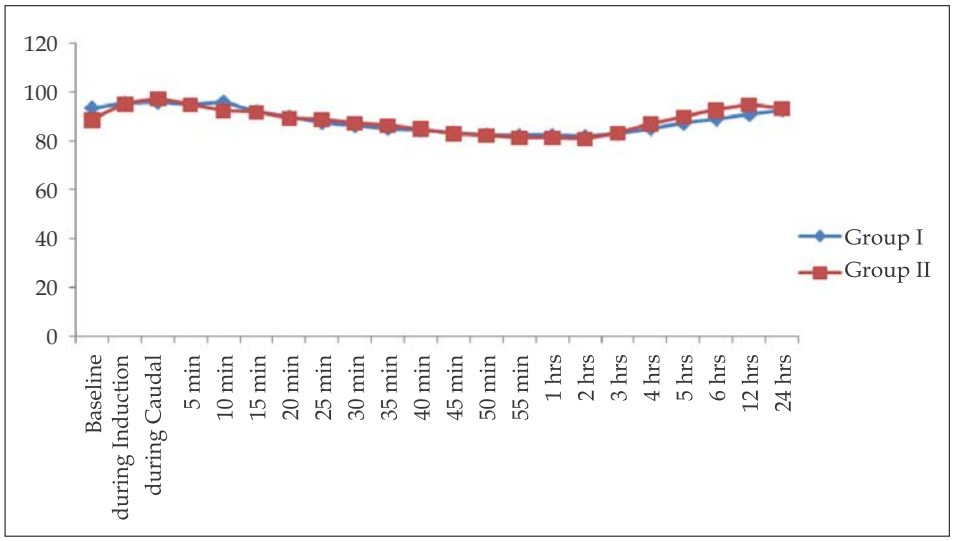

Fig. 2: Mean Systolic blood presure

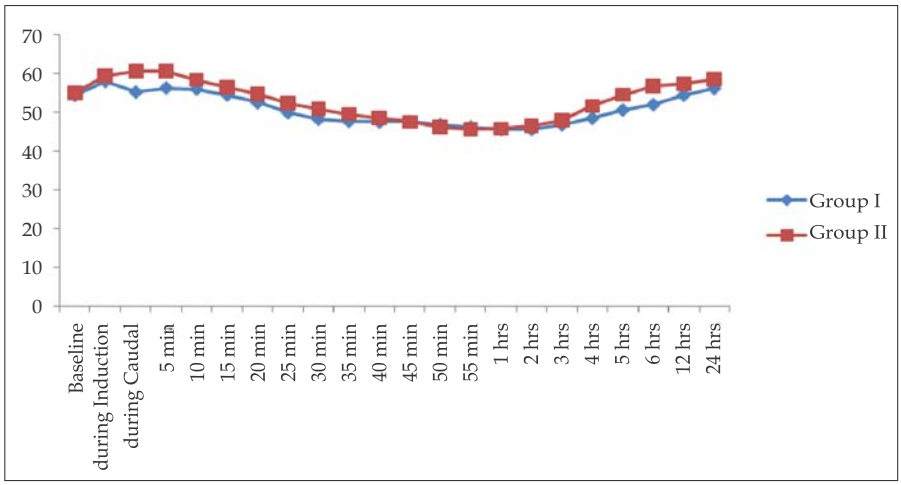

Fig. 3: Mean Diastolic blood presure

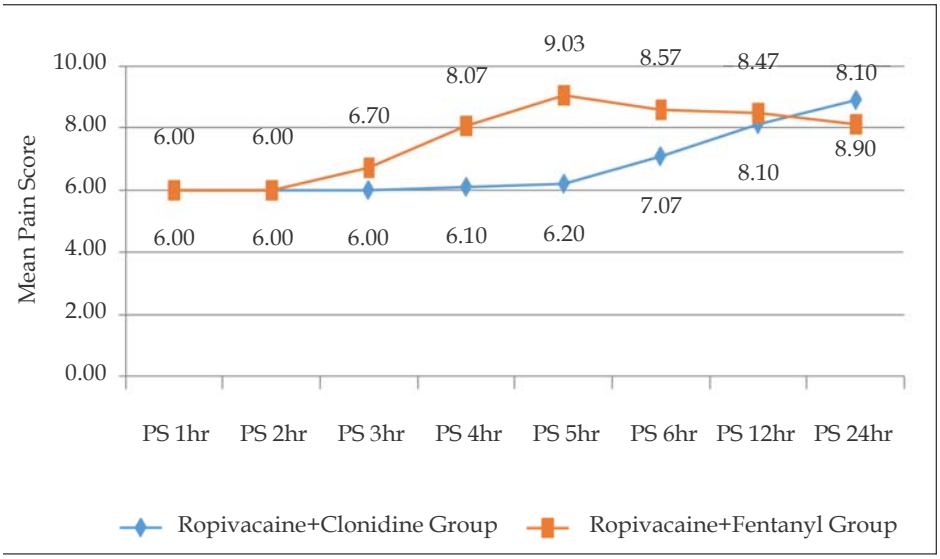

Fig. 4: Cheops Pain score

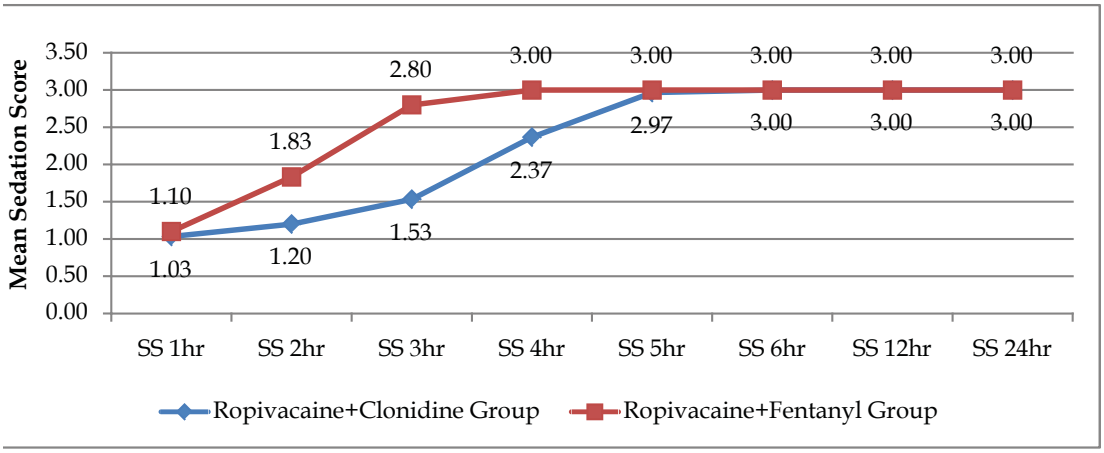

Fig. 5: Sedation score

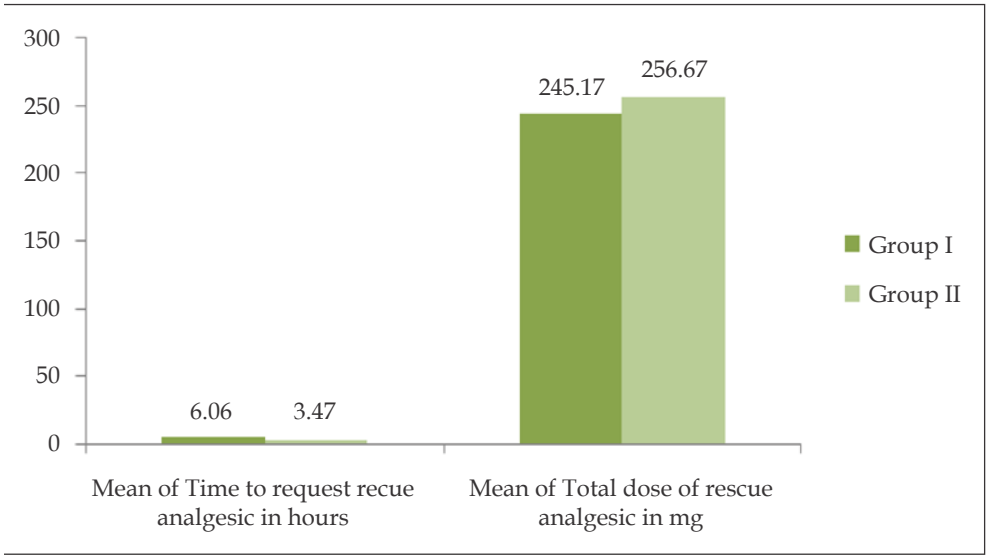

Fig. 6: Rescue analgesic

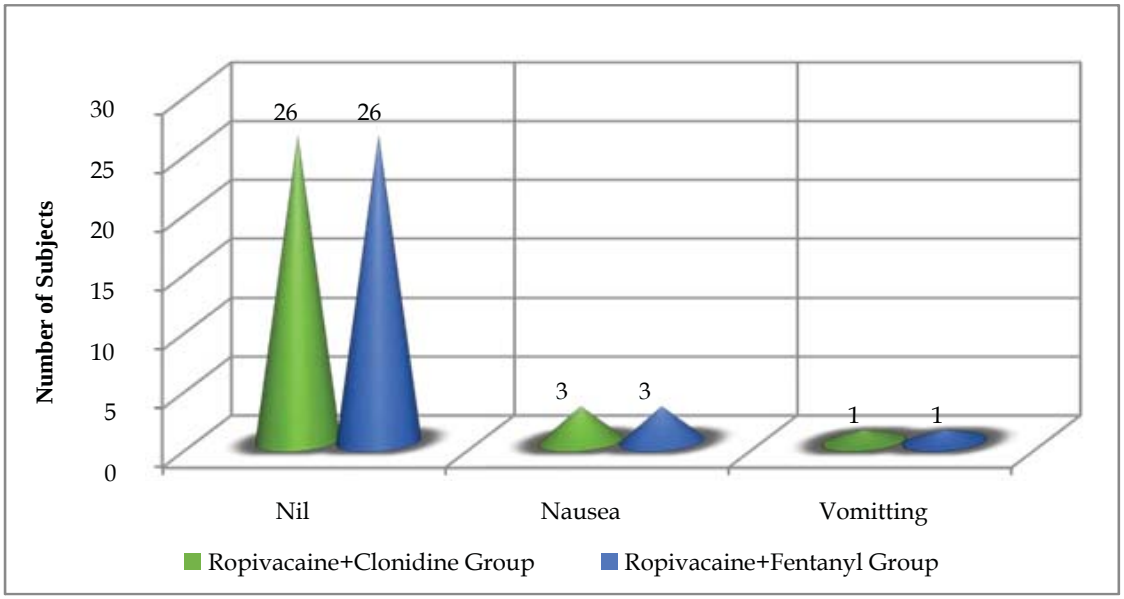

Fig. 7: Adverse effects

Discussion

Caudal block is a popular and routinely used technique to provide intra and posoperative analgesia in children. Ropivacaine and Bupivacaine are the most widely used local anesthetics in caudal blocks. In our study, we evaluated the effect of two additives— Clonidine and Fentanyl to Ropivacaine in prolonging postoperative analgesia. A limitation of a single shot caudal block is its short duration of action. A study was done by Samuel et al.[11], where they analyzed the effect of double caudal technique by injecting drug into the caudal space a second time at the end of the surgery. This gave way to concerns about the safety of injecting such high volumes in a short period of time. Bosenberg et al. conducted a study where they demonstrated that Ropivacaine 0.2% provided satisfactory postoperative pain relief where, 0.1% was less effective and 0.3% was associated with a higher incidence of motor block with minimal improvement in pain relief. In our study, we have used 0.2% Ropivacaine in both the study groups and no motor blockade was recorded in any patient.

In this study, our aim was to study about the postoperative analgesia and side effect profile provided by Clonidine and Fentanyl when used along with Ropivacaine. Shukla et al. conducted a similar study and concluded that the analgesic properties in both groups were comparable but the side effects were significantly lesser in the Clonidine Group but they had avoided muscle relaxant and analgesic dose and the route was different.[12]

Our study showed that the heart rates, blood pressures, and peripheral capillary oxygen saturation values were significantly lower in the Clonidine Group but none of the patient required clinically significant changes.

Clonidine is said to cause sedation in the postoperative period as stated in a study done by Lee et al.[13] In our study too, it was observed that the sedation scores were higher in the Clonidine Group which could be the cause for a decreased peripheral capillary oxygen saturation in them.

Clonidine is known to have antiemetic properties whereas Fentanyl and other opioids usually cause postoperative nausea and vomiting.[14] The adverse effects in both our study groups were comparable with equal number of patients having nausea or vomiting postoperatively.

Conclusion

We conclude that addition of Clonidine to Ropivacaine in a single shot caudal block is more advantageous than Fentanyl for postoperative pain relief without increasing the incidence of adverse effects.

Key messages: None.

Conflict of Interest: None.

Source(s) of support: Nil

Presentation at a meeting: Nil

Conflicting Interest (If present, give more details): Nil

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Original Research Article

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Comparative Study of Dexmedetomidine and Clonidine as Adjuvants to Isobaric Ropivacaine 0.75% for Epidural Anesthesia in Infraumbilical Surgeries

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Abstract

Background: Epidural anesthesia is very popular for infraumbilical surgeries. Epidural form of central neuraxial blockade techniques avoid the disadvantages associated with general anesthesia like airway manipulations, polypharmacy and other untoward effects like postoperative nausea, vomiting and need for supplemental intravenous analgesics. Amongst different local anesthetic drugs used, Ropivacaine, being pure S-enantiomer of bupivacaine is the recently introduced long acting amide anesthetic agent is claimed to be better in its cardiovascular profile. Alpha 2 (α_2) adrenergic receptor agonists have both analgesic and sedative properties when used as an adjuvant to local anesthetic in regional anesthesia. *Methodology:* A double blind prospective randomized control study conducted at tertiary health care institute to evaluate and compare the efficacy, block characteristics and postoperative analgesia of 1.5 µg/kg Dexmedetomidine in comparison to 2 µg/kg Clonidine as adjuncts to 0.75% isobaric Ropivacaine in epidural anesthesia for infraumbilical surgeries. *Results:* Meantime for onset of sensory and motor blockade, meantime for maximum sensory blockade and meantime for complete motor blockade was earlier with dexmedetomidine than with Clonidine as epidural adjuvant. Total duration of sensory and motor blockade was considerably longer in group receiving dexmedetomidine. Higher dermatomal level of sensory blockade, longer postoperative analgesia with better sedation was achieved by group receiving dexmedetomidine with comparative stable hemodynamics as compared to group receiving Clonidine. *Conclusion:* Dexmedetomidine is a better alternative to Clonidine as an adjuvant to 0.75% isobaric Ropivacaine in epidural anesthesia for providing early onset of sensory and motor blockade, desirable sedation and prolonged postoperative analgesia.

Keywords: Clonidine; Dexmedetomidine; Epidural anesthesia; Infraumbilical surgeries; Isobaric ropivacaine.

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Introduction

Central neuraxial blockade in the form of epidural anesthesia is very popular for lower abdominal and lower limb surgeries. Central neuraxial blockade techniques avoid the disadvantages associated with general anesthesia like airway manipulations, polypharmacy and other untoward effects like postoperative nausea, vomiting and need for supplemental intravenous analgesics.[1] Epidural

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anesthesia provides anesthesia for prolonged surgery with better hemodynamic stability than spinal anesthesia. Advantage of epidural anesthesia over general anesthesia is that the intubation and extubation responses are avoided and there will be a choice to provide postoperative analgesia.

Amongst different local anesthetic drugs used for epidural anesthesia, most popular are lignocaine and bupivacaine. Though bupivacaine is used popularly in epidural space, the fear of accidental intravascular injection lead to cardiac arrest which is difficult to resuscitate is a major problem. Ropivacaine being pure S-enantiome is a recently introduced long acting amide local anesthetic agent derived from bupivacaine is claimed to have lesser cardiovascular side effects compared to the later. It is said to be better in its cardiovascular profile as Ropivacaine was found to be less cardiac depressant, less arrythmogenic and less cardiotoxic and neurotoxic than bupivacaine.[2–5]

To alleviate anxiety due to awake status, large doses of sedation or even general anesthesia may be needed in epidural anesthesia technique. This defeats the novel purpose of regional anesthesia of continuous verbal contact with the patient. Hence to overcome this problem an adjuvant can be used with epidural local anesthetics which will provide sedation, stable hemodynamic conditions and ability to provide smooth and prolonged postoperative analgesia in addition to the reduction in the dose of Ropivacaine.

Alpha 2 (α_2) adrenergic receptor agonists have both analgesic and sedative properties when used as an adjuvant to local anesthetic in regional anesthesia.[6–11] Dexmedetomidine is a relatively selective α_2 adrenergic agonist. Majority of patients receiving Dexmedetomidine were effectively sedated yet were easily arousable, a unique feature not observed with other sedatives.[12] Dexmedetomidine suppresses descending noradrenergic pathway activity, modulates nociceptive neurotransmission and terminates propagation of pain signals leading to analgesia. The hypnotic and supraspinal analgesic effects are mediated by the hyperpolarization of noradrenergic neurons, which suppresses neuronal firing in the locus ceruleus along with inhibition of norepinephrine release and activity in the descending medullospinal noradrenergic pathway, secondary to the activation of central α_2 adrenergic receptors. This suppression of inhibitory control triggers neurotransmitters that decrease histamine secretion producing hypnosis similar to normal sleep, without respiratory depression, making Dexmedetomidine a near ideal sedative.[13]

Clonidine is an established α_2 adrenoceptors agonist with antihypertensive properties. When administered epidurally it has an analgesic action that is largely mediated through α_2 adrenoceptors in dorsal horn of spinal cord. Clonidine is useful adjuvant to opioids and local anesthetic agent for postoperative analgesia after major abdominal surgeries and orthopedic surgeries.[14] Clonidine enhances both sensory and motor blockade from epidural injection of local anesthetic. Hence to come up with a better adjuvant for epidural 0.75% isobaric Ropivacaine the present study had been planned.

Objectives

To compare between dexmedetomidine and clonidine as adjuvants to epidural 0.75% isobaric Ropivacaine with respect to the following parameters:

1. Time for onset of sensory and motor blockade;
2. Level of sensory blockade achieved;
3. Time required for two segment regression of sensory blockade;
4. Duration of sensory and motor blockade;
5. Duration of postoperative analgesia;
6. Hemodynamic changes;
7. Intraoperative and postoperative complications if any.

Materials and Methods

Study design: Randomized double blinded clinically controlled study

Study setting: Tertiary health care center.

Study population: 60 patients with *inclusion criteria*:

1. Patient giving valid informed written consent;
2. Age group of 18–60 years of both sexes;
3. ASA grade I or II;
4. Patients undergoing elective infraumbilical surgeries.

Exclusion criteria

- Patient refusal.
- ASA Grade III and onwards.
- Patients on α_2 antagonist treatment, allergic to local anesthetics or α_2 adrenergic agonists.
- Patients with infection at the site of injection, congenital abnormalities of lower spine.

- Patients with coagulopathy, uncorrected hypovolemia, active disease of CNS.
- Patients with uncontrolled systemic illness like diabetes mellitus, hypertension, neuromuscular diseases, etc.

The study population was randomly divided into following two treatment groups in a double blinded fashion based on a computer generated code: RC and RD.

Group RC - Group of 30 patients received 17 ml of 0.75% Ropivacaine + 2 µg/kg Clonidine diluted up to 1 ml with normal saline.

Group RD - Group of 30 patients received 17 ml of 0.75% Ropivacaine + 1.5 µg/kg Dexmedetomidine diluted up to 1 ml with normal saline.

After ethical committee approval and preanesthetic evaluation with basic laboratory investigations like Hemoglobin, complete blood count, blood sugar level, blood urea, serum creatinine, liver function test, chest X-ray, Electrocardiography (ECG) and urine investigations and thorough clinical examination, patients belonging to study population were interviewed and explained in detail about the surgical procedure, procedure of giving anesthesia, the pin prick method for assessing anesthesia, VAS score and how it will be checked to the patient in their own language. All the patients were reviewed in the previous night of proposed day of surgery and received tab. diazepam 10 mg and tab. ranitidine 150 mg given at bed and kept nil orally for appropriate duration.

On the day of surgery, patient's basal hemodynamic parameters were recorded. Multi-parameter monitor was connected which records heart rate, noninvasive measurement of Systolic Blood Pressure (SBP), Diastolic Blood Pressure (DBP), Mean Arterial Pressure (MAP), continuous Electrocardiogram (ECG) monitoring and oxygen saturation (SpO_2).

Assessment of sensory and motor blockade was done using pin prick and modified Bromage scale respectively.

Modified Bromage Scale

0	No motor blockade
1	Inability to raise extended leg or able to move knees and feet.
2	Inability to raise extended leg and move knee or able to move feet
3	Inability to flex ankle and foot

Cardio-respiratory parameters were monitored continuously and recordings were made every 5 min for first 30 min, every 10 min for next 30 min and every 15 min thereafter, during intraoperative period.

Block characteristics observed were:

1. Time for onset of sensory blockade;
2. Time for onset of motor blockade;
3. Time of maximum sensory blockade;
4. Time for complete motor blockade;
5. Maximum level of sensory blockade;
6. Time required for two segment regression;
7. Total duration of sensory blockade;
8. Total duration of motor blockade;
9. Time required for rescue analgesia (VAS ≥ 4).

Hypotension (i.e. systolic arterial blood pressure falling more than 20% mm Hg of baseline value) was treated with inj. mephenteramine 6 mg in bolus doses intravenous and bradycardia (heart rate < 60 beats/min) was treated with 0.6 mg of inj. atropine intravenously. Intravenous fluids were given as per body weight and operative loss requirements. During the surgical procedure, adverse event like anxiety, nausea, vomiting, shivering, dry mouth etc. were recorded. Nausea and vomiting were treated with 4 mg of intravenous inj. ondensetron.

Sedation Grading was done by 5 points scale:

I	Alert and wide awake
II	Arousable to verbal command
III	Arousable with gentle tactile stimulation
IV	Arousable with vigorous shaking
V	Not arousable

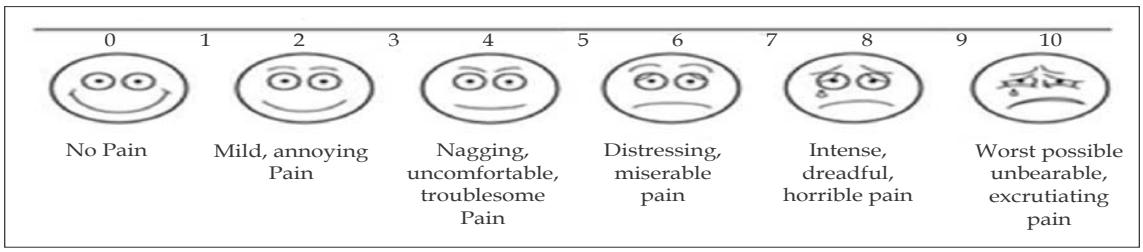

Fig. 1: Visual analog scale for assessment of pain

Sedation up to Grade III of this scale was desirable for surgical procedures.

Pain scoring was done using VAS score. Rescue analgesia given to the patient experiencing pain of VAS ≥ 4 with inj. Diclofenac sodium 75 mg by intramuscular or intravenous route.

After completion of surgery, the epidural catheter was removed. Patients were observed postoperatively as well.

Statistical Analysis

The findings were recorded in the case record forms. Data entries were done in Microsoft excel 2013. Statistical analyses were performed in SPSS software (version 20.0). for quantitative data unpaired t-test was applied and for qualitative data Chi-square test was applied. p - value less than 0.05 is taken as significant and p - value < 0.001 as highly significant.

Results

The demographic profile of the patients in terms of their age, sex, weight, duration of surgery and type of infraumbilical surgeries were comparable. The block characteristics and hemodynamic changes were as shown in Tables 1,2 and Figs. 1–5.

Discussion

Among local anesthetic agents, ropivacaine is a newer local anesthetic agent which is popular in the conduct of epidural anesthesia. Though ropivacaine is slightly less potent as compared to bupivacaine, its pharmacological profile is almost comparable to later. Various studies and literary evidence had concluded that cardiac toxicity of ropivacaine is far less than bupivacaine. In this study, 60 patients were randomly divided into two groups, each group had 30 patients, (n = 30).

Table 1: Comparison of block characteristics between Group RC and Group RD

Block Characteristics	Group RC	Group RD	*p* - value
Time for onset of sensory blockade at T 10 dermatome (min.)	12.53 ± 1.85	7.28 ± 0.97	0.000013
Time for onset of motor blockade (min.)	17.26 ± 3.42	14.02 ± 4.18	0.0017
Time for maximum sensory blockade (min.)	18.52 ± 2.33	12.05 ± 3.71	0.00007
Time for complete motor blockade (min.)	22.31 ± 2.67	18.25 ± 4.12	0.000089
Max. sensory level			
T4	3 (10%)	4 (13%)	
T6	21 (70%)	26 (86.67%)	0.01904
T8	6 (20%)	0 (0%)	
T10	0 (0%)	0 (0%)	
Total duration of sensory blockade Study (min.)	303.3 ± 27.7	324.7 ± 32.3	0.0078
Duration of motor blockade (min.)	206.3 ± 21.78	226.7 ± 23.96	0.0015
Time required for 2 segment regression (min.)	123.7 ± 13.4	146.3 ± 14.3	0.000034
Time required for rescue analgesia (minutes)	387.00 ± 41.14	423.3 ± 42.67	0.0014

Table 2: Comparison of sedation score & incidence of side effects between group RC & group RD

	Group RC	Group RD	*p*- value
Sedation score			
I	19 (61.33%)	4 (13.33%)	
II	9 (30%)	12 (40%)	
III	2 (6.67%)	14 (46.67%)	0.00067
IV and V	0 (0%)	0 (0%)	
Side effect			
Dry Mouth	3(10%)	3(10%)	
Nausea	2(6.67%)	5(16.67%)	>0.05
Vomiting	2(6.67%)	1(3.33%)	>0.05
Shivering	5(16.67%)	4(13.33%)	>0.05
Bradycardia	6(20%)	13(43.33%)	< 0.05
Hypotension	16(53.33%)	2(6.67%)	<0.001

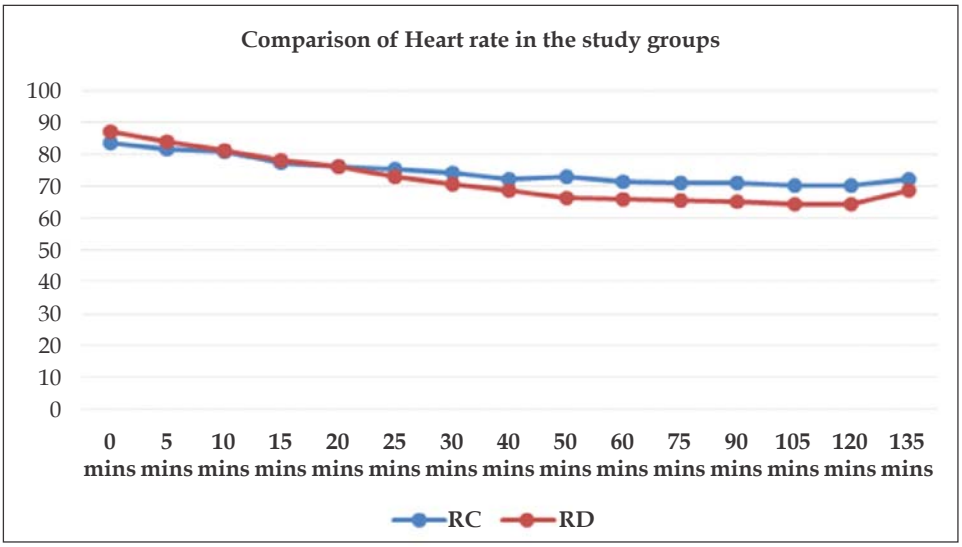

Fig. 2: Comparative changes in heart rate in study groups

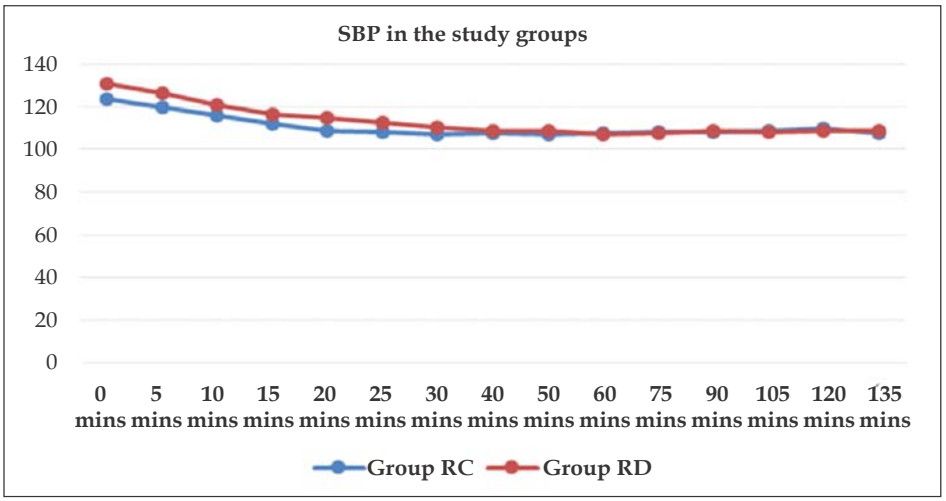

Fig. 3: Comparative changes in systolic blood pressure in study groups

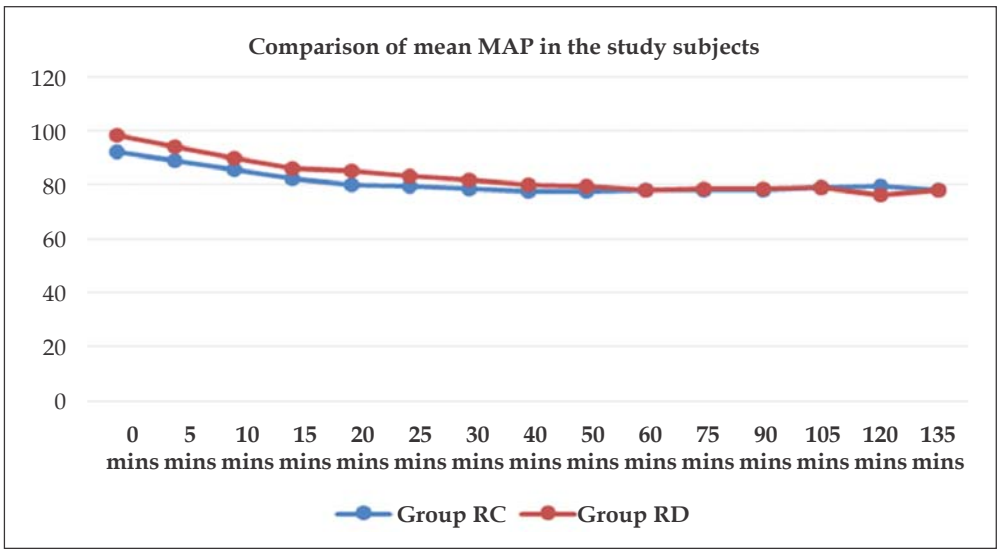

Fig. 4: Comparative changes in mean arterial pressure in study groups

Group RC: Received epidurally 17 ml of 0.75% isobaric ropivacaine with 2 µg/kg of Clonidine.

Group RD: Received epidurally 17 ml of 0.75% isobaric ropivacaine with 1.5 µg/kg of dexmedetomidine.

The demographic parameters like age, sex, weight, ASA Grading and duration of surgery were comparable.

The findings of our study were as follows:

The meantime for onset of sensory blockade in Group RC (12.53 ± 1.85 min.) was late than in Group RD (7.28 ± 0.97 min.). Bajwa, et al.[11] in their study observed onset time of sensory blockade to be 9.72 ± 3.44 min in Group RC and 8.52 ± 2.36 min in Group RD. Shivakumar M. Channabasappa et al.[15] 63 found onset of sensory blockade in group of patients receiving dexmedetomidine (14.53 ± 2.96 min.) earlier than group of patients receiving clonidine (16.72 ± 4.43 min.).

Thimmappa et al.[1] found onset of sensory blockade earlier in dexmedetomidine Group (8.90 ± 0.99 min.) than clonidine Group (9.17 ± 1.21 min.), similar to our study. Muhammad Rashid O, et al.[19] observed earlier onset of sensory blockade with dexmedetomidine (9.42 ± 1.41 min.) than clonidine. (10.80 ± 2.49 min.) Arunkumar S et al.[16] in their study found earlier onset of sensory blockade in patients receiving dexmedetomidine (8.53 ± 1.81 min.) as compared to patients receiving clonidine. (11.93 ± 1.96 min.) Harinath G et al.[13] in their study found earlier onset of sensory blockade in patients receiving dexmedetomidine (8.6 ± 12.38 min.) as compared to patients receiving clonidine. (9.84 ± 1.77 min.) These results support our study.

Meantime for onset of motor blockade in Group RC and Group RD were 17.26 ± 3.42 min. and 14.02 ± 4.18 min. respectively. The onset time of sensory and motor blockade, was significantly earlier in Group RD than in Group RC. The onset is faster in patients receiving dexmedetomidine than the patients receiving clonidine. The difference was found to be statistically significant.

Bajwa et al.[11] in their study found rapid onset of motor blockade in Group RD (17.24 ± 5.16 min.) than in the Group RC. (19.52 ± 4.06 min.) Thimmappa et al.[1] in their comparative study found that time required to attain motor blockade with Group RD was 15.77 ± 1.25 min. and with Group RC was 16.47 ± 1.38 min. Bajwa et al.[11] also found that addition of dexmedetomidine to epidural ropivacaine hastens the onset of motor blockade.

The meantime for maximum sensory blockade was 18.52 ± 2.33 min. in Group RC and 12.05 ± 3.71 min. in Group RD. Thus, time for maximum sensory blockade in Group RD was earlier than in Group RC which was statistically significant. Harinath G et al.[13] found time for maximum sensory blockade earlier (13.36 ± 2.62 min.) in patients receiving dexmedetomidine than in patients receiving clonidine. (15.56 ± 2.53 min.) Bajwa et al.[11] noticed time for maximum sensory blockade to be earlier in Group RD (13.14 ± 3.96 min.) as compared to Group RC (15.80 ± 4.56 min.) which was similar to our study.

Thimmappa et al.[1] unlike our study, found no any significant difference in attaining maximum

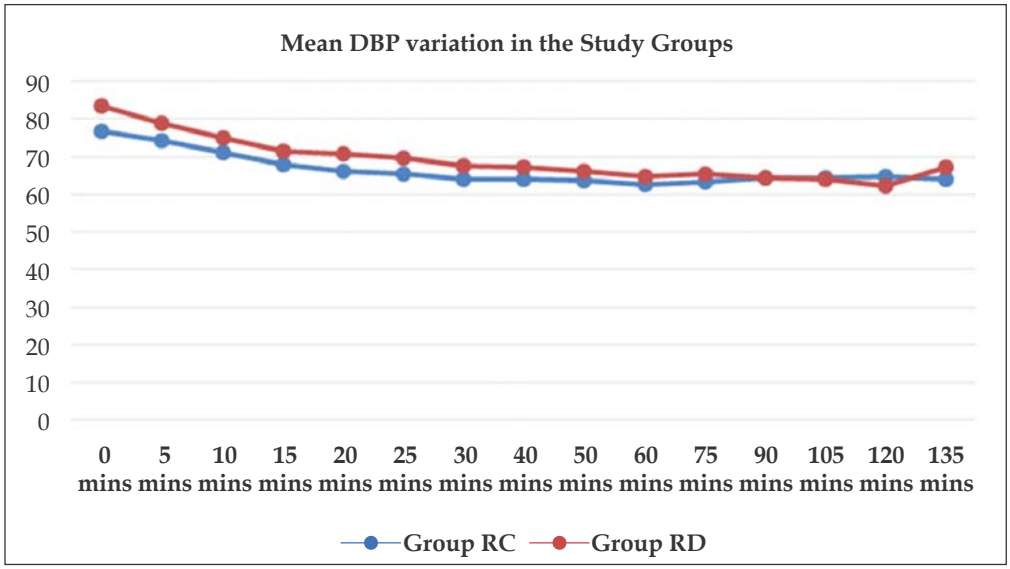

Fig. 5: Comparative changes in mean diastolic blood pressure in study groups

sensory blockade in patients receiving Clonidine (13.36 ± 1.46 min.) and dexmedetomidine (13.03 ± 1.33 min.).

In present study, meantime for complete motor blockade in Group RC was 22.3 ± 2.67 min and in Group RD was 18.25 ± 4.12 min. Tis finding suggest motor blockade to be earlier in Group RD as compared to Group RC which was statistically significant.

Bajwa et al.[11] in their study found that the meantime for complete motor blockade in Group RD (17.24 ± 5.16 min.) was earlier than in Group RC (19.52 ± 4.06 min.).

Muhammad Rashid O et al.[19] found time for complete motor blockade to be earlier in patients receiving dexmedetomidine (21.20 ± 3.36 min.) as compared to patients receiving Clonidine (28.40 ± 4.06 min.) Harinath G et al.[13] found time for complete motor blockade to be earlier in patients receiving dexmedetomidine (17.32 ± 2.71 min.) as compared to patients receiving Clonidine (19.6 ± 3.09 min.) which was similar to our study.

Thimmappa et al.[1] found no any significant difference in attaining complete motor blockade in patients receiving Clonidine (16.47 ± 1.38 min.) and dexmedetomidine. (15.77 ± 1.25 min.)

Arunkumar S et al.[16] also found no statistically significant difference in time required for complete motor blockade between two groups of patients i.e. patients receiving Clonidine (23.07 ± 4.63 min.) and dexmedetomidine. (23.00 ± 4.27 min.) Higher dermatomal level of sensory blockade was achieved by (T 4–5) than with Clonidine T 5–6). Harinath G et al.[13] found higher dermatomal level of sensory blockade in patients receiving dexmedetomidine (T 5–6) than those receiving Clonidine (T 6–7).

Bajwa et al.[11] found higher dermatomal level of sensory blockade in patients receiving dexmedetomidine (T 5–6) than those receiving Clonidine (T6–7).

uhammad Rashid O et al.[19] also found higher dermatomal level of sensory blockade in patients receiving dexmedetomidine (T 3–4) than those receiving Clonidine (T4–5). The findings of these studies were similar to our study. Bamne et al.[17] found highest dermatomal blockade T4 in both groups of patients receiving dexmedetomidine and Clonidine with no statistically significant difference.

Time taken for two segment regression in Group RC and RD were 123.7 ± 13.4 min. and 146.3 ± 14.3 min. respectively in present study i.e. significantly earlier in Group RC than in Group RD. Study by Bajwa et al.[11] found meantime to two segment regression to be statistically significantly earlier in Group RC (128.08 ± 7.54 min.), than Group RD (136.46 ± 8.12 min.) similar to our study. Harinath G et al.[13] found meantime to two segment regression to be statistically highly significant between Group RD (135.76 ± 7.63 min.) and Group RC (127.96 ± 6.79 min.) comparable to our study. Channabasappa S et al.[15] also found meantime for two segment regression to be statistically significant between group of patients receiving dexmedetomidine (123.2 ± 8.63 min.) and clonidine.(111.52 ± 7.21 min.)

Thimmappa et al.[1] also found time taken for two segment regression to be statistically significant between Group RC (120.63 ± 17.59 min.) and Group RD (163.67 ± 15.20 min.) patients.

Muhammad Rashid O et al.[19] also found statistically significant difference in Group RC (108 ± 7.21 min.) and Group RD (132.60 ± 9.25 min.) patients. These findings supports our study. Total duration of sensory blockade in present study was more in group RD (324.7 ± 32.3 min) as compared to Group RC (303.3 ± 27.7 min) which was statistically significant. Bajwa et al.[11] found total duration of sensory blockade to be more in patients receiving dexmedetomidine (316.64 ± 40.36 min.) as compared to clonidine (296.72 ± 35.52 min) which was statistically significant.

Saravana Babu et al.[12] found total duration of sensory blockade significantly more in patients receiving dexmedetomidine (407.00 ± 47.06 min.) than patients receiving clonidine (345.01 ± 35.02 min).

Arunkumar S et al.[16] also found total duration of sensory blockade significantly more in patients receiving dexmedetomidine (316.00 ± 31.15 min.) than patients receiving Clonidine (281 ± 37 min).

Salgado PF et al.[18] also found prolonged sensory blockade in group of patients receiving dexmedetomidine than in those receiving Clonidine.

Thimmappa et al.[1] unlike our study, found no statistical significant difference in total duration of sensory blockade in patients receiving Clonidine (261.00 ± 17.68 min.) and dexmedetomidine (291.33 ± 27.79 min.). Total duration of motor blockade in present study in Group RC was 206.3 ± 21.7 min and in Group RD it was 226.7 ± 23.96 min. Thus, the duration of motor blockade in Group RD was more than Group RC which was statistically significant.

Bajwa et al.[11] found duration of motor blockade to be more in Group RD (246.72 ± 30.46 min.) than in Group RC (228.84 ± 27.18 min.) Muhammad Rashid O et al.[19] found duration of motor blockade in patients receiving dexmedetomidine (180.4 ± 11.6 min.) to be significantly more than those receiving Clonidine (143.00 ± 5.16 min.) which was similar to our study. Salgado PF et al.[18] found duration of motor blockade in group of patients receiving dexmedetomidine to be about 390 min. Bajwa et al.[11] found in their study that duration of motor blockade was prolonged in patients receiving dexmedetomidine along with ropivacaine i.e. 259.62 ± 21.38 min. Their finding was similar to our study. Thimmappa et al.[1] found time for complete recovery of motor blockade to be nonsignificant between patients of Group RC and Group RD.

The time required for first rescue analgesia in Group RC was 387.00 ± 41.14 min. and in Group RD was 423.3 ± 42.67 min., suggesting duration of postoperative analgesia to be more in Group RD than in Group RC which was statistically significant. Bajwa et al.[11] found time for first rescue top up to be more in Group RD (342.88 ± 29.16 min.) than in Group RC (310.76 ± 33.76 min.). Harinath G et al.[13] found time for first rescue top up to be earlier in Group RC (200.56 ± 17.74 min.) than in RD (220.48 ± 21.43 min.) which was statistically highly significant.

Channabasappa S et al.[15] found time for first rescue top up to be earlier in Group RC (234.65 ± 23.76 min.) than in RD (286.76 ± 34.65 min.) which was statistically highly significant. Thimmappa et al.[1] found no statistical difference in the duration of postoperative analgesia between Group RC (261.00 ± 17.68 min.) and Group RD (291.33 ± 27.79 min.) Muhammad Rashid O et al.[19] also found time to first rescue top up to be prolonged in Group RD (306 ± 12.3 min.) than Group RC (224 ± 17.2 min.) patients.

Soni P et al.[14], Arunkumar S et al.[16] also found duration of analgesia to be more in Group RD patients than Group RC patients. The incidence of sedation score of Grade II and III was more in Group RD as compared to Group RC. While the incidences of sedation score of Grade I was found more in Group RC than in Group RD.

Studies by Bajwa et al.[11], Thimmappa et al.[1] also found sedation score to be significantly more in Group RD than Group RC patients. Harinath G et al.[13] observed sedation score during surgery between the two groups to be statistically significant in Grade I and III sedation score.

Arunkumar S et al.[16] and Muhammad Rashid O et al.[19] found higher sedation scores in group of patients receiving dexmedetomidine than those who received clonidine. The results were similar to our study. Hemodynamic parameters were preserved both in intraoperative and postoperative period in both groups. There was overall statistically significant difference in mean heart rate at various time intervals between patients of Group RD and RC. 13 patients (43.33%) who received dexmedetomidine and 6 patients who received clonidine (20%) had bradycardia, which was statistically significant. Bradycardia was easily reversed with 0.6 mg of inj. atropine IV in all the patients experiencing bradycardia. Thimmappa et al.[1] found bradycardia in 13.3% of patients in Group RC and 33.3% of patients of Group RD which was similar to our study.

Studies by Harinath G et al.[13] and Muhammad Rashid O et al.[19] found no statistically significant difference in heart rate between patients of Group RD and Group RC. Saravana Babu et al.[12] found stable heart rate in Group RC and RD patients. Arunkumar S et al.[13] found significant fall in heart rate in both the study groups by 20% in 30–50 min. following epidural injection.

Channabasappa S et al.[15] found slight decrease in heart rate in both groups which was statistically insignificant. In this study, statistically significant difference in mean arterial pressure at various time intervals observed. 16 patients in Group RC and 2 patients in Group RD developed hypotension requiring treatment. Fall in MAP was significantly more in patients of Group RC than in Group RD, which was managed by intravenous fluids and inj. mephenteramine 6 mg IV.

Harinath G et al.[13] found statistically significant difference in MAP between Group RC and Group RD patients with incidence of hyptension more in Group RC than Group RD. This finding was similar to our study.

Bajwa et al.[11], Saravana Babu et al.[12] 55 found stable cardiorespiratory parameters in both RD and Group RC of patients. Muhammad Rashid O et al. 70 and Arunkumar S et al.[13] did not find any statistically significant difference in deviation in Blood Pressure (BP) in both study groups.

Channabasappa S et al.[15] found a slight decrease in MAP in both the study groups which was statistically not significant. Incidence of side effects like nausea, vomiting, dry mouth, shivering and headache were observed in very few patients. The difference between the two study groups was statistically nonsignificant. No patients in either

group had any respiratory depression. Bajwa et al.[11] found incidence of dry mouth to be significantly higher in both the groups but it was statistically not significant on comparison. Incidences of other side effects were comparable were statistically not significant in both the groups. Studies by Muhammad Rashid O et al.[19] and Thimmappa et al.[1] did not find statistically significant difference in incidence of side effects in both the study groups.

Harinath G et al.[13] found incidence of dry mouth to be higher in both the study groups but it was statistically not significant on comparison.

Conclusion

The present study, concludes that dexmedetomidine is a better alternative to clonidine as an adjuvant in epidural anesthesia for providing early onset and prolonged duration of sensory and motor blockade, desirable sedation and prolonged postoperative analgesia.

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Comparison of Insertion Techniques of Classical Laryngeal Mask Airway Regarding Ease of Insertion and Complications

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Abstract

Introduction: LMAs is a valuable rescue device in both elective and emergency situations for both anticipated and unanticipated difficult airways. Many studies have shown that rotational technique has been proven to be much more effective in pediatric age group avoiding injury to pharynx without buckling the tip of LMA. This prompted us to study this rotational technique in adult population and compare it with the standard one. *Aims and Objectives:* To study the classic laryngeal mask airway insertion comparing standard and partial cuff inflated rotational technique with respect to ease of insertion and occurrence of complications. *Materials and Methods:* Ethical committee approval and informed consent obtained, 140 patients of age 18 to 70 years, ASA I and II posted for short surgical procedures under general anesthesia were randomized into Group S (Brain's Standard insertion Technique) and Group R (Partially inflated Rotational Technique). Appropriate sized LMA was inserted was hemodynamics monitored. *Data Analysis:* Continuous variables were analyzed with the unpaired *t*-test. Categorical variables were analyzed with the Chi-square Test and Fisher Exact Test. Statistical significance was taken as $p < 0.05$. *Results:* Both groups were comparable with respect to demography. Statistically significant difference among the group with respect to first attempt success and LMA insertion time. Hemodynamically both groups were comparable. There were no statistically significant difference in complications. *Conclusion:* We conclude that the Standard technique of LMA insertion is a better technique when compared to Rotational technique with respect to ease of insertion and lesser number of complications.

Keywords: Brain's standard insertion technique; Classic laryngeal mask airway; Partially inflated rotational technique.

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Introduction

Successful tracheal intubation required one to master the art of laryngoscopy to visualize the larynx, without causing undue trauma to the teeth and walls of the oropharynx.[1–3] In 1983, Archie Brain[3] invented the Laryngeal Mask Airway and introduced it as a safer and reliable alternative rescue device in both elective and emergency situations for both anticipated and unanticipated difficult airways. The Classic LMA became commercially available in 1988 in England. It is a reusable device and may be steam autoclaved up to 40 times. The mask consisted of three components, an inflatable cuff made of silicone rubber that provides a prelaryngeal seal, a semi rigid, semitransparent airway tube and an inflation line.

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The mask is oblong and based on the plaster cast of cadavers. Brain's technique[4] of insertion involved placing the head and neck in the normal intubating position and then inserting the deflated mask with its lumen facing forwards until a resistance was felt. This technique though popular is not without drawbacks. The main problem arises when the tip of the LMA folds against the posterior pharyngeal wall. It requires excessive force to push the LMA into proper position using the index finger, which could also lead to trauma to the guiding finger by the patient's teeth. This would often lead to multiple insertion attempts, trauma to the airway and failure to obtain a proper seal.

Various insertion techniques have been attempted in all age groups with regard to ease of insertion and time required to achieve proper placement of the mask. Among the various techniques used rotational technique has been proven[5–7] to be much more effective in pediatric age group, when compared to the standard Brain's technique. It avoided the structures in the anterior pharynx and the LMA slides along the posterior pharynx without buckling the tip of LMA. This prompted us to study this technique in adult population and compare rotational technique with the standard technique.

Aims

To study the classic laryngeal mask airway insertion comparing standard technique and partial cuff inflated rotational technique with respect to ease of insertion and occurrence of complications.

Objectives

Primary objectives: To evaluate and compare the ease of LMA insertion through the Standard and partially inflated Rotational LMA insertion technique with respect to:

Number of attempts;

Time to secure a successful airway.

Secondary objectives: To evaluate occurrence of complications during insertion process such as:

Hypoxemia (SpO_2 < 90%);

Laryngospasm;

Blood staining on LMA surface upon removal.

Materials and Methods

After getting the ethical committee approval and informed consent 140 patients in the age group of 18 to 70 years, ASA I and II posted for short surgical procedures under general anesthesia were included in the study.

Patients anticipated difficult airway risk for aspiration recent history of upper airway infection ASA III and IV were excluded from the study.

Patients were then randomized into two groups:

Group S: Brain's Standard insertion Technique;

Group R: Partially inflated Rotational Technique.

All the patients were kept nil per oral for a minimum of 8 hours preceding the procedure. All the patients received intravenous inj. midazolam 1 mg, inj. glycopyrollate 0.2 mg and inj. ondansetron 4 mg half an hour before the surgery in the preanesthetic room. On arrival in the operating room, after the placement of standard minimum monitoring devices patients were preoxygenated for three minutes with 100% oxygen. Anesthesia was induced with Inj. Propofol 1%, 2.5 mg/kg/IV and fentanyl 2/kg/IV. Patients were ventilated with oxygen for one minute by bag and mask, after which LMA was inserted according to the study group technique allotted by randomization.

Anesthesia was considered adequate for device insertion when the patient was unresponsive with no spontaneous respiration and had lost eye-lash reflex. Laryngeal mask airway of appropriate size according to the weight of the patient was lubricated using a water based KY jelly and once adequate depth achieved the device was inserted, bilateral air entry was checked and the device was secured with tape. Anesthesia was maintained with nitrous oxide and oxygen in a ratio 2:1 along with isoflurane and patient was maintained in spontaneous ventilation.

Group S: Brain's Standard insertion Technique:[13,14] The patient's head was positioned in sniffing position and LMA was inserted using the index finger which was placed at the junction of cuff and tube while the hood faced the nose and hard palate. The LMA was pushed inside the oral cavity until a resistance was felt. Then the LMA was stabilized using the other hand and the inserting hand was removed.

Group R: Partially inflated Rotational Technique:[15–22] The patient's head was positioned in sniffing position. The LMA cuff was partially inflated and faced the nose and hard palate. The LMA was pushed inside until a resistance was felt and rotated to 180° anti clock wise and position was confirmed.

Insertion Time

Insertion time was calculated from the time taken from picking up the airway in the hand to the successful placement of airway as confirmed by auscultation of bilateral equal air entry over the chest.

Number of Attempts

If an effective airway could not be achieved the LMA was removed and reinserted in the same technique a total of 3 attempts were permitted before failure of insertion was recorded. After 3 unsuccessful attempts, the trachea was intubated.

In the event of desaturation (SpO_2 < 95%) during the three attempts, rescue ventilation was planned with bag and mask and that time period will also be included in the total insertion time. Number of insertion attempts using either technique was recorded.

The following parameters were monitored prior to insertion at 0 and every minute until 10 minute and then every 5 minute until 30 minutes after securing the airway:

Heart Rate (HR) in beats per minute;

Systolic Blood Pressure (SBP) in mm/Hg;

Diastolic Blood Pressure (DBP) in mm/Hg;

Oxygen saturation (SpO_2) in percentage.

Airway Sealing Pressure

Airway sealing pressure was determined by closing the expiratory valve of the circle system at a fixed gas flow of 3L/min and recording the oropharyngeal leak pressure by detection of an audible noise using a stethoscope placed just lateral to the thyroid cartilage. The corresponding airway pressure displayed in the monitor was recorded.

At the end of the surgical procedure, anesthesia was discontinued and the device was removed while the patient was in a deeper plane of anesthesia and oxygen maintained by face mask.

LMA position confirmation:

Visible bilateral equal chest expansion;

Bilateral equal air entry on auscultation;

Appearance of end tidal carbon dioxide tracing;

Absence of audible air leak after standardized cuff inflation;

Fiber optic bronchoscope confirmation, shows in Table 1.

Table 1: FOB grading

Grade1	Larynx only (ideal position)
Grade 2	Epiglottis + larynx
Grade 3	Epiglottis impinging grill + larynx seen
Grade 4	Kinked LMA
Grade 5	Epiglottis down folded + larynx not seen

Complications assessed after device removal

Hypoxemia (SpO_2 < 90%);

Laryngospasm;

Presence of blood on airway device.

Data Analysis

Descriptive statistics was done for all data and were reported in terms of mean values and percentages. Continuous variables were analyzed with the unpaired *t*-test. Categorical variables were analyzed with the Chi-square Test and Fisher Exact Test. Statistical significance was taken as $p < 0.05$. The data was analyzed using SPSS version 16 and Microsoft Excel 2007.

Sample Size Estimation

Sample size was determined based on study done by Dileep Kumar[33] et al.

In this study statistically insignificant difference was found in incidence of blood stained LMA (22% difference).

Description

- The confidence level is estimated at 95%
- With a *z* value of 1.96
- The confidence interval or margin of error is estimated at ±8
- Assuming p % = 22 and q % = 78

  $n = p\ \% \times q\ \% \times [z/e\%]^2$

  $n = 22 \times 78 \times [1.96/8]^2$

  × = 103

Therefore, 103 is the minimum sample size required for the study.

In our study, we planned to recruit a minimum of 140 subjects (70 per intervention arm).

Results

Both the groups were comparable with respect to age, weight, gender distribution, mallampatti classification and ASA distribution, shows in Table 2.

Among the study subjects, there was no statistically significant difference in relation to

Table 2: Demograph

Parameters	Standard Group (n = 71)	Rotational Group (n = 69)	p - value
Age in years (mean SD)	35.51 ± 10.41	35.09 ± 10.23	0.8101
Gender			
Male	3	0	0.0843
Female	68	69	
Weight in kgs	56.82 ± 7.83	58.09 ± 7.50	0.3290
ASA			
I	59	56	0.7645
II	12	13	
Mallampatti Class			
I	48	50	0.5306
II	23	19	
Number of Attempts			
1	67	42	< 0.0001
2	4	12	
3	0	15	
Mean LMA insertion time	34.28 ± 10.20	69 ± 48.49	< 0.0001
LMA - Fiberoptic Grade Groups			
Grade 1	52	45	0.6642
Grade 2	16	19	
Grade 3	1	3	
Grade 4	2	2	
Mean Oropharyngeal Leak Pressure	38 ±1.68	37.48±1.8	0.07

Table 3: Complications

Complications	Standard Group (n = 71)	%	Rotational Group (n = 69)	%	p - value Fishers Exact Test
Hypoxemia	0	0.00	1	1.45	0.4929
Laryngospasm	0	0.00	1	1.45	0.4929
Blood Stain	1	1.41	5	7.25	0.1131

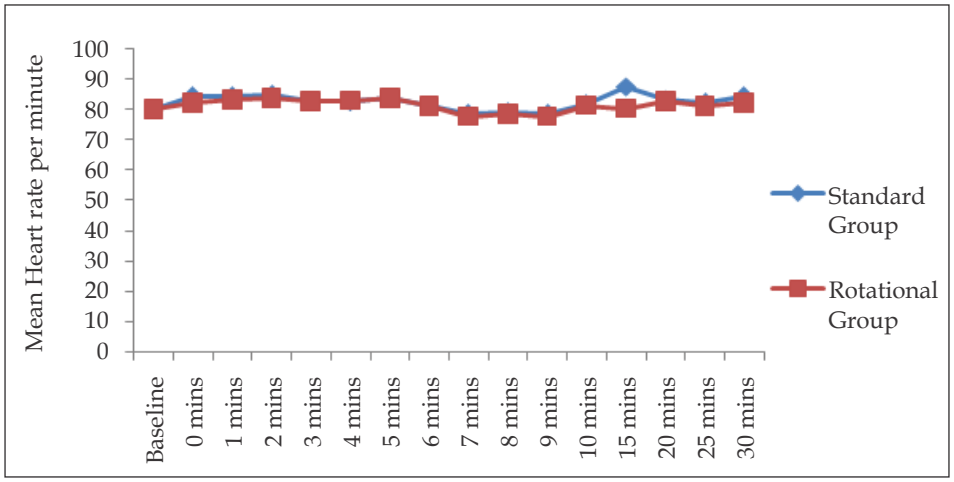

Fig 1: Mean Heart Rate

baseline and intraoperative heart rate, shows in Fig. 1, systolic blood pressure, shows in Fig. 2, diastolic blood pressure shows in Fig. 3 and oxygen saturation between rotational procedure group and standard procedure group during the observation period of 0 to 30 min (0 min and every minute until 10 minute and then every 5 minute until 30 minutes after securing the airway) *p* - value of > 0.05 as per unpaired *t*- test.

Among the study subjects, there was no

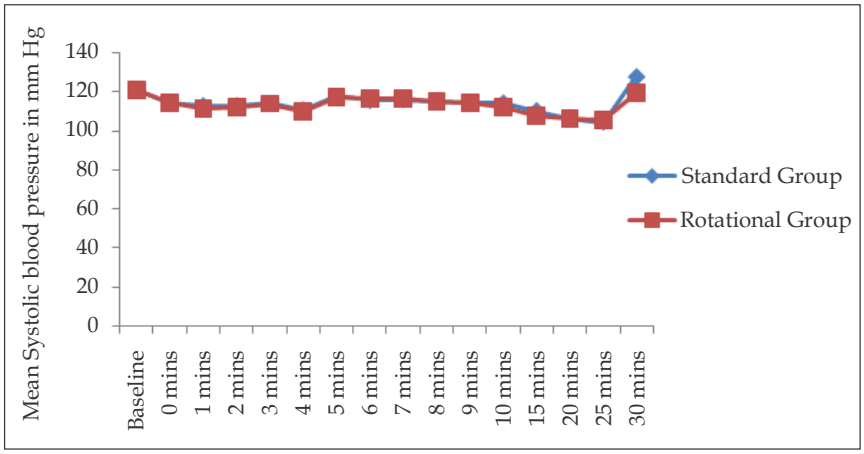

Fig 2: Mean Systolic Blood Pressure

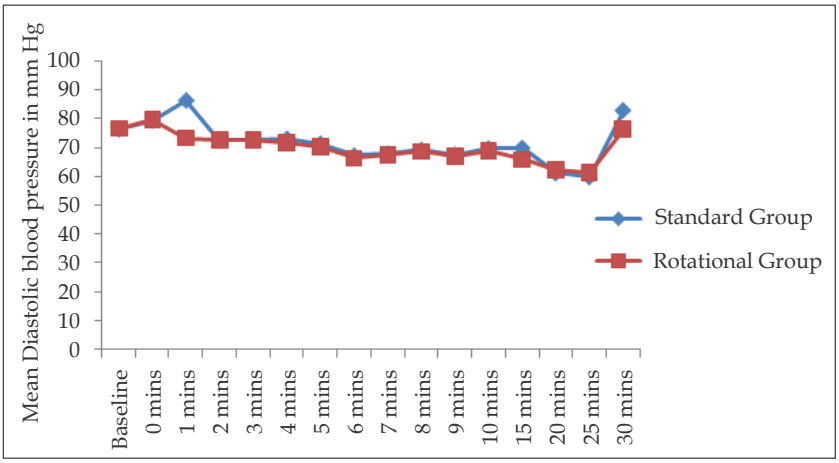

Fig 3: Mean Diastolic Blood Pressure

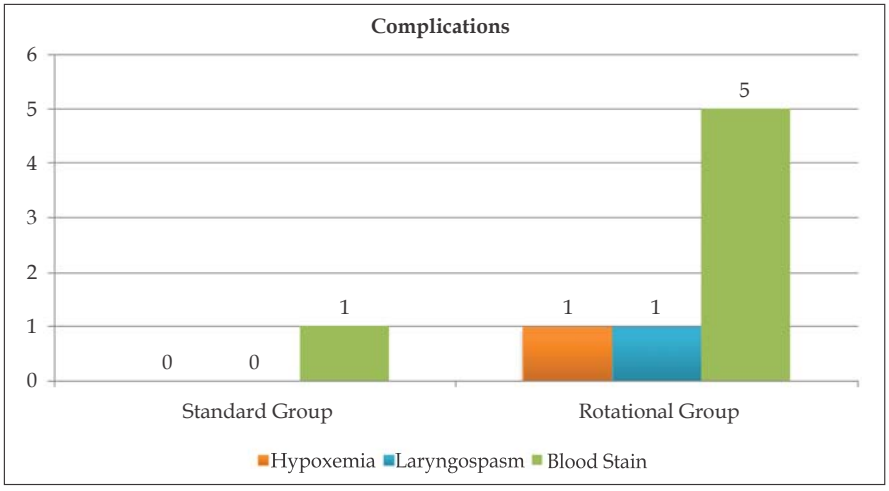

Fig 4: Complications

statistically significant difference in relation to complications status between standard procedure group and rotational procedure group when used in patients undergoing classic laryngeal mask airway insertion with a *p* - value of > 0.05 as per fishers exact test.

LMA insertion timetable shows that majority of the study subjects were distributed in 31–60 secs group (63.38% in standard procedure group and 42.03% in rotational procedure group). with a *p* - value of < 0.05 as per unpaired *t*-test. LMA fiberoptic grading table shows that majority of the study subjects were distributed in Grade I group (71.24% in standard procedure group and 65.22% in rotational procedure group). Among the study subjects, there was no statistically significant difference in relation to LMA fiberoptic grading status between standard procedure group and rotational procedure group LMA oropharyngeal leak pressure distribution between rotational procedure group (mean = 37.48) and standard procedure group (mean = 38.00) when used in patients undergoing classic laryngeal mask airway insertion with a *p* - value of > 0.05 as per unpaired *t*-test.

Incidence of hypoxemia, laryngospasm and blood stain is 0.00%, 0.00% and 1,41% respectively in standard procedure group and 1.45%, 1.45% and 7.25% in rotational procedure group *p* - value of > 0.05 as per fishers exact test, shows in (Table 3).

Discussion

Several techniques of insertion have been attempted in various age groups with regard to ease of insertion and time required to achieve proper placement of the LMA. Among the various techniques used rotational technique[15–22] has been found to have promising results in pediatric age group when compared to the standard Brain's technique.[13,14] Even though there have been several studies to prove the successful use and advantages of rotational technique of LMA in children, there have not been enough evidence to prove the same in adult population.

The main aim of our study is to compare the classical laryngeal mask airway insertion technique and rotational technique of LMA insertion with respect to ease of insertion and occurrence of complications in the adult age group. Based on a study done in the pediatric age group by Ghai B et al.[31] and Nakayama et al.[29] we decided to use partially inflated cuff in the rotational technique so, as to avoid failures and resultant complications. Insertion of an LMA in a similar fashion with the cuff partially inflated in the standard technique was observed by Brimacombe J[6] to be less successful than the cuff fully deflated. Jiwon An et al.[34] also had demonstrated this in his comparison of LMA with the cuff fully deflated and partially inflated in adults and had concluded that inserting the LMA with the cuff fully deflated was more accurate and gave rise to lesser complications. Hence, we decided to use the LMA in the standard technique group with cuff fully deflated as originally described by Archie Brain.[3] We recorded the ease of LMA insertion technique for each group by observing the number of attempts and the time taken to secure a successful airway way.

Both the groups were comparable and there was no statistically significant difference in relation to age, gender, weight, ASA status, Mallampati score, base line heart rate, systolic and diastolic blood pressure and peripheral oxygen saturation between the two groups.

Number of Attempts

In our study, the first attempt success rate for LMA insertion in using the Standard Brains technique was 94.37% which is relatively similar to Kumar D[33] study where they achieved a success rate of 86% using the standard technique. This can also be compared with Achmet Ali et al.[38] who had compared LMA classic with LMA supreme using the standard insertion technique, in the LMA Classic group, the LMA was successfully inserted in 27 patients (77%) at the first attempt and in 31 patients (88.5%) at the second attempt.

This lower insertion success rate on first attempt using the 180° rotational technique when compared to the standard technique had also been observed by Ata Mahmoodpoor et al.[35] in their study comparing three methods of LMA insertion in adults: Standard, Lateral and Rotational. They concluded that lateral 90° rotation technique to be a superior technique than 180° rotation because it did not require approaching the back of the mouth and needed lesser effort and thus led to lesser complications. The 90° rotation technique was studied using Proseal LMA by Jungwon Hwang et al.[32] who had observed that success rate of insertion at the first attempt was higher for the 90° rotational technique (100% *vs* 85% for the standard technique, *p* – value- 0.001). They also found that the overall success rate of the standard technique was 94%. The standard technique failed in five patients after three attempts, and a single attempt with the rotational

technique was successful in these patients.

Similarly Raghavan P et al. in 2016[37] while comparing standard insertion technique with 90° rotation technique found a significant increase in number of attempts in the standard group with *p* value = 0.0001.

In our study, the LMA first attempt success rate was significantly lower in rotational procedure group compared to standard procedure group by a percentage difference of 33.50. This difference is significant with a *p* - value of < 0.0001 as per fishers exact test. Also, noted was the statistically significant increased total number of attempts needed for a successful placement of airway using the Rotational technique with a *p* - value of < 0.05 as per fisher exact scale. This can be attributed to our relative inexperience of using the rotational technique and inability to achieve a proper seal over the laryngeal inlet leading to air leak and repeated attempts to achieve a successful placement around the laryngeal inlet.

It has been observed by Brimacombe J and Berry A[26] that rotational technique tends to result in mild residual rotation in the coronal plane. Even though our study showed statistically no significant changes in the fiberoptic grading of LMA position between the two groups, it is possible that mild residual rotation which was present during the initial attempts could have caused the air leak and improper chest expansion. This in turn could have led to repeated attempts until a perfect seal was achieved and ultimately showing a good fiberoptic grading of LMA placement. This was done in order to avoid putting the patient under risk of hypoxia while using the fiberoptic bronchoscope after every failed attempt at insertion. Hence, we conclude that even though a successful placement of LMA was possible with both techniques, the standard technique has a greater probability of getting a successful placement in the first attempt when compared to rotational technique.

LMA Insertion Time

Raghavan P et al.[37] in 2016, found statistically insignificant difference for the time of duration of LMA insertion when he compared lateral 90° rotational technique with the standard technique.

Jung-won Hwang et al.[32] when they compared Standard *versus* 90-degree Rotation technique of Proseal LMA Insertion technique made no difference to insertion time.

Kim et al.[36] observed that the insertion time at the first attempt in the standard group was longer than that in the rotation group.

In our study, LMA insertion time showed that majority of the study subjects were distributed in 31–60 secs group (42.03% in rotational procedure group and 63.38% in standard procedure group). Among the study subjects, there is a statistically significant difference in relation to LMA insertion time distribution between rotational procedure group and standard procedure group when used in patients undergoing classic laryngeal mask. The LMA insertion time was significantly higher in rotational procedure group (mean = 69.00 seconds) compared to standard procedure group (mean = 34.28 seconds) by a mean difference of 34.72 seconds Oropharyngeal leak pressure.

Kim et al.[36] in his study comparing Standard *vs* rotational insertion technique for I-gel placement found that the standard group had lower airway leak pressure than the rotational group.

Jiwon An, et al.[34] in his study compared fully deflated LMA cuff insertion technique with partially deflated LMA cuff insertion technique and concluded that there was no significant air leak among the groups.

In our study also, there was no statistically significant difference (*p* - value of > 0.05 as per unpaired *t* - test) in relation to LMA oropharyngeal leak pressure distribution between rotational procedure group (mean = 37.48) and standard procedure group (mean = 38.00) when used in patients undergoing classic laryngeal mask airway insertion.

Fiberoptic Grading

After confirming the successful LMA placement by auscultation method, fiberoptic grading of LMA placement was performed by an observer who was blinded to the technique of insertion, with the aid of an assistant holding the LMA in place. In a study, conducted by Jiwon An, et al.[34] comparing FOB grading after insertion by partially inflated cuff *vs* fully deflated cuff, it was found that the grade of fiberoptic view in the fully deflated group was Grade 1 in 94.2%, and Grade 2 in 5.8% of patients. In the partially inflated group, 80.2%, 18.6% and 1.2% of patients presented with fiberoptic view Grade 1, 2, and 3, respectively. This grading was statistically significant between the two groups ($p < 0.05$) Similarly in a study, conducted by CR SOH, ASB NG[28] comparing reverse and standard LMA insertion techniques in pediatrics there was no statistical significance ($p = 0.08$) between the two groups with respect to fiberoptic grading.

In our study, the LMA fiberoptic grading table shows that majority of the study subjects were distributed in Grade I group (71.24% in standard procedure group and 65.22% in rotational procedure group). Among the study subjects, there was no statistically significant difference (p - value of > 0.05 as per fishers exact test) between the groups in relation to LMA fiberoptic grading.

Hemodynamics

Kumar D[33] in his study, comparing standard *versus* rotational LMA insertion technique found no considerable differences in terms of Mallampati score, base line heart rate, baseline systolic and diastolic blood pressure and baseline peripheral oxygen saturation between both the study groups.

Raghavan P et al.[37] conducted a study in 2016 comparing lateral 90° rotation technique with standard technique and found no statistical significance in heart rate. However, the mean arterial pressure (78.58 and 79.87) was found statistically significant between the two groups.

In a study, conducted by Jiwon An, et al.[34] comparing fully deflated LMA cuff insertion technique with partially deflated LMA cuff insertion technique observed that there were no significant differences in hemodynamic variables between the groups.

Achmet Ali et al.[38] compared LMA classic insertion with LMA supreme insertion technique and found no statistically significant difference between the groups in terms of hemodynamic parameters

Jung-won Hwang et al.[32] did a study comparing Standard insertion technique *versus* 90-degree Rotation insertion technique of Proseal LMA. There was no statistical significance in change of heart rate, but the mean blood pressure changes showed statistical significance in the standard technique (p - valu*e* 0.001).

In our study also, there were no statistically significant difference in relation to heart rate, systolic BP, diastolic BP and peripheral capillary oxygen saturation between rotational procedure group and standard procedure group when used in patients undergoing classic laryngeal mask airway insertion

Injuries observed

At the end of the procedure after removing the LMA incidence of complications like hypoxemia, laryngospasm and blood staining of the LMA were recorded.

Jiwon An, et al.[34] in his study observed that the incidence rate of blood observed on the LMA at removal was significantly lower in the fully deflated group than in the partially inflated group (1.7% *vs* 16.3%, $p < 0.05$).

Raghavan p et al.[37] in his study observed that the incidence of blood staining and sore throat was significantly lower with the lateral 90° rotational technique (9% and 8%) than the standard technique (36% and 29%) respectively.

Jung-won Hwang et al.[32] compared Standard *versus* 90-degree Rotation technique of Proseal LMA and observed that the incidence of blood staining (9% *vs* 36%, $p < 0.001$) was lower with the rotational technique.

Kim et al.[36] in their study comparing Standard insertion *versus* rotational insertion for I-gel placement observed that the incidence of blood staining was higher in the standard group. In our study the incidences of hypoxemia, laryngospasm and blood stain was 1.45%, 1.45% and 7.25% in rotational procedure group and 0.00%, 0.00% and 1.41% respectively in standard procedure group were statistically insignificant (p - value > 0.05).

Conclusion

We conclude that Standard technique of LMA insertion is a better technique when compared to Rotational technique with respect to ease of insertion, and time taken for LMA to secure airway, with relatively lesser number of complications.

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Original Research Article

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Comparison between Conventional Technique and Ultrasound Guided Supraclavicular Brachial Plexus Block in Upper Limb Surgeries

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Abstract

Background: The conventional technique of supraclavicular brachial plexus block often requires multiple trials and error needle attempts, resulting in long procedure time, procedure related pain, discomfort and lethal complication. Ultrasound has improved the success rate of block with excellent localization as well as improved safety rates with lower complication rates. *Objectives:* To compare the effects of supraclavicular brachial plexus block using conventional blind technique and US technique in terms of success rate of technique, number of complications observed, Time taken for the procedure, Onset and duration of sensory and motor blockade, duration of postoperative analgesia. *Materials and Methods:* This was a prospective randomized nonblinded comparative study in which patients of ASA Grade I and II posted for upper limb orthopedic surgeries admitted during Nov 2015 to May 2017 to the Department of Orthopedics, GMERS Medical College, Hospital, Sola, Ahmedabad were enrolled in the study. There were total 100 patients enrolled who satisfies study selection criteria out of which 50 were randomized in Group C (Conventional) and 50 were randomized in Group US (Ultrasound Guided). *Results:* The block was successful in 72% of patients in Group C compared to 94% in Group US. In conventional group incidence of complications like vessel puncture 12%, pneumothorax 2% noted while in US Group vessel puncture 4% noted. Time for procedure for block in Group US is longer as compared to conventional Group C. Onset of sensory block & motor block in conventional group C is longer as compared to US Group. *Conclusion:* US guided supraclavicular block is more successful technique with less number of complications and longer duration of block compared to Conventional technique.

Keywords: Brachial plexus;Pneumothorax; Sensory block; Upper Limb.

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Introduction

Ultrasound continues to grow in popularity as a method of nerve localization and for the supraclavicular block, has the advantage of allowing real time visualization of the plexus, pleura and vessels along with the needle and local anesthetic spread. Successful peripheral nerve and plexus blockade can provide an excellent anesthetic outcome.[1,2] There is a possibility of prolonged postoperative analgesia. Regional anesthetic techniques have specific advantages both for anesthesia and as analgesic supplements for intraoperative and postoperative care. Among the various approaches of brachial plexus block, supraclavicular approach is considered easiest and effective. It is carried out at the level of

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trunks of brachial plexus. The first supraclavicular brachial plexus block was performed in 1912. The conventional paresthesia technique being a blind technique may be with a higher failure rate and injury to nerves and surrounding structures. To avoid some of these problems, the use of peripheral nerve stimulator was started which allowed better localization of the nerve/plexus. However, this technique may not be foolproof with a persistent risk of injury to surrounding structures, especially vascular structures, nerves, and pleura leading to pneumothorax.[3] Ultrasound (US) visualization of anatomical structure are only method offering safe blocks of superior quality by best needle positioning. US allow direct visualization of peripheral nerves, the block needle, and local anesthetic distribution. Hence, a study is planned for comparison of brachial plexus block by supraclavicular approach using conventional and US based technique in terms of success rate of technique, number of complications observed, Time taken for the procedure, Onset and duration of sensory and motor blockade and duration of postoperative analgesia.[4,5]

The main objectives of this study were to compare the effects of supraclavicular brachial plexus block using conventional blind technique and US guided technique in terms of success rate of technique, number of complication observed, Time taken for the procedure, Onset and duration of sensory and motor blockade and duration of postoperative analgesia.

Materials and Methods

We studied 100 patients of Grade-I and Grade-II of American Society of Anesthesiologist's (ASA) classification and allocated them randomly into equal groups who were admitted from Nov 2015 to May 2017. Ethics Committee approval was taken before initiation of the study. In present study, we have enrolled patients of either gender of age more than 18 years and who were admitted for upper limb surgeries and with American Society of Anesthesiologists (ASA) Grade I and II physical status. All those patients who had history of peripheral neuropathy and history of allergy to local anesthetic agents were excluded from the study and also patients who diagnosed with local skin infections at site of injection and suffering from respiratory or cardiac disease or patients who are receiving chronic analgesic therapy or anticoagulant therapy were also excluded from the study.

All the patients were fasted adequately and were premedicated with tablet diazepam 10 mg and tablet ranitidine 150 mg in the night before surgery and in the morning of surgery. In the operation theater, patients were monitored with pulse oximetry (SpO_2), noninvasive blood pressure, and electrocardiogram. No other sedation was given till the evaluation of the block was completed.

Allocation of Groups

The patients were randomly allotted by closed envelope technique into either of the two groups:

Group C (Conventional) - To receive conventional supraclavicular brachial plexus block;

Group US (US guided) - To receive US guided supraclavicular brachial plexus block.

All enrolled patients were underwent following investigation:

In Group US, block is performed after real-time visualization of the vessels, nerve, and bone. In plane approach, using 10 ml syringe containing LA was injected, and the drug distribution was noted. In Group C, conventional supraclavicular brachial plexus was performed by eliciting paresthesia in the forearm and hand and when paresthesia was obtained we withdrew the needle about 1–2 mm and then, the drug was injected.

The time taken for the procedure, the onset of sensory and motor blockade was noted. Intraoperatively hemodynamic was monitored at regular intervals. Following completion of surgery, the patients were monitored to assess the quality and duration of postoperative analgesia. At the time of each subsequent assessment, patients were observed and/or questioned about any subjective and/or objective side effects (sedation, nausea, vomiting or respiratory depression, and neurological injury).

The various parameters noted were:

Time taken for the procedure;

Onset and duration of sensory neural blockade;

Onset and duration of motor blockade;

Duration of Analgesia.

Investigations

The following investigations had been done:

Blood investigations: Hemoglobin (Hb)%; Blood sugar; Blood urea.

Urine: Albumin; Sugar and microscopy;

Electrocardiography (ECG) and chest *X*-ray posterior anterior view depending on the age and associated comorbidities;

Human immunodeficiency virus;

Hepatitis B surface antigen.

Statistical analysis

The data were analyzed using SPSS version 15 (SPSS Inc., Chicago, Illinois, USA). For all tests, confidence level and level of significance were set at 95% and 5% respectively.

Results

In present study, total 100 patients were enrolled and divided into Two Groups: Group C (Paresthesia) and Group US (USG). In both study groups, all the enrolled patients were in third decade of their age. It was also found that in both groups male patients were higher as compared to female patients, shown in Table 1.

In group USG, it was found that time taken for procedure, duration of sensory block (min), duration of motor blockade and duration of analgesia was significantly higher as compared to Group C and *p* - value was found < 0.0001. Whereas, time for onset of sensory block and motor block was found less in Group USG as compared to Group C and it was seen that time for onset motor block was significantly less in Group USG as compared to Group C, whereas, we did not find any significant difference between both study groups for time of onset of sensory block, shown in Table 2.

US Guided method was found total effective in 94% patients whereas, Conventional Method was

Table 1: Demographic Characteristics of the Study Population

Variables	Group C (Paresthesia) (*n* = 50)	Group US (USG) (*n* = 50)	*p* - value
Age (Yrs)	36.40 ± 12.02	36.84 ± 11.99	0.868
Weight (Kg)	57.18 ± 7.45	58.96 ± 8.01	0.250
Gender			
Male	28	35	0.21
Female	22	15	

Table 2: Comparison of various parameters among both groups

Parameter	Group C (Paresthesia) (*n* = 50)	Group US (USG) (*n* = 50)	*p* - value
Time taken for procedure (min)	6.05 ± 0.71	9.70 ± 1.21	< 0.0001
Onset of Sensory Block (min)	12.02 ± 1.16	11.82 ± 1.45	0.448
Onset of Motor Block (min)	17.02±1.281	15.81±1.24	< 0.0001
Duration of Sensory Block (min)	375.66 ± 17.478	402.56 ± 22.42	< 0.0001
Duration of Motor Blockade	355.88 ± 10.85	362.2 ± 17.02	0.0291
Duration of Analgesia	380.5 ± 21.31	412.52 ± 13.42	< 0.0001

Statistically significance at $p \leq 0.05$

Table 3: Comparison of Effectiveness among both groups

Parameter	Group C (Paresthesia) (*n* = 50)	Group US (USG) (*n* = 50)	test	*p* - value
Totally effective	36	47		
Partially effective	8	2	Chi-square test	0.013
Failure	6	1	8.629	
Total	50	50		

Statistically significance at $p \leq 0.05$

Table 4: Complication among both groups

Complication	Group C (Paresthesia) (*n* = 50)		Group US (USG) (*n* = 50)	
	N	%	N	%
Nerve injuries	0	0	0	0
Vessel puncture	6	12	2	4
Pneumothorax	1	2	0	0
Nil	43	86	48	96

found total effective in 72% of the patients and this shows total effectiveness was significantly higher in US guided Method as compared to Conventional method and this result was found statistically significant, *p* - value 0.013, shown in Table 3.

Discussion

Peripheral nerve blocks are cost effective anesthetic techniques used to provide good quality anesthesia and analgesia while avoiding airway instrumentation and hemodynamic consequences of general anesthesia. Patient satisfaction, a growing demand for cost effective anesthesia and a favorable postoperative recovery profile have resulted in increased popularity for regional techniques. Brachial plexus block is an easy and relatively safe procedure for upper limb surgeries.[5] Supraclavicular approach to brachial plexus block is associated with rapid onset and reliable anesthesia. It can be given either after eliciting paresthesia or using nerve stimulator. Frequently cited disadvantages of paresthesia technique include patient discomfort on eliciting paresthesia and that its success is highly dependent on the cooperation of the patient. The prevalence of pneumothorax after a supraclavicular block is 0.5% to 6% and diminishes with experience.[6] The supraclavicular approach is best avoided when the patient is uncooperative or cannot tolerate any degree of respiratory compromise because of underlying disease. Other complications include frequent phrenic nerve block (40% to 60%), Horner's syndrome, and neuropathy.[7-10] The paresthesia based method and nerve stimulator based methods are blind methods; an advanced technique like use of ultrasound allows direct visualization of the nerves, the block needle, and local anesthetic distribution. This imaging modality has proven highly useful to guide targeted drug injections and catheter placement. The last several years have witnessed a tremendous increase in the use of ultrasound guidance for regional anesthesia.[11-14]

This study is intended to compare the conventional method by eliciting paresthesia with ultrasound guided supraclavicular brachial plexus block in terms of time taken for the procedure, onset and duration of sensory blockade, onset and duration of motor blockade, success rate, the incidence of complications and overall effectiveness. This prospective randomized nonblind clinical study was done in patients undergoing upper limb surgeries with similar demographic profile, shown in Table 4.

We considered the block to be successful when there is complete blockade of all sensory dermatome and at the sametime inability to move any of the upper limbs joint. In our study, the block was successful in 72% of patients in Group C compared to 94% in Group US. In the study of M Veeresham et al.[1], the block was found successful in 66.6% of patients in Group C and 80% in US Group respectively which is similar to present study results whereas, Gajendra singh et al.[2] found in their study that the block was successful in 73.33% of patients in Group C compared to 90% in US Group respectively. Success rate was not statistically significant. B Jeyarani, S Saiprabha[7] were demonstrated in their study that in US Group success rate was 1/3 times higher as compared to US conventional group and these results were similar to our study results.

In present study, among the 50 cases in ultrasound group, only two patients had vascular puncture of subclavian artery which resolved immediately with compression for 15 minutes. There was no incidence of pneumothorax, nerve injury or local anesthetic toxicity in ultrasound group. Among the 50 patient in conventional group, 6 patients had vascular puncture, in which only one went for hematoma formation which resolved within two days. One patient develops pneumothorax. No other complication was elicited in this group. The difference between the two groups was not statistically significant ($p > 0.05$). In the study of M Veeresham et al[1], they reported that there were no complications observed in USG group while in conventional group 20% of patients experienced complications like vessel puncture and nerve injuries. This study results were similar to Present study findings. Gajendra Singh et al.[2] reported incidence rate of complication was 3.33% in USG group while in conventional group incidence rate of complication was 10.00%, similarly in the study of Punam Raghove[3], in conventional group incidence of complications like pneumothorax 3.33%, vessel puncture 16.66% noted while in US group no complication noted.

In present study, we found that the duration of motor blocks in the two groups were also statistically significant ($p < 0.05$). In contrast to present study, M Veeresham et al.[1] reported the duration of sensory block and duration of motor block in two groups were statistically insignificant.

The duration of analgesia in the two groups were statistically extremely significant, ($p < 0.05$). An advanced technique like use of ultrasound allows direct visualization of the nerves, the block

needle and local anesthetic distribution adjacent to nerve plexus which helps in prolonging duration of analgesia. Punam Raghove et al.[3] and Bidyut Borah et al.[4], reported the total duration of analgesia in the two groups were statistically significant.

Limitations of the Study

In this study, we have fixed the doses of bupivacaine and lignocaine which were not based upon patient's body weight that may have influenced the results described here.

Conclusion

US guided supraclavicular block is more successful technique with less number of complications and longer duration of block compared to Conventional technique.

Conflict of Interest: None

Source of Support: Nil

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Original Research Article

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Pretreatment with Three Different Doses of Lignocaine to Prevent Etomidate Induced Myoclonus

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Abstract

Introduction: Myoclonus is a common problem during induction of anesthesia with etomidate. We evaluated the effect of Lignocaine pretreatment on the incidence and severity of myoclonus in our study. *Methods:* This is a prospective randomized double blind study. Sample size was calculated with power of study 80% and alpha error 5%, 96 patients of ASA physical status I and II, aged 18 to 60 years scheduled for elective surgery under general anesthesia were included into three groups L1, L2, L3. Before induction, patients were pretreated with inj. 2% lignocaine 3 ml containing 40 mg, 50 mg, 60 mg diluted with normal saline depending on the random allocation by computer generated random number table. Patients were induced with 0.3 mg/kg etomidate within 30–60 sec, one minute after pretreatment with lignocaine. Patients were observed continuously for the time of initiation, grade and severity of myoclonus for 90 sec, *Results:* In our study, it was found that with Injection 2% lignocaine 60 mg IV 59.3%, 50 mg Lignocaine 37.5%, 40 mg Lignocaine group 9.3% of the patients had no myoclonus which was found to be significant $p < 0.001$. *Conclusion:* Both 2% IV Lignocaine 50 mg and 60 mg were effective in reducing the severity of myoclonus induced by Etomidate without causing side effects.

Keywords: Pretreatment Etomidate; Lignocaine; Myoclonus; Hemodynamics.

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Introduction

The intravenous route of the administration of drugs was long ago recognized as being the most convenient means for obtaining general anesthesia. In fact, the efficacy of this method was appreciated long before a suitable agent was available with the result that intravenous anesthesia awaited only the development of an ideal agent.

Ideal intravenous anesthetic agent for the induction of general anesthesia with all the desirable characteristics like stable in solution, absence of pain on injection, no histamine release, cadiovascular stability, rapid onset and complete return of consciousness and also absence of postoperative effects like nausea, vomiting, delirium, headache is yet to be developed.[1]

Etomidate is an imidazole-derived, sedative hypnotic agent. It acts directly on GABA receptor complex, blocking neuro excitation and producing anesthesia.

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Etomidate causes minimal histamine release and has a very stable hemodynamic profile. Etomidate's hemodynamic stability is due to its unique lack of effect on the sympathetic nervous system and on baroreceptor function. Even in cardiac patients induction dose of etomidate results in very stable hemodynamic. Etomidate has minimal effects on respiratory system also as compared to other induction agents and can be safely given in patients with reactive airway disease. However, pain on Injection and myoclonus are the most common side effects of this drug.[2] Pain on injection has been abolished by the new fat emulsion preparation of etomidate, but the new solvent has not reduced the incidence of myoclonus.[3] Myoclonus is a common problem during induction of anesthesia with etomidate, upto 80% of the nonpremedicated patients develop myoclonic movements[4], which maybe a problem in the nonfasting patients because of the risk of hypoventilation as well as regurgitation and aspiration.[5,6] Myoclonic movements may even raise the risk of prolapse of the vitreous in patients with open globe injury.[7] Although the probable mechanism of etomidate induced myoclonus is alteration in the balance of inhibitory and excitatory influence on the thalamocortical tract[4], a number of drugs have been investigated for their ability to suppress these myoclonic movements. Pretreatment with benzodiazepines (28%)[4], opioid (17%)[5], and Rocuronium (25%)[6] have been shown to reduce myoclonus to some extent. However, the drug of choice to prevent myoclonus induced by Etomidate is yet to be discovered.

Ideally, a pretreatment drug for preventing myoclonic movements should be short acting, should not have significant effects on respiration and hemodynamics, and should not prolong recovery from anesthesia[4] Lignocaine stabilizes the neuronal membrane and prevents the initiation and transmission of nerve impulses and has rapid onset of action. Lidocaine alters signal conduction in neurons by blocking the fast voltage gated Na+ channels in the neuronal cell membrane responsible for signal propagation.[8] The aim of our study, was to find the optimum dose of pretreatment with intravenous 2% lignocaine and to compare the incidence and severity of myoclonic movements along with any other side-effects linked to Etomidate.

Materials and Methods

A randomized, double blind clinical study protocol was approved by institutional ethical committee. Patients aged between 18 and 60 years with BMI of 20–25 kg/m^2, the American Society of Anesthesiology (ASA) physical status I and II undergoing elective surgery under general anesthesia were assigned to three groups, each containing 32 patients. Patients who were allergic to 2% lignocaine, on sedatives/opioids within 24 hours before surgery, patients with adreno cortical disorders, neurological, psychiatric disorders were excluded from the study. Patients underwent preanesthetic evaluation prior to surgery and nil per oral orders were followed. Alprazolam 0.5 mg given night before surgery. Antacids Inj. Ranitine 150 mg given 1 hour before surgery.

In our study, 96 patients were randomly allocated into three groups 32 patients in each group by computer generated random number table. Monitors like Noninvasive Blood Pressure (NIBP), Electrocardiography (ECG), pulse oximetry (SpO_2) and End Tidal Carbon Dioxide ($EtCO_2$) monitors were connected. Intravenous fluids were given according to the body weight of the patient and surgical loss. Group L1 received 40 mg 2% lignocaine diluted with 1 ml of normal saline, Group L2 received 50 mg 2% lignocaine diluted with 0.5 ml of normal saline, Group L3 received 60 mg 2% lignocaine. Patients were preoxygenated with 100% oxygen for 3 minutes. One min after pretreatment patients were induced with 0.3 mg/kg etomidate within 30–60 sec and were observed for the grade and severity of myoclonus for 90 sec. After administration of Etomidate and evaluation of myoclonus, all patients were injected with 2 mcg/kg Fentanyl, Inj. 0.05 mg/kg Midazolam, 0.1 mg/kg Vecuronium to facilitate tracheal intubation. Maintenance of anesthesia was provided by N_2O:O_2 5:3 along with Inj. Vecuronium 0.025 mg/kg plus Sevoflurane MAC of 1.5-3%. Study drugs were prepared in 5 ml syringes by coding them into three groups A, B, C and were decoded after 24 hours of observation byAnesthetist not participating in the study and were administered 1 min before induction with 0.3 mg/kg etomidate (Triomidate Troikaa) by some another anesthetist not participating in the study thus observer and the patient were blinded. The time to the loss of eye-lash reflex was recorded as the onset of induction, and an additional dose of etomidate was administered if necessary. Patients were observed continuously for the grade and severity of myoclonus for 90 sec. Vital signs pulse rate, blood pressure, ECG, SpO_2, $EtCO_2$ were monitored 1 min and 3 min after etomidate injection. Intraoperatively continuous hemodynamics monitoring was done. Postoperatively after thorough oral suction patients

was reversed with Inj. Neostigmine 0.05 mg/kg and Inj. glycopyrrolate 0.01 mg/kg. Tracheal extubation was performed on meeting the standard criteria of extubation. Postoperatively patients were assessed for 24 hrs for myalgia, headache, nausea and vomiting.

The Primary objective of this study, is to find the optimum dosage of Lignocaine required to prevent myoclonus and the secondary objective is to find the reduction in severity of Etomidate induced myoclonus, hemodynamic stability after induction of Etomidate.

Myoclonic movements are graded clinically as 0 = no myoclonus, 1 = mild myoclonus (short movement of a body segment, e.g.: a finger or wrist, 2 = moderate myoclonus (mild movement of two different muscle groups e.g.: face and arm, 3 = severe myoclonus (intense myoclonic movement in two or more muscle groups, fast adduction of a limb. Nausea and vomiting were assessed as 0 = no symptom, 1 = symptom present but treatment not required, 2 = symptom present and treatment given. Any other side effect of Etomidate like myalgia and headache were also noted upto 24 hours.

A power analysis based on article by Kahlon Singh et al. states that 66 patients are required to have 80% chance of detecting as significant at 5% level, a decrease in primary outcome measures myoclonus from 76% in the control group to 44% in the lignocaine groups, assuming the same decrease in the primary outcome, in a dose response to lignocaine with increasing strength of lignocaine a sample size of 96 patients of ASA physical status I and II of age group between 18 and 60 years scheduled for elective surgeries under general anesthesia were allocated to three groups n = 32 randomly after taking informed written consent.

The data was entered in Microsoft Excel and analyzed in EpiData analysis V2.2.2.184, Stata 12 and SPSS 20 software. The continuous variables such as age, height, weight, Body Mass Index, baseline value, 3 minutes and 5 minutes after induction vital parameters values (pulse rate, blood pressure), SpO_2 and time for myoclonus were reported as Mean (SD) or median (Inter Quartile Range) based on distribution of data. The categorical variables such as Group (L1, L2 and L3), gender, grading of severity of myoclonus, nausea, vomiting, post operative myalgia and headache were reported as proportions. The association between continuous variables and the Groups (L1, L2 and L3) were assessed using one way ANOVA or Kruskal Wallis test and the association between categorical variable and groups were assessed using Chi-square test. The difference between the groups over the time points and difference within the groups were measured using repeated measures of ANOVA. The p - value of < 0.05 was considered for statistical significance.

Results

Demographic data concerning patient's age, weight, BMI were comparable among all three groups. In our study, female population was comparatively (52%) more than the male population (48%) which was found to be significant $p < 0.001$. There was a significant ($p < 0.001$) height difference among the study population. Hemodynamic parameters from baseline value, 3 min and 5 min postinduction with Etomidate were comparable among the three groups $p > 0.005$. Time for myoclonus among the study participants in each group after induction in our study was not significant $p = 0.071$ (Table 1 and Fig. 1). Comparing the three groups the reduction in the severity of myoclonus postetomidate induction with lignocaine pretreatment was found to be significant $p < 0.001$ (Table 2 and Fig. 2). The incidence of postoperative nausea and vomiting in three groups was significant $p < 0.004$ (Table 3 and Fig. 3). There was no significant postoperative myalgia and headache with $p < 0.364$.

Table 1. Time for myoclonus among the study participants in each group after induction (N = 96)

Group	Number	Median (IQR) time for myoclonus (sec)	Range	*p* value*
L1	32	37.87 (20.7-62.3)	0-78.87	
L2	32	33.17 (0-59.2)	0-86.78	0.071
L3	32	7.56 (0-57.0)	0-90	

* *Kruskal Wallis test*

The table 1 shows the comparison of time of initiation of myoclonus in all the three groups was insignificant $p = 0.071$.

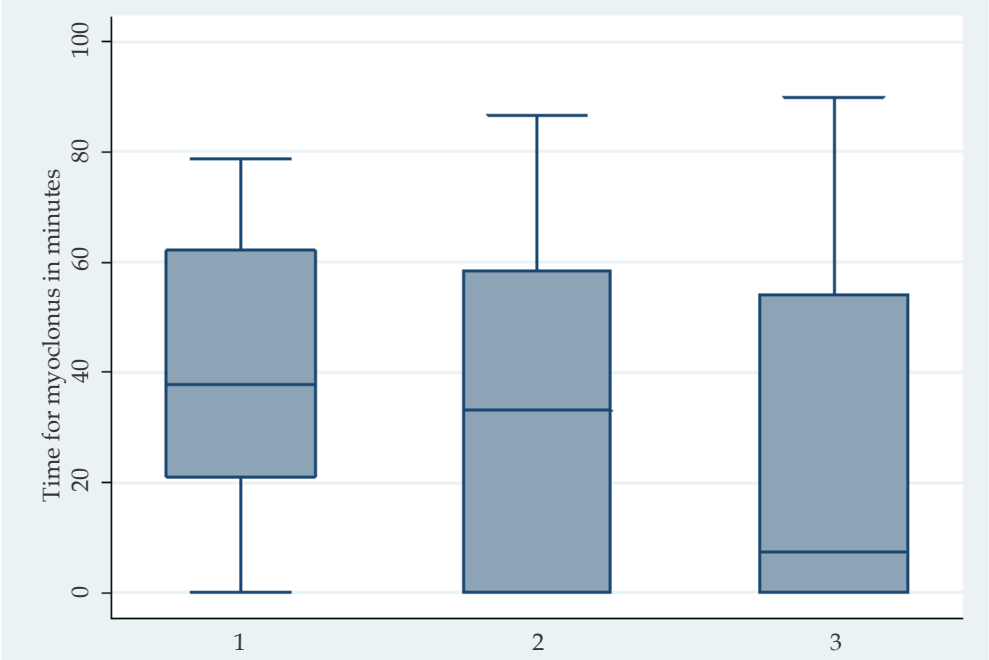

Fig 1: Time for myoclonus among the study participants in each group 5 minutes after in duction (N = 98)
**1,2,3 in X axis denotes group L1, L2 and L3 respectively*

Table 2. Severity of myoclonus among study participants in each group:

Groups	Number	Grade 0		Grade 1		Grade 2		Grade 3		*p* value#
		n	%	n	%	n	%	n	%	
L1	32	3	9.3	14	43.7	12	37.5	3	9.3	
L2	32	12	37.5	14	43.7	5	15.6	1	3.1	0.001
L3	32	19	59.3	5	15.6	8	25	0	0.00	
Total	96	34	35.4	33	34.3	25	26	4	4.1	

#chi square test

The table 2 shows the comparison of severity of myoclonus among the three groups L1, L2, L3 which was significant $p < 0.001$.

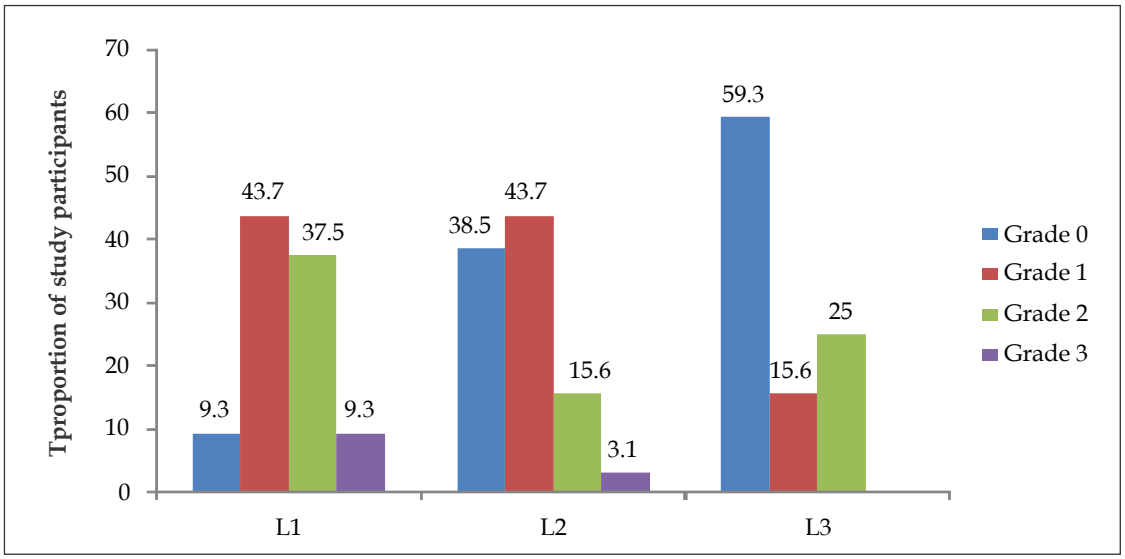

Fig 2: Severity of myoclonus among study participants in each group (N = 96)

Table 3. Severity of post-operative nausea and vomiting among study participants in each group

Groups	Number	Grade 0		Grade 1		Grade 2		*p* value#
		n	%	n	%	n	%	
L1	32	17	28.3	10	50.0	5	31.3	
L2	32	18	30.0	8	40.0	6	37.5	0.004
L3	32	25	41.7	2	10.0	5	31.3	
Total	96	60	100.0	20	100.0	16	100.0	

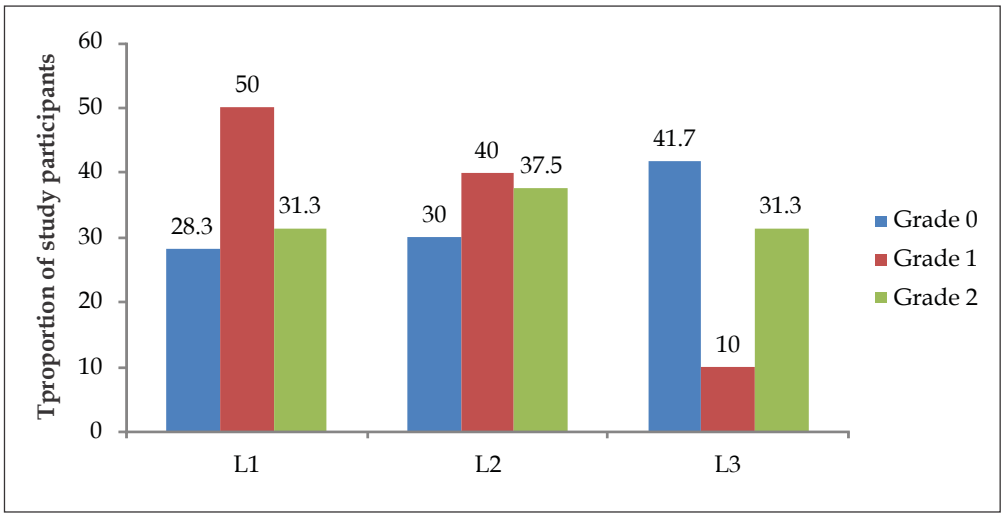

Fig 3: Severity of post-operative nausea and vominting among study participants in each group (N = 96)

Discussion

In this randomized double blind prospective clinical study, we compared the effects of different dose response of Lignocaine pretreatment on the incidence of etomidate induced myoclonus. To the best of our knowledge, there is shortage of literature studying Lignocaine pretreatment for etomidate induced myoclonus. Most of these studies have been done with 20 mg of Lignocaine IV in patients posted for elective surgery.

Etomidate is widely used as an induction agent in clinical practice. Several desirable properties, such as rapid onset, brevity of action, cardiovascular stability, protection of intracranial pressure, minimal histamine release, minimum respiratory depression and profound hypnosis makes it an ideal induction agent. However, etomidate is also associated with minimal side effects like pain on injection and myoclonus. Pain on injection has been largely eliminated by use of a lipid formulation of etomidate, but myoclonus remains a common problem during anesthesia induction.[4]

Ideally, a pretreatment drug for preventing myoclonic movements should be short-acting, should not have significant effects on respiration and hemodynamics and should not prolong recovery from anesthesia. Kahol et al. 1 in their study showed that 20 mg of Inj. 2% Lignocaine showed 56% reduction in the incidence of myoclonus.[9] Similar results were observed in the study by Gultop et al. Inj. 2% lignocaine (1 ml) and saline, was administered 30 sec before induction with etomidate, and it was observed that there was 56.6% incidence of myoclonus in the lignocaine group compared with 83% in the control group.[10] However, the mechanism by which lignocaine prevents myoclonus is unclear. Nyman and colleagues speculated that lignocaine reduces the excitability of the central nervous system, which is the cause of myoclonic movements.[2] In our study, we chose to compare escalating dose of 2% IV Lignocaine for reducing the severity of myoclonus as it does not have respiratory depression property unless toxic dose is given, is hemodynamically stable, helps in faster recovery from anesthesia as ithas antiinflammatory and analgesic properties.

We did not include control group in our study since it has already been proven that upto 80% of the patients develop myoclonus after induction with etomidate.[9,5] Thus, it would be unethical to subject the patients to myoclonus. Myoclonus may

be a problem in the nonfasting patient because of the risk of hypoventilation as well as theoretically regurgitation and aspiration[7] can occur. In patients with an open globe injury, myoclonus after etomidate raises intraocular pressure which increases the risk of vitreous prolapsed.[7] The study population included adult patients (18 to 60 years of age) of either sex, ASA Grades I and II undergoing elective general surgeries under general anesthesia who were randomly divided into three groups of 32 patients each.

There was no significant difference between the three groups regarding age, weight, BMI. In our study, female population was comparatively (52%) more than the male population (48%) which was found to be significant $p < 0.001$. There was a significant ($p < 0.001$) height difference among the study population because females were more than males in the study group. All the study population belonged to younger age group of 20 to 44 years. It was seen that there was not much change in the hemodynamic parameters from the baseline values, 3 min and 5 min postetomidate 0.3 mg/kg induction. These results have been further supported by Kahlon et al.[9] Huter et al.[6] and Lee et al.[11]

Various drugs have been used for reducing incidence and severity of myoclonus during IV injection of etomidate. Pretreatment with diazepam or flunitrazepam could not reduce myoclonus,[12] but midazolam reduced the incidence due to its faster onset of action.[4] Doenicke et al., reported that pretreatment with three different dosages (etomidate 0.03, 0.05 or 0.075 mg/kg IV) of etomidate used as premedicant reduced myoclonus.[4] Although studies have shown that fentanyl, alfentanil, or sufentanil are effective in reducing myoclonus, but these agents may cause residual apnea, sedation, nausea, vomiting, and delayed discharge from the hospital. Another study showed Remifentanil (1 $\mu g/kg^{-1}$) has faster onset of action, was very effective in reducing myoclonus after etomidate from 70% in the placebo group to 6.7% in the remifentanil group.[14] However, Remifentanil can cause severe bradycardia. Mizrak et al. concluded that pretreatment with dexmedetomidine or thiopental is effective in reducing the incidence and severity of etomidate-induced myoclonic muscle movements. Incidence of myoclonus was significantly low in Dexmedetomidine and Thiopental groups (34%, 36%) than in control groups (64%) ($p < 0.05$).[13] However, dexmetomidine can further cause hypotension and bradycardia, pretreatment with Thiopentone increases postoperative pain.[13]

In our study, the time of initiation of myoclonus was comparable among all the three groups. In our study, it was found that with Injection 2% lignocaine 60 mg IV, 59.3% of the patients in the group had no myoclonus. In patients who received 50 mg Lignocaine 37.5% had no myoclonus and 40 mg Lignocaine group 9.3% of the patients had no myoclonus. In L1 , L2 and L3 group 43.7%, 43.7% and 15.6 % of the population respectively had Grade 1 myoclonus. Grade 2 myoclonus was found to be 37.5% in L1 Group,15.6% in L2, 25% in L3 Group. In L1 and L2 Group 9.3% and 3.1% respectively had Grade 3 myoclonus. None of the patients in L3 Group had Grade 3 (severe) myoclonus. Comparing the three groups the reduction in the severity of myoclonus postetomidate induction with lignocaine pretreatment was found to be significant $p < 0.001$. This variation in our study could be due to ethnic variations or selection of a younger age group. The factors known to affect the incidence of myoclonus are age (the higher the age, the lesser the chances of development of myoclonus), sex of the patient (incidence is higher among male individuals), and the dose of etomidate.[11,14] It can be concluded from the above results that higher dose of Lignocaine is highly efficacious in suppressing myoclonus during induction with etomidate without causing hemodynamic instability and respiratory depression.

Kahlon A Singh et al.[9] concluded that pretreatment with lignocaine or midazolam is effective in reducing the incidence and severity of etomidate-induced myoclonic muscle movements. Incidence of myoclonus was significantly low in Lignocaine and Midazolam groups (28% and 44% respectively) than in control groups (76%) ($p < 0.05$).

Gultop et al.[10] observed in their study that Inj. 2% lignocaine (1 ml) and saline, when administered 30 sec before induction with etomidate, showed 56.6% incidence of myoclonus in the lignocaine group compared with 83% in the control group which was found to be significant $p < 0.005$.

Therefore, the results of our study are in concordance with the other studies which finds lignocaine efficacious in suppressing etomidate induced myoclonus.

The incidence of postoperative nausea and vomiting in three groups was significant $p < 0.004$. Around 30–38% patients in each group required treatment with antiemetics. Giese and colleagues[15] found the incidence of postoperative nausea and vomiting to be significant $p < 0.005$, when they used etomidate in their study.

The incidence of severity of postoperative myalgia and headache was found to be insignificant. No other side-effects of Etomidate was found in our study.

The absence of any recording of the electromyograph, time duration of myoclonus, incidence of myoclonus in extremes of age group after induction with etomidate, constant drug dosage was a limiting factor for our study. The present study was conducted with a fixed drug dosage instead lignocaine as pretreatment drug can be given according to the body weight which can further reduce the incidence and severity of myoclonus postetomidate induction.

Conclusion

In our study we found that both 2% IV Lignocaine 50 mg and 60 mg were effective in reducing the severity of myoclonus induced by Etomidate without causing any side effects. It was found that Lignocaine 60 mg to be more effective. Hence, with the escalating dose of Injection 2% Lignocaine IV within the toxic dose can limit myoclonus caused by Etomidate induction. However, more number of independent studies will prove it's efficacy.

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Comparison of Subclavian Vein Catheterization Using Supraclavicular Versus Infraclavicular Approach with Ultrasound

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Abstract

Background: Infraclavicular (IC) approach for Subclavian Vein (SCV) catheterization is widely used compared to Supraclavicular (SC) approach. Recently, SC approach for SCV catheterization has gained prominence because of its well-defined landmarks with more success and less complication rate. The primary aim of this study is to determine whether US guided SC approach or IC, provides the best SCV catheterization and the complications related to either approach. *Methodology:* A total of 110 patients were randomly divided into two groups of 55 patients each, the SC group (Group S) and IC group (Group I). All SCV catheterization were done by single trained anesthesiologist. The parameters recorded were access time, successful catheterization, number of attempts, catheter insertion time, ease of guide wire insertion and complications. *Results:* Mean access time in Group S was 32.4s compared to 39.24s in Group I. Successful catheterization and numbers of attempts were better in SC approach. Mean catheterization time was 55.4 ± 3.02s in Group S and 78.3 ± 8.605s in Group I and was significant ($p < 0.0001$). 96.4% patients in Group S and 92.7% patients in Group I was successfully catheterized and was associated with smooth insertion of guide wire. There were two cases of arterial puncture and one case of hemotoma in Group I as compared to only one case of hemotoma in Group S. *Conclusion:* SVC cannulation by US guided SC approach is better with respect to IC approach in terms of time for catheterization and complications.

Keywords: Central venous catheterization; Subclavian vein catheterization; Supraclavicular; Infraclavicular.

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Introduction

In modern day anesthesia, Central Venous Catheterization (CVC) is a mandatory for various purposes like volume resuscitation, CVP monitoring, transvenous cardiac pacing, Hemodialysis, in cancer patients with difficult venous access and for chemotherapy. There are mainly three large venous routes of central line insertion namely the internal jugular, subclavian or femoral veins, each with its own advantages, disadvantages and potential complications.[1]

SCV is the most preferred alternative to internal jugular vein for central venous catheterization,[2,3] because of a lower-risk of infection as compared with internal jugular or femoral sites, easy placement in immobilized severely traumatic patients, less interference while endotracheal

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intubation, mechanical ventilation during Cardiopulmonary Cerebral Resuscitation (CPCR) and less patient discomfort for long-term intravenous treatment.[4] It also carries a lower risk of thrombosis when compared to femoral or internal jugular vein cannulation.[5,6] Because of the close proximity of the vulnerable anatomic structures (subclavian artery and lungs), SCV catheterization can result in complications such as subclavian artery puncture causing hemotoma, hemothorax and pneumothorax.[3,8,9] Ultrasound is the gold standard of care for central venous catheterization. The benefit includes an increase success rate, great efficiency and decreased complications.[9] In a review of strategies to improve patient safety the agency for healthcare research and quality in the United States identified ultrasound guidance during CVC insertion as one of 11 risk reduction strategies unequivocally supported by evidence.[10,11] US guidance for CVL placement in the internal jugular and femoral veins has been the focus of numerous studies.[12] Less studies have assessed the use of US guidance for the placement of SCV.[13] This may be related to the overlying clavicle, which partly restricts the sonographic view.

SCV can be cannulated by supraclavicular and infraclavicular approaches. SCV are routinely cannulated by IC landmark technique. With US guidance sound waves are obscured by bony structures in infraclavicular but clear with supraclavicular approach.[14] To our knowledge, there are limited studies which have reported on US guidance for the SC approach. Therefore, this study was undertaken to compare the ultrasound guided IC and SC approach regarding access time, number of attempts, catheter insertion time, ease of guide wire insertion and complications related to either approach.

Materials and Methods

This prospective randomized comparative study was undertaken after approval of Institutional Research and Ethics committee. Written informed consent was obtained from patients requiring cannulation. Patients were randomized into two groups of 55 each, i.e. Group S and Group I, by computer generated random number table. The study population consists of 110 ASA Grading I, II, or III of either sex scheduled for elective and emergency procedure requiring central venous catheterization and patients requiring long-term management in ICU. Patients with ASA Grade > IV, local infection at puncture site, trauma to clavicle, upper thoracic region, cervical spine, deranged coagulation profile, morbidly obese patients, distorted anatomy of the neck and mentally retarded patients were excluded from the study.

Following detailed examination, Patients who fulfilled the required criteria were taken for the study. 18G IV line was secured. Routine monitors like ECG, NIBP, SpO_2 were connected and baseline vital parameters were noted.

Central venous catheterization of SCV was done by using Seldinger's technique using triple lumen 7 Fr cannula. Ultrasound machine (Phillips HD7) equipped with high resolution of 3–11 MHz, linear transducer was used.

In all patients the right SCV was selected. The patients were in supine position and head turned towards the left side. SCV was catheterized using Seldinger's technique using US guidance. Chest *X*-ray was done after the procedure to confirm the position of the catheter and rule out complications.

Following parameters were taken into consideration to measure the efficacy of either approach:

Access time was defined as the time from initial skin puncture to the aspiration of blood from SCV through the needle;

The number of attempts was defined as the number, required for each needle advance to puncture the vein. More than three attempts were considered as failure for the study purpose;

Catheter insertion time was defined as time from blood aspiration through the needle to free aspiration from the catheter;

Ease of guide wire insertion-smooth or failed;

All times are measured in seconds;

Successful catheterization – was confirmed by chest *X*-ray;

Complications like pneumothorax, hemothorax, arterial puncture were recorded and treated appropriately. Patients were followed up for 24 hours.

Statistical Analysis

Fragou M et al.[15] in their a study in 2011 comparing US guided subclavian vein cannulation and landmark guided technique and found the mean access time to be 26 ± 12.8. We used this to calculate the sample size. Taking into consideration power of the study 80% and confidence interval as 95% (α = 0.05), the sample size was calculated to be 52 in each group, to detect a difference in access time of atleast 8s based on the study done by Byon et al., where they found the difference in median puncture time to be 8s. To allow for dropouts, 55 pts. were included

in each group.[17] Numerical values are presented as mean and standard deviations for continuous data whereas as categorical data is represented as frequencies and percentages. Unpaired *t*-test is applied for comparing numeric parameters like access time, puncture time, number of attempts, and catheter insertion time. All data will be analyzed with SPSS-20, $p < 0.05$ was considered significant.

Results

The demographic data were comparable in both the groups. The mean access time in Group S was 32.4s compared to 39.24s in Group I which is statistically significant ($p < 0.0001$). Total number of patients successfully catheterized in Group S (53 out of 55) is much better than in Group I (51 out of 55), but difference was not statistically significant ($p = 0.6787$). Complications like hemotoma only seen in one patient in Group S and arterial puncture in two patients, catheter malposition in one patient and hematoma in one patient is seen in Group I, were treated appropriately. Mean catheter insertion time was 55.4 ± 3.02s in Group S compared to 78.3 ± 8.605s in Group I, which is highly significant ($p < 0.0001$). All successful catheterization, i.e., 53 (96.4%) patients. in Group S and 51 (92.7%) patients in Group I, were associated with smooth insertion of guidewire following subclavian vein puncture. This difference was not statistically significant (p 0.6787) (Table 1).

Table 1: Outcome measures in Group S and Group I

Parameters	Group S	Group I	*p* - value	Remarks
Mean access time (seconds)	32.4 ± 2.868	39.24 ± 7.17	< 0.0001	Significant
Successful Catheterization	53 (96.4%)	51 (92.7%)	0.6787	Not significant
No. of Attempts				Not significant
1st attempt	45 (81.8%)	42 (76.4%)		
2nd attempt	8 (14.6%)	9 (16.3%)	0.66	
Failed	2 (3.6%)	4 (7.3%)		
Complications				
Arterial puncture	0	2		
Catheter malposition	0	1		
Hemotoma	1	1		
Catheter insertion time (seconds)	55.4 ± 3.02	78.3 ± 8.605	< 0.0001	Significant
Ease of Guide wire Insertion	53 (96.4%)	51 (92.7%)	0.6787	Not significant

Discussion

In our study, in order to overcome the various access approaches, patient position, technique and individual expertise the procedure was conducted by the same anesthesiologist for either approach. The demographic profiles were comparable in both the group.

The access time is an important step in the process of catheterization, once the needle is in the vein the other steps usually follows most of the time. In the study of Raphael PO et al., the mean puncture time (access time) was significantly lower in the US guided SC group (39.86 ± 9.80s) when compared to US guided IC Group (54 ± 10.56s) with $p < 0.0001$.[20]

Fragou M et al., study showed US guided average access time was significantly reduced than the landmark guided for CVC ($p < 0.05$).[15]

Byon et al, also showed access time was significantly less in SC Group compared to IC Group.[17]

Similar results were also found in the study of Thakur A et al. while comparing SC and IC approaches by landmark technique.[16]

Our result also concurs with the above studies. This significant difference in SC and IC can attributed to the anatomical proximity of the vein to the clavicle and difficulty in getting the longitudinal visualization because of the acoustic shadow of the clavicle as reported in the Byon et al.[17] As far as successful catheterization and number of attempts are concerned, SC approach is better than IC approach but this was found to be statistically nonsignificant in our study.

Similar results were found in the study of Thakur A et al.[16] Kores et al. observed overall success of 97% in the SC and 94% in the IC approach. First attempt

success in the SC group was 73% as compared to 68% in the IC approach.[18]

Sterner et al. (n = 255) documented an overall success rate of 84.5% in Group SC and 80% in Group IC.[19]

Fragou M et al., study showed US guided success rate was 100% and landmark guided was 87.5%. Average number of attempts in US guided was 1.1 ± 0.3 (1.1–1.5) (n = 200) and in landmark guided was 1.9 ± 0.7 (1.5–2.7) (n = 201), which was significant ($p < 0.05$).[15]

Our results does not correlate from the study of Fragou M et al., may be because of the difference in sample size. Mean catheterization time in our study was 55.4 ± 3.02s in Group S and 78.3 ± 8.605s in Group-I, which was significant statistically ($p < 0.0001$).

Similar results were found in a study by Raphael et al., mean catheter insertion time was significantly shorter in SC Group (120.29 ± 8.61s) when compared to IC Group (132.29 ± 6.51s) with $p < 0.01$.[20]

Byon et al., also found similar results in their study.[17] In our study, all successful catheterization, i.e., 96.4% patients in Group S and 92.7% patients in Group I, guidewire and catheter insertion was found smooth with no resistance encountered at any step, which was nonsignificant. This was similar to Kores et al., they did not have difficulty in threading the guidewire.[18] Complications associated with subclavian venous catheter placement are pneumothorax, hemothorax, subclavian artery puncture and hematoma at the puncture site.

In Byon HJ et al., study incidence of guidewire misplacement was higher in IC than SC (20.4% *vs* 0%, $p = 0.001$).[17] Hussain S et al. in their study found complication rates were higher in SC Group, but the difference was not statistically significant.[21]

Palepu GB et al. in their study, the impact of USG on CVC catheterization found complications rates 14.3% for landmark technique and 11.4% for US guided technique. The age, sex and the operator adjusted odds ratio for complication was 0.9 (95% CI: 0.16–5.0; $p = 1$) for USG when compared to landmark technique.[22] This is in contrast with the established facts that USG reduces complications.

Bras P et al., in Cochrane database systematic review analysis of the available data suggested 2D US improves some but not all aspects of effectiveness of CVC catheterization.[23]

Complications in our study did not have any sequele. These results must be viewed with caution taking various factors into consideration like the sample size, power of study, operator experience, approach and technique. Further trials required with largest sample size with adequate experience and well-defined technique (in plane or out of plane approach) will help to decide the superiority of one technique over the other.

Conclusion

SCV catheterization by US guided SC approach has faster access time, shorter catheter insertion time and lesser complications as compared to US guided IC approach.

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Efficacy of Addition of Low Dose Oral Ketamine to Oral Midazolam Results in Better Premedication Than Either Drugs Given Alone in Children

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Abstract

Context: When we never induce anesthesia in a struggling adult patient, fearing hypertensive response, we never bother to properly sedate the pediatric patient before bringing the child to operation theatre. *Aims:* To Compare combination of midazolam and ketamine with midazolam or ketamine alone as oral preanesthetic medication in children undergoing elective surgeries. *Settings and Designs:* Hospital based comparative study was carried out at Department of Anesthesiology, SVS Medical College, Mahabubnagar *Methods:* 150 children of ASA Grade I and II in the age group of 2–10 years were included in the study and were randomly divided into three groups of 50 each. Group A received 0.5 mg/kg Midazolam in 5 ml orange syrup, Group B received Ketamine 6 mg/kg while Group C received a combination of oral Midazolam 0.5 mg/kg and oral Ketamine 3 mg/kg in 5 ml orange syrup. *Statistical Analysis:* The statistical analysis done by Chi-square test. *Results:* In Group A, 58% children were adequately sedated and 72% children were having an acceptable anxiolysis and parental separation scores. In Group B, acceptable sedation, anxiolysis and behavior at parental separation was obtained in 52% children. Group C shows an acceptable sedation in 68% children. Acceptable anxiolysis was observed in 82% of children. 80% children were calm with parental separation. Side effects were mainly seen in Ketamine group with 14% children showing nystagmus and 10% of children had excessive salivation. 8% children in Ketamine Group also developed hallucination. *Conclusion:* The present study showed that oral premedication with Midazolam 0.5 mg/kg alone produces as good results as the combination of Midazolam 0.5 mg/kg and Ketamine 3 mg/kg in children.

Keywords: Midazolam; Ketamine; Preanesthetic; Medication; Children; Elective surgeries.

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Introduction

Anesthesia and surgery represent an enormous time of stress for the child. The reasons for stress include primarily (a) separation from parents (ii) strange surroundings (iii) painful procedures (iv) frightening procedures and (v) survival.[1]

They are unable to understand the necessity for their surgery, nor arethey likely to be amenable to reasoned explanation. Eckenhoff demonstrated that stormy anesthetic induction in children leads to an increased incidence of postoperative behavioral problems. These problems can be diminished by psychologic preparation; however,

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a pharmacologic adjunct may be more reliable and better suited for efficient use of operating room time than psychologic preparation.[2]

Of the various aspects of pediatric anesthesia, the most neglected part is premedication. In most of the busy pediatric surgical theatres, it is very common to find children in waiting area in various stages of anxiety and distress emitting various tones of crying. Most of the time, the anesthetist will struggle with the child to start the intravenous line or induce inhalationally. When we never induce anesthesia in a struggling adult patient, fearing hypertensive response, we never bother to properly sedate the pediatric patient before bringing the child to operation theatre.[3]

A variety of premedications administered *via* various routes have been introduced. Route of administration is another important factor, for those patients who do not already have established venous access since, starting intravenous access to administer sedation may be as traumatic as the procedure itself. Therefore, an orally active agent could be especially preferable.[4]

Recent reports suggest that both oral Midazolamand oral Ketaminemay fulfil many of these criteria. The parenteral formulation of both Midazolam and Ketamineare effective as oral premedication in children. Ketamine has well-characterized sedative, anesthetic and analgesic properties. It also has advantages over other sedative anesthetic drugs, because it stimulates the cardiovascular system, usually associated with an unobstructed airway with preserved upper airway reflexes and causes minimal respiratory depression.[5]

Ketamine has been tried with a high overall success rate, without significant side effects. However, it is widely acknowledged that Ketamine IV or IM causes hallucinations in many patients. Even subanesthetic concentration of Ketamine produces psychedelic effects, when given IV.[6]

The combination of oral Ketamine 4–6 mg/kg, oral Midazolam 0.5 mg/kg and oral atropine 0.02 mg/kg provides a well-sedated patient. Studies have shown that a combination of Midazolam plus Ketamine provides better premedication than Midazolam or Ketamine alone. Benzodiazepines augment the action of Ketamine effects and attenuate emergence sequela.[7]

In the present study, an attempt is made to evaluate the scope of oral Midazolam 0.5 mg/kg, oral Ketamine 6 mg/kg and combination of Midazolam 0.5 mg/kg + Ketamine 3 mg/kg orally as a premedicant in pediatric age group.

Materials and Methods

This study was conducted on patients admitted to SVS Medical College, Mahabubnagar, during the period from December 2016 to September 2018, with cooperation from residents from Departments of General Surgery, ENT and Orthopedics. 150 patients of ASA Grade I and II, of either sex, aged between 2 and 10 years were included in this study. Children undergoing surgical procedure between 20 minutes and 2 hours duration were selected for the study. The children were divided into three groups of 50 each randomly.

Children of Group A received Midazolam 0.5 mg/kg orally Group B received Ketamine 6 mg/kg orally and Group C received Midazolam 0.5 mg/kg + Ketamine 3 mg/kg Orally. The premedication was prepared using orange syrup as a carrier 0.5 ml/kg up to a maximum of 10 ml. This was administered to children 30 minutes before induction. Those children who refused to take the whole dose we reexcluded from the study.

The child's condition was evaluated just before induction by the surgical resident with a scale assigning a score of 1 to 4 to the quality of sedation, anxiolysis and behavior at parental separation, while side effects were assessed by the anesthesiology resident conducting the case. All observers including anesthesiology residents, surgical residents and nurses were blinded about the contents of the oral premedicate.

Inclusion criteria

Patients coming for elective major or minor surgeries under general or regional anesthesia;

Age 2–10 years;

ASA Grade I and II.

Exclusion criteria

ASA Grade III and IV;

History of prematurity and chronic illness;

History of developmental delay;

Increased intracranial pressure;

Increased intraocular pressure;

Valvular heart disease;

Psychiatric disturbances.

The study was approved by the ethical committee of SVS Medical college, Mahabubnagar. Written, informed consent was obtained from parents for conducting study on their children.

Drugs and Dosages

In the preoperative room, baseline recordings of heart rate, respiratoryrate, systolic blood pressure and activity of child were noted.150 cases were divided into three groups of 50 each. Group A received Midazolam 0.5 mg/kg oral. Group B received Ketamine 6 mg/kg orally and Group C received a combination of Midazolam 0.5 mg/kg and Ketamine 3 mg/kg orally. This was given with orange syrup 0.5 ml/kg to mask the bitter taste of the drug, 30 minutes before induction of anesthesia.

The children were evaluated for quality of sedation, anxiolysis and behavior at parenteral separation, 30 minutes after administration of the premedicant by the concerned surgical resident and side effects such as tachycardia, bradycardia, hypertension, hypotension, hypertonia, nystagmus, vomiting, in voluntary movements, respiratory depression, apnoea, excitement, salivation, sweating and lacrimation were noted by the Anesthesiology resident. Children were observed for any signs of upper airway obstruction, respiratory depression, apnoea and oxygen desaturation.

Preanesthetic assessment

All patients were visited and evaluated for fitness for the intended procedure and anesthesia on the day prior to the surgery. During this visit, the procedure of the study planned was explained to the parents. An attempt was made to alleviate the anxiety of the patients. Parents were also instructed on the nil per oral guidelines. General clinical examination of the patient was performed including a general physical and systemic examination.

Laboratory investigations

The following laboratory investigations were performed on all the patients in the study:

Blood: Hb%, Blood Grouping and Typing, bleeding time, Clotting time, HIV and HBs Ag.

Urine: Albumin, Sugar, and Microscopy.

Chest *X*-ray: If required.

Preoperative fasting: No oral liquids up to 2 hours before the procedure;

Avoidance of milk/solids for 6 hours prior to the procedure.

Sedation was graded as follows:

Score 1: Alert

Score 2: Awake

Score 3: Drowsy

Score 4: Asleep

Anxiolysis was graded as follows:

Score 1: Panicky

Score 2: Moaning

Score 3: Composed

Score 4: Asleep, friendly

Behavior at parenteral separation was graded as follows:

Score 1: Combative, clinging to parents

Score 2: Anxious, consolable

Score 3: Calm

Score 4: Asleep

All monitors attached in operation theatre: The aesthetic agents administered were standardized Inj. Glycopyrrolate 0.04 mg/kg, Inj. Ondansetron 0.1 mg/kg and Inj. Fentanyl 1 mcg/kg was given.

General anesthesia was induced with Sevoflurane 6% and air & Oxygen (60:40), Trachea was intubated by appropriate size endotracheal tube after intravenous (IV) Atracurium 0.5 mg/kg. Intraoperative sedation was not given and analgesic was provided by caudal block with Inj. Bupivacaine 0.25% 1 ml/kg for intraoperative anesthesia. The neuromuscular blockade was reversed with Inj. Neostigmine (0.05 mg/kg), with Inj. Glycopyrrolate (0.01 mg/kg) Reversal and extubation was uneventful in all patients. Sedation score was estimated by single observer according to sedation scale.

Parameters observed were:

Level of sedation and score of sedation;

Emotional reaction: crying, apprehension and calm;

Separation reaction: crying, apprehension and good;

Acceptance reaction to face mask;

Side effects and recovery time.

Sedation, anxiolysis, cooperation was recorded immediately after giving oral drug at following intervals: 5 min, 10 min, 20 min, 30 min, 40 min. Heart rate and oxygen saturation were monitored throughout the procedure. The statistical analysis done by chi square test.

Results

Table 1 shows comparison of various parameters in three groups. All the three groups were comparable in terms of age, sex, mean weight and ASA Grade ($p > 0.05$).

Table 2 shows surgical procedures carried out in three groups. All the groups were almost similar in terms of surgical procedures carried out. The total number of children undergoing a particular surgery was similar in all the groups.

Table 3 shows comparison of sedation between the groups. Sedation was assessed on a 4-point scale. Acceptability was defined as a Score of III and IV. In Group A, an acceptable sedation was obtained in 58% (29 of 50) children. In Group B, an acceptable sedation was obtained in 52% (26 out of 50) childrens. In Group C, an acceptable sedation was obtained in 68% (34 out of 50) children. However, there is no significant difference between the Three Groups ($p > 0.05$).

Table 4 shows comparison of anxiolysis between the groups. Anxiolysis was similarly assessed on a 4-point scale. Acceptability was defined as a Score of III and IV. In Group A, acceptable anxiolysis was obtained in 72% (36 out of 50) children. In Group B, acceptable anxiolysis was obtained in 52% (26 out of 50) children. In group C, acceptable anxiolysis was seen in 82% (41 out of 50) children. Statistical studies show a significant difference between the study groups as a whole and between Groups B and C.

Table 5 shows comparison of behavior at parental separation between the Three Groups. Behavior at parental separation was also assessed by a 4-point scale. Acceptability was defined as a Score of III and IV. In Group A, an acceptable score for behavior at parental separation was seen in 36 (72%) out of 50 children. In Group B, an acceptable score for behavior at parental separation was seen in 26 (52%) children. In Group C, an overall acceptable score for behavior at parental separation was obtained in 40 (80%) children. Significant difference on statistical analysis is seen between study groups as a whole and between Groups B & C.

Table 1: Comparison of various parameters in three groups

Parameters Number		Group A		Group B		Group C	
		%	Number	%	Number	%	
Age (years)	2–5	20	40	21	42	14	28
	5–7	17	34	16	32	17	34
	8–10	13	26	13	26	19	38
	Mean ± SD	5.7 ± 2.6		5.4 ± 2.5		6.2 ± 2.6	
Sex	Male	39	78	37	74	35	70
	Female	11	22	13	26	15	30
Weight (kg)	Mean ± SD	18.22 ± 6.3		19.92 ± 5.69		19.22 ± 5.75	
ASA grade	I	42	84	44	88	45	90
	II	8	16	6	12	5	10

Table 2: Surgical procedures carried out in three groups

Surgical procedures	Group A		Group B		Group C	
	Number	%	Number	%	Number	%
Tonsillectomy	9	18	8	16	6	12
Circumcision	8	16	7	14	6	12
Orthopedic	6	12	5	10	11	22
Herniotomy	4	8	10	20	4	8
Tongue tie release	4	8	6	12	1	2
Other ENT	10	20	8	16	5	10
Others	9	18	6	12	17	34
Total	50	100	50	100	50	100

Table 3: Comparison of sedation between the groups

Sedation score	Group A		Group B		Group C	
	Number	%	Number	%	Number	%
I (Alert)	9	18	6	12	3	6
II (Awake)	12	24	18	36	13	26
III (Drowsy)	23	46	18	36	24	48
IV (Asleep)	6	12	8	16	10	20
Total	50	100	50	100	50	100

Table 4: Comparison of anxiolysis between the groups

Score	Group A		Group B		Group C	
	Number	%	Number	%	Number	%
I (Panicky)	6	12	10	20	1	2
II (Moaning)	8	16	14	28	8	16
III (Composed)	31	62	20	40	30	60
IV (Asleep, friendly)	5	10	6	12	11	22
Total	50	100	50	100	50	100

Table 5: Comparison of behavior at parental separation between the three groups

Score	Group A		Group B		Group C	
	Number	%	Number	%	Number	%
I (Combative clinging)	4	8	12	24	2	4
II (Anxious, consolable)	10	20	12	24	8	16
III (calm)	34	68	20	40	34	62
IV (Asleep)	2	4	6	12	9	18
Total	50	100	50	100	50	100

Table 6: Adverse effects between the groups

Adverse effects	Group A		Group B		Group C	
	Number	%	Number	%	Number	%
Vomiting	0	0	3	6	0	0
Nystagmus	2	4	7	14	2	4
Salivation	2	4	5	10	3	6
Tachycardia	2	4	1	2	4	8
Bradycardia	1	2	0	0	0	0
Excitement	0	0	4	8	0	0
Involuntary movements	2	4	1	2	0	0
Respiratory depression	1	2	0	0	0	0
Total	50	100	50	100	50	100

Table 6 shows adverse effects between the groups. The side effects with Midazolam, Ketamine and the combination are shown in Table 6. Vomiting was observed in 3 children in Ketamine Group (Group B) while it did not occur in either of other groups. Nystagmus was seen in 7 children in Group B while 2 children each in the other groups showed nystagmus. Group B also showed more incidence of salivation in 5 children, salivation was also observed in 3 children in Group C and 2 children in Group A. Tachycardia occurred in 4 children in Group C while Group A showed 2 and Group B had 1 child with tachycardia. One child in Midazolam group had bradycardia.

Discussion

In the present study, children in the three groups were of 2–10 years of age with mean age of 5.7 ± 2.6 years, weight of a mean of 19.12 kg with a male preponderance of 74%. This is in comparison; with studies conducted by Funk W et al.[8] who studied children in the age group of 2–10 years with a mean age of 5–7 years.

Prior studies have documented the effectiveness of 0.5 mg/kg oral Midazolam.[3,9]

Unfortunately, gastric absorption of Midazolam is variable and results in large difference in the time it takes for different patients to become adequately sedated. The sedative effect of Midazolam was found to be maximal at 30 minutes after oral administration in a study by Weldon BC et al.[10], Kazak Z et al.[4], observed that oral Midazolam 0.5 mg/kg promotes smooth and satisfactory induction of anesthesia and reduces the psychological effects of hospitalization in children.

Satisfactory sedation we got in our study was 58% which corresponded well with that obtained by Funk W et al.[8] (58%) when 0.5 mg/kg Midazolam was given. Funk W et al.[8] in their study with 0.5 mg/kg Midazolam found to obtainan acceptable anxiolysis in 75% of children. Similarly, studies by Feld LH[3] et al. and Warner DL et al.[11] showed that 69% and 65% of children were asleep or awake

and calm at induction of anesthesia after receiving Midazolam 0.5 mg/kg orally. We had a success rate of 72% which corresponds to the above studies.

Midazolam in the dose of 0.5 mg/kg provided an acceptable behavior at parental separation score in 72% of children in our study. Funk W et al.[8] in their study got a score of 68% for acceptable parental separation and Alderson PJ et al.[12] also got a score of 70%.

Funk W et al.[8] in their study got an acceptable sedation score in 47% children who were given Ketamine in dose of 6 mg/kg. This corresponds well with our study in which we got an acceptable sedation score in 52% of children. Studies by Warner DL et al.[11] showed an acceptable anxiolysis score in 42% of children, Masamaddi GS et al.[13] showed an acceptable anxiolysis score in 80% of children while Funk W et al.[8] had an acceptable score of 54% when 6 mg/kg Ketamine was given orally. This corresponds well with our result which showed an acceptable score in 52% of children with 6 mg/kg Ketamineorally.

Our studies showed an acceptable score for parental separation in 52% of children who were premedicated with 6 mg/kg Ketamine orally. This corresponds well with the studies by Funk W et al.[8] and Alderson PJ et al.[12] who got acceptable scores in 50% and 65% of children respectively.

Lin YC et al.[14] reported no difference in separation with Midazolam 0.75 mg/kg, Ketamine 6 mg/kg or the combination of 0.5 mg/kg and 3 mg/kg respectively. Their success rate with combination were about 80% at separation, and the incidence of oral secretions and nystagmus was lesser as compared to Ketamine. Warner DL et al.[11] found the combination of Midazolam 0.4 mg/kg and Ketamine 4 mg/kg to be significantly more effective than Midazolam 0.5 mg/kg or Ketamine 6 mg/kg alone. No psychological disturbances were noted in the immediate postoperative period. The success rate for anxiolysis and separation was found to be > 90% and only 70% for sedation with a combination of Midazolam 0.5 mg/kg and Ketamine 3 mg/kg by Funk W et al.[8]

We got an acceptable sedation score in 68% children with a combination of Midazolam 0.5 mg/kg with Ketamine 3 mg/kg. This corresponds well with the studies of Funk W et al.[8] who got an acceptable score in 70% children. Lin YC et al.[14] in their study got an acceptable anxiolysis score in 73% of children while Warner DL et al.[11] got an acceptable score in 85% ofchildren. This corresponds well with our results (82%) when the combination of 0.5 mg/kg Midazolam was given with 3 mg/kg Ketamine.

We got an acceptable score for parental separation in 80% of children who were premedicated with the combination. This corresponds well with the studies of Ghai B et al.[15] who got an acceptable behavior at parental separation score in 73% of children.

Lin YC et al.[14] also got similar results in 80% of children. In our study, there was no significant difference in sedation in the 3 groups, 30 minutes after receiving the study agents ($p > 0.05$). This corresponds to the results obtained by Pan AK et al.[16] and Funk W et al.[8] in their studies.

Also, both anxiolysis and behavior at parental separation scores were significantly better in Midazolam alone. These results are similar to the results obtained by Funk Wet al.[8] and Warner DL et al.[11]

The incidence of preoperative nystagmus was 14% with Ketamine and 4% each with Midazolam alone and with the combination. However, none of the children seemed distressed by the nystagmus. The reported incidence of nystagmus with Ketamine ranged from 26% to 60%. 9,22. An incidence of 13% for nystagmus with orally administered Midazolam was mentioned by Lin YC et al.[14]

The side effects noted in the present study were similar to the results obtained by Pan AK et al.[16] and were not clinically significant.

Conclusion

The present study showed that oral premedication with Midazolam 0.5 mg/kg alone produces as good results as the combination of Midazolam 0.5 mg/kg and Ketamine 3 mg/kg in children. Although, Midazolam 0.5 mg/kg produced lesser sedation than the combination, it was no disadvantage as separation from parents was successful and coincided with good anxiolysis.

The incidence of side effects was highest with Ketamine 6 mg/kg, especially nystagmus. The combination increased the cost factor, made preparation of premedication more complex and produced higher incidence of tachycardia as compared to Midazolam alone. Even though, the combination did not produce statistically better sedation, anxiolysis or behavior at parental separation than Midazolam, the combination did produce distinctly better premedication characteristics than either Midazolam or Ketamine alone when given through oral route.

Key Messages

Oral premedication with Midazolam 0.5 mg/kg alone can be used in children undergoing elective surgeries.

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Original Research Article

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Comparison of Effects of Oral Ivabradine and Oral Clonidine as Premedicants on Intraocular Pressure Changes Following Intubation with Succinylcholine

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Abstract

Background: Endotracheal intubation done with succinylcholine raises intraocular pressure which can be of significance in cases of traumatic open globe injury. *Aims:* The study was done to compare the efficacy of oral Ivabradine and Clonidine in lowering the intraocular pressure rise following intubation using succinylcholine. *Methods:* A total of 105 patients were enrolled. Three groups having 35 patients each were formed. Group I: Received oral Ivabradine 5 mg, Group II: Received oral Clonidine 0.1 mg & Group III received placebo one hour before intubation. Intraocular Pressure (IOP) was measured with schiotz tonometer preoperatively & at various intervals to assess the effect of clonidine and Ivabradine on IOP. *Results*: A total of 105 pateints were enrolled. Three groups having 35 patients each were formed. The mean IOP of the patients from 3 groups were comparable initially (p - 0.082). At all later time points, the mean IOP of patients from 3 groups was statistically different ($p < 0.001$). The mean IOP in patients who received clonidine was significantly lesser as compared to control group at all time points except at the baseline ($p < 0.001$). However, among patients who received Ivabradine, the mean IOP was significantly less than the control group only at T1, and T7. *Conclusions*: Oral Clonidine can be recommended as premedicant for obtunding the rise in IOP following endotracheal intubation using succinylcholine. Oral Ivabradine showed no effect on IOP during endotracheal intubation using succinylcholine.

Keywords: Clonidine; Ivabradine; Succinylcholine; Intraocular pressure.

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Introduction

Laryngoscopy contribute significantly to hemodynamic changes like increased heart rate, elevated systolic blood pressure, and cardiac arrhythmias along with increase in Intraocular Pressure (IOP).[1]

General anesthetics and nondepolarizing neuromuscular blocking drugs usually reduce IOP whereas studies have shown that succinylcholine increase IOP.[2] It has been found that IOP of 25 mm Hg or more is considered pathological. Some studies have shown transient elevation of IOP 2–4 minutes

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after IV injection of succinylcholine.[3] Increase in IOP is of clinical significance in setting of open eye injury. Clonidine is an alpha-2 adrenergic agonist with antiischemic activities[4,5] whereas Ivabradine controls heart rate.[6]

The present study was conducted to study the efficacy of oral Ivabradine and Clonidine in lowering the intraocular pressure rise following intubation using succinylcholine as a muscle relaxant.

Materials and Methods

This prospective, randomized study was conducted at a tertiary referral hospital for a duration of one year after obtaining approval from the hospital ethical committee and patients' written informed consent.

Sample size

We hypothesized that Clonidine and Ivabradine will decrease the IOP after IV injection of succinylcholine. For the calculation of sample size for this trial, the pooled standard deviation of IOP was taken as 2.8 mm Hg[7] and minimum detectable difference (effect size) of IOP was assumed to be 1.25 mm Hg. Assuming alpha error as 5%, power as 80%, and attrition rate as 10%, the sample size for each group was calculated as 35.

Adult patients aged between 18 and 50 years belonging to ASA Grade I and II, undergoing general anesthesia, were included in the study. Patient's refusal, patients with ocular diseases, patients with cardiovascular diseases and history of hypertension, pregnant and breast feeding females, patients with difficult airway, with Hepatic/renal impairment, in whom the study drugs were contraindicated and obese patients (BMI more than 30) were considered as exclusion criteria. Randomization, blinding and allocation concealment: Randomization of the participants was done using computer-generated random sequences into Test Groups or Control Group. The person allocating the treatment to the included participants was not aware of the randomization sequence as it was distributed in the sealed envelope.

To ensure blinding, the Test Groups as well as Control Groups were not informed regarding the drug which they were being given and the drugs were as identical as possible to avoid ascertainment bias. To ensure blinding, the assessor also was not aware of the treatment provided to the patient.

Group-I (Test Group): Received oral Ivabradine, 5 mg tab one hour before intubation,

Group II (Test Group): Received oral Clonidine 0.1 mg tab one hour before intubation,

Group-III (Control Group): Received placebo one hour before intubation.

Preanesthetic check-up and routine investigations like complete blood count, serum creatinine, chest *X*-ray & Electrocardiogram (ECG) were done. Patients were kept nil by mouth for 8 hours. Intraocular pressure was recorded in both eyes after instilling 2 drops of 4% Lignocaine in each eye, using schiotz tonometer under supervision of an ophthalmologist in the preop period just before administration of test/placebo drug which is given 1 hour prior to intubation.

Intravenous cannulation was done with 18G cannula and ringer lactate solution was started in preoperative room. After shifting the patient to the operation theatre all the standard monitorings were applied. IOP and other parameters were recorded just before premedication. Inj. Midazolam 0.07 mg/kg and Inj. Ondansetron 0.12 mg/kgwas given as premedicant intravenously just before induction.

All patients were given general anesthesia according to the standard protocol. The patient was induced by Inj. Propofol (2 mg/kg body weight) & intubation was facilitated using Inj. Succinylcholine 2 mg/kg intravenously. Intubation was achieved with an appropriate size oral cuffed, endotracheal tube by the aid of Macintosh laryngoscope blade. Intubation was performed by an experienced anesthesiologist in each case. After securing the airway, intraocular pressure was recorded in both eyes at set intervals by an Ophthalmologist. Difficult airway cart was ready for patients with difficult airway. Any patient where prolonged laryngoscopy of more than 60 second was done was excluded from the study. Surgery was not allowed to commence till the recordings were completed which was ten minutes in each case.

Anesthesia was maintained with 40:60 of oxygennitrous oxide mixture with 1% isoflurane and intermittent doses of vecuronium bromide. Extubation was performed, after reversing the neuromuscular blockade with neostigmine 0.05 mg/kg and glycopyrrolate 0.01 mg/kg, following thorough oral suctioning. All the patients were followed in the postoperative room for the next 3 hours for any complications like dizziness, deep sedation and bradycardia.

The IOP recordings were noted at various intervals. T0 - Preoperatively - just before administration of the study drug, T1 - Just before premedication inside OT, T2 - Just after intubation,

T3 - 1 minute after intubation, T4 - 3 minutes after intubation, T5 - 5 minutes after intubation, T6 - 8 minutes after intubation, T7 - 10 minutes after intubation.

Each patient was examined clinically and all parameters were recorded on a separate case record form and thereafter, entered on a Microsoft excel sheet for statistical analysis.

Statistical analysis

The statistical analysis was done using SPSS 17 (Armonk, NY: IBM Corp). The categorical variables are presented as percentages and continuous variables were presented as mean (SD) or median (IQR) as applicable. For the comparison of categorical variables, Chi-square test was used. For comparison of more than 2 means, ANOVA (Analysis of variance) was used. p - value of < 0.05 was considered statistically significant.

Results

The study was conducted over a period of one year from May 2016 to April 2017. Data from 105 patients was analyzed in this study. There was no significant difference in the demographic profile of the three groups with respect to age, sex, nutritional status and ASA status, (Fig. 1).

Systolic blood pressure was recorded at various time intervals in all the three groups and was not found to be statistically significant except at T2, (Fig. 2).

Difference in heart rate of patients of three groups was not found to be statistically significant at baseline (T0). Thereafter, at all the periods of observation from T1–T7 mean heart rate of patients of Group III were found to be significantly higher than that of Group I and Group II, (Fig. 3).

In Group I, change in baseline IOP was found to be statistically significant at all the periods of observation except at T6 (p = 0.064). In Group II, change in baseline IOP was found to be statistically significant only at T1, T6 and T7. In Group III, change in baseline IOP was found to be statistically significant at all the periods of observation except at T6 (p = 0.169) and T7 (p = 0.147), (Table 1).

Mean IOP of patients of Group III was found to be statistically significant only at T1, T3, T4 and T7. Mean IOP of patients of Group III was found to be statistically higher than that of Group II at all the periods of observation except at T0, (Table 1).

Difference in IOP among patients of three groups at T0 was not found to be statistically significant. At T1 mean IOP of patients of Group III (14.47 ±

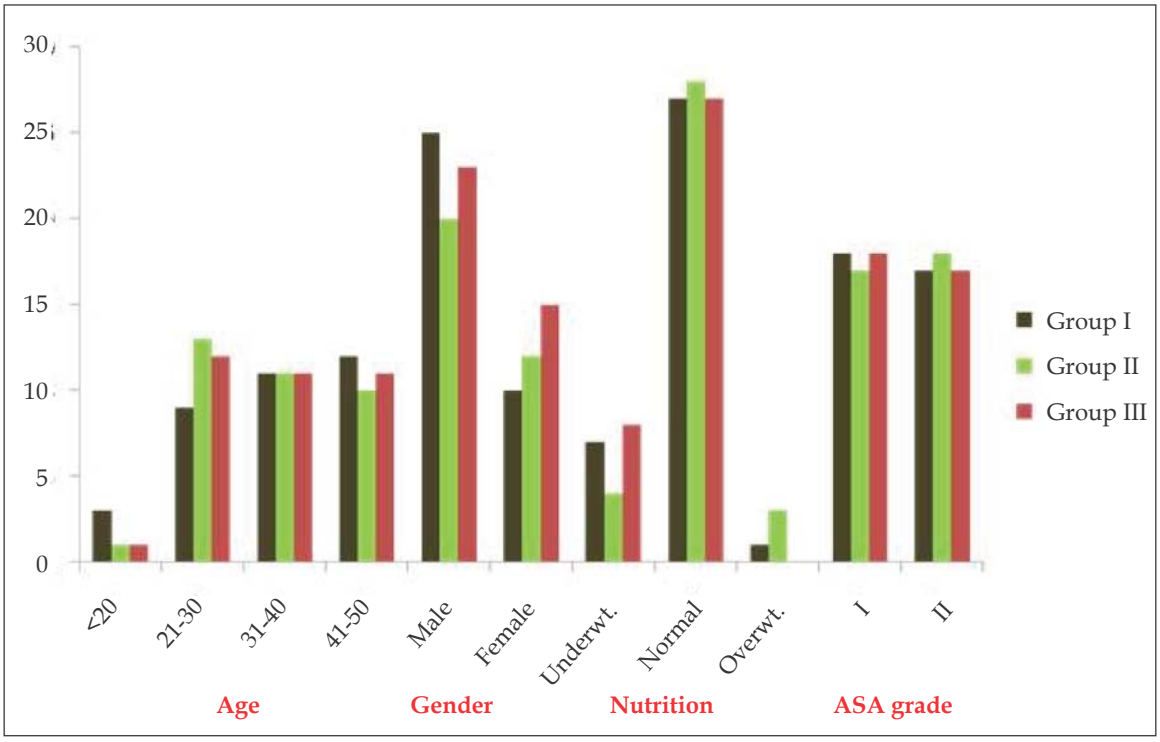

Fig. 1: Comparison of Demographic data between the study groups

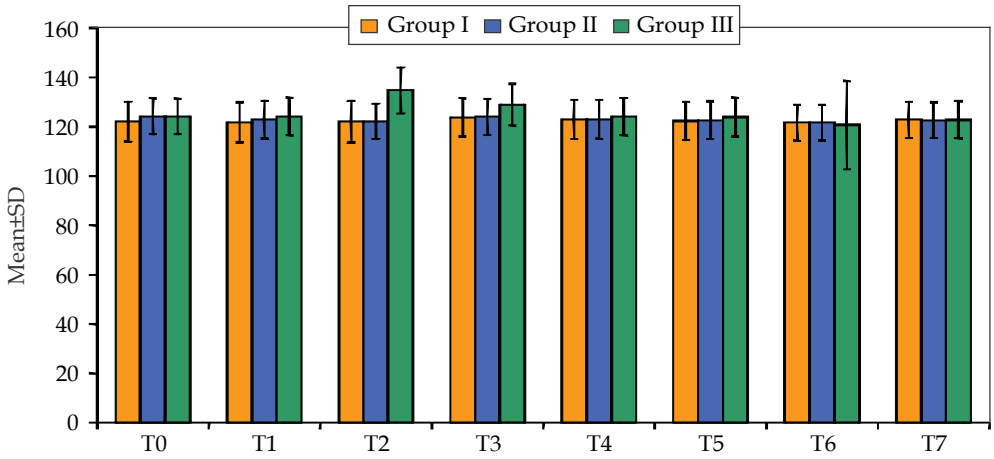

Fig. 2: Comparison of Systolic blood pressure between groups at various time interval

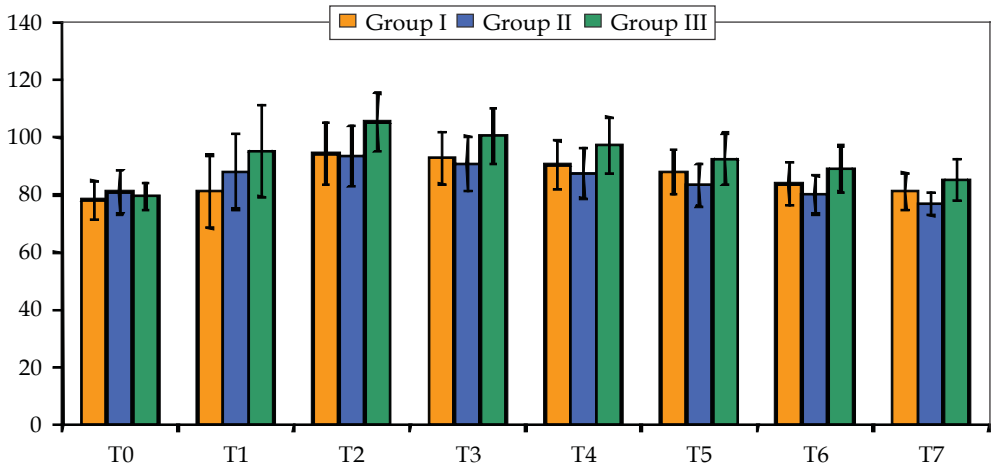

Fig. 3 : Comparison of Heart rate between groups at various time interval

Table 1: Intragroup Change in Baseline Mean IOP at different time intervals

	Group I					Group II					Group III				
	Mn ch.	SD	% ch.	't'	'p'	Mn ch.	SD	% ch.	't'	'p'	Mn ch.	SD	% ch.	't'	'p'
T1	-1.04	0.35	-7.99	-17.58	<0.001	-0.29	0.46	-2.14	-3.688	0.001	0.84	0.54	6.18	9.247	<0.001
T2	2.39	1.36	18.27	10.37	<0.001	0.34	1.45	2.56	1.395	0.172	2.39	0.76	17.50	18.616	<0.001
T3	1.96	1.24	14.99	9.301	<0.001	0.17	1.50	1.28	0.674	0.505	2.23	1.10	16.35	11.981	<0.001
T4	1.50	1.08	11.49	8.233	<0.001	0.06	1.53	0.43	0.221	0.827	1.69	1.18	12.37	8.434	<0.001
T5	1.39	1.03	10.61	7.962	<0.001	-0.29	1.47	-2.14	-1.152	0.257	1.16	1.08	8.49	6.360	<0.001
T6	0.31	0.97	2.41	1.915	0.064	-0.63	1.33	-4.70	-2.795	0.008	0.31	1.32	2.31	1.405	0.169
T7	-0.86	0.48	-6.56	-10.60	<0.001	-1.26	1.42	-9.40	-5.233	<0.001	-0.34	1.37	-2.52	-1.486	0.147

Table 2: Inter Group Comparison of Mean IOP at different time intervals

	Group I Vs Group II			Group I Vs Group III			Group II Vs Group III		
	Mean diff.	SE	'p'	Mean diff.	SE	'p'	Mean diff.	SE	'p'
T0	-0.31	0.25	0.431	-0.57	0.25	0.066	-0.26	0.25	0.568
T1	-1.07	0.26	<0.001	-2.46	0.26	<0.001	-1.39	0.26	<0.001
T2	1.73	0.36	<0.001	-0.57	0.36	0.264	-2.30	0.36	<0.001
T3	1.47	0.34	<0.001	-0.84	0.34	0.040	-2.31	0.34	<0.001
T4	1.13	0.32	0.002	-0.76	0.32	0.048	-1.89	0.32	<0.001
T5	1.36	0.25	<0.001	-0.34	0.25	0.372	-1.70	0.25	<0.001
T6	0.63	0.24	0.028	-0.57	0.24	0.051	-1.20	0.24	<0.001
T7	0.09	0.16	0.853	-1.09	0.16	<0.001	-1.17	0.16	<0.001

1.23 mm Hg) was found to be significantly higher as compared to Group I (12.01 ± 0.08 mm Hg) and Group II (13.09 ± 1.46 mm Hg). At T2 difference in mean IOP of patients was found to be statistically significant between Group I and II and Group II and III. Difference in mean IOP of patients of three groups were found to be statistically significant at all the periods of observation from T3–T7, (Table 2).

No complication like dizziness, deep sedation and bradycardia was observed in any of the patients in the postoperative room during the 3 hours observation period.

Discussion

Patient with difficult airway who require tracheal intubation in cases of open globe injury often require succinylcholine to facilitate intubation, Succinylcholine is also one of the commonly used muscle relaxants during rapid sequence induction and intubation which is often done in trauma patients as they are considered full stomach. Succinylcholine produces an undesirable rise in intraocular pressure which may prove disastrous in patients with penetrating eye injuries.

Intraocular Pressure (IOP), in normal conditions, ranges from 12 to 20 mm Hg which is influenced by several factors such as central venous pressure, choroidal blood volume changes, and extraocular muscle tonicity. Sudden increase in blood pressure, as occurs after laryngoscopy and endotracheal intubation, results in the choroidal blood volume increase and eventually a 10 to 20 mm Hg increase in IOP. This increase in IOP can be troublesome during ophthalmic surgeries, especially in the presence of glaucoma or open eye trauma. Increase in (IOP) following endotracheal intubation during general anesthesia is commonly reported as a side effect while using depolarizing muscle relaxant, Succinylcholine.

Lignocaine, Diazepam, other previously studied drugs and substitution of nondepolarizing drugs of intermediate duration like Atracurium[8] or rocuronium[9] for succinylcholine have all been ineffective with inconsistent results. In the recent year's alpha-adrenergic agonist like Clonidine have shown a considerable attenuating effect on hemodynamic rise including intraocular pressure.[10] Recently, Ivabradine, a novel sinus node inhibitor, has shown attenuating effects for hemodynamic with promising ability and with minimal side effects.[11]

Ivabradine binds to hyperpolarization voltage-gated channels which carry the I (h) current in the eye, leading to transient, dose-dependent changes of the electroretinogram.[12] Considering the promising hemodynamic effect of Ivabradine, we were encouraged to evaluate its impact on rise of intraocular pressure among patients scheduled to undergo laryngoscopy and endotracheal intubation under succinylcholine. For a reference, Clonidine, one of the premedication that has proven attenuating effect on pressor response following laryngoscopy and endotracheal intubation, was used.

The major outcome of present study was the difference in IOP between baseline value and just before premedication value. Ivabradine showed a 7.99% decline in IOP while Clonidine showed a 2.14% decline during the period. Thus, both the trial drugs indicated an onset of IOP attenuating effect before intubation itself. However, during the same period, in placebo group an IOP increase of 6.18% was observed. While the reductions in IOP in both the trial groups could be attributed to the attenuating effect of the drugs, the increase in IOP in placebo group can be attributed to a psychological stress and anxiety among patients undergoing surgery. Presence of preoperative anxiety and its hemodynamic effect has been recorded in several studies previously[13–15] and use of some antianxiety drugs or nonpharmacological management modalities is advised in some instances.[16–18] In present study, no such intervention to tackle the anxiety/stress induced IOP rise was done between preoperative IOP assessment and just before induction period. The findings in turn suggest that patients having premedication of either of two drugs may have a positive impact on the anxiety-stress related hemodynamic changes too.

In present study, following intubation an increase of 18.27% and 17.50% in IOP was observed in Ivabradine and placebo groups, however, Clonidine showed an increase of 2.56% only. Thus, showing that premedication with Ivabradine did not help to attenuate the intraocular pressure rise following intubation. Interestingly during the entire observation period (up to 10 minutes after intubation), the IOP values were minimum in Clonidine group as compared to placebo and ivabradine groups. Despite having mean IOP values much below the placebo group just after premedication inside OT (T1), Ivabradine had significantly lower mean IOP as compared to placebo only at 3 out of six postintubation observations. Thus, indicating that at the given dose of 5 mg oral premedication, Ivabradine was only marginally

better than placebo. However, Clonidine was able to attenuate the IOP rise effectively. Although, IOP rise following intubation can be as high as 10–20 mm Hg[19] however, no such increase was observed in present study in any of the study groups.

The present study showed the efficacy of clonidine in controlling the IOP rise following intubation. As far as effect of Ivabradine on IOP was concerned, the present study failed to elucidate the same. Ivabradine despite showing a higher reduction in IOP between premedication to preintubation period failed to exercise the IOP attenuating effect. This could be attributed probably to a shorter half-life of the drug. It is pertinent to mention here that Clonidine has almost 3–12 times longer half-life as compared to that of Ivabradine. Similarly, bioavailability of Clonidine is also almost 1.5 times higher as compared to Ivabradine. The initial better attenuation of IOP in Ivabradine group (between premedication and preintubation interval) could be attributable to the faster onset of the drug. As such it is difficult to comment on the optimal dosage of the drug as we used 5 mg drug only which is the minimum dose available commercially. It might be possible that higher dosages may provide a better outcome. For this interventions using variable dosages of Ivabradine are recommended. Though there are a number of studies supporting the role of Clonidine premedication in maintenance of hemodynamic stability among patients undergoing endotracheal intubation[20,21] there are limited studies regarding the role of clonidine and ivabradine in the maintenance of IOP.

Although the primary objective of the study was to evaluate and compare the attenuation of IOP rise following endotracheal intubation between oral Clonidine and ivabradine premedication groups, during the course of study, we felt that IOP rise to succinylcholine intubation did not reach to a considerably high level to need any particular intervention even in placebo group, that means, that among patients with baseline IOP in normal range, IOP rise following intubation does not hold much value. On reviewing the previous studies too, we did not find that during endotracheal intubation period there was any considerable and substantial rise in IOP, however, during postoperative period within 24 hours, some studies have reported considerable rise in IOP 5–6 hours after the surgery, hence, whether premedication for IOP attenuation during endotracheal intubation is required among patients having normal IOP at baseline itself requires a reconsideration.

Further studies with variable drug-dose combinations are recommended to find the optimal dose of ivabradine required to control IOP similar to the effect produced by oral clonidine 0.1 mg.

Conclusion

Based on the outcome of the present study, we conclude that oral Clonidine (0.1 mg) can effectively be recommended as premedicant for obtunding the rise in IOP following endotracheal intubation after administration of succinylcholine. Oral Ivabradine, 5 mg do not prevent increase in IOP following intubation with succinylcholine.

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Original Research Article

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Comparative Effects of Supraclavicular Perivascular and Infraclavicular Brachial Plexus Block for Upper Limb Surgeries

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Abstract

Background: Supraclavicular and infraclavicular both approaches have identical distributions of anesthesia. Proximal blocks generally have rapid onset than blocks which are distal. *Objective*: To compare the clinical effect of supraclavicular perivascular technique and infraclavicular brachial plexus block for upper limb surgery. *Methods:* A prospective randomized clinical trial was performed among hundred patients receiving upper limb surgery under infraclavicular or supraclavicular brachial plexus block. The infraclavicular brachial plexus block was achieved by using the vertical technique with 30 ml of 0.5% ropivacaine. The supraclavicular block was performed using the plumb bob technique with 30 ml of 0.5% ropivacaine. The pain related to block administration was evaluated. The sensory and motor block extent as well as the complications were assessed. *Results:* No significant differences were observed in the block administration related pain, evolution of sensory and motor block quality, or the success of the block. There was significant differences in the patient's satisfaction. *Conclusions:* Both infraclavicular and supraclavicular block had effects which were similar. When considering the complications, the infraclavicular approach may be preferred to the supraclavicular approach.

Keywords: Supraclavicular perivascular block; Upper limb surgery; Infraclavicular brachial plexus block; Pneumothorax; Nerve Injury.

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Introduction

Four approaches are there to a brachial plexus block namely interscalene, supraclavicular, infraclavicular and axillary. Associated to the axillary approach, at the level of the clavicle, a brachial plexus block can anesthetize all 4 distal upper extremity nerve areas without need of separate musculocutaneous nerve block. The supraclavicular approach has a supplementary advantage of a blockade at a level where the brachial plexus elements are firmly grouped, which eases an injection at single point and is supposed to result in onset rapidly.[1] In all patients, the infraclavicular approach should be feasible. It is also the theoretical way of both the supraclavicular and axillary approaches which are anatomical distribution of plexus structures allowing single injection of local anesthetics and a reduced risk of pneumothorax. Both supraclavicular and infraclavicular approaches have similar distributions of anesthesia.[2] Proximal blocks have rapid onset than distal blocks (infraclavicular and axillary), but there are lacuna in literature. So,

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this Interventional study was programmed for comparing both approaches to the brachial plexus using nerve stimulation in patients under going upper limb surgery.

Materials and Methods

Type of study - Prospective study;

Study design - Interventional study;

Study population - Patients enrolled for Upper limb surgery;

Study place - Department of Anesthesia of Tertiary care Institution;

Study duration - 6 months (February 2019 to July 2019);

Sampling technique - Consecutive sampling Technique;

Sample size - 100 consecutive patients.

Inclusion criteria

- > = 18 years;
- Scheduled to undergo surgery of the elbow, forearm, or hand underbrachial plexus anesthesia.

Exclusion criteria

- Coexisting lung, heart, liver, or kidney disease;
- Pregnancy;
- Inability to understand the information provided;
- Allergy to local anesthetics;
- Chest deformities; previous clavicle fractures;
- Neurologicaldisorders.

Methodology

The patients were randomly distributed to receive either infraclavicular plexus block (Group I, $n = 50$) or supraclavicular block (Group S, $n = 50$). All blocks were performed by the same anesthesiologist. Standard monitoring (noninvasive blood pressure, pulse oximetry and ECG) was commenced upon arrival to the preoperative holding area.

A 22-gauge 50-mm insulated stimulation short bevel needle (Stimuplex® A, B/Braun Medical, Germany) connected to a nerve stimulator (Stimuplex® -DIG, B/Braun, Germany) was used for all blocks. The nerve stimulator settings initially were 1.5 mA with a duration of impulse of 0.1 ms. The position of needle was decent when the response of motor in the hand or wrist was obtained and remained visible with a maximum current of 0.5 mA. 30 ml 0.5% ropivacaine was used as local anesthesia and it was injected slowly for about 60 seconds with periodic aspiration. The infraclavicular approach was done in position of supine with the side of upper arm, but with the elbow flexed and the hand resting on the lower-chest or abdomen. After landmarks identification, the site of puncture was marked halfway between the notch of jugular and the most ventral part of the acromion. The needle was injected vertical to the horizontal plane.

The supraclavicular Perivascular block was performed according to the original procedure reported by Brown et al.[3] In the supine position, the patient was placed with their head turned toward the opposite side. The point at which the lateral border of the sternocleidomastoid muscle joins the superior aspect of the clavicle was marked, and a needle was inserted at this point in a direction that is directly. The needle was pierced until a motor response was elicited. During the initial insertion, if a motor response in the hand or wrist was not obtained, or in small steps, the needle was redirected cephalad, if the first rib was not contacted, until a motor response in the hand or wrist was obtained or until it was angled approximately 30°.

Immediately after removing the needle, assessment of block performance pain was done by asking the patient to verbally quantify the pain level using a score between 0 and 10; 0 = meaning no pain and 10 = meaning excruciating pain. As a point of reference, a simultaneous comparison of the sensory and motor function in the contralateral limb was used. After the injection, a block assessment was assessed at 10 min intervals until 50 min. The sensory block for each nerve (radial, median, ulnar, musculo-cutanoeus, and media cutaneous of forearm) was ranked as follows: 0 = no difference from an unblocked extremity; 1 = less cold than unblocked extremity; and 2 = no sensation of cold.

The evaluation of motor block was performed using the forearm flexion and scored as follows: 0 = no loss of force; 1 = reduced force compared with the contralateral arm; and 2 = incapacity to overcome gravity.

The quality of the block was evaluated in the intraoperative time: (a) Satisfactory block—Surgery without patient discomfort or the need for supplementation; (b) Unsatisfactory block—A sensory region involved in the surgery was not completely anesthetized and the block was supplemented by the continuous infusion of propofol at 50 μg/kg/min and sufentanil 0.1–0.3

µg/kg IV; and (c) Complete failure— If the patient still experienced pain despite supplementation, general anesthesia was induced by the attending anesthesiologist using his/her preferred technique.

The duration of the sensory block was noted as time between the end of the local anesthetic injection and the total recovery of sensation. The side effects and complications namely intravascular injection, blood vessel puncture, overdose and dyspnoea, were noted. The satisfaction of patient with the anesthetic procedure was assessed after postanesthesia care ward arrival using a 2-point scale (0 = unsatisfied, 1 = satisfied).

Ethical Consideration - The study was approved by Institutional Ethics Committee.

Consent Type - Written Informed consent.

Statistical Analysis

Recorded observation were analyzed using SPSS. The values were expressed as the mean ± SD. Group sizes (50 patients per group) were determined using the proportion sample size estimates. Unpaired *t*-test and Chi-quare test was performed for analysis. A p - value of < 0.05 is considered statistically significant.

Results

Table 1: Demographic and Clinical details of the study participants

Features	Group I (n = 50)	Group S (n = 50)
Age (years)	46 ± 18*	47 ± 18
Male / Female	27/23	26/24
Height (cm)	164 ± 8	163 ± 7
Weight	60 ± 8	62 ± 10
Type of Surgery		
Wrist	1	2
Elbow	45	42
Forearm	4	6
Duration of Surgery (min)	70 ± 32*	64 ± 30

*p < 0.05 is statistically significant.

Shown as per Table 1 demographic and surgical features of the patients were studied. Mean age of Group I was 46 years and it was found to be statistically significant when compared with mean age of Group S. The study was male preponderance in both groups. Height and weight in both groups were nearly similar and were not significant (p > 0.05). Most of the upper limb surgeries included elbow. Duration of Surgery was higher using Infraclavicular plexus block and it was found to be significant (p < 0.05).

Table 2: Duration of Sensory and Motor Block

Duration	Group I (n = 50)	Group S (n = 50)
Sensory (min)	821 ± 170	760 ± 200
Motor (min)	820 ± 2015	772 ± 230

Shown as per Table 2 determines the duration of sensory and motor block between the groups. Duration of both sensory and motor in Group I was higher than Group S but was not to be statistically significant (p > 0.05).

Table 3: Quality of Block

Quality	Group I (n = 50)	Group S (n = 50)
Satisfied	48	42
Unsatisfied	2	5
Complete failure	0	3

Shown as per Table 3 satisfactory block was achieved in 96% of patients who undergone Infraclavicular plexus block which was statistically significant, while 84% are satisfied with supraclavicular perivascular block. An unsatisfactory block was reported more in supraclavicular block. While a complete failure was seen in 3 patients of Group S which was significant. (p < 0.05).

Table 4: Patient's Satisfaction

Level	Group I (n = 50)	Group S (n = 50)
Satisfied	48	47
Unsatisfied	2	3

According to Table 4 Ninety six percent of patients were satisfied with infraclavicular block and 94% were satisfied with supraclavicular block. More patients are unsatisfied with Group S block. There were no statistically significant differences in the level of patient's satisfaction between the groups. One patient in Group S had a pneumothorax after the block, and one patient in the Group I was unhappy with the prolonged sensory and motor block with ropivacaine.

Table 5: Side Effects and Complication due to Blocks

Side effects & Complication	Group I (n = 50)	Group S (n = 50)
Dyspnoea	2	28
Pneumothorax	0	2
Vascular Puncture	3	5
Horner Syndrome	7	7

Shown in Table 5 presents side effects and complications. No systemic reactions to the local anesthetic were reported. Horner's syndrome was observed in 7 patients in Group S (14%) and I (14%), respectively. Vascular puncture happened while performing the blocks occurred in both groups, 10% (n = 5) in Group S and 6% (n = 3) in Group

I. 28 patients from Group S versed with dyspnea that was resolved after applying 6 L of oxygen by a mask. A pneumothorax was observed in 2 patients in Group S (4%), but none in Group I. A thoracostomy tube was not traced.

Discussion

In this study, no important clinical differences were shown using neurostimulation, the supraclavicular and infraclavicular approach except for the patient satisfaction, high incidence of Horner's syndrome and the pneumothorax in 2 patients with the supraclavicular approach. A brachial plexus block could be done using several approaches. Selection of the selected approach is decided by the innervations of the site of surgery, risk of regional anesthesia complications, as well as the exposure of the anesthesiologist. Other factors which may be considered such as the reliability, rapidity and ease, patient comfort during block performance.

Compared with the axillary block, the supraclavicular approach to the brachial plexus offers a marked advantage in upper limb surgery, particularly a rapid onset of a dense block with a single injection using minimal local anesthesia.[4] However, many anesthetists do not perform this procedure for fear of causing a pneumothorax. To avoid pneumothorax, the plumb - bob technique was used as supraclavicular approach. Enough surgical analgesia in the vertical infraclavicular approach was reported by Kilka et al.[5] in 95% of patients at 30 min using 40 ml of prilocaine 1.5% and 10 ml of bupivacaine 0.5%. Neuburger et al.[6], without specifying the time of assessments, reported enough surgical anesthesia in 87% and 88% of patients. In the supraclavicular block, Franco et al.[1] reported a 97.2% success rate using the subclavian perivascular technique in 1,001 patients. Possible reasons for the lower succes rate observed in both groups include the lower volume of local anesthesia used, operator's inexperience, different local anesthetics used or the definition of success. There are no reports comparing the supraclavicular with infraclavicular method using neurostimulation. In several studies, the supraclavicular approach with the infraclavicular approach with ultrasound were compared. No significant difference in either the block performance or onset times or block efficacy was reported in Arcand et al.[7] and they compared ultrasound-guided supraclavicular with infraclavicular blocks. In contrast, Koscielniak et al.[8] reported that an ultrasound - guided infraclavicular block had a faster onset, better surgical efficacy and fewer adverse events than a supraclavicular block. Recently, Fredrickson et al.[9] compared an ultrasound - guided supraclavicular block using multiple injection with ultrasound-guided triple injection infraclavicular block. The incidence of vessel puncture was similar in both groups. None of them resulted in serious complications, such as seizures or hematoma. This might be due to the slow injection technique with repeated aspiration and the use of a traumatic needles. According to Rettig et al[10], Horner's syndrome is a clinically significant sign (100%) that predicts changes in hemidiaphragmatic movement. However, in their patients, changes in hemidiaphragmatic movement were also observed without Horner's syndrome. In this study, Horner's syndrome was observed in 7 patients in both groups respectively. When the complication rates between the supraclavicular and infraclavicular approaches are compared, an impairment in diaphragmatic movements can be rated as 100% for interscalene[11], 50% to 77% for supraclavicular[12,13], 24% to 26% for proximal infraclavicular[10], and 0% for more distal infraclavicular blocks[14,15]. This has also been reported after interscalene[16], coracoid and vertical infraclavicular blocks. The noted incidence of pneumothorax after a supraclavicular block is 0.5% to 6.1%. To reduce the risk of pneumothorax, the plumb-bob and subclavian perivascular approaches were designed. The pneumothorax risk in tall, thin patients might be reduced by initially directing the needle 45° cephalad during the supine plumb-bob technique, than directly toward the floor. This magnetic resonance imaging finding has not been confirmed clinically. The pneumothorax incidence is likely to be decreased by the operator's experience, using needles which are shorter, and taking extra care with tall, thin patients who are more likely to have high apical pleural reflections or in patients with emphysema.

Conclusion

The results of the present study, concludes that both the supra-clavicular and infra-clavicular method to the similar clinical efficacy, but the supraclavicular block caused more dyspnoea, pneumothorax and has less patient satisfaction. For hand, forearm, and/or elbow surgery, these results suggest that the infraclavicular approach might be preferable.

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Conflict of Interest: None declared.

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Original Research Article

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A Comparative Study of 0.5% Levobupivacaine and 0.5% Bupivacaine in Spinal Anaesthesia in Geriatric Patients Undergoing Lower Limb Surgeries

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Abstract

Background: The geriatric population faces serious problems. When combined with the tendency for older population to have more unsteady balance and vision problems, it becomes a recipe for increased risk of fracture. *Aims:* Hemodynamic stability during perioperative period is of paramount importance in such scenario and hence the technique of choice becomes neuraxial block. The anesthetist's traditional approach to provide anesthesia for geriatric population has been the emphasis on maintaining hemodynamic stability by maintaining heart rate, saturation, blood pressure and by avoiding hypotension, bradycardia etc. This study aimed to compare the efficacy of intrathecal 0.5% Bupivacaine and 0.5% Levobupivacaine in geriatric patients. *Methods*: After ethical committee permission, a comparative study was conducted in the department of Anesthesia at BLDE (DU's) Shri BM Patil Medical College, Hospital and Research Center, Vijayapur. With prior informed written consent, study was conducted on total of 120 geriatric patients above 60 years of age with American society of anesthesiologist (ASA) Grade II–III scheduled for lower limb surgeries under spinal anesthesia. The patients either received 0.5 % hyperbaric Inj. Bupivacaine 3 ml (60 patients) Group B (Bupivacaine) or 0.5 % hyperbaric Inj. Levobupivacaine 3 ml (60 patients) Group L (Levobupivacaine) The time for onset of sensory block between the two groups was the primary endpoint. Other measurements included were time to Grade 4 motor blockade and time to 2 segment regression, Hemodynamic changes (RR, SpO_2, MAP, HR), Time to rescue analgesia and side effects if any. *Results*: Statistical analysis was done using Chi-square test and Unpaired *t*-test. Time to onset of sensory blockade was significantly faster (p – value < 0.001) in Levobupivacaine Group compared to Bupivacaine Group. Also, there was a significant increase in heart rate, respiratory rate in patients of Group L with $p < 0.001$. Time to Grade 4 motor blockade, time to 2-segment regression and time to rescue analgesia were also increased in Group L patients with $p = 0.872$, $p < 0.046$ and $p < 0.002$ respectively. Mean arterial pressure was increased in Group B patients with $p < 0.02$. Side effects like hypotension was significantly less (p - value < 0.001) with Group Levobupivacaine compared to Group Bupivacaine. *Conclusion*s: Increased incidence of intraoperative hypotension with Bupivacaine suggests that Levobupivacaine is a better drug in maintaining perioperative hemodynamics in a geriatric patient undergoing lower limb orthopedic surgery.

Keywords: Geriatric; Lower limb surgeries; Neuraxial block.

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Introduction

The geriatric population faces serious problems as they age. Their bone mineral density decreases as they grow old. This is in particular a problem in postmenopausal women. Decreased mineral levels tend to translate into weaker and more brittle bones. When combined with the tendency for older adults to have more unsteady balance and vision problems, it becomes a recipe for increased risk of fractures. According to Population census 2011, there are nearly 104 million elderly persons (aged 60 years or above) in India; 51 million males and 53 million females.[1]

Anesthetic technique of choice for lower limb orthopedic surgeries is neuraxial blockade. A clinically precise and skillful anesthetic management of geriatric population requires in-depth knowledge of the numerous patho-physiological alterations and functional changes at this advanced age due to altered and more variable pharmacokinetics and pharmacodynamics and associated comorbidities.[2]

In elderly patients, neuraxial anesthetic blockade has a definite advantage over general anesthesia, as it reduces surgical stress by decreasing sympathetic efferent nerve activity and blocking nociceptive impulses from the operative site. Cardio-respiratory complications and overall morbidity and mortality are also minimized.[3] Evaluating the safety and efficiency of 0.5% levobupivacaine and 0.5% bupivacine (hyperbaric) in spinal anesthesia for lower limb surgeries in geriatric patients, was the sole purpose of this study.

Aims and Objectives

To compare the efficacy of 0.5% Bupivacaine and 0.5% Levobupivacaine in geriatric patients with regard to:

1. Time of onset of sensory blockade and maximum level of sensory blockade;
2. Time to Grade 4 motor blockade and time to 2 segment regression;
3. Time to rescue analgesia, hemodynamic changes (RR, SpO_2, MAP, HR) and side effects if any.

Materials and Methods

Study Design

After receiving approval from the institutional research and ethical committee a comparative study was conducted on 120 geriatric patients undergoing elective lower-limb surgeries under subarachnoid block at Department of Anesthesiology, BLDE (DU's) Shri BM Patil Medical College, Hospital and Research Center, Vijayapura. The study duration was from December 2017–August 2019.

Inclusion criteria

1. Patients age group above 60 years;
2. Patients with ASA Grade II and III;
3. Patients undergoing elective lower-limb surgeries.

Exclusion criteria

1. Patients having deformities of spine;
2. Patients having infection at the site of insertion of spinal needle;
3. Patients having bleeding disorders, coagulation abnormalities, raised Intracranial Pressure (ICP) and neurological deficits.

Preanesthetic examination and preparation

The study protocol received ethical clearance from the institution. Preanesthetic check-up was performed one day prior to the surgery. Patients were evaluated with history, general physical examination, systemic examination of cardiovascular, respiratory, central nervous system and spine examination for deformity was also performed. Investigations like hemogram, bleeding time, clotting time, blood glucose, blood urea, serum creatinine were done. ECG and Chest *X*-ray were done wherever necessary. Patient's weight, height were also recorded prior to surgery. All patients were kept nil orally for 6–8 hours. The procedure of spinal anesthesia was explained to the patients and written informed consent was obtained

Premedication

Patients were premedicated with Tab. Ranitidine 150 mg, on the previous night of surgery. Each patient was preloaded with an IV infusion of 500 ml of Ringer Lactate solution and 50 mg IV Ranitidine, 30 min prior to surgery.

Methods

120 patients were randomly divided into 2 Groups of 60 each:

Group B: 60 patients received 3 ml hyperbaric Inj. 0.5% bupivacaine intrathecally;

Group L: 60 patients received 3 ml hyperbaric Inj. 0.5% levobupivacaine intrathecally.

Preparation of operating room

Anesthesia machine was checked and cock pit drill performed. Appropriate size endotracheal tubes, working laryngoscope with medium and large size blades, stylet, bougie, other emergency airway equipment and working suction apparatus were kept ready prior to the procedure.

After shifting the patient to operating room, patients were monitored for Noninvasive Blood Pressure (NIBP), Heart Rate (HR) and percentage of oxygen saturation (SpO_2). Under all aseptic precautions, subarachnoid block was performed using a 25G Quincke needle, with the patient in the lateral or sitting position depending on the patients comfort, at the L_3-L_4 interspace. The study solution was administered slowly. Patient was repositioned gently to supine position without elevation of extremities and tested every 5 minutes until maximal spread of sensory block and then every 15 minutes during the surgery.

Parameters evaluated

Sensory Blockade

This was assessed by loss of sensation to alcohol cotton swab on each side and patients asked about the sensation–

a. *Time to onset of sensory block:* Defined as the time between injection of the drug to the time of loss of sensation at L_2 level;
b. *Time to maximum sensory block:* Defined as the time to reach highest dermatomal level with loss of sensation;
c. *Time to two segment regression:* Defined as the time period to regain sensation at two dermatomes lower to the initial level of highest dermatome;
d. *Time to rescue analgesia:* Defined as the time at which patient complained pain at the site of surgery intraoperatively or postoperatively.

Motor Blockade

The degree of motor block was assessed using "Bromage Scale". Motor blockade was assessed at 5 minutes and then for every 30 seconds till Grade IV block was achieved. And then every 15 minutes until return of normal motor function.

Onset time for motor block

It is defined as the time between injection and Grade IV block. Heart Rate (HR), Mean Arterial Pressure (MAP), Percentage Saturation of Oxygen (SpO_2) and Respiratory Rate (RR) were recorded every 5 minutes for the first 30 minutes and then every 1 hourly for 3 hours throughout the surgery.

Patients were considered hypotensive when their MAP decreased to < 65 mm Hg, and were treated with Inj. Ephedrine 5 mg IV dose titrated according to response. A decrease in the heart rate to < 50 bpm was treated with Inj. Atropine 0.3–0.6 mg IV.

Parameters recorded intraoperatively

- Time of onset of sensory blockade;
- Time to maximum level of sensory blockade;
- Time to Grade IV motor blockade;
- Time to 2 segment regression;
- Time to rescue analgesia;
- Percentage of oxygen saturation (SpO_2);
- Heart Rate (HR);
- Mean Arterial Pressure (MAP);
- Respiratory Rate (RR).

Bromage Scale

Grade motor activity:

1. Free movement of legs or feet;
2. Just able to flex knees with free movement of feet;
3. Unable to flex knees but with free movement of feet;
4. Unable to move legs or feet.

Complications such as nausea, vomiting and shivering were treated accordingly and the treatment given was recorded.

All the patients were kept under observation in the postoperative period for 4 hrs and Heart Rate (HR), Mean Arterial Pressure (MAP), Percentage of Oxygen Saturation (SpO_2) and Respiratory Rate (RR) were recorded at interval of every 30 min till 4 hours. All the patients were assessed for pain at regular intervals and rescue analgesia was given accordingly.

Statistical Analysis

All characteristics were summarized descriptively. For continuous variables, the summary statistics of mean ± Standard Deviation (SD) were used. For categorical data, the number and percentage were used in the data summaries and diagrammatic presentation. Chi-square (χ^2) test was used for association between two categorical variables.

The formula for the Chi-square statistic used in the Chi-square test is:

$$\chi_c^2 = \Sigma \frac{(O_i - E_i)^2}{E_i}$$

The subscript "*c*" stands for the degrees of freedom, "O" is observed value and E is expected value.

The difference of the mean of analysis variables between two independent groups was tested by unpaired *t*-test.

The *t* statistic to test whether the means are different can be calculated as follows:

$$t = \frac{(\overline{x_1} - \overline{x_2}) - (\mu_1 - \mu_2)}{\sqrt{\frac{s_1^2}{n1} + \frac{s_2^2}{n2}}}$$

Where X_1 = mean of sample 1

X_2 = mean of sample 2

n_1 = number of subjects in sample 1

n_2 = number of subjects in sample 2

s_1^2 = variance of sample 1 = $\frac{Ó(x_1 - \overline{x}_1)^2}{n_1}$

s_1^2 = variance of sample 2 = $\frac{Ó(x_2 - \overline{x}_2)^2}{n_1}$

If the *p* - value was < 0.05, then the results were considered to be statistically significant otherwise it was considered as statistically insignificant. Data were analyzed using SPSS software V.23.0. on Microsoft office 2007.

Results

One Hundered Twenty patients were chosen for the study. 60 patients were assigned into each of the groups. Group B patients received 3 ml hyperbaric 0.5% bupivacaine and Group L patients received 3 ml hyperbaric 0.5% levobupivacaine.

Time to onset of sensory blockade was significantly faster (*p* – value < 0.001) in Levobupivacaine group compared to Bupivacaine Group. Also, there was a significant increase in heart rate, respiratory rate in patients of Group L with *p* < 0.001. Time to Grade 4 motor blockade, time to 2-segment regression and time to rescue analgesia were also increased in Group L patients with *p* = 0.872, *p* < 0.046 and *p* < 0.002 respectively. Mean arterial pressure was increased in Group B patients with *p* < 0.02. Side effects like hypotension was significantly less (*p* - value < 0.001) with Group Levobupivacaine compared to Group Bupivacaine.

The Table 1 shown, the comparison of mean time of onset of sensory blockade between the bupivacaine and levobupivacaine groups. The mean time of onset of sensory blockade in bupivacaine group was 2.4 ± 0.8 min, while in the levobupivacaine group it was 3 ± 0.8 min, above shown as (Fig. 1).

Table 1: Comparison of mean time of onset of sensory blockade between Bupivacaine and Levobupivacaine Groups.

Time of onset of sensory block	Bupivacaine		Levobupivacaine		*p* - value
	Mean	SD	Mean	SD	
	2.4	0.8	3.0	0.8	< 0.001

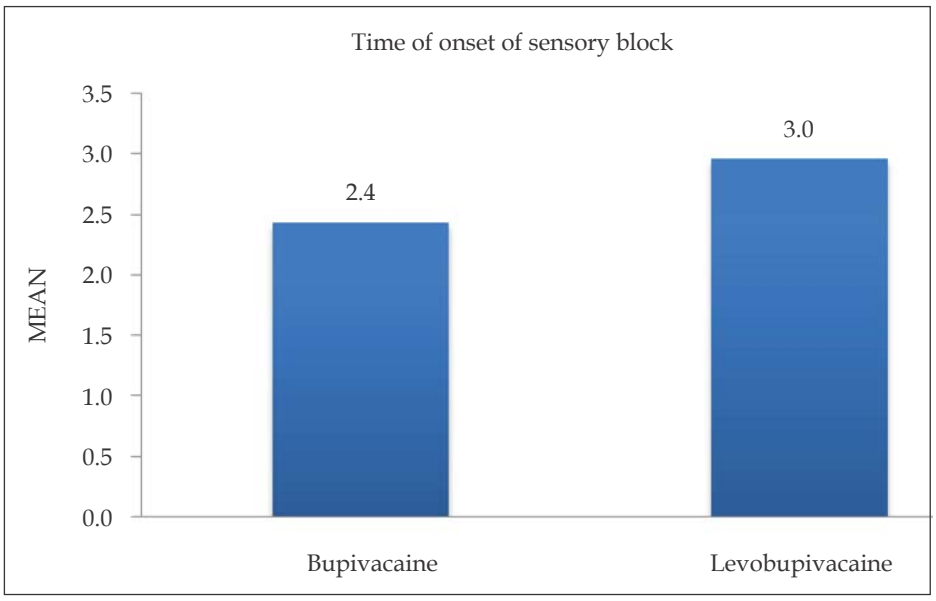

Fig. 1: Time of onset of sensory block

Table 2: Comparison of mean time to 2 segment regression between Bupivacaine and Levobupivacaine Groups.

Time to reach 2-segments regression	Bupivacaine		Levobupivacaine		*p* - value
	Mean	SD	Mean	SD	
	101.7	7.2	104.3	7.2	0.046*

Note: *Significant at 5% level of significance ($p < 0.05$).

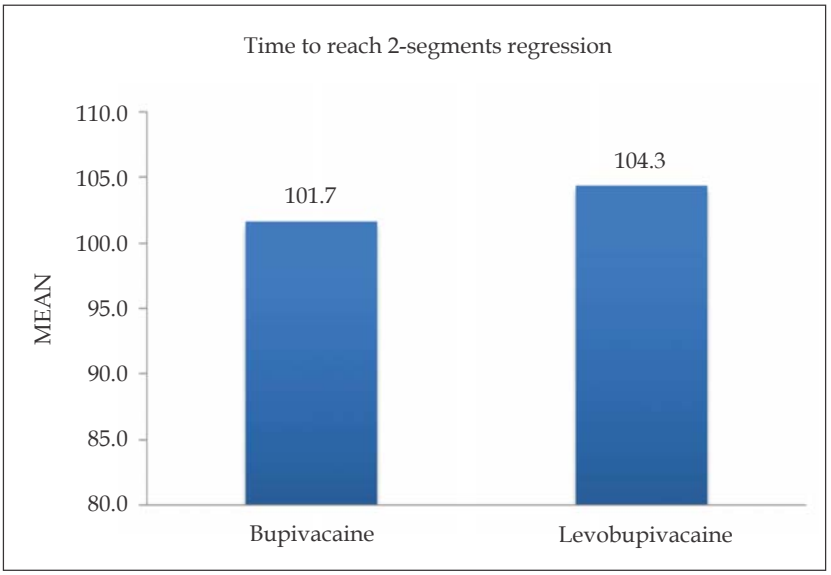

Fig. 2: Time to reach 2-segment regression

The Table 2 shows, the comparison of mean time to 2 segment regression between the bupivacaine and levobupivacaine groups. The mean time to 2 segment regression in bupivacaine group was 101.36 ± 7.76 min, while in the levobupivacaine group it was 104.76 ± 7.62 min, as shown in Fig. 2.

Table 3: Comparison of mean time to rescue analgesia between Bupivacaine and Levobupivacaine Groups.

Time to rescue analgesia	Bupivacaine		Levobupivacaine		*p* - value
	Mean	SD	Mean	SD	
	147.0	14.1	155.5	15.0	0.002*

Note: *Significant at 5% level of significance ($p < 0.05$).

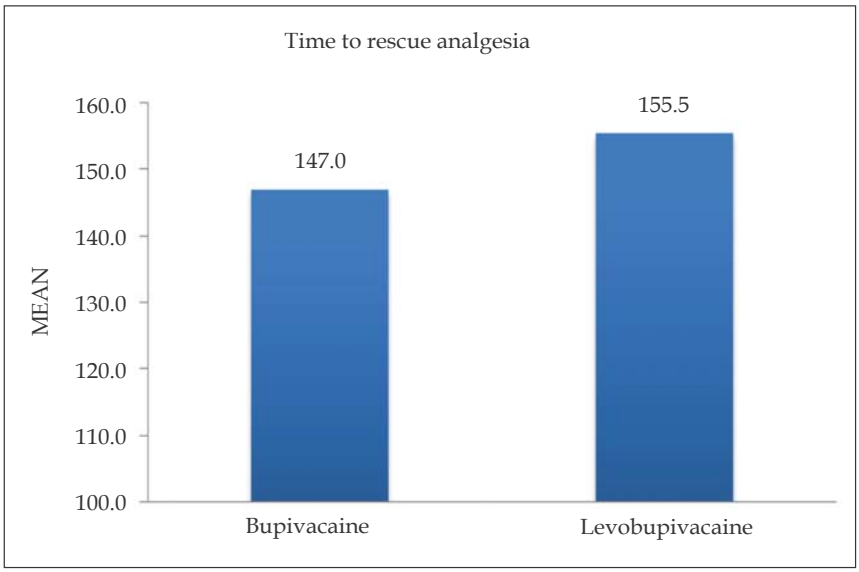

Fig. 3: Time to rescue analgesia

The Table 3 shows, the comparison of mean time to rescue analgesia between the bupivacaine and levobupivacaine groups. The mean time to rescue analgesia in bupivacaine group was 146.22 ± 15.46 min, while in the levobupivacaine group it was 152.04 ± 14.88 min, shown as in Fig. 3.

Table 4: Distribution of patients according to hypotension

Hypotension	Bupivacaine		Levobupivacaine		*p* - value
	N	%	N	%	
YES	21	35.0%	5	8.3%	
NO	39	65.0%	55	91.7%	< 0.001*
Total	60	100.0%	60	100.0%	

Note: *Significant at 5% level of significance ($p < 0.05$).

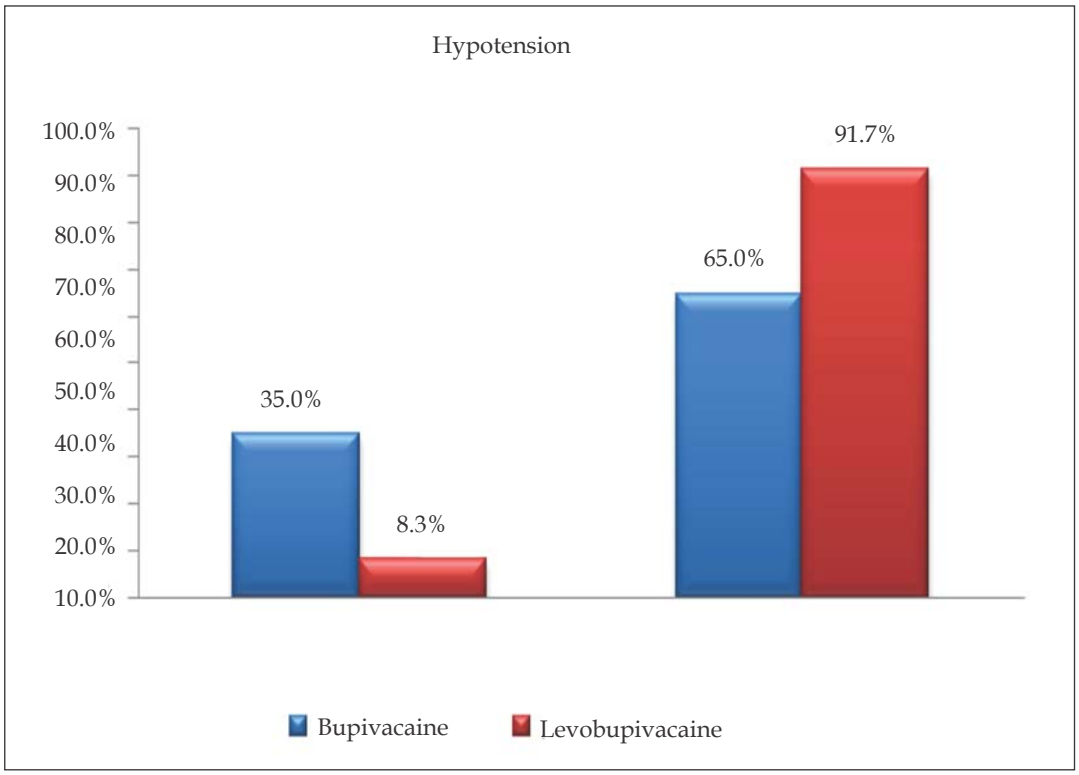

Fig. 4: Hypotension

The Table 4 shows, the distribution of patients as per hypotension in bupivacaine and levobupivacaine groups. In the bupivacaine group, 21 (35%) patients had hypotension, while in the levobupivacaine group 5 (8.3%) patients had hypotension, shown as in Fig. 4.

Discussion

Lower limb fractures are most commonly seen in geriatric population like neck of femur fracture or shaft of femur fracture etc. Various factors such as altered cognitive function, neuromuscular degeneration, reduced bone mineral density and environmental factors are responsible for trivial injury in geriatrics. Surgical fixation of fracture is the definitive treatment. Ageing is a universal and progressive physiological phenomenon clinically characterized by degenerative changes in both the structure and the functional capacity of organs and tissues.

In general, geriatric patients are more sensitive to anesthetic agents. Less medication is usually required to achieve a desired clinical effect, and drug effect is often prolonged. The most important outcome and overall objective of perioperative care of geriatric population, is to speed recovery and avoid functional decline. Spinal anesthesia is a widely used anesthetic technique for lower limb

surgery in the elderly. Spinal anesthesia is often preferred for its efficacy, rapidity, minimal effect on mental status, reduction of blood loss, and protection against thrombo-embolic complications. But risk of severe and prolonged hypotension is associated with spinal anesthesia. This is due to the rapid extension of the sympathetic block, hindering cardiovascular adaptation and causing significant morbidity and mortality. This study largely focuses on the relative potencies, systemic effects, particularly cardiovascular system and the relative degree of sensory and motor blockade with bupivacaine and levobupivacaine in geriatric patients who are undergoing lower limb surgeries.

Comparison of meantime of onset of Sensory Blockade

In present study, the time for sensory block to reach the L2 level were shorter in the bupivacaine group, difference was found to be statistically significant with p - value < 0.05.

This study is comparable with study of Erdil et al.[4] which compared the effect of intrathecal levobupivacaine and bupivacaine in 80 elderly patients and showed mean onset time for sensory blockade at T10 dermatome was about 6.4 minute and 7.8 minute for bupivacaine and levobupivacaine respectively with p - value < 0.05.

Our study also showed the p - value of < 0.05 which is highly significant. Celik et al.[5] studied the effectiveness of bupivacaine and levobupivacaine in hip surgery which showed no significant difference in onset time of sensory blockade. This study was conducted in age group between 18–65 yrs with low dose of drug.

Casati et al.[6] studied the effectiveness of bupivacaine, levobupivacaine and ropivacaine for unilateral spinal anesthesia for inguinal hernioplasty which showed there was no significant difference in onset time of sensory blockade between these drugs. Overall in our study time of sensory blockade was almost similar in bupivacaine and levobupivacaine groups.

Comparison of mean time to two Segments Regression

The study shows that the mean time to two segments regression in bupivacaine group was 101.70 ± 7.2 min, while in the levobupivacaine group it was 104.3 ± 7.2 min. The difference was found to be statistically significant (p - < 0.05), with a higher time for two segments regression in levobupivacaine group in comparison to bupivacaine group.

The study conducted by Erdil et al.[4] for the comparison of effects of levobupivacaine and bupivacaine in elderly observed that the time taken for the two segment regression was 78.3 for bupivacaine and 80.3 for levobupivacaine with p - value > 0.05. But in our study, we found the two segment regression was higher for levobupivacaine than bupivacaine. This difference may be due to the difference in the drug dosages in both the studies.

Comparison of mean time to Rescue Analgesia

This study shows that the mean time to rescue analgesia in bupivacaine group was 147.0 ± 14.1 min, while in the levobupivacaine group it was 155.5 ± 15.0 min. The difference was found to be statistically significant (p - < 0.05), thus, time to rescue analgesia in was earlier in bupivacaine group than in levobupivacaine group.

Erbay et al. (2010)[7] studied 60 patients scheduled for urological procedure undergoing subarachnoid block with bupivacaine and levobupivacaine (hyperbaric solutions) and similar to our study found that the requirement for analgesia was earlier in Group Bupivacaine (305 ± 50 min) than in Group Levobupivacaine (389 ± 146 min), (p - = 0.004).

Comparison of Complications

This study shows that in the bupivacaine group, 21 (35%) patients had hypotension, while in the levobupivacaine group, 5 (8.3%) patients had hypotension. In bupivacaine group, there was higher number of hypotension seen in comparison to levobupivacaine group.

Guler et al. (2012)[8] compared the clinical efficacy of spinal anesthesia for cesarean section in sixty females with bupivacaine and levobupivacaine (hyperbaric solutions). Conclusion was made that as motor blockade time was lesser with fewer adverse effects (fall in blood pressure, heart rate, vomiting), levobupivacaine would make a better alternative, which is similar to the finding in our study. Overall hypotension was most common complication seen with bupivacaine.

Conclusion

From the results obtained from this study, we conclude that even though there was no major statistically significant difference between the efficacy of levobupivacaine and bupivacaine when used in a volume of 3 ml for spinal anesthesia with respect to:

1. Time of onset of sensory blockade;
2. Time to maximum level of sensory blockade;

3. Time to Grade 4 motor blockade;
4. Time to 2 segment regression;
5. Time to rescue analgesia;
6. Hemodynamic change (RR, SpO_2, MAP, HR);
7. Side effects like hypotension.

But the increased incidence of intraoperative hypotension with bupivacaine suggests that levobupivacaine is a better drug in maintaining perioperative hemodynamics in a geriatric patient undergoing lower limb orthopedic surgery.

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Original Research Article

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Evaluation of Clonidine as an Additive to Bupivacaine for Central Neuraxial Blockade

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Abstract

Context: Advantages of Epidural anesthesia over spinal anesthesia like lesser incidence of hemodynamic instability and postdural puncture headache are offset by delayed onset time and unreliable motor blockade. Clonidine has been used as an additive in epidural and spinal anesthesia to prolong the duration of action. *Aims:* To compare the effect of Clonidine as an Additive in Epidural and Spinal Anesthesia. *Settings and Designs:* We designed this study to compare the effect of clonidine in epidural and spinal anesthesia in 75 adult patients scheduled for lower abdominal surgeries. *Materials and Methods:* Seventy five adult patients were randomized to receive intrathecal 0.5% hyperbaric Bupivacaine, 3 ml (Group ITB), 0.5% hyperbaric Bupivacaine + 30 μg clonidine, 3 ml (Group ITBC) or 16 ml 0.5% Bupivacaine with 75 μg clonidine at L3-L4 inter vertebral space, 16 ml (Group EDBC). Onset time of sensory blockade, duration and degree of sensory and motor blockade, heart rate, blood pressure and sedation were noted periodically. *Statistical Analysis:* Analysis was done by one way ANOVA (variables over time), Turkey's posttest (parametric variables), Kruskal-Wallis test (Nonparametric variables). *Results:* Group EDBC had similar onset time of Group ITB. Sensory blockade was increased by 37% in EDBC and 27% in ITBC compared to ITB (212.2 ± 12.4 min, 230.4 ± 13.6 min and 166.8 ± 8.5 min respectively). EDBC had motor blockade similar to that of ITB. Hypotension and bradycardia were more severe in ITBC. *Conclusions:* Epidural bupivacaine with clonidine has better hemodynamic stability compared to intrathecal bupivacaine with similar sensory and motor blockade characteristics.

Keywords: Additive; Clonidine; Epidural; Intrathecal; Spinal; Subarachnoid.

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Introduction

Many drugs have been tested to prolong the highly desirous properties of single dose neuraxial block. Opioids have been most successful in this regard but respiratory depression, urinary retension and pruritis are annoying side effects. In this background, clonidine an α_2-adrenergic agonist, stands out but its propensity to cause bradycardia and hypotension and sedation is well-known. Besides this, neuraxially administered clonidine also has antihyperalgesic action which is highly beneficial in postoperative period.[1]

Epidural has certain advantages over intrathecal anesthesia in terms of the lesser chance of postdural puncture headache and the relatively slower onset

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of hypotension. However, its failure to consistently ensure adequate muscle relaxation makes it a less attractive choice for many anesthesiologists in lower abdominal surgeries. Besides this, onset of blockade is delayed in epidural compared to intrathecal route. Addition of clonidine has been shown to improve the muscle relaxation. We designed this study to directly compare the effect of clonidine through epidural route with that with intrathecal route as there are very few studies addressing this.

Materials and Methods

After obtaining approval by the institutional research and ethics committee, 75 patients aged between 20 and 60 of ASA-I and ASA-II physical status scheduled for elective lower abdominal surgery were recruited. ASA-III and IV patients, those with significant cardiovascular, renal, hepatic dysfunction, morbidly obese, and those having an allergy to either clonidine or bupivacaine were excluded from the study.

After the informed consent the patients were randomly allocated into one of the following Groups: Group ITB (intrathecal bupivacaine 0.5% hyperbaric Bupivacaine, 3 ml), Group ITBC (0.5% hyperbaric Bupivacaine + 30 μg clonidine, 3 ml), Group EDBC (16 ml 0.5% Bupivacaine with 75 μg clonidine at L3-L4 inter vertebral space, 16 ml).

Inside the OR, base line pulse rate, noninvasive blood pressure (Systolic BP, Diastolic BP and Mean BP) and oxygen saturation were recorded. Preloading was done with Ringer's lactate solution. Depending on the group allocated the anesthetic technique was performed. Noninvasive blood pressure, oxygen saturation, heart rate were monitored and recorded every five minutes. Onset of sensory level, maximum level of sensory blockade, duration of analgesia (the time of patient's first demand for analgesics) was also noted. Two segment regression level, degree of motor blockade by Bromage score (1-No impairment of movement of legs and feet, 2-Barely able to flex knees and no impairment of movement of legs, 3-unable to flex knees and barely able to move feet and 4-unable to move feet) and sedation Score 1–4 (1-agitated and uncomfortable, 2-awake and comfortable, 3-sleeping intermittently, 4-asleep wakes to touch) were assessed periodically during the surgery and 6 hours postoperatively.

The other parameters assessed were surgical relaxation as assessed by the surgeon, respiratory rate and oxygen saturation.The mephenteramine and atropine requirements were also recorded. Hypotension and bradycardia were treated with routine protocolized management measures.

Statistical Analysis

Statistical analysis was performed using SPSS version 17.0 and Graph Pad InStat 3.10. Statistical analysis of variables over time was evaluated by one way analysis of variance with repeated measures. Statistical analysis of parametric variables between groups was done by One Way ANOVA followed by Tukey's posttest. Intergroup comparisons between nonparametric variables were accomplished using Kruskal-Wallis test with posttest. Variation of nonparametric variables within a group was assessed by Friedman test.

Results

All three groups, were similar in their demographic characteristics. The three groups were similar with respect to baseline parameters *viz* heart rate, mean blood pressure, respiratory rate, hemoglobin oxygen saturation and sedation score.

Sensory Level

Addition of clonidine resulted in a faster onset of sensory level in both spinal and epidural group. The onset of sensory level to T10 was significantly faster in Group ITBC compared to Groups ITB and EDBC. There was no statistical difference between Groups ITB and EDBC in the time to onset of sensory level, (Table 1).

Table 1: Onset of sensory level in all three groups

Group	Onset of sensory level in minutes (Mean ± SD)
Group ITB	2.08 ± 0.5*
Group ITBC	1.52 ± 0.5*
Group EDBC	2.44 ± 0.6*

*$p < 0.05$.

ITB - Intrathecal Bupivacaine

ITBC - Intrathecal Bupivacaine with clonidine

EDBC - Epidural bupivacaine with clonidine

Duration of analgesia

Duration of analgesia was significantly prolonged in both the clonidine groups. Time to request for first analgesic was significantly more prolonged in Group EDBC when compared to the other Two Groups. Group EDBC > Group ITBC > Group ITB, (Table 2).

Table 2: Duration of analgesia in all three groups

Group	Time to request for first analgesic (minutes) (Mean ± SD)
Group ITB	166.8 ± 8.5*
Group ITBC	212.2 ± 12.4*
Group EDBC	230.4 ± 13.6*

*$p < 0.05$.

ITB - Intrathecal Bupivacaine

ITBC - Intrathecal Bupivacaine with clonidine

EDBC - Epidural bupivacaine with clonidine

Two segment regression time

The two segment regression time was significantly longer in Group EDBC when compared to the other Two Groups. Group EDBC > Group ITBC > Group ITB. The regional block was successful in all patients and none of the procedures required conversion to general anesthesia, (Table 3).

Table 3: Two segment regression time in all three groups

Group	Two segment regression (minutes) (Mean ± SD)
Group ITB	83.6 ± 14.76*
Group ITBC	112.8 ± 17.45*
Group EDBC	135.4 ± 28.02*

*$p < 0.05$.

ITB -Intrathecal Bupivacaine

ITBC- Intrathecal Bupivacaine with clonidine

EDBC- Epidural bupivacaine with clonidine

Motor blockade

Motor blockade as assessed by the Bromage score was significantly more prolonged in the Group ITBC when compared to the other Two Groups, (Fig. 1).

There was no statistical difference in the surgical relaxation score as assessed by the surgeon between the Group's $p = 0.2219$, (Table 4).

Table 4: Surgical relaxation as assessed by surgeon

Group	Surgical relaxation score (1–10) #
Group ITB	8 (7–9)
Group ITBC	9 (8–9)
Group EDBC	8 (7–10)

Median (range)

ITB - Intrathecal Bupivacaine

ITBC - Intrathecal Bupivacaine with clonidine

EDBC - Epidural bupivacaine with clonidine

Hemodynamics

Addition of clonidine resulted in a greater drop in heart rate. The drop in heart rate occurs earlier in the Group ITBC as compared to Group EDBC. In Group ITBC statistically significant drop in heart rate was observed from 10 min onwards. In Group EDBC drop in heart rate was observed from 60 min onwards. The heart rate in Group ITBC was significantly lower than in Group EDBC between 2 min and 20 min. Heart rate at 60 min was significantly lower in Group EDBC when compared to Group ITB. There was significant difference between the heart rate in Group ITB and Group ITBC from 30 min onwards. Fig. 2. In Group ITBC there were three episodes of bradycardia that required treatment with atropine (12%). In the other Groups, there was no significant bradycardia that required use of atropine.

A statistically significant drop in mean arterial pressure was observed in Group ITB and Group ITBC from 2 min while similar trend in Group EDBC from 5 min onwards. MAP was significantly lower in Group ITBC than in Group ITB at 2 min, 5 min and from 30 min up to 120 min. There was a statistically significant difference in MAP between Group ITBC and Group EDBC from 2 min onwards, (Fig. 3). Among patients in Group ITBC mean mephenteramine requirement was significantly more than those in Group EDBC ($p < 0.05$). Between other Groups there was no statistically significant difference in the usage of mephenteramine, (Table 5).

Table 5: Requirement of atropine and vasopressors

Group	Atropine	Mephenteramine (mg/patient) #	Total me phen teramine (mg)
Group ITB	0 (0%)	4.6 ± 2.7	114
Group ITBC	3 (12%)	5.5 ± 2.9*	138
Group EDBC	0 (0%)	3.5 ± 2.1*	87

Mean ± SD

*$p < 0.05$

ITB - Intrathecal Bupivacaine

ITBC - Intrathecal Bupivacaine with clonidine

EDBC- Epidural bupivacaine with clonidine

Sedation

Clonidine added to spinal or epidural bupivacaine makes the patient more sedated. Sedation is more intense in Groups ITBC and EDBC when compared to Group ITB as indicated by higher median sedation scores. Between Groups ITBC and EDBC more intense sedation is noted with Group ITBC. Statistically significant sedation is seen in Group EDBC till 3 hours after the block while it is seen in Group ITBC till 4 hours, (Fig. 4).

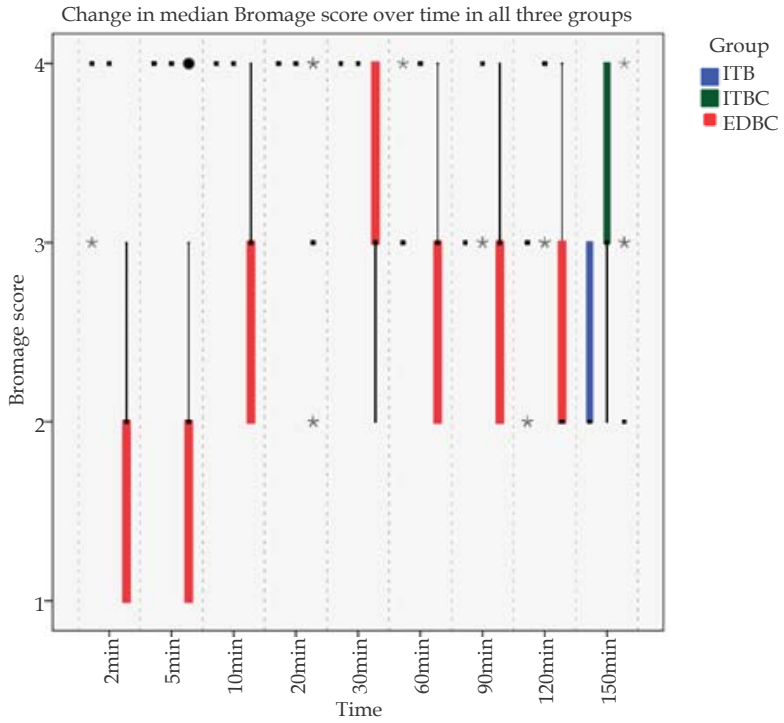

Fig. 1: Change in median Bromage score
ITB -Intrathecal Bupivacaine
ITBC- Intrathecal Bupivacaine with clonidine
EDBC- Epidural bupivacaine with clonidine

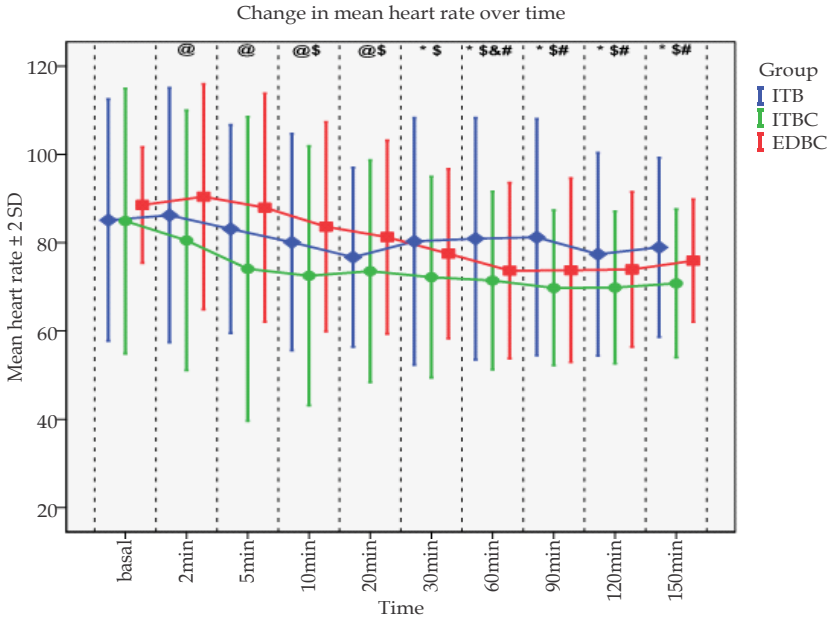

Fig. 2: Change in mean heart rate over time
ITB -Intrathecal Bupivacaine
ITBC- Intrathecal Bupivacaine with clonidine
EDBC- Epidural bupivacaine with clonidine
@ $p < 0.05$ between group ITBC and group EDBC
* $p < 0.05$ between group ITB and group ITBC
& $p < 0.05$ between group ITB and group EDBC
# $p < 0.05$ within group EDBC when compared to basal heart rate
$ $p < 0.05$ within group ITBC when compared to basal heart rate

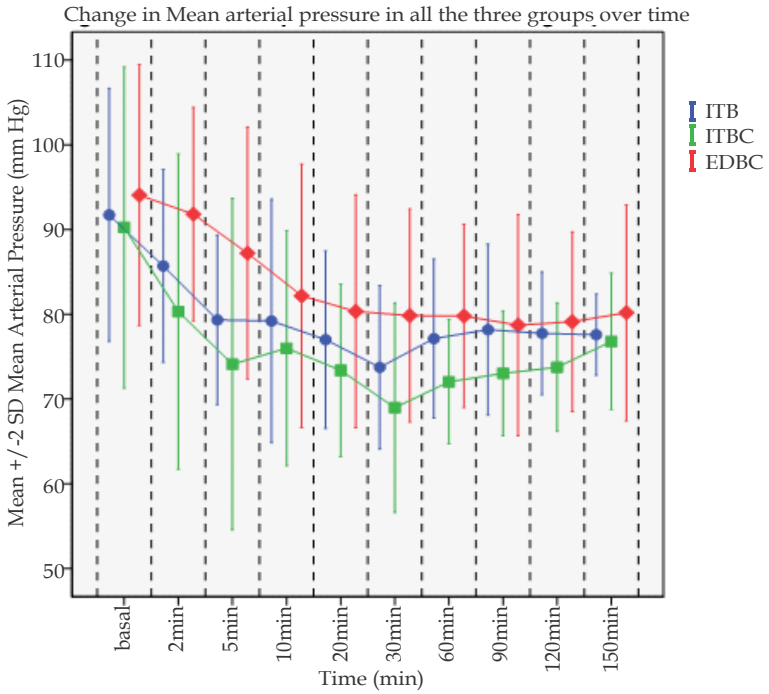

Fig. 3: Change in Mean Arterial Pressure
ITB -Intrathecal Bupivacaine
ITBC- Intrathecal Bupivacaine with clonidine
EDBC- Epidural bupivacaine with clonidine
@p < 0.05 between group ITBC and group EDBC
* p < 0.05 between group ITB and group ITBC
& p < 0.05 between group ITB and group EDBC
# p < 0.05 within group EDBC when compared to basal heart rate
$ p < 0.05 within group ITBC when compared to basal heart rate

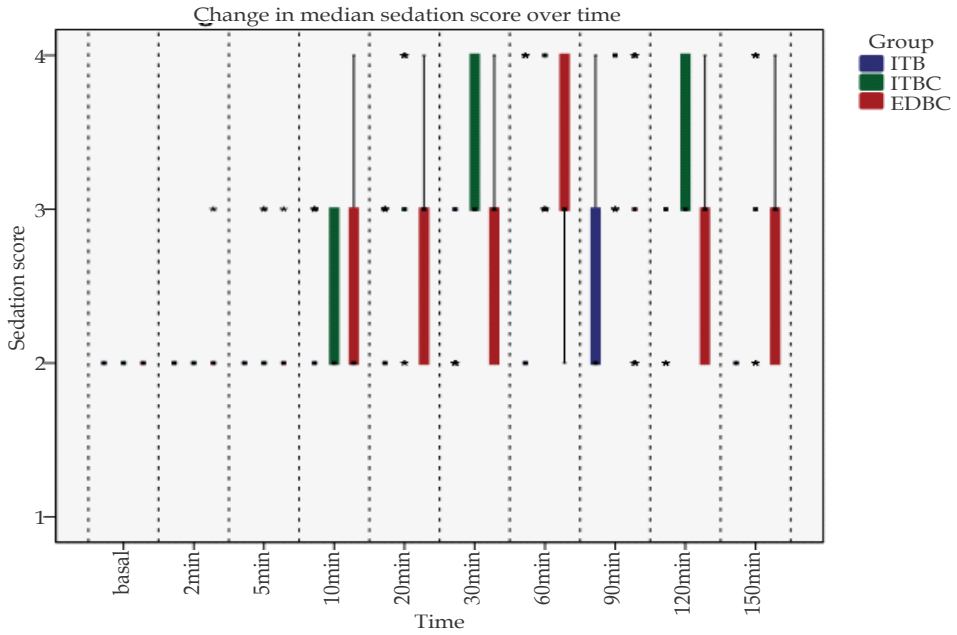

Fig. 4: Change in median sedation score
ITB -Intrathecal Bupivacaine
ITBC- Intrathecal Bupivacaine with clonidine
EDBC- Epidural bupivacaine with clonidine

Respiratory rate and Oxygen saturation

There was no significant drop in respiratory rate or oxygen saturation in the intraoperative or immediate postoperative period in all Three Groups. There were no intergroup differences in the blood pressure and the heart rate in the immediate postoperative period (6 hours).

Discussion

We observed that the addition of clonidine to epidural or intrathecal bupivacaine increased the duration of analgesia as assessed by the first request for analgesia by about 37% in Epidural Group and 27% in Intrathecal Group compared to bupivacaine - only intrathecal group (212.2 ± 12.4 min in Group ITBC, 230.4 ± 13.6 min in Group EDBC when compared to 166.8 ± 8.5 min in Group ITB), Table 2. Similarly the two segment regression time was significantly increased ($p < 0.05$) in groups receiving clonidine with 60% increment in epidural group and 37% increase in intrathecal group compared to plain bupivacaine intrathecal group (112.8 ± 17.45 min in Group ITBC, 135.4 ± 28.02 min in Group EDBC as compared to 83.6 ± 14.76 min in Group ITB), Table 3. Onset of sensory block is generally slower with epidural than with intrathecal anesthesia. However, we found that the onset of blockade when clonidine was added in the epidural group was comparable to the control intrathecal group, Table 1. This would reduce the time lost in waiting for the epidural anesthesia to take effect.

Motor blockade as assessed by Bromage score was significantly more in patients who had received intrathecal clonidine when compared to the other two groups till four hours postoperatively ($p < 0.05$). In Group ITBC the motor blockade outlasted the sensory blockade as assessed by the request for systemic analgesics. Therefore, we infer that addition of clonidine to bupivacaine to intrathecal space results in intense motor blockade which outlasts the sensory blockade. Several studies have reported similar finding of improved sensory and motor blockade.[2,3]

Clonidine by itself does not cause any motor blockade.[4] However, it potentiates the motor blockade caused by intrathecal local anesthetic.[5] Epidural clonidine exerts its effect through its escape into the intrathecal space and action in the spinal cord, direct action on the Aδ and C nerve fiber in the epidural space and through the vasoconstrictor effect which potentiates and augments the action of local anesthetic by increasing the effect site concentration.[6] The CSF concentration of clonidine after epidural and intrathecal administration is similar after 2 hrs.[7] So, the greater sensory and motor blockade observed in epidural group in our study may have been because of the other two actions.

As expected after a neuraxial block, there was a drop in mean arterial pressure in all the three groups, Fig. 3. This drop due to sympathetic blockade occurred later in the epidural group compared to the other Two Groups. Mean blood pressure in Group EDBC was significantly higher than in Group ITB during the first 10 min. This is as expected because epidural anesthesia is slower to set in compared to intrathecal blockade. After 10 minutes there was no significant difference in blood pressure between Groups ITB and EDBC. This shows that the addition of clonidine does not negate the better hemodynamic profile in epidural route.

Between the intrathecal groups, addition of clonidine resulted in lower blood pressure at 2 min, 5 min and from 30 min onwards till 120 min. Between the clonidine groups, epidural group had significantly higher mean arterial pressure than intrathecal group at all-time intervals. Addition of clonidine to intrathecal or epidural space is known to cause hypotension but the degree of hypotension is more severe in the case of intrathecal clonidine.[7] Clonidine produces hemodynamic effects due to their action in the brain stem and peripheral blood vessels after systemic absorption as well as the direct inhibition of sympathetic preganglionic neurons in spinal chord.[8,9] Epidural clonidine rapidly penetrates into the intrathecal space with peak concentration in the CSF is observed at 30–60 min.[9] In our study, the peak reduction in mean arterial pressure in epidural clonidine group occurred at 60–90 minutes after the procedure, (Fig. 3).

However, in the immediate postoperative period (6 hours) there was no significant drop in blood pressure in all the Three Groups from the baseline. This makes clonidine a safe additive for neuraxial blockade if the intraoperative hypotension is managed well.

Heart rate was significantly lower in clonidine groups compared to control, Fig. 2. Intrathecal route caused lower heart rate than epidural route. Decrease in heart rate which occurred earlier in intrathecal group as compared to epidural clonidine. In 3 out of the 25 patients (12%) receiving intrathecal clonidine, there was a significant drop in heart rate which required the use of atropine, (Table 5).

The patients in groups receiving clonidine were more sedated than the control group, Fig. 3. Sedation to some extent with anxiolysis is a desirable property in a patient undergoing neuraxial blockade. Sedation commonly accompanies the use of clonidine for regional anesthesia due to its systemic absorption and action in the locus coeruleus in brain.[10] Contrary to expectation, cephalad migration in CSF producing delayed sedation does not happen. As a result, the amount of sedation should be regardless of the route of administration.[9] However, this was not what we observed. Intrathecal route produced more sedation due to clonidine than epidural group in our study, (Fig. 4). We could not find many studies comparing epidural clonidine to intrathecal clonidine to compare our observation.

Despite the increased sedation in clonidine groups, there was no statistically significant difference in the respiratory rate and the oxygen saturation between the three groups nor were these parameters significantly lower than the baseline in any of the groups. This reiterates the safety of neuraxial clonidine through neuraxial route. However, caution must be observed in patients who are prone for airway obstruction or when sedation is not desirable.

The 30 μg of clonidine used in the intrathecal group in our study might sound very small compared to the other studies where up to 150 μg were used.[1] However, despite a large number of trials, the optimum dose of intrathecal clonidine remains unknown.[11] Clonidine comes in 100–150 μg/ml preparations. 150 μg of clonidine will have a volume of 1–1.5 ml. When this volume is added to the local anesthetic, it dilutes the local anesthetic. The diminished action due to the dilution is made up by the addition of clonidine! Besides this, many studies comparing varying doses of intrathecal clonidine, topped up the final drug solution to a constant volume in order to ensure blinding between the groups. However, this is not how drug is administered in general practice. For example 2 ml of bupivacaine 0.5% heavy added with 50 μg of clonidine (0.3 ml of 150 μg/ml preparation) and made up to the final volume of 3.2 ml with saline (0.9 ml of saline)[10] is not same as the same preparation without saline. This factor should not be forgotten when applying the findings of these studies to practice. In our study, we did not use any saline to make up the volume. The total volume in the intrathecal groups were maintained at 3 ml by sacrificing the bupivacaine dose in the ITC Group. This factor should be kept in mind in attempting to replicate the finding we observed.

Epidural has certain advantages over intrathecal anesthesia in terms of the lesser chance of postdural puncture headache and the relatively slower onset of hypotension. However, its failure to consistently ensure adequate muscle relaxation makes it a less attractive choice for many anesthesiologists in lower abdominal surgeries. Our study reveals that this short coming of epidural can be circumvented by the addition of clonidine which makes it at par with intrathecal route with distinct advantages.

Conclusion

We observed that low-dose clonidine as an additive to bupivacaine in central neuraxial blocks improves the analgesic efficacy and block characteristics (onset of sensory level, muscle relaxation) but intrathecal clonidine was associated with more hemodynamic alterations. Addition of 75 μg Clonidine in epidural makes the onset comparable to intrathecal route, sensory and motor blockade longer while preserving the hemodynamic stability and maintaining optimum level of sedation.

Key Messages

Addition of clonidine to epidural bupivacaine makes it similar to intrathecal bupivacaine with better hemodynamic stability.

Source(s) of support: NIL

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Conflicting Interest (If present, give more details): NIL

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Comparison of Esmolol and Lidocaine for Attenuating Cardiovascular Stress Response to Direct Laryngoscopy and Endotracheal Intubation

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Abstract

Aims: Cardiovascular response was increase by direct laryngoscopy and endotracheal intubation. The aims of this study the hemodynamic change and compare the best among the two drugs in prevention of cardiovascular response to direct laryngoscopy and Endotracheal intubation. *Background:* This study also evaluates the efficacy of intravenous Esmolol (1 mg/kg) and intravenous Lidocaine (1.5 mg/kg) in attenuating cardiovascular stress response during direct laryngoscopy and endotracheal intubation in normotensive patients undergoing plan routine surgeries. *Materials and Methods:* This prospective study was conducted from June 2017 to May 2019 after informed consent was obtained from 120 patients. The study population consisted of ASA physical status I or II, and Mallampatti Score 1 or 2. All patients had enrolled our study are between the age of 20 years and 65 years and are scheduled for various elective surgical procedures. This study was a prospective, randomized, and clinical comparison study in rural tertiary referral health center. The Sample size for the study was 120 generated using a sample size calculator. The study participants were divided into Three Groups. A study patient (Group A) who was received intravenous esmolol 1 mg/kg two minutes before intubation. In Group B, who was received intravenous Lidocaine 1.5 mg/kg, two minutes before intubation and Group C, who received only prescribed premedication and listed in Control Group. All drugs were diluted in 10 milliliters of distilled water. All patients were monitored Heart Rate (HR), Systolic Blood Pressure (SBP), Diastolic Blood Pressure (DBP), and Mean Arterial Pressure (MAP) with respect to time. All patients were kept unaware of the drug injected to enable double-blinding. *Results:* Group C had statistically highly significant ($p \leq 0.0001$) value of HR, SBP, DBP, and MAP at all time interval after intubation when compared to Group B and Group C had statistically significant ($p \leq 0.05$) higher values of hemodynamic variable at all time interval when compared to Group A. *Conclusions:* Intravenous lidocaine (1.5 mg/kg) and esmolol (1 mg/kg) are effective agents in suppressing the hemodynamic response to laryngoscopy and intubation without any deleterious effect. Esmolol 1 mg/kg appears to be very effective and should be viewed as potential treatment strategy for attenuating hemodynamic changes during induction of anesthesia.

Keywords: Direct Laryngoscopy; Intubation; Esmolol; Lidocaine; Cardiovascular response.

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Introduction

Direct laryngoscopy and endotracheal intubation is not only an integral part of modern day balanced anesthesia but is also the most delicate phase in general anesthesia. Cardiovascular complications are one of the most common causes of anesthesia-related morbidity and mortality.[1] Direct laryngoscopy and endotracheal intubation frequently induces a cardiovascular stress response characterized by hypertension and tachycardia due to reflex sympathetic simulation. The response is transient occurring 30 sec after intubation and lasting for less than 10 min.[2] It may be well-tolerated in healthy people, but may be hazardous in patients with hypertension, tachycardia, myocardial infarction, and other complications.[3] Various pharmacological approaches have been used to attenuate the pressure responses to direct laryngoscopy and endotracheal intubation.[4] Direct laryngoscopy and endotracheal intubation causes mechanical stimulation to the oropharynx, laryngopharynx and the tracheobranchial tree causing increased reflex sympathetic activity and it's hence increase in blood pressure and heart rate, as reflected by an increase in the level of circulating catecholamine's and stress hormone. Direct laryngoscopy was a more potent stimulus to develop hypertension than the endotracheal intubation. The stimulation of the sympathetic system occurs as a result of the direct laryngoscope pressing on the base of tongue and lifting the epiglottis thus, stimulation the mechanoreceptors concentrated in the proximal portion of the trachea-bronchial tree. The stimulation of Sympathetic system lead to a transient rise in systolic arterial blood pressure of approximately 20–25 mm Hg and peaks up to 30–45 seconds after direct laryngoscopy. The degree of reflex response to laryngeal stimulation appears to vary with the depth of anesthesia, duration and difficulties encountered during endotracheal intubation as well as on patients dependent variables, including age and chronic diseases.

Expertise in establishing a definitive airway is not limited to being able to successfully intubation but also in a manner that does not significantly alters the vital parameters or increases the myocardial oxygen demand of patients. These techniques for attenuation of intubation related stress response depend on reduction input of stimuli or the blockage of the adrenergic responses. It can be achieved by minimizing the duration of direct laryngoscopy to less than 15 seconds, deep inhalation anesthesia, antihypertensive drugs, use large dose of opiates and alpha-2-agonists. Lidocaine is the oldest and most widely use drugs for the purpose of attenuating oropharyngeal and laryngopharyngeal reflexes.

Perioperative myocardial infarction is a leading cause of postoperative morbidity and mortality due to hypertension and tachycardia. Such anesthesia-related deaths could be reduced by controlling the hemodynamic changes that occur due to myocardial ischemia. There is increasing evidence that the control of the heart rate and blood pressure response to direct laryngoscopy and endotracheal intubation is essential in preventing adverse cardiovascular outcomes, as Rate Pressure Product (RPP) acts as an indicator of oxygen demand by the heart at the onset of ischemia,[9] there is therefore, a need for assessment in this direction as.

The present study, is designed to compare and select the best among the two drugs in prevention of cardiovascular response to direct laryngoscope and endotracheal intubation. To evaluate the efficacy of intravenous Esmolol (1 mg/kg) and intravenous Lidocaine (1.5 mg/kg) in attenuating stress response during direct laryngoscopy and endotracheal intubation, both above mentioned drugs are given two minutes before induction of general anesthesia. The hemodynamic status and electrocardiographic assessment are monitoring of all normotensive patients. Efforts are being made in practice safe anesthesia and reduce perioperative complication and mortality during anesthesia.

Aims and Objectives

Cardiovascular response was increase by direct laryngoscopy and endotracheal intubation. The aims of this study the hemodynamic change and compare the best among the two drugs in prevention of cardiovascular response to Direct laryngoscopy and Endotracheal intubation. This study also evaluates the efficacy of intravenous Esmolol (1 mg/kg) and intravenous Lidocaine (1.5 mg/kg) in attenuating cardiovascular stress response during direct laryngoscopy and endotracheal intubation in normotensive patients undergoing plan routine surgeries.

Materials and Methods

This prospective study was conducted from June 2017 to May 2019 after informed consent was obtained from 120 patients. The study population consisted of ASA physical status I or II, and Mallampatti Score 1 or 2. All patients had enrolled

our study are between the age of 20 years and 65 years and are scheduled for various elective surgical procedures.

Study Design

This study was a prospective, randomized, and clinical comparison study in rural tertiary referral health center. The Sample size for the study was 120 generated using a sample size calculator. The study participants were divided into Three Groups. A study patient (Group A) who was received intravenous esmolol 1 mg/kg two minutes before intubation. In Group B, who was received intravenous Lidocaine 1.5 mg/kg, two minutes before intubation and Group C, who received only prescribed premedication and listed in Control Group. All drugs were diluted in 10 milliliters of distilled water. All patients were monitored Heart Rate (HR), Systolic Blood Pressure (SBP), Diastolic Blood Pressure (DBP), and Mean Arterial Pressure (MAP) with respect to time. All patients were kept unaware of the drug injected to enable double-blinding.

Inclusion Criteria

For the study was ASA Class I or II, age range 20–65, oropharyngeal anatomy of Mallampati Class I or II and elective operation other than cardiac and neurosurgery performed under general anesthesia with direct laryngoscopy followed by endotracheal intubation.

Exclusion Criteria

For the study included patients who were morbidly obese, patients with cardiovascular disease, heart rate < 60 beats per minute (bpm), basal SBP < 100 mm Hg and other conditions such as bronchial asthma, diabetes mellitus, chronic kidney diseases, liver diseases, cardiovascular diseases, drug allergies, and total duration of Direct laryngoscopy was noted and in cases where duration exceeded 15 sec, and patients refuse was excluded from study.

Presurgical protocol

All selected patients underwent a preanesthetic evaluation with special consideration to elicit a history of hypertension, dyspnoea, chest-pain, cough, wheezing, convulsions, and diabetes mellitus as well as previous anesthetic history and drug sensitivity prior to surgery. Information collected also included weight, nutritional status, and airway assessment by the Mallampatti scoring system, a detailed examination of the respiratory, cardiovascular, and central nervous system. A preoperative routine investigations such as hemoglobin, hematocrit, total lymphocyte count, differential lymphocyte count, serum electrolytes, blood group/Rh typing, blood urea nitrogen, serum creatinine, fasting blood sugar, chest radiography, and electro-cardiogram in all patients. Patients were advised to fast the night prior to surgery. All selected patients were given uniformly premedication on tablet diazepam 5 mg at night before surgery and same dose at 6 a.m. on day of surgery with sip of water and with Inj. pethidine 1 mg /kg, Inj. Phenergan 0.5 mg/kg I.M. 45 min. before induction of general anesthesia.

Surgical protocol

All selected patient identification a short preoperative history was taken; clinical examination and routine investigations were rechecked in all patients. Study objective and procedure were explained to the participant's patients and a written informed consent was obtained from each participant patients.

In all the groups, after shifting the patients to Operation Theater base line parameters were recorded. All the patients were pre oxygenated for 3 minutes with 100% oxygen and intravenous access was secured and infusion of Ringer's lactate solution started. All patients were then shifted to the operating room after which routine noninvasive monitor was applied and vital signs monitored. The patient was preoxygenated for 3 minutes with 100% oxygen. All the patients were induced with 5 mg kg^{-1} IV thiopentone sodium in incremental doses until loss of eyelash reflex occurred, then Injection succinylcholine 1.5 mg/kg IV after check ventilation, followed up by administering the study drugs (normal saline, esmolol, or lidocaine) 2 min before laryngoscopy and intubation. The study drug was randomly allocated to patients in a double blinded manner. General anesthesia was maintained with oxygen 40%, Nitrous oxide 60%, Isoflorane, Vecuronium 0.10 mg/kg/ IV and supplemented as needed, Controlled ventilation was employed using Bain's circuit system. At the end of surgery action of muscles relaxant was reversed with Injection Neostigmine 0.05 mg/kg and Injection atropine 0.02 mg/kg/IV.

All parameter were monitored and recorded like HR, SBP, DBP, MAP, RPP (rate pressure product), SpO_2 (oxygen saturation), and ECG (electrocardiogram) before induction (Basal) and after tracheal intubation at 1, 3, 5,10, 15 and 30 minutes for the purpose of this study. No manipulation like painting and draping the area of operation was allowed till 10 min after the study drug administration.

Parameters and statistical analysis

Summary statistics of patient gender, age, and weight for all three groups were reported as means ± standard deviation. HR, SBP, DBP, and MAP were recorded before induction (Baseline), after tracheal intubation at 1, 3, 5, 10, 15, and 30 minutes during monitoring. From the data RPP was calculated by multiplying heart rate with systolic blood pressure. Patients were also observed for complications like hypotension, hypertension, arrhythmias, and hypoxemia. Statistical analysis was done by student *t*-test and *P* - values were calculated. Hemodynamic variables were represented by mean ± SD. ANOVA with repeated measures was used to compare the changes in HR, MAP, and RP*P* values. Bonferroni›s multiple comparison tests were applied to evaluate intragroup comparisons. The statistical package SPSS® 17.0 and Graph pad prism 5 was used. $p < 0.05$, $p < 0.001$ were considered significant and highly significant, respectively, for the study.

Results

The present study is designed to compare and select the best among the two drugs in prevention of cardiovascular response to direct laryngoscope and endotracheal intubation. To evaluate the efficacy of intravenous Esmolol (1 mg/kg) and intravenous Lidocaine (1.5 mg/kg) in attenuating stress response during direct laryngoscopy and endotracheal intubation, both above mentioned drugs are given two minutes before induction of general anesthesia. A study patient (Group A) who was received intravenous esmolol 1 mg/kg two minutes before intubation. In Group B, who was received intravenous Lidocaine 1.5 mg/kg, two minutes before intubation and Group C, who received only prescribed premedication and listed in control group. All drugs were diluted in 10 milliliters of distilled water. All patients were monitored Heart Rate (HR), Systolic Blood Pressure (SBP), Diastolic Blood Bressure (DBP), and Mean Arterial Pressure (MAP) with respect to time. All patients were kept unaware of the drug Injected to enable double-blinding.

All the demographic profiles in the Group C-control, Group-B-lidocaine, and Group-A-esmolol were comparable shown in Table 1. The mean age of patients in group A is 34.15 years. There was no significant difference in mean age among the groups ($p < 0.05$). In Group A and Group C there were 14 male and 26 female and Group B there were 18 male and 22 female patients. Overall there was no significant difference in the sex distribution of the Groups ($p < 0.05$). In Groups A and B 36 patients were of ASA Grade 1 and 4 patients were Grade ASA 2. In Group C-32 and 8 patients belonged to ASA Grades 1 and 2 respectively ($p < 0.05$).

An increase in HR, MAP, and RPP from the base line and maximum at 1 min after intubation was observed in Group-C, however in the Groups-L and E there was no significant variation of HR, MAP, and RPP from the base line after 1 min of intubation, (Table 2).

Table 1: Distribution of patient's demographic profile

Parameters		Group A (Esmolol)	Group B (Lidocaine)	Group C (Control)	*p* - Value (A/B, A/C, B/C)
Age		34.15 ± 7.3	34.05 ± 9.63	36.8 ± 9.8	0.97, 0.34, 0.38
Sex	Male	14	18	14	0.754
	Female	26	22	26	(Overall)
ASA	1	36	36	32	0.562
	11	4	4	8	(Overall)

($p < 0.05$ is significant)

Table 2: Baseline hemodynamic parameters

Parameters	Group A (Esmolol)	Group B (Lidocaine)	Group C (Control)	*p* - Value (A/B, A/C, B/C)
HR	92 ± 11	97 ± 16	90 ± 12	0.2, 0.28, 0.15
SBP	131 ± 5	134 ± 6	130 ± 12	0.1, 0.53, 0.11
DBP	83 ± 12	86 ± 5	82 ± 9	0.32, 0.32, 0.31
MAP	99 ± 10	100 ± 5	97 ± 9	0.17, 0.45, 0.19
RPP	11641 ± 1663	12731 ± 2100	11751 ± 2269	0.13, 0.52, 0.17
Spo_2	100 ± 1	100 ± 1	100 ± 1	0.41, 0.19, 0.62

Data are presented as means standard deviation. HR = Heart Rates, SBP = Systolic Blood Pressure, DBP = Diastolic Blood Pressure, MAP = Mean Arterial Pressure, RPP = Rate Pressure Product. ($p < 0.05$ is significant)

Table 3: Hemodynamic parameters after administrating the drugs (esmolol and lidocaine) two minutes before and during induction

Parameters of study drugs	Group A (Esmolol)		Group B (Lidocaine)		Group C (Control)		*p* - Value (A/B, A/C, B/C)	
	2 Minutes before induction	During induction	2 Minutes before induction	During Induction	2 Minutes before induction	During Induction	2 Minutes before induction	During induction
HR	78 ± 10	80 ± 12	94 ± 18	95 ± 13	94 ±14	98 ± 13	< 0.001, < 0.001, < 87	< 0.001, < 0.001, 0.42
SBP	122 ± 7	122 ± 9	131 ± 5	128 ± 8	129 ± 11	125 ± 11	< 0.001, 0.03, 0.48	0.043,0.38 0.38
DBP	77 ± 9	77 ± 10	85 ± 6	85 ± 8	82 ± 10	80 ± 15	< 0.001, 0.11, 0.19	0.008, 0.445, 0.2
MAP	92 ± 7	92 ± 8	101 ± 5	100 ± 7	97 ± 9	94±13	< 0.001, 0.05, 0.12	0.002, 0.53,0.08
RPP	9475 ± 1545	9791 ± 1980	12292 ± 2086	12177 ± 1991	12071 ± 2350	12358 ± 2259	< 0.001,< 0.001, 0.75	0.001,< 0.001,0.79
SpO_2	99 ± 1	99 ± 1	99 ± 1	99 ± 1	99 ± 1	99 ± 1	0.28, 0.23, 0.2	0.4,0.08,0.09

Data are presented as means standard deviation. HR = Heart Rates, SBP = Systolic Blood Pressure, DBP = Diastolic Blood Pressure, MAP = Mean Arterial Pressure, RPP = Rate Pressure Product. ($p < 0.05$ is significant)

Table 4: Hemodynamic parameters immediately after Intubation

Intubation	Group A (Esmolol)	Group B (Lidocaine)	Group C (Control)	p - Value (A/B, A/C, B/C)
Heart Rate	98 ± 11	116 ± 15	129 ± 14	< 0.001, < 0.001, 0.01
SBP	140 ± 5	149 ± 9	161 ± 16	< 0.001, <0.001, 0.01
DBP	88 ± 11	97 ± 8	105 ± 12	0.006. < 0.001, 0.01
MAP	106 ± 8	114 ± 7	123 ± 12	< 0.001, < 0.001, 0.022
RPP	13680 ± 1770	17483 ± 2788	20801 ± 3625	< 0.001, < 0.001, 0.01
SpO_2	99 ± 1	99 ± 1	99 ± 1	0.83, 0.12, 0.14

Data are presented as means standard deviation. SBP = Systolic Blood Pressure, DBP = Diastolic Blood Pressure, MAP = Mean Arterial Pressure, RPP = Rate Pressure Product. ($p < 0.05$ is significant)

Table 5-A: Percentage change in Hemodynamic parameters, Percentage change in Heart Rate (HR)

Percetage change in Heart Rate	Baseline *Vs* Study drugs (*p* - Value)	Baseline *Vs* Induction (*p* - Value)	Baseline *Vs* Intubation (*p* - Value)
Group A (Esmolol)	↓ 9.7 (0.023 A/B)	↓ 7.5 (0.102 A/B)	↑ 13.71 (0.112 A/C)
Group B (Lidocaine)	↓ 2.4 (<0.001 A/C)	↓ 0.86 (< 0.001 A/C)	↑ 21.53 (< 0.001 A/C)
Group C (Control)	↑ 3.44 (0.008 B/C)	↑ 9.23 (0.003 B/C)	↑ 44 (< 0.001 B/C)

($p < 0.05$ is significant)

All hemodynamic parameters were recorded at specified intervals in each of the group and tabulated as follows:

p - value between Group A and B, A and C, and B and C were more than 0.05, i.e. there were no significant difference in the hemodynamic parameters of patients between any two groups at the baseline. SpO_2 was similar among all the groups at the intervals (Table 3).

A Significant decrease in heat rate, systolic blood pressure, diastolic blood pressure and mean arterial pressure was noted after administration of esmolol as compared to lidocaine ($p < 0.05$). ON calculation, rate pressure product was found to be significantly low in Esmolol Group as compared to Lidocaine Group ($p < 0.05$). There was a significant fall in heart rate, SBP, RPP ($p < 0.05$) in Esmolol Group as compared to control group.

All the vital parameters noted were significantly lower in the Esmolol Group compared to Lidocaine Group ($p < 0.05$) and heart rate and rate pressure product ($p < 0.05$) was statistical significance decrease as compared to the control group. No statistical significance was found in parameters with compare to Control Group ($p < 0.05$).

All the parameters were increase at intubation in all three groups. The percentage increases was significantly higher in the control group as compared to esmolol and Lidocaine Groups ($p < 0.05$). All the parameters were increase minimum in Esmolol Group, shown as in Table 4. In Lidocaine Group, all the parameters were significantly higher than in Esmolol Group (< 0.05).

We noted a decrease in heart rate after giving the study drugs and after induction in groups receiving Esmolol (Group A) and Lidocaine (Group B). After

Table 5-B: Percentage change in Systolic Blood Pressure (SBP)

Parameters	Baseline *Vs* Study drugs (*p* - Value)	Baseline *Vs* Induction (*p* - Value)	Baseline *Vs* Intubation (*p* - Value)
Group A (Esmolol)	↓ 7.14 (0.009 A/B)	↓ 6.7 (0.333 A/B)	↑ 6.7 (0.048 A/B)
Group B (Lidocaine)	↓ 2.6 (< 0.001 A/C)	↓ 4.55 (0.048 A/C)	↑ 11 (< 0.001 A/C)
Group C (Control)	↓ 0.56 (0.150 B/C)	↓ 3.16 (0.429 B/C)	↑ 24 (< 0.001 B/C)

(p < 0.05 is significant)

Table 5-C: Percentage change in Diastolic Blood Pressure (DBP)

Parameters	Baseline *Vs* Study drugs (*p* - Value)	Baseline *Vs* Induction (*p* - Value)	Baseline *Vs* Intubation (*p* - Value)
Group A (Esmolol)	↓ 6.9 (0.004 A/B)	↓ 6.97 (0.034 A/B)	↑ 7.28 (0.128A/B)
Group B (Lidocaine)	↓ 0.87 (<0.001 A/C)	↓ 1.39 (0.026 A/C)	↑ 13 (<0.001 A/C)
Group C (Control)	↑ 2.33 (0.08 B/C)	↓ 0.27 (0.703 B/C)	↑ 31 (<0.001 B/C)

(p < 0.05 is significant)

Table 5-D: Percentage change in Mean Arterial Pressure (MAP)

Parameters	Baseline *Vs* Study drugs (*p* - Value)	Baseline *Vs* Induction (*p* - Value)	Baseline *Vs* Intubation (*p* - Value)
Group A (Esmolol)	↓ 6.5 (0.006 A/B)	↓ 6.4 (0.066 A/B)	↑ 7.5 (0.098 A/B)
Group B (Lidocaine)	↓ 1.3 (< 0.001 A/C)	↓ 2.1 (0.083 A/C)	↑ 12 (< 0.001 A/C)
Group C (Control)	↑ 0.6 (0.10 B/C)	↓ 2.4 (0.878 B/C)	↑ 28 (< 0.001 B/C)

(p < 0.05 is significant)

Table 5-E: Percentage change in Rate Pressure Product (RPP = HR × SBP)

Parameters	Baseline *Vs* Study drugs (*p* - Value)	Baseline *Vs* Induction (*p* - Value)	Baseline *Vs* Intubation (*p* - Value)
Group A (Esmolol)	↓ 15.66 (0.007 A/B)	↓ 13.0 (0.069 A/B)	↑ 22 (0.005 A/B)
Group B (Lidocaine)	↓ 2.28 (< 0.001 A/C)	↓ 2.64 (< 0.001 A/C)	↑ 39 (< 0.001 A/C)
Group C (Control)	↑ 3.0 (0.194 B/C)	↑5.67 (0.082 B/C)	↑ 79 (< 0.001 B/C)

(p < 0.05 is significant)

administration of study drugs, both Esmolol and Lidocaine Groups showed significant decreases in heart rate, with fall in esmolol group being significantly more than in lidocaine group. In the control group there was a significant increase in heart rate after induction as compared to study to study drugs. After intubation all groups showed an increase in heart rate but the less increase in esmolol group as comparable between Esmolol (13.7%), Lidocaine (21.53%) and Control group (44%) but each of these groups showed a statistically significant difference from control group, shown in (Table 5-A).

Systolic blood pressure decreased after administration of study drugs in the entire group, but significantly maximum fall systolic blood pressure was seen after Esmolol (7.14%). After induction fall in systolic blood pressure was comparable between esmolol and lidocaine group and lidocaine and control groups, but significant fall in systolic blood pressure was seen in esmolol group as compared to control group. After intubation all patients had a rise in systolic blood pressure but Control Group (24%) has highly significant as compared to study drugs. The rise in systolic blood pressure was significantly in Esmolol Group (6.7%) as compared to Lidocaine Group (11%), shown in (Table 5-B).

Diastolic blood pressure decreased significantly after administration of study drugs as compared to Control Group. Esmolol showed significantly highest fall among the Group (6.9%). Whereas no statistically significant drop diastolic blood pressure was seen in Lidocaine Group as compared to Control Group. After induction Diastolic Blood Pressure (DBP) fall in the entire group; Esmolol Group showed significant DBP drop as compared to the Lidocaine and Control Group, though no significant difference in DBP was seen in control and Lidocaine Group. After intubation the entire three groups showed increase in DBP, but this rise was comparable between Esmolol (7.28%) and Lidocaine (13%) Groups and each of these groups showed statistically significant lower rise in DBP as compared to Control Group (31%), shown in (Table 5-C).

Mean arterial pressure showed significant drop after administration of Esmolol (6.5%) as compared to Lidocaine and Control Groups, though it increased in the control group. After induction, the MAP fell in all groups but this was statistically insignificant even after Esmolol (6.4%) administration. After intubation, MAP was increased in the entire group, but significantly higher in Control Group (28%) as compared to study group, shown in (Table 5-D).

Increase in rate pressure product after intubation was significant in all the groups but it was significantly lower in Esmolol Group (22%) as compared to Lidocaine (39%) and Controls (79%) Groups. Lidocaine Group showed significantly lower rise in RRP as compared to Control Group, shown in (Table 5-E).

All the parameters were recorded in 1 min., 3 min., 5 min., 10 min., 15 min., and 30 minute after intubation they were significantly lower in the esmolol group as compared to the lidocaine and control groups. Heart rate and rate pressure product were significantly lower in esmolol compared with lidocaine and control groups ($p < 0.05$), (Table 6).

In Groups C, B, and A maximum increase in mean heart rate over the baseline values were 90.00 ± 12, 97.00 ± 16, and 92.00 ± 11, respectively, and at 1 minute was 119.00 ± 14, 110.00 ± 16, and 91 ± 12 after intubation, respectively. The difference between means from baseline value and 1 minute were 30.00 bpm, 13.00 bpm, and 0.40 bpm in Groups-C, B, and A, respectively. The mean difference in the heart rate between Groups C-B, C-A, and B-A recorded at 1 minute were 7.00, 29.60, and 12.60 bpm [$p < 0.0001$], (Table 6).

In all Three Groups the vitals remained attenuated for 5 min after intubation; however, the vitals returned to baseline values after 15 to 30 minute. Control Group patients undergoing laryngoscopy and intubation showed an incidence of 8% ventricular ectopics and 5% dropped beats however no such findings were recorded in the lidocaine and esmolol groups.

Table 5-F: Percentage change in SpO_2

Parameters	Baseline *Vs* Study Drugs (*p* - Value)	Baseline *Vs* Induction (*p* - Value)	Baseline *Vs* Intubation (*p* - Value)
Group A (Esmolol)	↓ 0.5	↓ 0.02	↓ 0.24
Group B (Lidocaine)	↓ 0.35	↓ 0.5	↓ 0.5
Group C (Control)	↓ 1.0	↓ 1.0	↓ 1.26

Over all, there was no significant change in the peripheral oxygen saturation at any time in any of the groups p - value was between any two groups < 0.05, (Table 5-F)

Table 6: Hemodynamic change were significantly lower in esmolol compared with lidocaine and control groups.

Parameter	Basal	1 Min. After Intubation	3 Min. After Intubation	5 Min. After Intubation	10 Min. After Intubation	15 Min. After Intubation	30 Min. After Intubation	p Value
A. heart Rate								
1. Group A. (Esmolol)	91 ± 11	91 ± 12	88 ± 10	84 ± 14	77 ± 13	75 ± 9	75 ± 6	<0.001
2. Group B. (Lidocaine)	97 ± 16	110 ± 16	102 ± 13	97 ± 14	91 ± 11	89 ± 13	86 ± 11	<0.001
3. Group C. (control)	90 ± 12	119 ± 14	115 ± 14	108 ± 16	104 ± 15	101 ± 15	96 ± 13	<0.001
B. SBP								
1. Group A. (Esmolol)	131 ± 5	128 ± 10	123 ± 10	121 ± 10	123 ± 10	125 ± 9	126 ± 9	<0.001
2. Group B. (Lidocaine)	134 ± 6	144 ± 12	139 ± 9	133 ± 12	134 ± 9	132 ± 9	130 ± 23	<0.001
3. Group C. (control)	130 ± 12	147 ± 15	138 ± 12	135 ± 14	134 ± 11	131 ± 11	130 ± 10	<0.001
C. DBP								
1. Group A. (Esmolol)	83 ± 12	95 ± 10	83 ± 9	83 ± 10	83 ± 11	83 ± 10	83 ± 12	<0.001
2. Group B. (Lidocaine)	86 ± 5	99 ± 10	94 ± 8	91 ± 9	92 ± 10	89 ± 8	88 ± 10	<0.001
3. Group C. (control)	82 ± 9	95 ± 9	92 ± 11	89 ± 10	91 ± 10	86 ± 10	83 ± 10	<0.001
D. MAP								
1. Group A. (Esmolol)	99 ± 10	100 ± 10	96 ± 8	95 ± 9	97 ± 10	97 ± 9	97 ± 10	<0.001
2. Group B. (Lidocaine)	100 ± 5	114 ± 10	109 ± 6	105 ± 9	106 ± 9	103 ± 8	104 ± 9	<0.001
3. Group C. (control)	970 ± 9	112 ± 11	107 ± 10	104 ± 10	105 ± 9	101 ± 9	99 ± 9	<0.001
E. RPP								
1. Group A. (Esmolol)	11641 ± 1663	11765 ± 2224	11013 ± 1839	10290 ± 2205	9645 ± 1709	9539 ± 1394	9571 ± 1229	<0.001
2. Group B. (Lidocaine)	12731 ± 2160	15891 ± 2482	14115 ± 1677	12840 ± 2025	12204 ± 1576	11744 ± 1948	11642 ± 1877	<0.001
3. Group C. (control)	11751 ± 2269	17577 ± 2974	15908 ± 2610	14632 ± 2930	13943 ± 2649	13233 ± 2370	12425 ± 1941	<0.001
Spo2								
1. Group A. (Esmolol)	100 ± 1	99 ± 1	99 ± 1	99 ± 1	99 ± 1	99 ± 1	99 ± 1	<0.001
2. Group B. (Lidocaine)	100 ± 1	99 ± 1	99 ± 1	99 ± 1	99 ± 1	99 ± 1	99 ± 1	<0.001
3. Group C. (control)	100 ± 1	99 ± 1	99 ± 1	99 ± 1	99 ± 1	99 ± 1	99 ± 1	<0.001

Data are presented as means standered deviation. SBP = Systolic Blood Pressure, DBP = Diastolic Blood Pressure, MAP = Mean Arterial Pressure, RPP = Rate Pressure Product. ($p < 0.05$ is significant)

Discussion

So, far we have come to know that direct laryngoscopy and intubation evokes stress response in all individuals, and various study have come up to establish one maneuver or one drug over the other for prevention of this response. King et al. described the hemodynamic stress response due to laryngoscope and intubation more than 60 years ago.[23] Orotracheal intubation consists of two phases: Direct Laryngoscopy and passing of endotracheal tube through the vocal cords and trachea.[24] It has been seen in various studies that increase in HR occurs during endotracheal intubation whereas the greatest increase in BP occurs during laryngoscopy.[25] Both sympathetic and parasympathetic element has been found as a mechanism to this intubation response. The sympathetic response is a polysynaptic pathway due to glossopharyngeal and vagus nerve forming the afferent arc to the sympathetic nervous system through the brain stem and spinal cord causing increased firing of the cardio-accelerator fibers and release of adrenergic mediators including norepinephrine, epinephrine, and vasopressin. The net effect of this autonomic surge is an increased BP, HR, pulmonary artery wedge pressure, and decreased ejection fraction. On the other hand, the parasympathetic reflex is monosynaptic, more common in children but can occur in some adults. The reflex is mediated by the increased vagal tone at the SA node.[26] Lidocaine is the oldest among this list of drugs and esmolol is a relatively new drug. The present study was designed to compare the efficacy of these two drugs in maintaining the prelaryngoscopy and intubation hemodynamic after these most critical events during general anesthesia.

Lidocaine is a sodium channel blocker in the nerve cell membrane and on the myocardial cell membrane. This explains its local anesthetic. Myocardial depressant, Peripheral Vasodilator,[16] and antiarrhythmic action, and is also the proposed mechanism for its role in prevention of adverse effects of the stress response generated upon direct laryngoscope and intubation[17-19].

Beta-blockers are generally less effective in hypertensive as a result of the tendency toward a low-renin state and with increased peripheral resistance. Higher doses of beta-blockers are therefore, required to achieve target blood pressures.[10] Esmolol is an ultra short acting $ß_1$-blocker, its possesses several properties which make it a valuable agent to obtund the cardiovascular response by prevent the hemodynamic change. Firstly, it is a cardio selective agent, and secondly it has ultra short duration of action (9 min)[11] and finally, significant drug interaction with commonly used anesthetics has not been reported.[12] Korpinen *et al*. (1998) reported that the administration of esmolol bolus 2 mg kg^{-1} IV 2 min before laryngoscopy and intubation suppressed the increase in the heart rate rather than arterial blood pressures.[11] Bostana and Eroglu (2012) reported that IV esmolol in dose of 1 mg kg^{-1} before intubation was effective in suppressing the heart rate and arterial blood pressure.[14] Kumar *et al*. (2003) have also claimed optimal results while using higher doses of esmolol in Asian population, i.e., 2 mg kg^{-1} without any incidence of unplanned hypotension or bradycardia. However, no consensus has been reached regarding the optimum dose and timing of its delivery.[15] The hemodynamic changes in HR, MAP, and RPP from baseline values 1 min after tracheal intubation, in esmolol group were highly significantly less than those in lidocaine. Our failure to detect any significant effect of lidocaine as compared to esmolol on stress response could be due to the fact that we performed this study in patients without heart disease while Stoelting *et al*. included patients with heart disease and reported a favorable response.[20] Studies have shown that there is increased incidence of myocardial infarction when intraoperative heart rates are more than 110 beats min^{-1}.[21] In our study, none of the patients in study groups showed heart rate > 110 beats min^{-1}. Heart rate, Systolic blood pressure and Rate Pressure Product (RPP) found fall after intubation.[27] Blood Pressure and Heart rate was found decrease in patients pretreated with intravenous lidocaine prior to induction and overall decreases in cardiovascular complications.[28] RPP is a good estimate of myocardial oxygen requirement. The RPP levels close to 20,000 are normally associated with angina and myocardial ischemia.[22] RPP 1 min after intubation remained less than 20,000 in study drug groups. This finding confirms the cardio-protective effect of study drugs during laryngoscopy and intubation. Rate Pressure Product (RPP) was significantly lower after intubation in esmolol group as compared to lidocaine group with same dose of both intravenous lidocaine and esmolol are 1.5 mg/kg. These results are similar to the finding of our study; we have also found that the maximal difference in percent rise of parameters when esmolol was compared to lidocaine or the control group was in term of SBP and RPP, Table 5-E.[29] Lidocaine and Esmolol, both in the dose of 2 mg/kg intravenous showed that both were efficacious in attenuation of moderate

hemodynamic response to intubation,[30] which are same in our study. Intravenous lidocaine (1.5 mg/kg) and esmolol (2 mg/kg) are effective agents in suppressing the hemodynamic response to laryngoscopy and intubation without any deleterious effect.[31] In conclusion, the present our data suggest that lidocaine 1.5 mg kg^{-1} when injected 2 min before intubation can blunt the cardiovascular responses to laryngoscopy and tracheal intubation successfully. However, the prophylactic therapy with esmolol 1 mg kg^{-1} when injected 2 min before intubation is significantly more effective than lidocaine in suppressing hemodynamic changes to laryngoscopy and tracheal intubation in normotensive patients. The dosage and timing of administration of drugs are important factors that determine whether they will have beneficial effect on the laryngoscopy and tracheal intubation, therefore further research is necessary to elucidate the effects of different doses of esmolol in black population.

Conclusion

Intravenous lidocaine (1.5 mg/kg) and esmolol (1 mg/kg) are effective agents in suppressing the hemodynamic response to laryngoscopy and intubation without any deleterious effect. Esmolol 1 mg/kg appears to be very effective and should be viewed as potential treatment strategy for attenuating hemodynamic changes during induction of anesthesia.

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Conflict of Interest None declared.

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Study of Intraperitoneal Bupivacaine-Tramadol with Bupivacaine-Magnesium Sulphate for Pain Relief after Laparoscopic Cholecystectomy

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Abstract

Introduction: Cholecystectomy is surgical removal of the gall bladder. Intraperitoneal administration of other drugs along with the local anesthetics will reduce the consumption of supplementary postoperative analgesic medication. *Aims:* To compare between $MgSO_4$ and Tramadol when used along with Intraperitoneal Local Anesthetics (IPLA) by instillation of drug for postoperative pain relief in terms of Visual Analog Scores. *Materials and Methods:* Prospective analytical study in Sixty adult patients of Class I and Class II as per American Society of Anesthesiology (ASA) of either sex were posted for elective laparoscopic cholecystectomy. These patients participated in prospective open randomized study for postoperative pain relief after laparoscopic cholecystectomy. *Results:* Bupivacaine along with Magnesium sulphate instillation significantly reduced VAS pain scores over 24 hrs. Prolonged duration of analgesia was noted with Magnesium sulphate. Total analgesic required over 24 hrs was less with Magnesium use. No signs of drug allergy and toxicity were observed. *Conclusions:* Bupivacaine and Magnesium sulphate are safe and efficacious in reducing postoperative pain following intraperitoneal instillation in laparoscopic surgeries. Thus, the intraperitoneal instillation of Bupivacaine-$MgSO_4$ combination provides good analgesia in first 24 hours after surgery, with longer duration of pain free period.

Keywords: Cholecystectomy; Intraperitoneal Bupivacaine; Tramadol.

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Introduction

Cholecystectomy is surgical removal of the gallbladder. It took a significant amount of time before the risk of the procedure was low enough to justify its routine use. The benefits of a minimally invasive procedure were joined with a century long proven treatment of gallbladder disease. Laparoscopy involves insufflation of the abdomen by gas, so, that the endoscope (usually 6–10 mm in diameter) can view the intraabdominal contents without being in direct contact with the viscera or tissues. It is widely practiced now-a-days, because of its potential benefits as compared to conventional open cholecystectomy. Diminished surgical trauma, associated low morbidity, net low-cost of procedure has made laparoscopy, a standard technique for removal of the diseased gallbladder.

Postoperative pain is reduced in laparoscopic, as compared with open traditional cholecystectomy,

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but effective analgesic treatment after LC has remained a clinical challenge.[1] Patients complain more of a parietal pain after open cholecystectomy, whereas after Laparoscopy mostly visceral pain results. In 17–41% of the patients, pain is the main reason for staying overnight in the hospital on the day of surgery.[2] Postoperative pain associated with laparoscopic cholecystectomy, although less severe and of shorter duration than that after open cholecystectomy, is still a dominating complaint and the primary reason for prolonged convalescence after LC.[3] Characteristically, overall pain after LC carries a high interindividual variability in intensity and duration and is largely unpredictable.

Visceral pain accounts for most of the discomfort experienced in the early postoperative period. Its intensity quickly decreases after the first 24 hours postoperatively. Parietal pain is less intense than visceral pain, owing to the small abdominal incisions and the limited damage to the abdominal wall. Shoulder-tip pain, insignificant during the first postoperative hours, increases thereafter, to become the main complaint on the second day postoperatively. Optimal management of postoperative pain has a potential for shortening of hospital stay and for speeding up of recovery. There are varieties of anesthetic techniques available to control postoperative pain after LC. Administration of intraperitoneal local anesthetic (LA), either during or after surgery, is a common practice by many surgeons as a method of reducing postoperative pain. This technique was first evaluated in patients undergoing gynecological laparoscopic surgery.[4] Injection of LA subcutaneously into the incisional site, into the periportal fascia, and into the muscle and parietal peritoneum to provide pain relief after LC has been documented in the literature. LA can be injected into the peritoneum through the ports created either before the start of surgery or prior to closure. It may be injected over the visceral peritoneum through the trocar site or into the surgical bed after the excision of the organ or under the diaphragm. Injection of subdiaphragmatic LA is given to decrease the incidence of shoulder pain.

Intraperitoneal administration of other drugs along with the local anesthetics will reduce the consumption of supplementary postoperative analgesic medication. Administration of local anesthetic in combination with opioids, steroids dexmedetomidine, ketamine, NSAIDs, tramadol, $MgSO_4$ for the relief of postoperative pain, has already been reported after laparoscopic cholecystectomy.

Effectiveness of local anesthetics, instilled intraperitoneally, solely or mixed with other drugs, has been shown in a number of studies on laparoscopic cholecystectomy, but there is no agreement regarding the dose, concentration, site and manner of administration. Therefore, in our study an effort has been made to compare primarily the antinociceptive effects of $MgSO_4$ with bupivacaine to tramadol with bupivacaine.

Materials and Methods

Prospective analytical studybetween March 2017 and August 2018 conducted in Osmania General Hospital. Sixty adult patients of Class I and Class II as per American Society of Anesthesiology (ASA) of either sex were posted for elective laparoscopic cholecystectomy. These patients participated in prospective open randomized study for postoperative pain relief after laparoscopic cholecystectomy. After the informed and written consent was obtained, these patients were randomly allocated using computer generated table to one of the Two Groups:

Group BT (30 ml of 0.25% bupivacaine along with 100 mg tramadol) (30 patients)

Group BM (30 ml of 0.25% bupivacaine along with 50 mg/kg of $MgSO_4$) (30 patients)

Dose of bupivacaine not exceeding 2.0 mg/kg BW.

Inclusion Criteria

Age 18–65 years**,** Elective Casesand ASA-I & ASA-II patients.

Exclusion Criteria

Patients with history of allergies to bupivacaine, $MgSO_4$ or tramadol, with acute cholecystitis, Emergency and urgency for surgery, Patient known for hypomagnesemia or $MgSO_4$, Chronic alcoholism, heart block, renal failure and cognitive impairment or mental retardation, progressive degenerative disorders of CNS, Patients with peritoneal drain after surgery.

A thorough examination of the patient was done which included a detailed history, general and systemic examination. The BMI of all the patients was noted. The baseline investigations were done and Other investigations were done as per individual patient assessment and requirement.

All the patients underwent thorough preanesthetic evaluation one day prior to surgery. Clinical assessment with detailed history was taken. All

systems were examined including the airway. The procedure to be carried out was explained and the patients were made familiar with Visual Analog Scale (0–10 cm; 0- no pain and 10- the worst possible pain) and its employment in pain assessment. All the patients were kept nil peroral as perthe fasting guidelines. All of the received Tab. Alprazolam 0.25 mg orally the night before surgery and Tab. Ranitidine 150 mg the night before and on the morning of surgery. A written informed consent was taken.

After confirming adequate starvation for 8 hours, written informed consent, verifying PAC, patient was attached for continuous electrocardiogram monitoring. Preoperative Heart Rate (HR), systolic and diastolic blood pressure and respiratory rate were recorded 5 min before induction (i.e., baseline parameters). An intravenous line was secured and Ringer lactate infusion started.

The patients were premedicated withInjection Glycopyrrolate 0.005 mg/kg IV, Injection Ranitidine 1mg/kg IV, Injection Ondansetron 0.1 mg/kg IV and Injection Midazolam 0.05 mg/kg IV.

Injection Fentanyl 2 mcg/kg IVwas administered for intraoperative analgesia. Anesthesia was induced with intravenous (IV) lignocaine 1.0 mg/kg, propofol 2.0 mg/kg. IV vecuronium 0.1 mg/kg was administered to facilitate endotracheal intubation. Intraoperative anesthesia was maintained with O_2: N_2O (40:60), sevoflurane 1–2%, closed circuit with controlled ventilation. Intermittent doses of injection Vecuronium IV was administered for muscle relaxation. The patients were monitored intraoperatively for pulse, blood pressure, oxygen saturation, and end tidal CO_2, intraabdominal pressure, urine output and blood loss. All the patients received Ringer Lactate at 5 ml/kg/hr for intraoperative fluid requirements. Intraabdominal pressure was maintained between 12–14 mmHg and end tidal CO_2 was maintained between 30–40 mmHg during the period of surgery.

Operating Technique

Position

Patient with Supine with 15° head up and 15° tilt to left.

Creating Pneumo-peritonium

Small infraumbilical incision about 1cm is taken. Then, blunt tip veress needle with safety valve is introduced with the needle pointing towards the sacral promontory. Confirmation of intraperitoneal location of the needle tip is made by the saline drop test and CO_2 insufflations is started. Maximum pressure is set at around 12 mmHg and initial flow rate around 1:2 lit/min. Later the rate was increased to 4–6 lit/min. The machine has automatic shut off the gas, if the pressure rises above the maximum pressure set.

Primary port placement

It was introduced blindly by a 10 mm trocar with a finger guard, after lifting the abdominal wall. Through this a 10 mm telescope was introduced and a peritoneoscopy was done. The other ports were placed as shown below under vision.

Dissection of the triangle of calot

Dissection should be close to gall bladder and to the right of the hepatic duct. Adhesiolysis is done taking care of surrounding structures. Cystic duct and cystic artery are clearly dissected and then clipped. The cystic artery should be doubly clipped.

Dissection of gall bladder from its bed

During dissection, gentle traction is applied to the gall bladder, moving it from side to side so that loose areolar tissue can be demonstrated. With a hook or spatula, the dissection was carried down the under surface of the gall bladder. The fundic attachment should be preserved till the end as it helps in the elevation of the gall bladder and the fossa can be inspected for any ooze or blood or bile. Before final detachment of the gallbladder, the cystic artery and duct stumps are reexamined, and a through wash given. Then the gall bladder was detached and held over the liver.

Extraction of gall bladder

Through the epigastric port, gall bladder was held with an Ellis forceps at its neck. Care was taken to avoid spillage of stone or billiary sludge. If the gallbladder was tense, it was decompressed by suction and opened to remove the stone. The camera is withdrawn last under vision after final inspection. A drain if required is kept through one of the 5 mm ports. The ports are closed with vicryl and skin stitches. Light dressings are applied.

Instillation of study drugs

After the gall bladder was extracted, 15^0 of head up and left tilt position was removed and CO_2 was stopped, 15^0 of head low and right till position was given. A preaspirated syringe of 30 ml of study drug was instilled in the same position over the gall bladder fossa and right subdiaphragmatic space under direct vision by the operating surgeon. After the drug was instilled the head low and right till position was maintained for the next 10 minutes.

Pneumoperitoneum was completely evacuated by the surgeon before closing port sites by manual compression of the abdomen. At the end of surgery muscle relaxant was reversed with Inj. Neostigmine 0.06 mg/kg IV and Injection Glycopyrrolate 0.01 mg/kg IV. The total duration of surgery was recorded for all the patients. The patients in the both groups were instilled with 30ml of study drug by the same method described above.

In the postoperative period the patients continued to receive intravenous fluid and all the patients were monitored for the following:

Hemodynamic monitoring: The pulse rate and the systolic and diastolic blood pressure were recorded for all of the patients every 5 min for the first 20 min after the administration of study drugs and during postoperative period at intervals of 30 min,1 h, 2h,4h, 5h,6h, and 24 h after surgery.

Respiratory rate monitoring: The respiratory rate was recorded for all the patients at 0, 2, 4, 8, 12, 18 and 24 hrs after surgery.

VAS pain score Assessment: The patients were asked to indicate their pain scores on a 10 cm visual analog pain scale where "0" indicated no pain and "10" indicated worst possible pain. The VAS was recorded at 0, 1, 2, 4, 6, 8, 12 and 24 h after surgery, (Fig. 1).

Rescue analgesia: Rescue analgesic (Inj. Paracetamol 1g IV) was administered when the VAS was 3 or when the patient demanded an analgesic. The time taken to the first dose of rescue analgesia and the total dose of rescue analgesics received by each patient were recorded.

Site of pain: The site of pain was determined by asking the patient to indicate the site of discomfort. Also, the patient was asked whether he was experiencing shoulder tip pain.

Associated side effects: The patients were monitored for side effects such as Nausea and Vomiting (NV), loss of tendon reflex, hypotension (defined as more than 20% reduction of SBP and/or DBP from baseline) rise in temperature, drowsiness, respiratory depression, itching and toxic effects of bupivacaine such as arrhythmias, respiratory depression, and restlessness, tremors, convulsions.

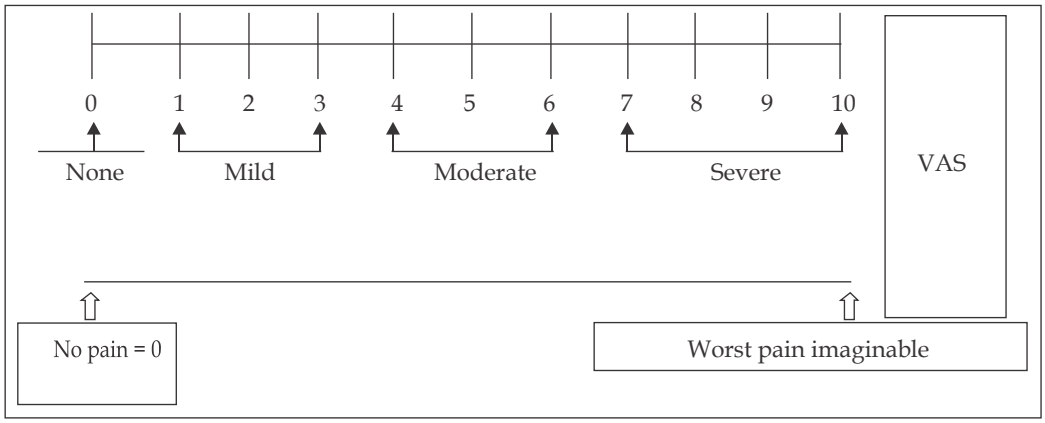

Fig. 1: Visualanalog scale

Results

There was no statistically significant difference in age and weight between the two groups. Both groups had female population in greater proportions,accounting for 60% or more of the total study population in each group (Table 1).

Both the groups were comparable in terms of ASA status of either ASA I or II with 60–70% of the sample falling within ASA I Group (Table 2).

Sample population in both the study groups were comparable with respect to SBP, DBP, MAP, and HR with p - value > 0.05 (Table 3).

Intraoperatively the differences in systolic blood pressure were not statistically significant throughout the period (Fig. 2).

There were no significant differences in diastolic blood pressures in both the groups throughout the intraoperative period (Fig. 3).

In Group BM, heart rate was recorded at 5 min interval and compared with baseline HR and found that the difference was statistically significant (p <

Table1: Comparison of demographic details in between the two groups

Parameters		Group BM	Group BT	*t*-test
Age (years)	Mean	36.63	36.90	
	SD	9.46	9.28	0.3891
Weight (in kgs)	Mean	66.96	65.33	
	SD	6.16	4.81	0.258
Gender				
Male	No. of patients	12	10	
	Percentages	40%	33.3%	0.688
Female	No of patients	18	20	
	Percentages	60%	66.6%	

0.05). After instillation HR was slightly less than baseline and stable thereafter, in Group BM. There were no significant differences in heart rate in both the groups during intraoperative period (Fig. 4).

No significant differences were noted in SBP trends postoperatively between both the groups. No Significant differences in DBP were observed postoperatively. Postoperatively there were no significant differences between both the groups in terms of HR in the first 24 hrs.

Mean VAS scores though statistically significant at all intervals, lower in first 3hrs after instillation.

Table 2: ASA status comparision

ASA physical status	Group BM	Group BT	*p* - Value (Fischer's Exact Test)
ASA I	21(70%)	18(60%)	
ASA II	9(30%)	12(40%)	0.59
Duration of surgery	59.73/+-9.74	59.27/+-10.72	0.86 Not significant
Duration of anaesthesia	76.73/+-10.41	74.70/+-8.19	0.40 Not significant

Table 3: Preoperative hemodynamic data

Parameters	SBP	DBP	MAP	HR
Group BM	119.57±10.4	77.2±9.99	91.3±8.52	90.7±11.88
Group BT	123.07±10.5	78.53±7.95	93.5±6.98	92.3±12.94
p value	0.2708	0.57	0.28	0.62

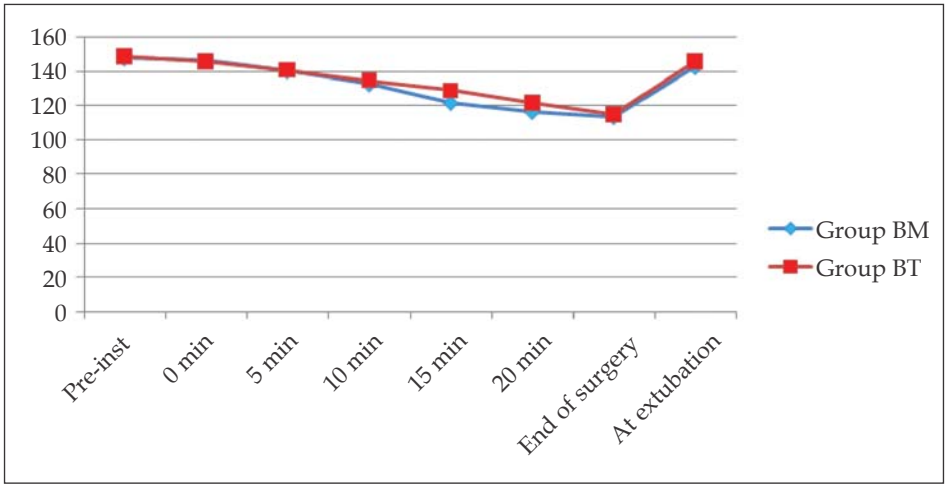

Fig. 2: Intraoperative systolic blood pressure

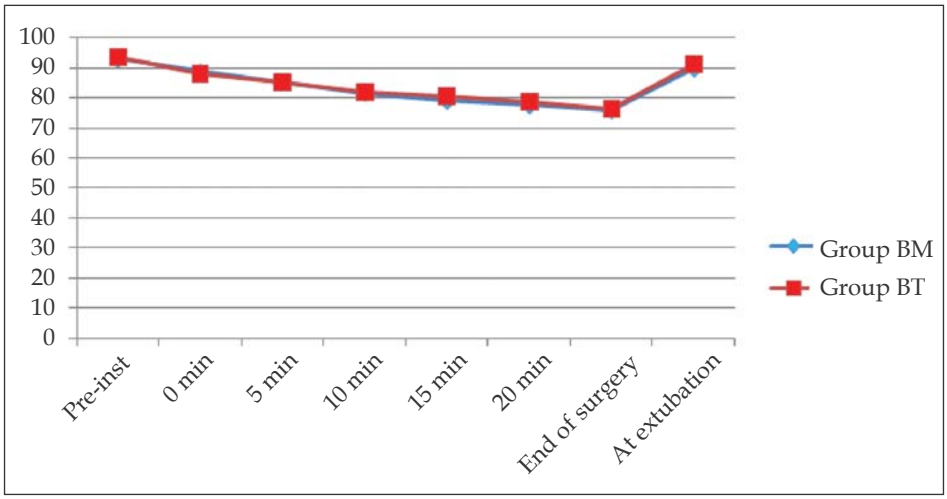

Fig. 3: Intraoperative diastolic blood pressure trend

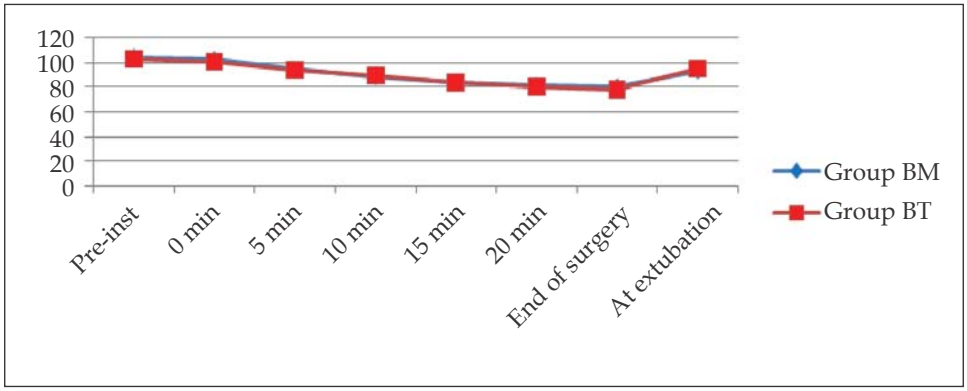

Fig. 4: Intraoperative heart rate trend between two groups

Table 4: VAS pain scores(values expressed in terms of mean and standard deviation and *p* values).

Time interval	**VAS score**		
Post OP	**Group BM**	**Group BT**	***p* - Value**
0 min	1.73 ± 1.11	3.36 ± 1.56	0.0117
30 min	2.03 ± 0.99	3.86 ± 1.19	0.0001
1 hr	2.26 ± 1.14	3.43 ± 1.30	0.0005
2 hr	2.5 ± 1.01	3.9 ± 1.21	0.0001
3 hr	2.63 ± 1.32	4.4 ± 0.81	0.0001
4 hr	1.96 ± 0.92	4.76 ± 1.43	0.0001
6 hr	2.19 ± 0.80	2.96 ± 1.12	0.0035
8 hrs	1.83 ± 1.14	2.76 ± 0.97	0.0005
12 hrs	2.23 ± 1.25	2.93 ± 1.04	0.001
24 hrs	1.77 ± 0.82	2.67 ± 1.42	0.022

It Increased after 3hrs and statistically significant. There was a slight increase in VAS scores 3 hrs of postoperative period in both the groups probably due to increasing intensity of pain and waning off of the effect of Bupivacaine. At 24 hrs the scores were reduced indicating reduction in intensity of postoperative pain (Table 4).

Mean Time taken for administration of rescue analgesia was 8.24 ± 0.51 hrs in Group BT and 4.06 ± 0.0.93 hrs in Group BM which was statistically significant (p = 0.0001). Earliest and longest time of administering rescue analgesia in Group BM was required 7 and 9.1 hrs respectively and in Group BT was 2.2 and 6.2 hrsrespectively (Fig. 5).

Mean of Total rescue analgesic dose required in Group BM was 1.27 ± 0.61 mg *vs* 2.27 ± 1.14 mg in Group BT which was not very statistically significant (p = 0.06). However, a total of 15 individuals in Group BT (50% of study group) and 8 individuals in Group BM (26.6% of study group) required 2nd dose of rescue analgesia in 24 hrs. This probably reflects the difference of efficacy in analgesia provided by Magnesium and Tramadol. There is no incidence of PONV in Group BM *vs* 13.3% in Group BT and was statistically not significant. (p - value: 0.54). There are no complication in both groups (Fig. 6).

Discussion

Laparoscopic surgeries being minimally invasive surgeries are associated with a relatively minor surgical trauma. They also have evolved as day

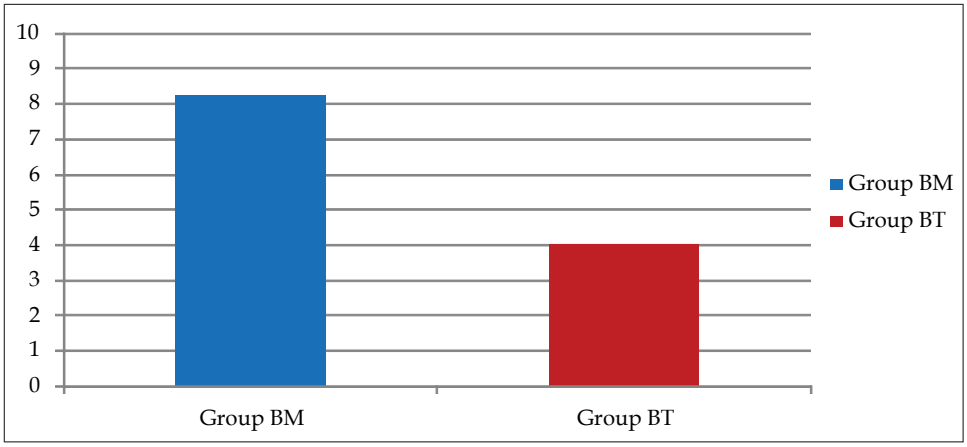

Fig. 5: Time required for first rescue analgesic (hrs) and total analgesic dose (Paracetamol) values expressed in terms of mean and standard deviation.

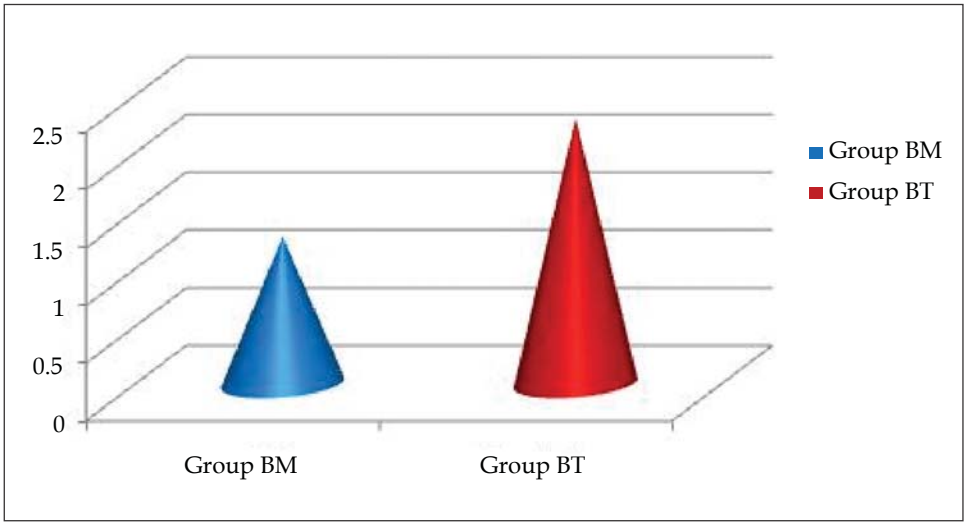

Fig. 6: Total dose of rescue analgesic

care surgeries owing to significantly reduced stress responses, postoperative pain and opioid requirements, improved postoperative pulmonary function, reduced overall morbidity resulting in rapid recovery, earlier ambulation thus, a reduced risk of DVT and a rapid return to normal activities. Top priorities for successfully discharging patients of day care surgeries are the four A's: Alertness, Analgesia, Ambulation and Alimentation. Excessive pain, nausea and vomiting and fatigue will delay the discharge. The success of fast tracking depends on effective pain management by simple techniques.

Postoperative pain in laparoscopic surgeries is multi-factorial in origin. Intraperitoneal infusion of normal saline at the end of the procedure is effective way to remove the carbon dioxide from the subdiaphragmatic area. The carbon dioxide gas between liver and diaphragm increases the space between them, producing tension of the peritoneal reflection and shoulder pain through mechanical irritation of the right phrenic nerve.The 37^0C temperature of the infused normal saline improves the hypothermia caused by carbon dioxide gas used for pneumoperitoneum. The heating of the peritoneum reduces the freezing peritoneal irritation and thus abdominal and shoulder pain.

Bhardwaj et al., conducted study in patients undergoing laparoscopic cholecystectomy. He instilled 20 ml 0.5% bupivacaine only at the end of surgery in the Trendelburg position. Postoperatively they assessed for vital signs (heart rate, blood pressure and respiratory rate), pain scores (VAS, VRS and shoulder pain) and analgesic consumption. They found that it reduced postoperative cholecystectomy pain and analgesic consumption.[5] There is a contradictory opinion about when to administer the local anesthetic. Few authors suggested early instillation of intraperitoneal local anesthetics as it provides better control of postoperative pain when compared with instillation at the end of the surgery, but few others have contradicted this and suggested otherwise. In our study, we have instilled the study drugs intraperitoneally at the end of the surgery.

The efficacy of local anesthetic instillation in pain control has been demonstrated in numerous other studies in laparoscopic cholecystectomy. Some used bupivacaine 0.125% while others used 0.25% bupivacaineand found a good postoperative pain relief. Joris et al. studied the characteristics of pain after laparoscopic cholecystectomy and the effect of intraperitoneal instillation of 80 ml of 0.125% bupivacaine with adrenaline. A systematic review and meta-analysis for the effect of intraperitoneal local anesthetic in laparoscopic cholecystectomy was done and 12 out of 24 studies reported a significant improvement in pain during early postoperative period.[6] The results correlate well with the results claimed in our study.The present study, hypothesized that the use of more than one modality to prevent postoperative pain may be more efficacious, (Tables 1–3).

The underlying mechanism of attaining analgesia by $MgSO_4$ is thought to be due to the reduction of calcium influx to the cell by magnesium. Magnesium also antagonises N-methyl-D-aspartate (NMDA) receptors, which are critical for neuronal signalling as well as pain processing in the central nervous system, thus reducing postoperative pain as both somatic and visceral pain fiber are blocked.Conventionally in laparoscopic cholecystectomy, $MgSO_4$ is given in various routes such as an IV bolus, continuous infusion, epidural infusion and in the subarachnoid space. Recently it has been shown that intraperitoneal local anesthetics alone or in addition to $MgSO_4$ improved postoperative pain after laparoscopic cholecystectomy.

A second reason to choose this combined regimen is that the effectiveness of individual analgesics was enhanced by the additive or synergistic effect of two or more drugs that relieve pain by different mechanisms

Buyukakilli B et al. carried out a study on frog sciatic nerves and found a better conduction blockwith $MgSO_4$ plus bupivacaine but not with Tramadol and bupivacaine.[7] AdjuvantTramadol and Magnesium sulphate potentiates the impulse inhibition by local anesthetics supporting our findings. Golubovic et al. in their study reported that the analgesic effects of the intraperitoneal injection of bupivacaine and/or tramadol in patients with laparoscopic cholecystectomy were both effective for the treatment and management of pain after the surgery and there was less requirement of postsurgical analgesics.[8] In our study also, we found similar results with mild to moderate pain in the patients. However, in the patients with bupivacaine plus Magnesium sulphate, the pain was significantly lower, with not even one patient experiencing more than mild pain and discomfort.

Akinci SB et al. compared the effectiveness of tramadol given IV and intraperitoneally regarding the postoperative analgesia after laparoscopic cholecystectomy and found that IV tramadol produced a better postoperative analgesia than intraperitoneal dose of tramadol.[9] Shukla U et al.

compared the effectiveness of bupivacaine alone, bupivacaine with tramadol and intraperitoneal instillation of bupivacaine in combination with dexmedetomidine. They found that intraperitoneal instillation of bupivacaine in combination with dexmedetomidine was superior to other two in reducing postoperative pain.[10] Our study also showed, a significant difference in pain intensity in the early postoperative period and the number of patients in both the studies was similar.

The graphic representation also shows, a rise in pain scores in study groups after 3 hrs postoperatively indicating that the effect of bupivacaine instillation slowly wanes with time. And also, the pain scores at 24 hour were significantly lower in Group BM and BT indicating reduction in intensity of postoperative pain, Table 4. We found that in this study, in comparison with the patients belonging to Bupivacaine-Tramadol Group, the patients of Bupivacaine-Magnesium Sulphate Group experienced statistically significantly reduced VAS pain scores after 1, 2, 4, 6 and 24 h of surgery ($p< 0.05$). Our findings are in accordance with Yadava A et al.[11] Similar results were found in the study by Maharjan SK et al. They compared intraperitoneal instillation of bupivacaine, solely and in addition to $MgSO_4$ in a dose of 50 mg/kg and found that the patients receiving intraperitoneal bupivacaine with $MgSO_4$ at the end of the surgery had better pain relief for a period of 2–5 hours compared with patients who were given only intraperitoneal bupivacaine.[12] Time for first requirement of rescue analgesic is also more in Bupivacaine-Magnesium sulphate when compared to Bupivacaine-Tramadol group of patients 8.29 ± 0.75 *Vs* 4.03 ± 0.93, Fig. 5. Rania M. Alia et al. in their study comparing intraperitoneal instillation of Bupivacaine-magnesium sulphate in laparoscopic cholecystectomy for analgesic effect using 0.9% Normal saline in control group found that the first requirement for first rescue analgesia was 9.2±3 hrs.[13] These findings are almost comparable to present study.In their study, comparing analgesic efficacy of intraperitoneal bupivacaine and bupivacaine plus magnesium sulphate for postoperative pain relief after laparoscopic cholecystectomy found that there is longer pain free period of average 5.53 ±4.33 hours after surgery compared to 3.16 ± 1.59 hours in sole bupivacaine group.[13]

In our study, there was also reduction in total analgesic consumed over 24 hrs for which total rescue analgesia consumption in 24 h was analyzed, Fig. 6. BT Group had 2.390 g (2.39 g, mean) and BM Group had 1.27 g, mean) of paracetamol (rescue analgesia) consumption in 24 h which was statistically significant. (p=0.06). And found that total rescue analgesic requirement reduced by half compared to BT Group.Edmunds S et al. reported that when magnesium sulphate was used as an adjunct for anesthesia, it reduced the doses of analgesics required and their action was strengthened but there was no prolongation of analgesic effects.[14] None of the patients, belonging to either group complained of shoulder tip pain this study.

Instillation of drugs in Trendelenburg's position might facilitate intraperitoneal local anesthetic flow over the celiac plexus and phrenic nerve endings giving better results.

Out of 6 Randomized placebo controlled studies to check the effectiveness of Intraperitoneal local anesthetics, four reported reduced overall pain after intraperitoneal instillation of local anesthetics in patient undergoing laparoscopic cholecystectomy, Table 5. Our study showed effective analgesia, statistically significant difference during the first 24 hours. Our present study also showed, significant reduction in shoulder tip pain but it was in contradiction with the findings of Chundrigar et al.[15]

We also found that the addition of $MgSO_4$ to bupivacaine decreased the heart rate slightly less

Table 5: Randomized controlled studies on effect of intraperitoneal analgesia onshoulder tip and overall pain after laparoscopic cholecystectomy.

First author and Ref. no.	No. of patients	Shoulder pain	Overall pain (incisional and visceral)
Chundrigar[15]	58	N	Y
Mraovic[16]	80	=	Y
Pasqualucci[17]	109	=	Y
Szem[18]	55	N	Y
Joris[6]	40	N	N
Raetzell[19]	24	N	N

N-not significant difference from placebo;
Y-significant effect in the treatment group
=not investigated.

than baseline and became stable thereafter, when compared to patients who were given bupivacaine and tramadol after laparoscopic cholecystectomy, Fig. 2,3,4. Our findings are in agreement with that of Jee D et al.SBP was recorded at 5 minute intervals in both groups after the intraperitoneal instillation of study drugs.[20] When SBP during the observation period was compared with baseline SBP, the difference was found to be statistically insignificant (p>0.05). Similarly DBP was also recorded at 5 minute intervals in both groups and DBP during the observation period was compared with baseline DBP, the difference was found to be statistically insignificant (p> 0.05).

After intraperitoneal instillation of the study drugs, the HR was recorded at 5 min interval in BTGroup patientsand compared with baseline HR and found that the difference was not statistically significant (p> 0.05). In BM Group, HR was recorded at 5 min interval and compared with baseline HR and found that the difference was statistically significant (p < 0.05). The HR after $MgSO_4$ plus bupivacaine instillation intraperitoneally was slightly less than baseline and stable thereafter. Jee D et al. in their study found a significant reduction in the mean arterial pressure was found with intravenous administration of Magnesium sulphate 50 mg/kg immediately before pneumoperitoneum, which was not found in our study.[20]

Maharjan SK et al. observed that there was no incidence of shoulder tip pain in patients receiving intraperitoneal bupivacaine solely compared to in addition to $MgSO_4$ in a dose of 50 mg/kg. There is 100% reduction in shoulder tip pain.[21] Rania M Alia et al. in their study found no significant difference in intraperitoneal magnesium sulfate group compared to 0.9% normal saline control group contradicting our study results though there is minimal shoulder pain.[13] Narchiet al. showed that intraperitoneal instillation of 100 mg bupivacaine did not cause toxicity.[22] This technique is safe with good pain relief in initial few hours. This drug possesses antiinflammatory activity that may further reduce pain when administered locally. Intraperitoneal instillation of 30 ml of 0.25% bupivacaine provides effective analgesia with plasma concentration below toxic levels (0.92–1.14 µg/ml). Several reports have revealed that the range of mean plasma concentration after plain intraperitoneal bupivacaine administration (100–150 mg) is well below the toxic concentration of 3 µg /ml.

In our study, we used lower doses (75 mg) of bupivacaine not more than 2 mg/kg body weight doses less than those believed to cause local anesthetic systemic toxicity, none of our patients exhibited features of toxicity such as arrhythmias, hypotension, delayed awakening. There is no record of clinical signs of local anesthetic systemic toxicity or signs of hypermagnesemia amongst all the previous studies. We recorded nausea and vomiting in four patients in the BT Group but not in any patient in the BM Group. There was no statistically significant difference in the proportion of patients with PONV. It would be more emetogenic potential of tramadol when compared to Magnesium sulphate. The results of Menteset al., who used preoperative infusion of $MgSO_4$ (50 mg/kg) in laparoscopic cholecystectomy, were in agreement with ours, as the incidence of nausea in the magnesium group was lower than in the control group.[23] Magnesium blocks NMDA receptors, which lie in both emetic pathways and structures associated with the final common pathway for vomiting. NMDA antagonists have the potential to be broad-spectrum antiemetics; however, there are no current data available on the direct effect of $MgSO_4$ on postoperative nausea and vomiting.

Conclusion

Bupivacaine along with Magnesium sulphate instillation significantly reduced VAS pain scores over 24 hrs. Prolonged duration of analgesia was noted with Magnesium sulphate. Total analgesic required over 24 hrs was less with Magnesium use. No signs of drug allergy and toxicity were observed.

Thus, the intraperitoneal instillation of Bupivacaine-$MgSO_4$combination provides good analgesia in first 24 hours after surgery, with longer duration of pain free period when compared to Bupivacaine-Tramadol combination, with almost no side effects in both the groups.

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Comparative Study of Granisetron and Ondansetron for the Prevention of Post Operative Nausea and Vomiting in Patients Undergoing Total Abdominal Hysterectomy Under General Anaesthesia

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Abstract

The aim of this study was to compare the efficacy of intravenous granisetron and intravenous ondansetron for prevention of postoperative nausea and vomiting in patients undergoing total abdominal hysterectomy under general anesthesia. In this prospective double-blind randomized controlled clinical trial, 60 American Society of ASA Grade I and II patients aged between 18 and 60 years scheduled for elective total abdominal hysterectomy under general anesthesia were selected. The patients were divided in the following Groups of 30 patients each: *Group 1 (Granisetron):* 30 patients were given 1 mg of Granisetron was diluted in NS to make upto 10 ml; *Group 2 (Ondansetron):* 30 patients were given 4 mg of Ondansetron was diluted in NS to make upto 10 ml. Postoperative Nausea and Vomiting (PONV), hemodynamic and side effects were observed at scheduled intervals. The incidence of PONV was significantly lower in Group 1 (Granisetron) than in Group 2 (Ondansetron). Requirement of rescue antiemetic was significantly lower in Group 1 (Granisetron) 6.7% as compared to Group 2 (Ondansetron) 33.3%. At all times the changes in the vital parameters like pulse rate, systolic blood pressure, diastolic blood pressure, mean arterial pressure and SpO_2 were within the normal physiological limits. There was no statistical significant difference between the groups. It was observed that there was no significant difference in adverse effects amongst the groups as well. We conclude that granisetron is more effective, potent and longer acting antiemetic as compared to ondansetron for reducing PONV in patients undergoing Total Abdominal Hysterectomy under general anesthesia.

Keywords: Granisetron; Ondansetron; PONV; Total Abdominal Hysterectomy.

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Introduction

Postoperative Nausea and Vomiting (PONV) constitutes a most common anesthesia related undesirable event. Its incidence in the available literature is reported to vary between 20 and 80%[1] PONV has significant adverse effects. It can cause profound distress to the patients. Oral administration of drugs, fluids and nutrients can be delayed and can lead to dehydration and alkalemia. It is an important cause of delayed discharge. It may be associated with poor surgical outcome.

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Vomiting can disrupt neck, abdominal and eye sutures. PONV is often severe on movement and may delay postoperative mobilization.[2]

The aetiology of PONV is multifactorial[3] with increased incidence in pediatric patients, adult females, obese and in patients with a history of motion sickness. The surgery related factors are after strabismus surgery, orchidopexy, middle ear surgery, intraabdominal and orthopedic surgeries. Anesthesia related factors like Intravenous anesthetic agents are associated with differing degrees of emesis. Perioperative use of opioids is associated with an increased incidence of PONV. It is generally accepted that nitrous oxide is responsible for a significant degree of emesis. Inhalational agents like halothane and isoflurane also cause PONV, though to a lesser extent.[4]

Prophylaxis for PONV in recent times include decreasing baseline risk for PONV,[5] use of non pharmacological measures,[6] change of anesthetic techniques and use of new antiemetic drugs. Drugs used to treat PONV are usually antihistaminic, anticholinergic, phenothiazine derivatives and dopamine receptor antagonist with side effects like extrapyramidal symptoms, sedation, tachycardia, dysphoria and restlessness.[7]

The treatment of nausea and vomiting has improved greatly in today's world with use of 5-hydroxytryptamine (5-HT_3, serotonin) receptor antagonist. Ondansetron is commonly used drug to prevent PONV. These drugs act by binding to the serotonin 5-HT_3 receptor in the chemoreceptor trigger zone (CTZ) and at vagal afferent supply in the gastrointestinal tract.[8]

Another 5-HT_3 receptor antagonist Granisetron is more effective and longer acting against Cisplatin induced emesis than Ondansetron. Granisetron is highly selective for 5-HT_3 receptors (1000:1) compared to Ondansetron which has a selectivity of 250–400:[9] Elimination half life of granisetron is 9 hrs which is 2.5 hrs longer than ondansetron[7] and its duration of action is more than 24 hrs.[7] This study was done to compare the antiemetic effect of Granisetron and Ondansetron in prevention of PONV in patients undergoing Total Abdominal Hysterectomy under General Anesthesia (GA).

Materials and Methods

A prospective, randomized, double blind study was conducted with 60 patients to compare the effects of granisetron and ondansetron for the prevention of Postoperative Nausea and Vomiting (PONV) in patients undergoing hysterectomy under general anesthesia. The patients were divided in the following Groups of 30 patients each:

Group 1 (Granisetron): 30 patients were given 1 mg of Granisetron was diluted in NS to make upto 10 ml;

Group 2 (Ondansetron): 30 patients were given 4 mg of Ondansetron was diluted in NS to make upto 10 ml.

Study design: Hospital based prospective, randomized, double blind study.

Study duration: 1 year.

Study area: The study was done at DY Patil Medical College, Hospital and Research Center, in the Department of Anesthesiology.

Study population: 60 ASA-I and ASA-II fit patients (30 in each Group) scheduled for elective total abdominal hysterectomy under general anesthesia that fulfilled the inclusion criteria.

Sample size: By keeping the significance level of 5%, power of study at 95% the sample size was calculated by WinEpi Statistical Package. The minimum sample size required was 25 in each Group. Keeping in mind dropouts or exclusions, we conducted the study in 60 patients after dividing 30 patients in each Group.

Inclusion criteria:

1. ASA Grade I and ASA Grade II patients;
2. Age between 18 and 60 years;
3. Hemodynamicaly stable patients with all routine investigations within normal limits and without any other comorbidity;
4. Availability of informed consent and willingness of the patient to be a part of the study.

Exclusion criteria:

1. Patients with ASA physical status III or more;
2. Patients below 18 years and above 60 years of age;
3. Patients with history of motion sickness or previous PONV;
4. Patient who have taken antiemetic drugs within 24 hours before surgery;
5. Patients with history of neurological or renal disease.

Methodology: After approval from the Institutional Ethics Committee, valid informed written consent was taken from patients and patient's attendant.

Once the patients were enrolled for the study, a thorough history and physical examination was done as per proforma.

Sixty patients of ASA-I and ASA-II in age group of 18 to 60 yrs. undergoing elective total abdominal hysterectomy were selected randomly after applying already mentioned stringent inclusion and exclusion criteria. The patients were divided into Two Groups of 30 each. The patients were allocated to respective groups by application of lottery method to ensure removal of selection bias and proper randomization:

Group 1 (Granisetron): 30 cases received 1 mg Granisetron diluted in NS to make up to 10 ml;

Group 2 (Ondansetron): 30 cases received 4 mg Ondansetron diluted in NS to make up to 10 ml.

Materials Required:

1. Standard anesthesia machine (Boyle's apparatus);.
2. Intravenous cannula 20G;
3. Intravenous fluids – Crystalloids and colloids;
4. Bain's circuit with face mask of appropriate size;
5. Monitoring equipments such as pulse oximeter, ECG monitor noninvasive blood pressure apparatus;
6. Anesthetic drugs – Inj. Glycopyrrolate, Inj. Midazolam, Inj. Pentazocine, Inj. Propofol, Oxygen, Nitrous oxide, Isoflurane;
7. Equipments of endotracheal intubation;
8. Disposable syringe;
9. Drugs and instruments necessary for resuscitation;
10. Injection Granisetron ampoule;
11. Injection Ondansetron ampoule.

All preparations that are drugs and equipment's necessary for resuscitation for general anesthesia were kept ready.

Procedure:

Patients enrolled in the study were visited a day prior to surgery. Detailed history, general and systemic examination of cardiovascular, respiratory and central nervous system was done. Routine laboratory investigations such as hemogram, Liver Function Tests (LFTs), Renal Function Tests (RFTs), serum electrolytes, urine routine, Bleeding Time and Clotting Time (BT-CT), were done. Patients were nil by mouth from midnight prior to surgery.

Preoperative pulse, noninvasive blood pressure, ECG and oxygen saturation were noted. Peripheral venous access with 20 gauge intravenous cannula was established and Intravenous (IV) fluids were given.

Three readings of systolic, diastolic blood pressure and heart rate were obtained at three minutes of interval with patient in supine position. Lowest reading of blood pressure and highest reading of heart rate were taken as baseline values to minimize influence of anxiety in patients with high initial values. Highest Nausea and Vomiting Score value was taken as baseline.

Drugs were given

Group 1 (Granisetron): 1 mg diluted in NS to make up to 10 ml;

Group 2 (Ondansetron): 4 mg diluted in NS to make up to 10 ml.

These drugs are given by double blinding method. Patients were preoxygenated for 3 minutes. Then patients were premedicated with Inj. Glycopyrolate 0.2 mg, Inj. Midazolam 1 mg and Inj. Pentazocine .03 mg/kg then patients were induced with propofol 2 mg/kg body weight, Inj. succinylcholine 2 mg/kg body weight. Patient was intubated with appropriate ET tube, bilateral air entry was confirmed by auscultation, tube was fixed. Maintenance of anesthesia was done with nitrous oxide (60%) and oxygen (40%) and isoflurane as required using Intermittent Positive Pressure Ventilation (IPPV) with Bain's circuit. On completion of surgery patients pts. were given reversal and were shifted to recovery room after regaining satisfactory tone and then to the respective wards after confirming as adequate level of consciousness and intact reflexes. The incidence of PONV was recorded within first forty eight hours after surgery at an interval of 30 mins, 1 hour, 6 hours, 12 hours and 48 hours. Postoperative nausea and vomiting were recorded by spontaneous complaints by the patient. Pulse, blood pressure and oxygen saturation were recorded preoperatively, intraoperatively and postoperative period.

Score table to assess postoperative nausea and vomiting is as follows:

Score Table:

0 = No symptom;
1 = Mild sausea;
2 = Severe nausea but no vomiting;
3 = Vomiting.

Statistical Analysis:

All the cases were completed in the stipulated time. Data was collected, compiled and tabulated. The statistical analysis was done using parametric test and the final interpretation was based on *Z*-test (standard normal variant) with 95% level of significance.

Quantitative data was analyzed by *Student 't'-test.*

Qualitative data was analyzed by *Chi-square test.*

Results

A total of 60 patients were enrolled in the present study and were randomized into two groups of 30 each, both the groups were comparable with respect to age, sex, BMI, duration of surgery, and the duration of anesthesia. The mean age of the patients in Group 1 (Granisetron) was 44.27 ± 12.54 years; and patients in Group 2 (Ondansetron) was 45.03 ± 8.64 years (p =.785), (p =.785) (Table 1).

Table 1: Comparison of demographic data between Groups

		Group 1 (Granisetron)	Group N (Ondansetron)	p - Value
1	Age (yrs)	44.27 ± 12.54	45.03 ± 8.64	> 0.05
2	BMI (kg/m^2)	25.03 ± 3.50	25.73 ± 3.41	> 0.05
4	ASA I/II	22/8	24/6	> 0.05

The incidence and severity of PONV was significantly lower in Group 1 (Granisetron) as compared to Group 2 (Ondansetron) at all time intervals (Table 2).

Postop 30 min: 20% pts. from Group 1 vomited (Score 3) *versus* 50% in Group 2; Postop 1 hr: 16.7% pts. from Group 1 vomited as compared to 46.7% in Group 2;

Postop 6 hrs: 10% pts. from Group 1 vomited as compared to 40% in Group 2;

Postop 12 hr: 3.3% pts. from Group 1 vomited as compared to 33.3% in Group 2;

Postop 48 hrs: No. pts. from Group 1 vomited as compared to 16.7% in Group 2;

There was statistical significant difference between the Groups as per Chi-square test (p < 0.05).

The requirement of rescue antiemetic was significantly lower in Group 1 (Granisetron) as compared to Group 2 (Ondansetron) as per Chi-square test (p < 0.05), shown in Table 3.

Table 2: Comparison of incidence of PONV between Groups

Incidence of PONV N			Group 1 (Granisetron)		Group 2 (Ondansetron)		p - Value
			%	N	%		
Postop mins	30	Score 0	10	33.3%	2	6.7%	< 0.05
		Score 1	8	26.7%	3	10%	
		Score 2	6	20%	10	33.3%	
		Score 3	6	20%	15	50%	
		Total	30	100%	30	100%	
Postop hr	1	Score 0	18	60%	3	10%	< 0.05
		Score 1	3	10%	4	13.3%	
		Score 2	4	13.3%	9	30%	
		Score 3	5	16.7%	14	46.7%	
		Total	30	100%	30	100%	
Postop hrs	6	Score 0	24	80%	6	20%	< 0.05
		Score 1	1	3.3%	4	13.3%	
		Score 2	2	6.7%	8	26.7%	
		Score 3	3	10%	12	40%	
		Total	30	100%	30	100%	
Postop hrs	12	Score 0	26	86.7%	9	30%	< 0.05
		Score 1	2	6.7%	5	16.7%	
		Score 2	1	3.3%	6	20%	
		Score 3	1	3.3%	10	33.3%	
		Total	30	100%	30	100%	
Postop hrs	48	Score 0	29	96.7%	15	50%	< 0.05
		Score 1	1	3.3%	7	23.3%	
		Score 2	0	-	3	10%	
		Score 3	0	-	5	16.7%	
		Total	30	100%	30	100%	

Table 3: Comparison of Requirement of Rescue Antiemetic between Groups

Requirement of Rescue Antiemetic	Group 1 (Granisetron)		Group 2 (Ondansetron)		p - Value
	N	%	N	%	
Yes	2	6.7%	10	33.3%	
No	28	93.3%	20	66.7%	< 0.05
Total	30	100%	30	100%	

Discussion

Postoperative Nausea and Vomiting (PONV) is a frequently encountered problem and distressing symptom in surgical patients. General anesthesia using inhalational agents is associated with incidence of PONV in 20–30% surgical patients.[10] These incidents are largely dependent on

preoperative patient characteristics, anesthesia, operation, gender, intensity of pain and its postoperative management.

Postoperative vomiting harms skin flaps, abdominal wall sutures and vascular anastomoses. It causes increases in intraocular, intracranial pressure and may also lead to tachycardia, electrolyte imbalance, wound dehiscence, oesophageal tears and aspiration pneumonitis.[11] It may at times lead to serious complications like Mallory Weiss syndrome and oesophageal rupture.[3] PONV especially after minor and ambulatory surgery causes delay in hospital discharge.

Four neurotransmitter systems seem to play an important role in elicitation of an emetic response these are dopaminergic, histaminic, cholinergic, muscaranic and 5-HT_3. As there are 4 different types of receptors involved in emesis so there are at least 4 sites for antiemetic dugs to act.[7] The advent of $5HT_3$ (serotonin) receptor antagonists in 1991 ushered in a new era in the treatment of PONV because of lack of side effects that were commonly observed with the use of antiemetic drugs.[12] Every $5HT_3$ receptor antagonist has the same basic double nitrogen ring backbone in their chemical structure, this maybe the chemical site of action of $5HT_3$ receptor antagonist.[7] Commonly used antiemetic agent from $5HT_3$ receptor antagonist class is ondansetron. Other alternatives are dolasetron, tropisetron, ramosetron.[13] Recent addition to this group is granisetron, which is more potent and has a longer half life of 8–9 hrs as compared to ondansetron's 3 hrs thus, it is much more effective and longer acting antiemetic agent.[5] The $5HT_3$ receptor antagonists caused no extra pyramidal symptoms, no sedation or any adverse effects on vital parameters and do not have any drug interaction with other anesthetic agents.

The present study was conducted with 60 patients belonging to ASA-I and ASA-II between the age of 18 and 60 years undergoing Total Abdominal Hysterectomy under general anesthesia to compare the effects of granisetron and ondansetron for the prevention of postoperative nausea and vomiting (PONV).

The incidence and severity of PONV was significantly lower in Group 1 (Granisetron) as compared to Group 2 (Ondansetron) at all time intervals. The requirement of rescue antiemetic was significantly lower in Group 1 (Granisetron) 6.7% as compared to Group 2 (Ondansetron) 33.3% as per Chi-square test ($p < 0.05$).

It was observed that there was no significant difference in adverse effects amongst the groups as per Chi-square test ($p > 0.05$).

Conclusion

Granisetron is more effective, potent and longer acting antiemetic as compared to ondansetron for reducing PONV in patients undergoing Total Abdominal Hysterectomy under general anesthesia.

Limitations

Following are the limitations of our study:

1. No placebo control group was included in the study as both Granisetron and Ondansetron are well-known drugs to prevent PONV;
2. Quality of oral intake couldn't be analyzed as this was TAH being an abdominal surgery patient needed to be nill per oral for a longer time till there was return of adequate intestinal motility postoperatively.

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Comparative Study of Nalbuphine and Fentanyl for Total Intravenous Anaesthesia in Short Surgical Procedures

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Abstract

Background: Total Intravenous Anesthesia (TIVA) can be defined as a technique of general anesthesia using a combination of agents given solely by the intravenous route and in the absence of all inhalational agents including nitrous oxide (Gas Anesthesia). Total intravenous anesthesia, based on the administration of Propofol combined with an opioid, has become a popular anesthetic technique. This study is to compare the analgesic effects of nalbuphine with fentanyl as well as associated side effects as adjuncts in TIVA along with propofol. *Aim:* To study the effect of nalbuphine and fentanyl when used as analgesic in total intravenous anesthesia along with propofol. *Methods:* This study was conducted on 60 adult patients belonging to American association of anesthesiologists (ASA) Grade I/II and posted for short minor surgical and gynecological procedures. They were divided into two equal groups of 30 each, using statistical table of random number: *Group N:* Preinduction medication with Inj. Nalbuphine 0.05 mg/kg; *Group F:* Preinduction medication with Inj. Fentanyl 1 mcg/kg. HR, BP, SPO_2, just before induction, immediately after induction and then at every 5 minute-intervals till 2 hours were recorded. Additionally, VAS scoring, Modified Aldrete scoring, Time for rescue analgesia, Respiratory rate were noted after 30 minutes. *Results:* Hemodynamic parameters like heart rate, systolic blood pressure, mean arterial pressure were controlled better in the fentanyl group at 5 min, 10 min, 15 min intraoperatively. Postoperative analgesia was better with nalbuphine group with reduced visual analogue scale with reduced respiratory depression. *Conclusions:* Fentanyl provided better intraoperative hemodynamic stability whereas, nalbuphine provided better postoperative analgesia with lesser respiratory depression.

Keywords: Total Intravenous Anesthesia (TIVA); Nalbuphine; Fentanyl.

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Introduction

Total Intravenous Anesthesia (TIVA) can be defined as a technique of general anesthesia using a combination of agents given solely by the intravenous route and in the absence of all inhalational agents including nitrous oxide (Gas Anesthesia).[1] TIVA has reduced incidence of postoperative nausea and vomiting, reduced atmospheric pollution, more predictable and rapid recovery, greater hemodynamic stability, preservation of hypoxic pulmonary

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vasoconstriction, reduction in intracerebral pressure and reduced risk of organtoxicity.

The most commonly utilized groups of drugs include hypnotics and short-acting opioids.[2]

Total intravenous anesthesia, based on the administration of Propofol combined with an opioid, has become a popular anesthetic technique. It allows independent modulation of the different components of anesthesia.[3]

Propofol is generally combined with an analgesic, the popular combination being either Propofol with Fentanyl or Ketamine, as pain relief to patient is an important constituent of balanced anesthesia.[4]

Fentanyl is a popular analgesic because of its relatively short-time to peak analgesic effect, rapid termination of effect and cardiovascular safety. Dose for achieving analgesia is 2-50 mcg/kg. Fentanyl decreases the anesthetic requirement for Thiopentone or Propofol by providing antinociceptive effects that the intravenous hypnotics do not provide.[5,6]

Nalbuphine is a member of the opioid family. It is an antagonist of μ receptor but agonist of kappa receptors.[7] It was synthesized in an attempt to produce analgesia without the undesirable side effects of alpha 1 agonist. Respiratory depression and abuse potential with nalbuphine is very less. Although very commonly used, fentanyl is costlier and needs narcotic licensing. Thus, this study is to compare the analgesic effects of nalbuphine with fentanyl as well as associated side effects.

Materials and Methods

Type of study:

Prospective Double blind Randomized Study.

Period required for data collection:

1.5 years.

Period required for data analysis:

Reporting: 6 months;

Sampl Size: 60 cases.

After approval from institution ethics committee, this study was conducted on 60 adult patients belonging to American association of anesthesiologists (ASA) Grade I/II and posted for short minor surgical and gynecological procedures under General Anesthesia.

They were divided into two equal groups of 30 each, using statistical table of random number:

Group N: Preinduction medication with Inj. Nalbuphine 0.05 mg/kg;

Group F: Preinduction medication with Inj. Fentanyl 1 mcg/kg.

Inclusion criteria:

1. ASA Grade I & II;
2. Ages between 18 and 60 of either gender;
3. Hemodynamically stable patients with normal laboratory investigations;
4. Patients willing to be a part of the study;
5. Surgery duration < 30 mins.

Exclusion criteria:

1. ASA Grade 3 and more;
2. Patients not willing to be a part of the study;
3. Patients on pain perception modifying drugs;
4. Patients with known sensitivity to any of the drugs understudy;
5. Surgery duration > 30 min.

Sample size:

By keeping the significance level of 5%, power of study at 95 %, the sample size was calculated by WinEpi Statistical Package. The minimum sample size required was 25 in each group. Keeping in mind dropouts or exclusions, we conducted the study in 60 patients after dividing 30 patients in each group.

Procedure and Conduct of Study Masking:

The anesthesiologist loading the drugs and administering the premedication was different than the one conducting the case and managing patients in postanesthesia care unit. Thus, both the anesthesiologists were blinded to the assignment.

Preop Evaluation

All patients were subjected to detailed preanesthetic evaluation and relevant laboratory investigations. Written informed consent was obtained from all the patients as per the hospital protocol given at appendix A. They were counseled with regards to sedation, general anesthesia as well as the operative procedure.

Intraoperative

On arrival in operation theatre, nil by mouth was confirmed and baseline vitals recorded.

Patient was premedicated with Inj. Ondansetron 4 mg, Inj. Glycopyrrolate 0.2 mg IV. Preoxygenation

done with 100% oxygen was done. Patient was given the randomly allotted drug (either Fentanyl or nalbuphine).

Propofol was administered 5 mins after the test drug fentanyl and nalbuphine were given as premedications to the participants.

It was given intermittently as per the vitals and clinical signs of the patient.

The initial bolus for induction was 0.8–1.2 mg/kg at the rate of 30 mg/10 sec till the desired clinical effect was achieved. 20–30 mg increment boluses were given to keep the patient deeply sedated.

Propofol was stopped 5–10 mins prior to the desired time of emergence.

Rescue analgesia was given when VAS is > 5. Inj. Diclofenac 75 mg IM was given as rescue analgesic.

All the intraoperative vitals were recorded and VAS score, Modified aldrete score, side effects and respiratory rate were noted in the postoperative period for 2 hours.

Patient was shifted to postanesthesia care unit and monitored for hemodynamic parameters, duration of analgesia, VAS & Modified Aldrete Scoring and adverse effects, if any, immediately on arrival in PACU & every 30 mins (till 2 hours) thereafter, till transfer to surgicalward.

Data analysis:

The comparison of quantitative data was done by using test of significance based on '*t*'-test. Unpaired *t*-test for intergroup & paired *t*-test for within the group comparisons. Qualitative parameters were analyzed by Chi-square test.

p - value ≤ 0.05 was taken as significant and *p* < 0.001 was taken as highly significant.

Results

The age and weight of the patients were comparable in both the groups and was found to be clinically insignificant.

Propofol given in fentanyl group was 151.6 ± 7.8 mg and in the nalbuphine group was 153.8 ± 6.9. There was no significant difference in the doses in both the groups.

The intraoperative heart rate is higher at 5, 10 ,15 minute in the nalbuphine group and is clinically significant, (Table 1).

The systolic Blood Pressure is lower at 1 minute, 2 minute, 5 minute, 10 minute, 15 minute and 30 minute in the fentanyl group and is clinically significant, (Table 2).

The mean diastolic blood pressure was comparable and there was no significant difference.

The mean arterial pressure was lower in the fentanyl group at 2, 5, 10, 15 minutes and was clinically significant, (Table 3).

The mean SpO_2 was on the lower side in fentanyl at 1 hour and 2 hour (postoperative) and was clinically significant, (Fig. 1).

Table 1: Comparison of mean heart rate between Fentanyl and Nalbuphine at different time internal

Time interval	Fentanyl (Mean ± SD)	Nalbuphine (Mean ± SD)	*p* - Value
Baseline	72.63 ± 8.54	73.13 ± 8.41	0.820
1 Minute	71.90 ± 7.59	72.70 ± 8.09	0.694
2 Minute	70.53 ± 7.50	73.70 ± 8.09	0.121
5 Minute	69.13 ± 7.31	74.10 ± 8.30	0.017
10 Minute	68.30 ± 6.58	77.47 ± 8.06	0.000
15 Minute	69.90 ± 7.18	74.93 ± 8.17	0.014
30 Minute	71.20 ± 8.04	71.87 ± 8.40	0.755
1 Hour	72.63 ± 8.54	71.67 ± 6.77	0.629
2 Hour	72.33 ± 8.51	71.30 ± 5.93	0.587

Table 2: Comparison of mean systolic blood pressure between Fentanyl and Nalbuphine at different time internal

Time interval	Fentanyl (Mean ± SD)	Nalbuphine (Mean ± SD)	*p* - Value
Baseline	117.47 ± 7.60	123.37 ± 14.66	0.055
1 Minute	115.40 ± 8.08	123.30 ± 13.94	0.009
2 Minute	113.30 ± 7.42	125.00 ± 13.35	< 0.001
5 Minute	111.53 ± 7.28	125.40 ± 13.29	< 0.001
10 Minute	110.67 ± 6.78	128.17 ± 12.69	< 0.001
15 Minute	112.67 ± 7.04	123.40 ± 12.48	< 0.001
30 Minute	114.50 ± 7.85	120.23 ± 13.30	0.047
1 Hour	117.70 ± 8.30	117.67 ± 10.75	0.989
2 Hour	116.73 ± 8.39	116.47 ± 9.89	0.989

Table 3: Comparison of mean arterial pressure between Fentanyl and Nalbuphine at different time internal

Time interval	Fentanyl (Mean ± SD)	Nalbuphine (Mean ± SD)	*p* - Value
Baseline	92.00 ± 5.91	92.67 ± 10.17	0.757
1 Minute	89.87 ± 5.95	92.60 ± 9.98	0.203
2 Minute	88.73 ± 5.53	93.73 ± 9.91	0.019
5 Minute	87.33 ± 5.43	93.93 ± 9.84	0.002
10 Minute	86.53 ± 5.14	95.67 ± 9.65	< 0.001
15 Minute	88.27 ± 5.15	92.87 ± 9.57	0.024
30 Minute	90.00 ± 5.62	90.77 ± 9.85	0.713
1 Hour	92.00 ± 5.91	91.97 ± 9.89	0.987
2 Hour	92.00 ± 5.91	91.97 ± 9.65	0.987

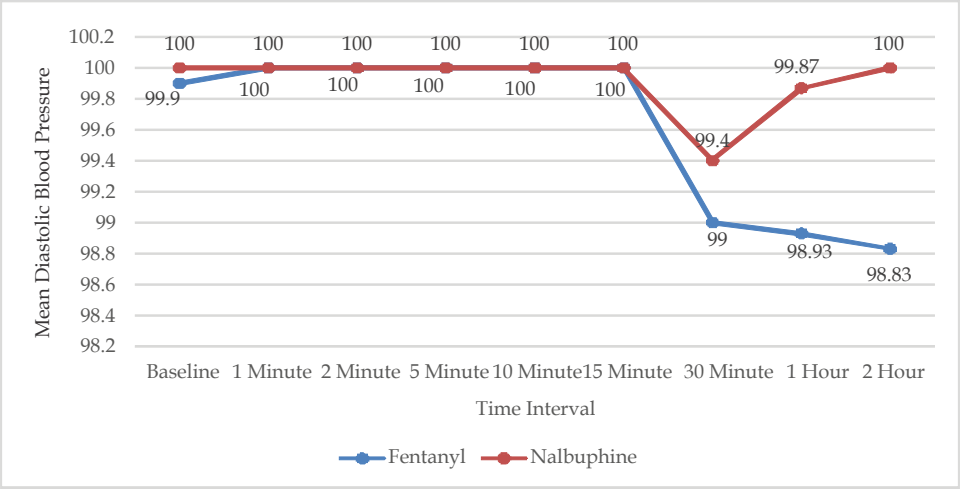

Fig. 1: Comparison of SpO_2 in both groups

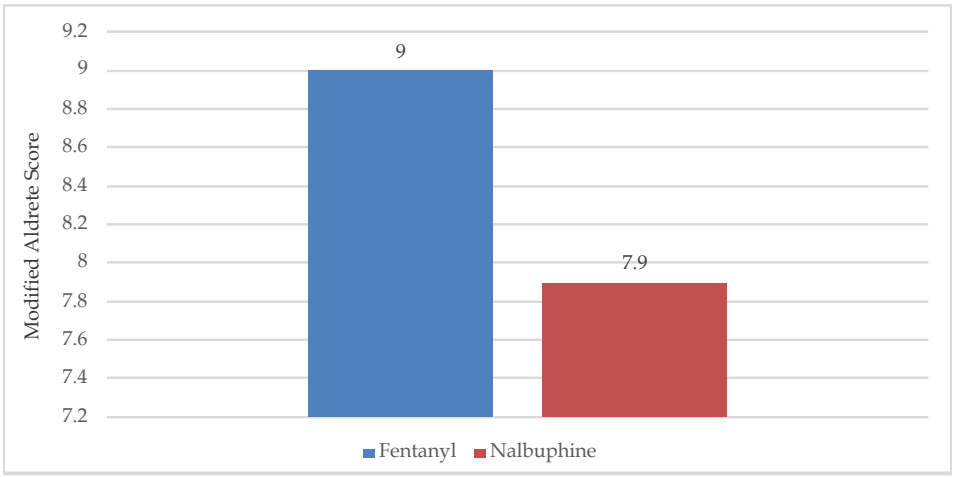

Fig. 2: Comparison of modified aldrete score in both the groups

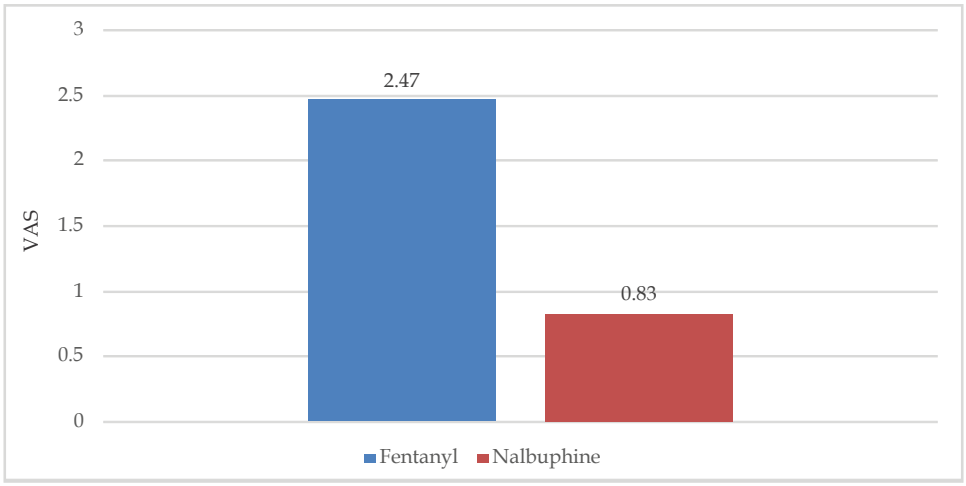

Fig. 3: Comparison of visual analog scale in both the groups

Modified aldrete score was lower in nalbuphine group in the postoperative period and the difference was clinically significant, (Fig. 2).

The visual analog scale was lower in the postoperative period in the nalbuphine group and was clinically significant, (Fig. 3).

Rescue analgesia time was significantly higher in the nalbuphine group with fentanyl needing rescue analgesia at 65.30 ± 8.82 minutes and nalbuphine at 139.87 ± 8.99 minutes.

The respiratory rate was on the lower side in the fentanyl group and it was clinically significant as per (Fig. 4).

No difference was found in the incidence of nausea in both the groups;

Vomiting was observed in one patient in nalbuphine group;

Pruritis was observed in 3 patients in fentanyl group.

Discussion

Demographic Profile

The demographic data age, weight, and type surgery in both the groups were comparable. The difference between both groups was statistically insignificant.

The nature of the procedure in the study was same. Any procedure extending beyond 30 minutes were excluded from the study.

Kay and Rolly[8] introduced Propofol in 1977 during their search for an ideal intravenous anesthetic agent. There was lack of analgesic properties of Propofol which led to development of use of supplementary agents during TIVA, like Ketamine and Fentanyl.

In our study, we are comparing propofol-fentanyl and propofol-nalbuphine and studying the efficacy of nalbuphine as adjunct.

Comparison of hemodynamic stability

Comparison of Heart Rate

Both in nalbuphine group and in fentanyl group the heart rate was within 20 percent of the baseline with nalbuphine showing intraoperative increase in heart rate which was clinically significant at 5 min, 10 min and 15 min and postoperative reduction of heart rate which was not clinically significant.

Similar findings were found in a study conducted by *FA Khan in 2002,*[9] when nalbuphine was compared to fentanyl in total intravenous anesthesia where nalbuphine showed a much higher positive variation compared to fentanyl group especially after incision. The study was conducted in 60 ASA 1 patients undergoing laparoscopic cholecystectomy. Both the drugs, nalbuphine 0.2 mg/kg and fentanyl 2 mcg/kg were given 5 minutes before induction. Anesthesia was induced with propofol 2 mg/kg followed by vecuronium 0.1 mg/kg.

Another study conducted by *Khanday et al. in 2019*,[10] where they compared fentanyl *versus* nalbuphine for attenuation of hemodynamic response to laryngoscopy and endotracheal intubation in general anesthesia. In this study, the variation was more in nalbuphine group than fentanyl but the difference was statistically insignificant.

Thus, both the studies had similar findings as ours.

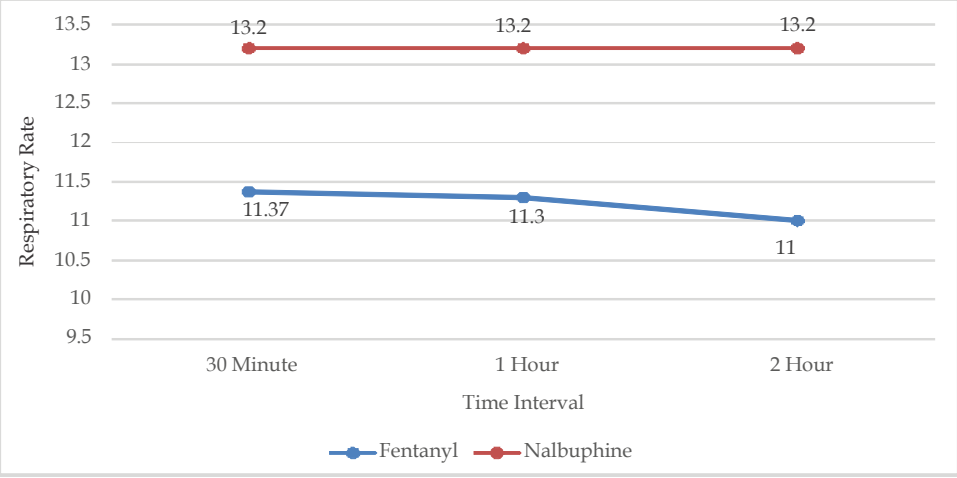

Fig. 4: Comparison of respiratory rates in both the groups

Comparison of Systolic Blood Pressure

There was significant difference in the systolic blood pressure at 5 min, 10 min, 15 min postinduction with increase in the systolic blood pressure in the nalbuphine group which later falls in the postoperative period but is not clinically significant. There was a fall in systolic blood pressure in the fentanyl group at 5, 10, 1 5 min which was statistically significant. However, the variation was within 20 percent of baseline at all times.

Similar findings were found in the study conducted by *Khan et al. in 2002*[9] where there was a significant difference in systolic blood pressure at 2, 3 , 5 minutes postinduction when the maintenance doses of propofol was started and at the time of incision with higher values in the nalbuphine group.

Comparison of Diastolic Blood Pressure

Nalbuphine group showed an increase in the diastolic blood pressure till 10 minutes which was not found to be statistically significant and later a fall in diastolic blood pressure after 30 mins. Fentanyl group showed a fall in Diastolic Blood Pressure (DBP) which was not found to be statistically significant.

In a study, conducted by *Neha Sharma et al. in 2014,*[11] group nalbuphine had a significant rise in systolic and diastolic blood pressure compared to fentanyl postintubation with a maximum rise in systolic blood pressure and diastolic blood pressure to be 14.9 % and 8.9% in nalbuphine group and 4.8 % and 4.5% in fentanyl group. The rise in nalbuphine group lasted longer in nalbuphine group than fentanyl.

Our findings were similar.

Comparison of Mean Arterial Pressure

In our study, there was a fall in mean arterial pressure in the fentanyl group which was found to be statistically significant at 2, 5, 10, 15 minutes. Nalbuphine showed a fall in mean arterial pressure in the immediate postoperative period after 30 mins which was similar to fentanyl.

In *Khan et al. in 2002*[9] study, the changes in mean arterial pressure was similar to their diastolic blood pressure findings, where the variation was within 20 % in both the groups but there was a much higher rise in nalbuphine which was found to be statistically significant. These findings were congruous to our study.

Channaiah et al. in 2008[12] noted in their study that inter group MAP yielded significant attenuation in the Fentanyl group for all recorded time periods and it was similar to our study.

Recovery Profiles

Comparison of modified Aldrete Score

We used modified aldrete score in our study to compare the recovery profile and to compare the safety in discharging patients from postanesthesia care unit. The modified aldrete score was lower in the nalbuphine group than in fentanyl, showing a better and earlier recovery in the fentanyl group.

According to *Khan et al. in 2002*,[9] the recovery profile was same in both the groups but an earlier recovery was noted in the fentanyl group.

Comparison of Visual Analog Scale

We used the Visual analog scale to compare the postoperative analgesia, and nalbuphine provided better analgesia in the postoperative period than fentanyl and it was statistically significant.

These findings were similar to *Khan et al. in 2002*[9] study.

Comparison of Rescue Analgesia Time

The rescue analgesia time was significantly higher in the nalbuphine group with a mean of 139 minutes in the nalbuphine group and 65 mins in the fentanyl group.

Similar findings were found in *Khan et al. in 2002*[9] study.

Comparison of respiratory depression in postoperative period

Fentanyl produced a lower saturation level than nalbuphine at one hour and two hour without Oxygen supplement which was found to be statistically significant.

The mean respiratory rate at 30 min, 1 hour and 2 hour was lower in fentanyl group which was 11.3 per minute and nalbuphine was 13.2 per min. This difference was statistically significant.

Similar findings were found in a study conducted by *Rawal et al. in 1990*[13] where within the first 15 min following recovery, increasing $Paco_2$ and $ETco_2$ as well as respiratory rates below 10/min were noted considerable patients in fentanyl group.

Side effects

The incidence of nausea was 10% in nalbuphine group and vomiting was 3%. Fentanyl reported of nausea in 10%. So, nausea was comparable in both the groups.

A study conducted by Bone E et al. (1988)[14] found no significant difference in the incidence of nausea and vomiting in the study Comparison of nalbuphine with fentanyl for postoperative pain relief following termination of pregnancy under day care anesthesia, which is congruous to our findings.

Pruritis occurred in 10 percent patients of fentanyl group in the postoperative period. Similar findings were found in the study conducted by Hari Prasad et al.[15] (2016) in the study Comparative Study of Analgesic Potential of Nalbuphine *versus* Fentanyl during General Anesthesia. Pruritis was not reported in the nalbuphine group.

Side effects like shivering, headache, bradycardia were not noted in our study.

Conclusion

Based on this study we can conclude that,

1. Fentanyl had better control on intraoperative hemodynamics as compared to nalbuphine;
2. Nalbuphine had better analgesia in the postoperative period;
3. Fentanyl showed earlier and better recovery;
4. Respiratory depression was more in the fentanyl group in the postoperative period, which is undesirable.

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Original Research Article

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Comparative Study to Evaluate the Efficacy of Intrathecal Clonidine Versus Clonidine with Fentanyl in Laparoscopic Surgeries Under General Anaesthesia

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Abstract

Background: Laparoscopic surgeries are known to cause hemodynamic repercussions due to pneumoperitoneum despite being minimally invasive surgeries. Various studies have been conducted to minimize hemodynamic alterations in laparoscopic surgeries. *Aim:* The aim was to compare the efficacy of intrathecal clonidine *versus* intrathecal clonidine with fentanyl in maintaining hemodynamic stability and to assess postoperative analgesia in patients undergoing laparoscopic surgeries under general anesthesia. *Materials and Methods:* A randomized double-blind study was done in 60 patients of either sex, with American Society of Anesthesiologists Grade I and II, aged between 18 and 55, posted for laparoscopic surgeries. Group CL (n = 30) received intrathecal clonidine 150 micrograms and Group CF (n = 30) received intrathecal clonidine 75 micrograms followed by intrathecal fentanyl 25 micrograms before general anesthesia. Assessment parameters included hemodynamics, postoperative analgesia and sedation scores. *Results:* Intraoperative heart rate, systolic, diastolic and mean arterial blood pressures at intubation, pneumoperitoneum and extubation were significantly reduced in Group CL ($p < 0.05$) when compared to Group CF. Mean duration of postoperative analgesia was significantly prolonged in Group CL (10.30 ± 1.24 hours, $p < 0.001$) when compared to Group CF (5.53 ± 1.11 hours). Mean sedation score was significantly higher in Group CL (2.07 ± 0.25 *versus* 1.90 ± 0.31; $p = 0.025$). No adverse effects were recorded during study. *Conclusions:* Intrathecal clonidine 150 micrograms is highly effective in maintaining intraoperative hemodynamic stability during laparoscopic surgeries under general anesthesia along with prolonged postoperative analgesia in comparison to combination of intrathecal clonidine 75 micrograms with fentanyl 25 micrograms.

Keywords: Intrathecal Clonidine; Fentanyl; Hemodynamics; Analgesia.

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Introduction

Minimally invasive surgeries such as laparoscopic procedures offer the advantage of less trauma and shorter hospital stay to the patients. Laparoscopic surgeries are usually performed by insufflation of gases like carbon dioxide into the abdominal cavity.[1]

However, the creation of pneumoperitoneum along with frequent change in patient positions

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resulted in marked pathophysiological alterations which includes significant cardiovascular and respiratory effects.[2] Intrathecal clonidine (partial alpha 2 receptor agonist) is found to reduce the hemodynamic stress response and anesthetic requirements in a laparoscopic surgery with prolonged postoperative analgesia.[3,4] As a matter of fact, we know that clonidine can cause hypotension and bradycardia. Fentanyl is a synthetic opioid agonist with profound analgesia and no significant motor blockade.[5] A combination therapy of opioid and alpha 2 adrenoreceptor agonist has been under utilized clinically in spite of a large body of evidence describing their synergistic action.[6] So, we attempted to combine these two drugs hypothesizing that there will be lesser side effects and hemodynamic disturbances without compromising the quality of postoperative analgesia. Hence, we compared between a single-dose of clonidine (150 micrograms) *versus* half-dose of clonidine (75 micrograms) along with an opioid such as fentanyl (25 micrograms) to investigate if this addition provided a better hemodynamic stability with increased duration of postoperative analgesia.

Aims of Study

The major aims of the study were to compare the intraoperative hemodynamic variables along with the hemodynamic response to intubation and extubation. Duration of postoperative analgesia and postoperative sedation was also assessed.

Materials and Methods

After approval of the Institutional Ethics Committee, a prospective double blinded randomized study was conducted in 60 patients, aged between 18 and 50 years, of either sex, with Body Mass Index between 18 and 30 kg/m^2, who belonged to American Society of Anesthesiologists Grade I and II posted for elective laparoscopic general surgeries lasting less than or equal to two hours. They were selected and divided into two groups of 30 each by using computer generated randomization table. Patients with contraindication to spinal technique, known allergy to clonidine and all patients with significant cardiovascular and respiratory diseases were excluded from our study.

Group 'CL' included 30 patients who received intrathecal clonidine 150 micrograms followed by conventional general anesthesia.

Group 'CF' included 30 patients who received intrathecal clonidine 75 micrograms followed by intrathecal fentanyl 25 micrograms followed by conventional general anesthesia.

Preanesthetic examination including detailed history and systemic examination as well as airway examination were conducted prior to enrollment of the patient for the study. Informed written consent was obtained from the patients after explanation of the anesthesia technique. All patients received premedication with Tablet Ranitidine 150 mg and Tablet Anxit 0.5 mg the night before surgery. The selected patients were kept fasting overnight for a period of eight hours.

An 18-gauge intravenous line was secured onto either of the upper limbs. The patients were preloaded with 500 milliliters (ml) of Ringer's lactate. On shifting the patient to the operation theater, monitors including electrocardiogram, noninvasive blood pressure monitor and pulse oximeter were connected. Baseline heart rate, systolic blood pressure, diastolic blood pressure, mean arterial pressure, oxygen saturation and end tidal carbon dioxide were measured and recorded.

Under aseptic precautions, a lumbar puncture was performed in the patients in the left lateral position using 25-gauge Quincke type spinal needle at the L3-L4 intervertebral space by midline approach to get a free flowing, clear cerebrospinal fluid. Patients allotted to the Group CL received Injection clonidine 150 micrograms (1 ml) which was kept loaded in two separate syringes as 75 micrograms (0.5 ml) each, injected intrathecally one after the other. Whereas, patients allotted to Group CF received Injection clonidine 75 micrograms (0.5 ml) followed by Injection fentanyl 25 micrograms (0.5 ml), one after the other intrathecally. In either of the two groups, a trained anesthesiologist different from the anesthesiologist performing lumbar puncture was made to load the injections required for intrathecal administration in two separate syringes so as to ensure proper blinding. The patients were made supine immediately. A five minutes interval was given for recording of post injection hemodynamic parameters prior to general anesthesia.

Patients were premedicated with Injection Glycopyrrolate 0.004 mg/kg, Injection Midazolam 0.02 mg/kg and Injection Fentanyl 2 micrograms/kg. After adequate preoxygenation, conventional general anesthesia was administered to the patients. The intravenous induction agent propofol was given in graded doses so as to attain a Bispectral Index (BIS) value of 60 after which it was stopped. The volatile inhalational agent, isoflurane was used in lowest possible concentration necessary to keep

the mean arterial pressure and heart rate within 20 percentage (%) of baseline and at the same time maintaining bispectral index between 40 and 60. At the end of the procedure, residual neuromuscular blockade was adequately reversed and patients were extubated after adequate recovery. Heart rate, systolic blood pressure, diastolic blood pressure, mean arterial pressure, end tidal carbon dioxide and oxygen saturation were recorded during intubation, appropriate intervals during surgery and during extubation. Any incidence of hypotension, hypertension, bradycardia and tachycardia was also noted. Duration of surgery was recorded at the end of surgery. Patients were shifted to the postoperative ward and monitored for heart rate, blood pressure and oxygen saturation. Level of pain and sedation was assessed using Visual Analog Scale (VAS) and Ramsay Sedation Score (RSS) respectively. Time to the first rescue analgesic was noted as the duration of postoperative analgesia which corresponded to VAS > 3. Rescue analgesia was given with Injection paracetamol 1 g intravenous infusion over 15 minutes. Sedation was assessed in the postoperative period ten minutes post extubation.

Variation in basal mean arterial pressure less than 20% was treated with intravenous Injection Ephedrine 6 mg and more than 20% was managed with increase in volatile inhalational agent. Heart rate less than 60 beats per minute was treated with intravenous Injection atropine 0.6 mg. Heart rate more than 20% of the baseline was treated with intravenous Injection fentanyl 0.5 micrograms/kg. Postoperative nausea and vomiting was treated with intravenous Injection Ondansetron 4 mg.

The qualitative parameters were represented using frequencies and percentage and the quantitative parameters were depicted using Mean (Standard Deviation) and Median (Inter Quartile Range). Student's *t*-test was used for normally distributed quantitative data and Mann Whitney *U* test was used for skewed data. Chi–square or Fisher's exact probability test was used for qualitative variables. Data was analyzed by using SPSS 22 Version Software and *p* - value less than 0.05 was considered statistically significant.

Results

A total of 60 patients were randomly assigned into two groups of 30 each. None of these patients were excluded from the study.

Mean age in Group CL was 39.9 ± 8.2 years and 38.5 ± 9.5 years in Group CF (p = 0.5). There were 13 males and 17 females in Group CL and 15 males and 15 females in group CF (p = 0.6). The duration of surgery (62.5 ± 10.1 minutes *versus* 62.25 ± 10.8 minutes) was also similar in both groups (p = 0.96). Mean body mass index was 23.8 ± 1.9 kilogram per meter square (kg/m^2) in Group CL whereas it was 24.0 ± 1.6 kg/m^2 in Group CF (p = 0.6). Baseline hemodynamic data were recorded in both the groups. Demographic data were comparable in both the groups and none of them were statistically significant.

After intubation, heart rate showed a median decrease of 6 beats/minute in Group CL whereas a median increase of 4 beats/minute was seen in Group CF which was statistically significant. (p < 0.001). At Pneumoperitoneum, a median decrease of 11 beats/minute in Group CL and 10 beats/minute in Group CF was observed which was of no statistical significance

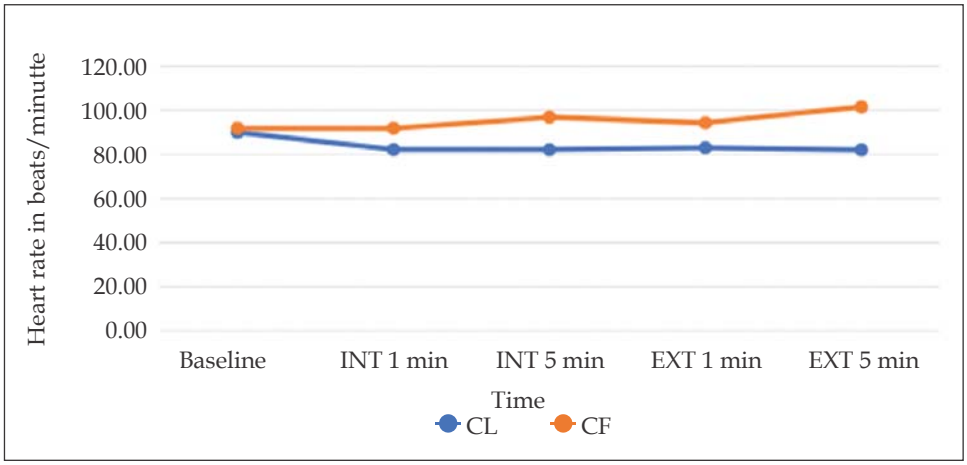

Fig. 1: Graph showing the comparison of Heart rates during intubation and extubation between both the groups.

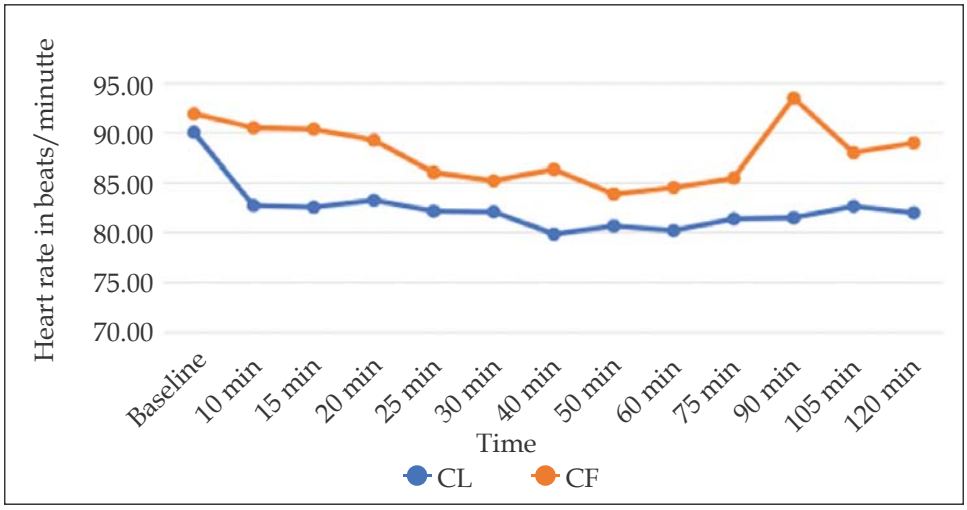

Fig. 2: Graph showing the comparison of Heart rates during pneumoperitoneum between both the groups.

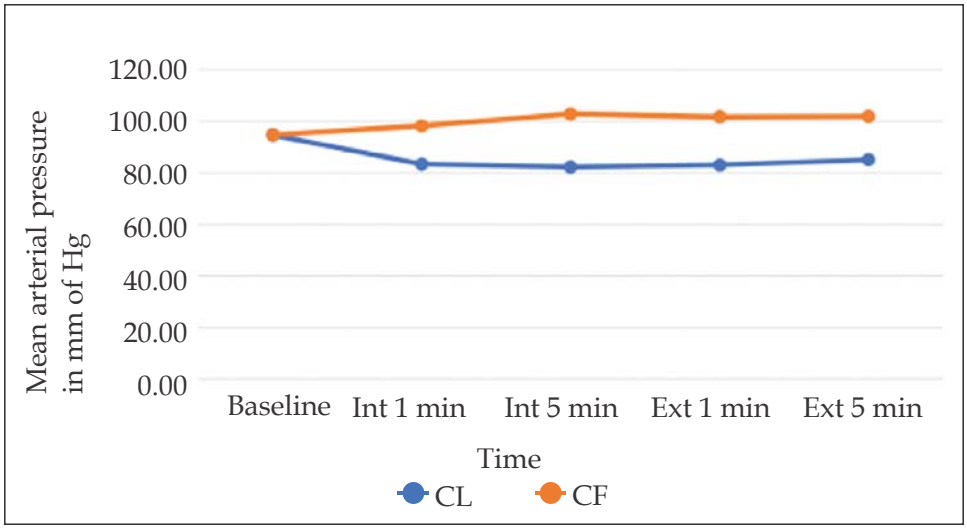

Fig. 3: Graph showing the comparison of Mean arterial pressures during intubation and extubation between both the groups.

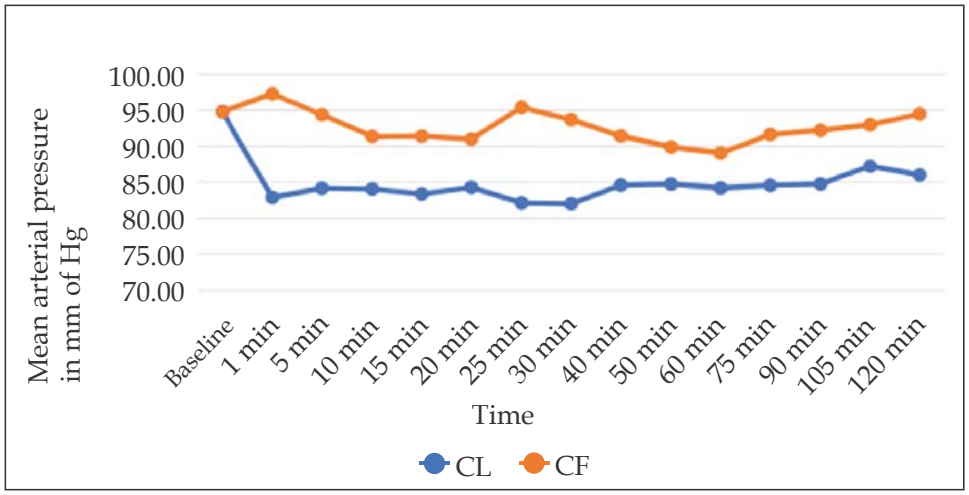

Fig. 4: Graph showing the comparison of Mean arterial pressures during pneumoperitoneum between both the groups.

(p = 0.75). Also, at extubation, a median decrease of 6 beats/minute in Group CL was found and a median increase of 11.5 beats/minute in the Group CF was observed which was statistically significant. (p < 0.001), (Figs. 1 and 2).

Systolic blood pressure after intubation showed a median decrease of 16 mm Hg in Group CL and a median increase of 10 mm Hg in Group CF (p < 0.001) whereas at extubation showed a median decrease of 15 mm Hg in Group CL and a median increase of 13.5 mm Hg in Group CF was noticed (p < 0.001), both of which were of statistical significance.

Diastolic blood pressure after intubation showed a median decrease of 6 mm Hg in Group CL and a median increase of 9 mm Hg in Group CF (p < 0.001). At extubation, a median decrease of 6 mm Hg in Group CL and a median increase of 10 mm Hg in Group CF was observed in the diastolic blood pressure (p < 0.001). These were considered significant statistically.

In the values of mean arterial pressure after intubation, a median decrease of 9 mm Hg in Group CL and a median increase of 9.5 mm Hg in Group CF was observed (p < 0.001). However, at extubation, a median decrease of 10 mm Hg in Group CL and median increase of 11.5 mm Hg in the Group CF was noticed (p < 0.001) which were of statistical significance.

At pneumoperitoneum, a median decrease of 16 mm Hg in Group CL and a median decrease of 13 mm Hg in Group CF was observed (p = 0.09) which was not significant statistically. Similarly, at pneumoperitoneum, systolic and diastolic blood pressures showed a median decrease, how so ever, both of these were not of statistical significance (p < 0.05), (Figs. 3 and 4).

The duration of postoperative analgesia is significantly greater in Group CL (10.30 ± 1.24 hours) in comparison to Group CF (5.53 ± 1.11 hours), (Fig. 5).

Hypertension was seen in 11 Patients of Group CF (p = 0.001) which was statistically significant. 6 patients had tachycardia in Group CF. 2 patients had hypotension and 1 patient had hypertension in Group CL. No patients had bradycardia episodes. None of the other side effects were statistically significant.

Sedation was comparatively greater in Group CL than Group CF (Mean RSS 2.07 ± 0.25 *versus* 1.90 ± 0.31; p = 0.025) but none of the patients in both the groups had RSS > 3.

Discussion

The creation of pneumoperitoneum in a laparoscopic surgery increases the systemic vascular resistance and blood pressure thereby producing significant hemodynamic alterations along with nociception. The use of different class of drugs like opioids, beta blockers, dexmedetomidine and nitroglycerine have been tried to minimize these changes but they have their own demerits.

Clonidine being an alpha 2 adrenoreceptor agonist is known to reduce the sympathetic outflow. Also, alpha 2 agonists induce analgesia by acting

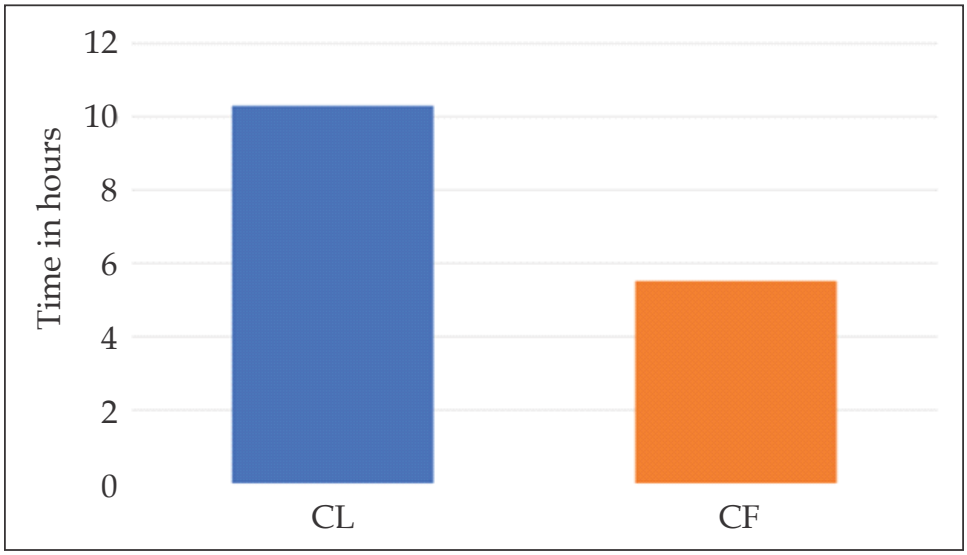

Fig. 5: Bar Diagram showing the comparison of Mean duration of postoperative analgesia between both the groups.

at different sites such as brain, brain stem, spinal cord and peripheral nerves.[7] Clonidine can be administered *via* various routes – oral, intramuscular, intravenous, epidural, intrathecal etc.

However, less literature is available with regard to the effect of intrathecal clonidine in laparoscopic surgeries under general anesthesia. The combination of two anesthesia techniques was chosen to add to their advantages and limit the side effects of each drug.

Also, clonidine is known to cause side effects like bradycardia, hypotension, sedation etc. So, we decided to compare the combination of two drugs, intrathecal fentanyl with clonidine *versus* intrathecal clonidine alone to observe if addition of fentanyl could help us reduce the dose of clonidine thereby limiting its side effects without a compromise in the intraoperative hemodynamic stability and postoperative analgesia.

Intrathecal fentanyl was chosen for combination in our study because of its rapid clearance from spinal cord sites and no motor paralysis.[8] We have avoided the use of local anesthetics through spinal route to prevent motor blockade thereby helping in early ambulation of the patients making it useful in a day care surgery.

The present study was done in 60 patients in two groups posted for elective laparoscopic surgeries under general anesthesia. Group 'CL' received intrathecal clonidine 150 micrograms whereas Group 'CF' received intrathecal clonidine 75 micrograms with fentanyl 25 micrograms followed by conventional general anesthesia.

A similar study was conducted in 2012 by Mohamed AA et al. which was a double-blind randomized trial in 90 patients to assess the safety profile and analgesic efficacy of intrathecally administered dexmedetomidine or dexmedetomidine combined with fentanyl in patients undergoing major abdominal cancer surgery.[9] They found that intrathecal dexmedetomidine improved the quality and duration of postoperative analgesia and provided analgesic sparing effect in patients undergoing major abdominal cancer surgery. They observed that addition of fentanyl had no valuable clinical effect. In our study, we also found that clonidine 150 micrograms alone was superior in maintaining hemodynamic stability along with prolonged postoperative analgesia. We observed that addition of fentanyl did not abolish the response to intubation and extubation but it maintained hemodynamic stability during pneumoperitoneum.

Our study results are in agreement to the work of Sripriya R et al. in 2018 in a study to compare the stress response attenuating effect of equal does of intrathecal and intravenous clonidine on pneumoperitoneum in 75 patients.[7] The results of the study showed that intrathecal clonidine was more effective than intravenous clonidine in suppressing hemodynamic stress response without causing much sedation.

In 2015, Sharma AN et al. studied the hemodynamic stability with intrathecal fentanyl 25 micrograms alone in laparoscopic hysterectomies under general anesthesia in 60 patients.[8] In their study, they concluded that intrathecal fentanyl (25 micrograms) is superior to intravenous fentanyl in maintaining hemodynamic stability in patients undergoing laparoscopic hysterectomies under general anesthesia. We have also done a similar study with a dose of intrathecal fentanyl 25 micrograms in combination with clonidine to assess the hemodynamic stability in laparoscopic surgeries.

There have been a few studies with the usage of high-doses of sole intrathecal clonidine. Chiari et al, in a study on analgesic and hemodynamic effects of intrathecal clonidine as the sole analgesic agent conducted in 1999, studied the effects on three different doses of clonidine 50, 100 and 200 micrograms on parturients.[10] They concluded that intrathecal clonidine produced a dose dependent analgesia with the duration and quality of analgesia being more pronounced with 100 and 200 micrograms. Also, the hypotension required significantly more often treatment with ephedrine only in the group of 200 micrograms in their study. We observed hypotension only in two patients of Group CL which was treated with one dose of intravenous injection ephedrine.

In contrast to this study, Filos et al. compared 150, 300 and 450 micrograms intrathecal clonidine as a sole agent for postoperative analgesia following cesarean section and observed a decrease in mean arterial pressure of more than 20 % from baseline with intrathecal clonidine.[11] However, we have observed hypotension only in two patients in our study with a dose of 150 micrograms of clonidine (not significant statistically) probably due to our patients being subjected to surgical stress and pneumoperitoneum in laparoscopic surgeries that encountered the vasodilating properties of clonidine unlike other studies.

We observed in our study, that the two groups, intrathecal clonidine with fentanyl combination and intrathecal clonidine group alone did not show

any statistically significant difference with regard to the heart rate, mean arterial pressure, systolic blood pressure and diastolic blood pressure at pneumoperitoneum. This implied that the intrathecal clonidine and fentanyl combination is effective and hence can be used to blunt the hemodynamic responses to pneumoperitoneum in laparoscopic surgeries even though it could not abolish the hemodynamic response to intubation and extubation.

The limitation of our study was that we had not monitored sedation for a longer duration in the postoperative period as a result of which we cannot comment upon the discharge of the patient from the postanesthesia care unit. Also, the other side of effects of clonidine such as dry mouth, constipation, postural hypotension etc. was not followed up.

Conclusion

A single dosage of Intrathecal clonidine 150 micrograms is associated with better hemodynamic stability throughout the intraoperative period and prolonged postoperative analgesia when compared to combination of clonidine 75 micrograms and fentanyl 25 micrograms.

Key Messages

The study aimed to observe the effect of sole intrathecal clonidine to attenuate the hemodynamic alterations in laparoscopic surgeries along with quality of analgesia offered. Fentanyl was used in combination with a low-dose clonidine to look for any synergistic response in terms of attenuation of hemodynamic response and enhancement of analgesia

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Comparison of Bolus Phenylephrine, Ephedrine and Mephentermine for the Management of Hypotension during Spinal Anaesthesia in Caesarean Section: A Clinical Study

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Abstract

Background: The delivery of the infant into the arms of a conscious and pain free mother is one of the most exciting and rewarding moments in medicine. To compare the efficacy of vasopressors by measuring Systolic and Diastolic blood pressure, Heart rate, Nausea and Vomiting, Neonatal APGAR scores in all Three Groups. *Methods:* A Prospective comparative clinical study was conducted in 30 patients coming for elective lower segment Cesarean section. Parturients were divided into 3 Groups (P, E, M) of 30 each as per the study drugs. Patients meeting the criteria were incorporated into the study. Randomization achieved by sealed envelope technique. Patient's height and weight were measured during the preanesthetic visit. Baseline values for maternal systolic blood pressure, diastolic blood pressure and heart rate were recorded. Epi-info 7 was used for analysis. *Results:* No statistically significant differences were found in all the 3 Groups with regards to baseline heart rate, baseline systolic blood pressure and baseline diastolic blood pressure. There was significant statistical difference in the total dose of Phenylephrine, Ephedrine and Mephentermine used ($p < 0.05$). No Significant differences were observed between heart rate changes in Ephedrine and Mephentermine group. *Conclusion:* Phenylephrine, Mephentermine and Ephedrine effectively maintained arterial blood pressure during spinal anesthesia for cesarean section. Phenylephrine has quicker onset and peak effect in comparison to ephedrine and mephentermine and its predictable carotid sinus reflex effect causes reduction in heart rate, which may be advantageous in cardiac patients and patients in whom tachycardia is undesirable.

Keywords: Phenylephrine; Mephentermine; Ephedrine; Cesarean section; Vasopressor.

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Introduction

The delivery of the infant into the arms of a conscious and pain free mother is one of the most exciting and rewarding moments in medicine. With the increasing boom in the incidence of cesarean section,[1] the anesthesiologist is trapped in a delicate web of decision making over the type of anesthetic technique to be employed which guarantees the safety of both the mother

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and fetus. However, in the recent decades there has been a worldwide shift in obstetric anesthesia practice in favor of regional anesthesia with spinal anesthesia being the most popular among them.[2] Spinal anesthesia was introduced into clinical practice by German Surgeon Karl August Bier in 1898.[3] In cesarean section under spinal anesthesia hypotension has been reported in as many as 85% of the patients.[4] Maternal hypotension is associated with distressing symptoms like dizziness, nausea, vomiting and may also interfere with surgical procedure and can cause fetal bradycardia[5] and acidosis. The rationale behind the study was bolus Phenylephrine, Ephedrine and Mephentermine for the management of hypotension during spinal anesthesia in Cesarean section. Compare the efficacy of vasopressors by measuring heart rate, nausea and vomiting, neonatal APGAR scores in all three groups.

Materials and Methods

Study design:

Prospective comparative clinical study.

Study population:

Parturients coming for elective lower segment Cesarean section.

Study settings:

Gandhi Medial College and Hospital, Secunderabad.

Sampling Technique:

Simple random sampling: Parturients were divided into 3 groups of 30 each as per the study drugs. Patients meeting the criteria were incorporated into the study. Randomization achieved by sealed envelope technique.

Sample size: After approval from the Institutional ethics committee, ninety parturients ASA I and II scheduled for elective cesarean section who developed hypotension after Subarachnoid block (SAB) were studied. All parturients were at term, had uncomplicated singleton pregnancy with cephalic presentation and did not weight more than 70 kg.

Inclusion criteria:

- Patients scheduled for elective lower segment Cesarean section;
- Aged between 20–35 years;
- Patients with ASA Class I and II;
- Baseline systolic blood pressure between 100–140 mm Hg and diastolic blood pressure between 70–89 mm Hg.

Exclusion criteria:

Patients with medical complications like diabetes mellitus, cardiovascular diseases, severe anemia, and cerebrovascular diseases;

Patients with obstetrical complications like antepartum hemorrhage, pregnancy induced hypertension, cord complications (nuchal cord or cord prolapse), fetal malformations or malpresentations;

Patients with autonomic neuropathy, spinal deformities, other neurological diseases, infections in the lumbar area, coagulation abnormalities and hypovolemia due to any cause.

Methodology:

Parturients were divided into 3 Groups of 30 each as per the study drugs:

Group P: Phenylephrine 100 μg (0.1 mg) in 1 ml as IV bolus

Group E: Ephedrine 6 mg in 1 ml as IV bolus and

Group M: Mephentermine 6 mg in 1 ml as IV bolus.

The protocol was explained to all patients in detail in their own language and informed written consent was taken.

Patient's height and weight were measured during the preanesthetic visit. Baseline values for maternal systolic blood pressure, diastolic blood pressure and heart rate were recorded. Before surgery, Ranitidine 50 mg and Metaclopramide 10 mg were given intravenously. Patients were transported to the operating theater in left lateral position with an 18G intravenous cannula in a peripheral vein.

Lumbar puncture was performed under strict aseptic precautions in left lateral position by a midline approach using 23G Quincke Babcock spinal needle inserted at L2-3 or L3-4 vertebral interspace. After establishing a free flow of clear cerebrospinal fluid, 12.5 mg (2.5 ml) of hyperbaric bupivacaine 0.5% was injected.

Statistical Analysis:

Sample size of 30 per group is taken for the study. Data like Age, Weight, Height, Base line BP, Diastolic BP, HR were expressed as mean ± SD. Comparability of groups were analyzed with Analysis of Variance (ANOVA) test to elicit the statistical significance

of variation when 3 variables are taken together Student's two-tailed '*t*' test applied to analyzed parametric data. Nonparametric Chi-square test is used for testing statistical significance for variables measured qualitatively. *p* - value < 0.05 was considered significant.

Results

As per shown in Table 1, hence age, height and weight were comparable in all 3 groups and were found to be statistically not significant. Baseline heart rate, baseline systolic blood pressure and baseline diastolic blood pressure were analyzed. The mean values for baseline heart rate in Group P were 90.13 ± 7.47 per minute, in Group E were 88.33 ± 7.93 per minute and in Group M were 92.97 ± 8.90 per minute. Similarly mean values for basal diastolic blood pressure in Group P, Group E and Group M patients were 78.80 ± 3.18 mm Hg, 78.40 ± 4.46 mm Hg and 76.33 ± 4.90 mm Hg respectively. No

Table 1: Preoperative details of the Study Participants

Parameters	Study Groups	n	Mean	SD	*F* Value	*p* - Value
Age (yrs)	Group P	30	23.17	2.51	0.66	0.51
	Group E	30	22.73	2.32		
	Group M	30	22.53	1.59		
Height (cms)	Group P	30	153.20	4.26	1.3	0.27
	Group E	30	151.83	4.66		
	Group M	30	151.43	4.33		
Weight (kg)	Group P	30	54.33	3.07	0.26	0.76
	Group E	30	54.93	4.62		
	Group M	30	54.27	3.81		
Pulse Rate	Group P	30	90.13	7.47	2.4	0.09
	Group E	30	88.33	7.93		
	Group M	30	92.97	8.90		
Systolic BP	Group P	30	123.47	4.98	2.1	0.11
	Group E	30	124.20	5.86		
	Group M	30	121.13	6.80		
Diastolic BP	Group P	30	78.80	3.18	2.9	0.059
	Group E	30	78.40	4.46		
	Group M	30	76.33	4.90		

Table 2: Clinical Parameters and Characteristics

Parameters	Study Groups	N	Mean	SD	*F* Value	*p* - Value	Significance
SAB Hypotension Time (Mins)	Group P	30	7.00	1.02	0.3	0.73	NS
	Group E	30	7.20	1.00			
	Group M	30	7.13	1.01			
SAB Del Interval (Mins)	Group P	30	9.33	1.21	1.5	0.22	NS
	Group E	30	9.40	0.50			
	Group M	30	9.00	1.29			
UI-Del Interval (secs)	Group P	30	51.50	6.45	2.4	0.095	NS
	Group E	30	46.60	3.78			
	Group M	30	48.80	12.99			
Total dose (mgs)	Group P	30	0.13	0.05	73.38	0.001	HS
	Group E	30	9.56	4.62			
	Group M	30	9.78	4.01			
APGAR 1	Group P	30	8.89	0.58	0.88	0.41	NS
	Group E	30	8.67	0.72			
	Group M	30	8.50	0.77			
APGAR 5	Group P	30	8.78	0.58	0.88	0.41	NS
	Group E	30	8.67	0.72			
	Group M	30	8.50	0.77			

Table 3: Variations in the Heart Rate with Time

Time of Assessment (min)	Mean Diff with Hypotension			*p* - Value	Significance	Significant Pairs
	Group P	Group E	Group M			
1	18.90	-1.47	3.47	$p < 0.001$	HS	P & E, P & M
2	23.97	-2.57	3.47	$p < 0.001$	HS	P & E, P & M
3	24.17	-1.47	4.33	$p < 0.001$	HS	P & E, P & M
4	23.73	4.86	6.87	$p < 0.001$	HS	P & E, P & M
5	23.70	5.46	6.87	$p < 0.001$	HS	P & E, P & M
6	23.30	8.06	6.73	$p < 0.001$	HS	P & E, P & M
7	22.83	7.86	6.33	$p < 0.001$	HS	P & E, P & M
8	22.83	9.60	10.47	$p < 0.001$	HS	P & E, P & M
9	22.97	9.53	10.47	$p < 0.001$	HS	P & E, P & M
10	22.50	9.73	11.20	$p < 0.001$	HS	P & E, P & M
11	22.43	10.06	11.27	$p < 0.001$	HS	P & E, P & M
12	23.30	10.53	11.33	$p < 0.001$	HS	P & E, P & M
13	25.80	10.93	11.53	$p < 0.001$	HS	P & E, P & M
14	22.73	10.93	11.80	$p < 0.001$	HS	P & E, P & M
15	22.73	10.80	11.87	$p < 0.001$	HS	P & E, P & M
16	23.97	11.73	11.93	$p < 0.001$	HS	P & E, P & M
17	23.97	11.60	11.93	$p < 0.001$	HS	P & E, P & M
18	23.70	12.73	11.93	$p < 0.001$	HS	P & E, P & M
19	22.50	12.80	11.93	$p < 0.01$	S	P & E, P & M
20	21.67	12.53	12.27	$p < 0.01$	S	P & E, P & M
25	21.67	13.06	12.67	$p < 0.01$	S	P & E, P & M
30	22.03	13.53	13.33	$p < 0.01$	S	P & E, P & M
35	22.03	14.00	13.67	$p < 0.05$	S	P & E, P & M
40	22.17	14.40	13.87	$p < 0.05$	S	P & E, P & M
45	21.83	15.40	14.13	$p < 0.05$	S	P & E, P & M
50	21.10	16.20	16.33	$p < 0.05$	S	P & E, P & M
55	20.30	17.50	16.53	$p < 0.05$	S	P & E, P & M
60	19.63	17.56	17.06	$p < 0.05$	S	P & E, P & M

Table 4 (A): Changes in Systolic Blood Pressure

Time of Assessment (min)	Mean Diff with Hypotension			*p* - Value	Significance	Significant Pairs
	Group P	Group E	Group M			
1	15.53	11.00	10.73	$p < 0.001$	HS	P & E, P & M
2	22.47	19.67	19.27	$p < 0.001$	HS	P & E, P & M
3	22.60	19.73	19.93	$p < 0.05$	S	P & E, P & M
4	24.53	22.20	22.00	$p < 0.05$	S	P & E, P & M
5	25.40	22.47	22.87	$p < 0.05$	S	P & E, P & M
6	26.67	24.20	23.93	$p < 0.05$	S	P & E, P & M
7	24.40	24.47	24.73	$p > 0.05$	NS	-
8	26.73	26.67	26.20	$p > 0.05$	NS	-
9	26.60	26.67	26.33	$p > 0.05$	NS	-
10	27.40	27.27	27.33	$p > 0.05$	NS	-
11	27.53	27.33	27.00	$p > 0.05$	NS	-
12	27.53	27.00	27.00	$p > 0.05$	NS	-
13	27.87	27.33	29.93	$p > 0.05$	NS	-

(Contd.)

Time of Assessment (min)	Mean Diff with Hypotension			*p* - Value	Significance	Significant Pairs
	Group P	Group E	Group M			
14	28.40	28.13	28.33	$p > 0.05$	NS	-
15	27.80	28.00	27.60	$p > 0.05$	NS	-
16	28.93	28.63	28.60	$p > 0.05$	NS	-
17	29.00	28.93	28.67	$p > 0.05$	NS	-
18	30.67	29.07	28.87	$p > 0.05$	NS	-
19	30.87	29.67	28.27	$p > 0.05$	NS	-
20	31.80	29.87	29.40	$p > 0.05$	NS	-
25	30.80	29.87	29.00	$p > 0.05$	NS	-
30	30.27	30.07	29.27	$p > 0.05$	NS	-
35	30.20	30.73	28.67	$p > 0.05$	NS	-
40	30.20	31.13	28.40	$p > 0.05$	NS	-
45	30.87	31.27	28.93	$p > 0.05$	NS	-
50	32.20	32.33	32.27	$p > 0.05$	NS	-
55	33.20	33.13	33.00	$p > 0.05$	NS	-
60	33.47	33.13	33.07	$p > 0.05$	NS	-

Table 4 (B): Changes in Diastolic Blood Pressure

Time of Assessment (min)	Mean Diff with Hypotension			*p* - Value	Significance	Significant Pairs
	Group P	Group E	Group M			
1	13.40	10.87	10.53	$p < 0.05$	S	P & E, P & M
2	15.40	12.67	12.40	$p < 0.05$	S	P & E, P & M
3	15.73	12.67	12.20	$p < 0.05$	S	P & E, P & M
4	16.73	13.73	13.07	$p < 0.05$	S	P & E, P & M
5	16.73	13.80	13.40	$p < 0.05$	S	P & E, P & M
6	17.13	16.20	12.40	$p < 0.05$	S	P & E, P & M
7	17.07	17.00	17.07	$p > 0.05$	NS	-
8	17.27	17.13	17.27	$p > 0.05$	NS	-
9	17.47	17.20	17.13	$p > 0.05$	NS	-
10	18.07	17.80	18.13	$p > 0.05$	NS	-
11	18.07	17.93	18.20	$p > 0.05$	NS	-
12	16.87	16.80	16.60	$p > 0.05$	NS	-
13	17.40	17.00	17.13	$p > 0.05$	NS	-
14	18.60	18.33	18.33	$p > 0.05$	NS	-
15	18.67	18.73	18.53	$p > 0.05$	NS	-
16	18.47	18.87	18.20	$p > 0.05$	NS	-
17	17.87	18.73	18.00	$p > 0.05$	NS	-
18	17.80	18.60	17.73	$p > 0.05$	NS	-
19	18.47	18.73	18.47	$p > 0.05$	NS	-
20	19.60	19.47	19.20	$p > 0.05$	NS	-
25	19.53	19.13	19.20	$p > 0.05$	NS	-
30	19.53	19.40	19.07	$p > 0.05$	NS	-
35	19.13	19.40	19.27	$p > 0.05$	NS	-
40	19.67	19.87	19.60	$p > 0.05$	NS	-
45	19.47	19.60	19.67	$p > 0.05$	NS	-
50	20.20	19.87	19.87	$p > 0.05$	NS	-
55	20.27	20.07	20.07	$p > 0.05$	NS	-
60	20.27	20.07	20.07	$p > 0.05$	NS	-

Table 5: Side Effects in Study Participants

Side Effects		Drug		
		Group P	Group E	Group M
Nausea & Vomiting	Count	2	5	5
	%	6.67	16.67	16.67
Nil	Count	28	25	25
	%	93.33333	83.333333	83.33333

Chi-square = 1.730, $p > 0.05$, Nonsignificant

statistically significant differences were found in all the 3 groups with regards to baseline heart rate, baseline systolic blood pressure and baseline diastolic blood pressure.

The mean value with standard deviation of total Phenylephrine dose in Group P, total Ephedrine dose in Group E and total Mephentermine dose in Group M were 0.13 ± 0.05, 9.56 ± 4.62 and 9.72 ± 4.01 respectively. There was significant statistical difference in the total dose of Phenylephrine, Ephedrine and Mephentermine used ($p < 0.05$), shown as in Table 2.

Heart rate raised in all three groups during hypotension. In Group P, poststudy drug values of heart rate were decreased significantly from the values at onset of the hypotension till the end of the surgery when compared to other Two Groups ($p < 0.001$). No Significant differences were observed between heart rate changes in Ephedrine and Mephentermine group, shown in Table 3.

On intergroup comparison rise of systolic blood pressure at 2, 4 and 6 minutes poststudy drugs were significantly less in Ephedrine Group and Mephentermine Group as compared to Phenylephrine Group ($p < 0.05$), shown as in Table 4 (A and B).

Shown in Table 5, side effects observed were only nausea and vomiting. 6% developed nausea and vomiting in Group P, whereas 16% developed in Group E and Group M. APGAR score did not reveal any untoward effect on fetal status, since, all newborn of three groups had APGAR score greater than 7.

Discussion

Regional anesthesia, especially spinal anesthesia, proved to be the most preferred technique for cesarean section.[6] The reason being, the unique potential of spinal anesthesia to provide Subarachanoid block with a blend of low-degree of physiological changes and with profound degrees sensory denervation and muscle relaxation. Thus, the safety of spinal anesthesia is of dual nature, pharmacological as well as physiological, when compared to general anesthesia.

The results of the present study, correlate well with the study by *Dinesh Sahu and colleagues*.[7] They studied 60 patients undergoing elective as well as emergency cesarean section under spinal anesthesia who developed hypotension after subarachnoid block. They were randomly allocated to one of three groups to receive an IV bolus of the following Group P Phenylephrine 100 µg (n = 20), Group E Ephedrine 6 mg (n = 20) or Group M Mephentermine.

Thomas and Colleagues[8] reported that bolus phenylephrine 100 µg is as effective as ephedrine 5 mg in restoring maternal arterial pressure100 mm Hg. More than 50% of women given phenylephrine in their study developed significant bradycardia. But in our study, decrease in heart rate was seen but not below 60 beats/min than with Ephedrine and Mephentermine Groups.

Taylor JC et al.[9] who reported two cases of overdose resulting in extreme hypertension and headache. In one case she developed decreased blood pressure after induction of spinal anesthesia to 110/59 mm Hg and there were symptoms of faintness and nausea. She was given phenylephrine 250 µg IV. These side effects are may be due to larger doses of phenylephrine when compared to the present study where the dose was given in small incremental doses.

Ramanathan and colleagues[10] studied in 127 healthy patients undergoing elective cesarean section under epidural anesthesia. They concluded that transient maternal hypotension does not affect neonatal acid – base status, both ephedrine and phenylephrine do not cause fetal acidosis, when used for treating maternal hypotension.

Casey study[11] showed that 10-point APGAR score as affective as umbilical artery pH measurement to assess the condition and prognosis of new born. Hence, APGAR score was used to predict neonatal outcome in our present study.

Conclusion

Phenylephrine, Mephentermine and Ephedrine effectively maintained arterial blood pressure during spinal anesthesia for cesarean section. Phenylephrine has quicker onset and peak effect in comparison to ephedrine and mephentermine and its predictable carotid sinus reflex effect causes reduction in heart rate, which may be advantageous in cardiac patients and patients in whom tachycardia is undesirable. Thus, it can be concluded that IV Phenylephrine, Ephedrine and Mephentermine can be safely used during spinal anesthesia for cesarean section for treatment of hypotension.

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Original Research Article

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A Study on Hemodynamic Response During Induction with Etomidate, Propofol or Combination of Etomidate and Propofol in General Anaesthesia

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Abstract

*Introduction***:** Patient's safety is the most important aspect of patient management in general anesthesia. Stress response during laryngoscopy and intubation leads to hemodynamic changes. In all the methods used for induction of anesthesia, it is aimed to preserve the hemodynamic balance and to provide optimal conditions by reducing the side effects. The purpose of this study was to compare hemodynamic response during induction with propofol, etomidate or combination of propofol and etomidate with special reference to pain on injection and myoclonus in patients requiring endotracheal intubation in elective surgeries. *Materials and Methods:* It is a prospective randomized comparative study. After getting ethical committee clearance, a group of ninety patients aged 18 to 65 years of either sex and ASA physical status I or II scheduled for elective surgery under general anesthesia were assigned randomly to Three Groups Group (P) was induced with Injection. Propofol (2 mg/kg) intravenously Group (E) with Injection. Etomidate (0.3 mg/kg) intravenously and Group (P + E) with Injection. Propofol (1 mg/kg) plus Injection. Etomidate (0.15 mg/kg) intravenously. Heart Rate (HR), Systolic Blood Pressure (SBP), Diastolic Blood Pressure (DBP), Mean Arterial Blood Pressure (MAP) and Oxygen Saturation (SpO_2) were noted at different time intervals. Presence of pain on injection and myoclonus were also observed. *Statistical Analysis:* Data will be analyzed by descriptive Statistics. Student's *t*-test was used to compare the significant difference between two means. ANOVA for three groups. The Chi-square test was used for categorical data such as gender, American Society of Anesthesiologist physical status, injection pain and myoclonus. A value of $p < 0.05$ is considered as statistically significant. *Results:* There was significant difference in mean HR ($p < 0.001$) between the 3 groups within 1–5 minutes of induction. MAP among all three groups decreases after induction and it was more in Group P than in Group E and Group P + E. The incidence of myoclonus in Group E was 80% while in Group P + E was 1.3% and none in Group P. The incidence of pain on injection in Group P was 86.7%, Group E was 10% and none in Group P + E. *Conclusion:* The incidence of hemodynamic instability, pain on injection, myoclonus is less with E + P group. Therefore, we concluded that combination of etomidate & propofol can be considered as valuable alternative as an induction agent.

Keywords: Etomidate; Propofol; Hemodynamics; Injection Pain; Myoclonus.

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Introduction

Anesthesia induction is commonly initiated by intravenous administration of induction agents. Anideal induction agent should have properties such as hemodynamic stability, minimal respiratory side effects, rapidclearance, minimal drug interactions etc. Over the years, there has been a continuous search for better and safer intravenous induction agents.

Propofol, an alkyl phenol derivative is one of the most widely used induction agents with rapid onset and short duration of action.[1] But it is associated with significant blood pressure reduction and decrease in systemic vascular resistance especially in volume depleted and cardiac patients.[2] A significant decrease in heart rate is also observed with this agent.[3] Many patients also report some degree of pain and discomfort with intravenous administration.[4] Etomidate is a hypnotic agent with minimal effect on cardiovascular system having a very stable hemodynamic profile.[5] But it has side effects like pain on injection and also myoclonus.[6] Rarely it can inhibit enzymatic synthesis if adrenal steroids which can last up to 6–8 hours even after single induction dose.[7] Patient's safety is the most important aspect of patient management in general anesthesia. Stress response during laryngoscopy and intubation leads to hemodynamic changes. In all the methods used for induction of anesthesia, it is aimed to preserve the hemodynamic balance and to provide optimal conditions by reducing the side effects.

With this background, we hypothesize that, with the use of average doses of combination of etomidate and propofol would reduce the hemodynamic deterioration. Therefore, the present study was designed to evaluate the effect of combination of both these drugs while used and the primary objective was to compare the hemodynamic parameters associated with etomidate propofol combination and sole use of each drugs. Secondary objective was defined as incidence of myoclonus and injection pain.

Materials and Methods

After obtaining approval from institutional ethical committee and informed written consent from each patient. 90 patients scheduled for elective surgery under general anesthesia in hospitals attached to Bangalore Medical College and Research Institute during the period from February 2019 to June 2019.

Patients aged 18–65 years, scheduled for elective surgeries under general anesthesia with endotracheal intubation, and patients belong to ASA class 1 & 2 were included in the study. Patient refusing to participate in the study, Patients with preexisting hypertension, IHD, on beta blockers, ASA physical status III and IV, patient with history of hypersensitivity to Propofol /Etomidate were excluded from the study.

Based on previous study, Meena K, et al.,[8] heart rate after two minutes of induction is taken in Group E was 96.37 ± 6.031 and and in Group P + E was 91.17 ± 6.747. To detect a minimum of difference of 5.22 beats/min.

Sample size is calculated using the formula,

$n = 2 (Z\alpha + Z_{1-\beta})^2 \sigma^2/d^2$

Where Zα = standard table value for 95% CI = 1.96

$Z_{1-\beta}$ = Standard table value for 80% Power = 0.84

σ = Standard Deviation = 40.8d = Effect Size = 5.22

$n = 26.4$

A minimum of 30 patients would be required in each group, keeping confidence interval (α) at 95% and power of study (β) at 80%.

Patients were randomly allocated into one of the Three Groups comprising 30 each, using numbers generated from www.random.org.

For induction, *Group P* received Injection. Propofol 2 mg/kg IV, *Group E* received Injection. Etomidate 0.3 mg/kg IV and Group *P + E* received Injection Propofol 1 mg/kg plus Injection. Etomidate 0.15 mg/kg IV.

A prior preanesthetic evaluation was done on the previous day of surgery. On arrival at Operation Theater, a 18G/20G intravenous (IV) cannula was secured in the nondominant hand and suitable intravenous fluid was started. Standard anesthesia care monitors were attached and baseline hemodynamic parameters were noted. Patients were premedicated with Inj. Glycopyrrolate 4 mcg/kg, Inj. Midazolam 0.03 mg/kg and Fentany l2 mcg/kg 2 minutes prior to induction and were preoxygenated with 100% oxygen for 3 minutes.

For induction Group P received Injection. Propofol 2 mg/kg IV, Group E received Injection. Etomidate 0.3 mg/kg IV, Group P + E received Injection Propofol 1 mg/kg plus Injection. Etomidate 0.15 mg/kg IV.

After induction, hemodynamic variables were recorded. One minute after loss of consciousness & inability to respond to verbal commands, Injection

Vecuronium (0.1 mg/kg) was given after which patient was ventilated with bag and mask. 3 minutes after the administration of muscle relaxant, laryngoscopy and endotracheal intubation was done using an adequately sized endotracheal tube. Depth of anesthesia was further maintained by isoflurane 1-1.5% and equal mixtures of oxygen-nitrous oxide (3–4 L/ min) along with intermittent bolus of vecuronium (0.02 mg/kg) as required throughout the surgery.

Heart Rate (HR), Systolic Blood Pressure (SBP), Diastolic Blood Pressure (DBP), Mean Arterial Blood Bressure (MAP) and Oxygen Saturation (SpO_2) were continuously monitored. Hemodynamic parameters before induction, after induction and at 1 minutes, 2 minutes, 3 minutes, 5 minutes, 10 minutes, 15 minutes, 30 minutes after induction were recorded.

Statistical Analysis:

Data was entered in Microsoft excel and was exported into SPSS Version 21.0. Data was analyzed by descriptive Statistics; Student's *t*-test was used to compare the significant difference between two means. ANOVA was e used to compare the significant difference between three or more groups. The Chi-square test was used for categorical data such as gender, American Society of Anesthesiologist physical status, injection pain and myoclonus. A value of $p \leq 0.05$ is considered as statistically significant.

Results

The demographic features of the patients recruited in the three groups were comparable regarding age, sex and BMI ($p > 0.05$), Table 1. There is a statistically significant fall in heart rate in Group P at 2 minutes, 3 minutes and 5 minutes postinduction compared to other Two Groups ($p < 0.05$), Fig. 1. There is a significant fall in systolic blood pressure in Group P from 1 minute to 10-minute postinduction compared to others given ($p < 0.05$), Fig. 2.

There is a significant fall in diastolic blood pressure in group P from 3 minutes post induction which sustained up to 30 minutes ($p < 0.05$), (Fig. 3).

There is a significant fall in mean Arterial Blood Pressure (MAP) in Group P which started at 3 minutes and persisted upto 30 minutes when compared to other groups ($p < 0.05$), Fig. 4. The incidence of pain on injectionin Group P was 86.7% of total patients in that group, while it was 10% of patients in Group E and none in Group P + E (Fig. 5).

There was 80% incidence of myoclonus in Group E compared with Group P and Group P + E which were 0% and 1.3%, respectively, (Fig. 6).

Table 1: Demographic details of patients recruited in the present study

Demographic data	Group P	Group E	Group P + E
Age (years)	34.5	33.63	35.48
Gender (male/female)	14/16	15/15	13/17
BMI (Kg/M2)	21.76	21.95	21.43

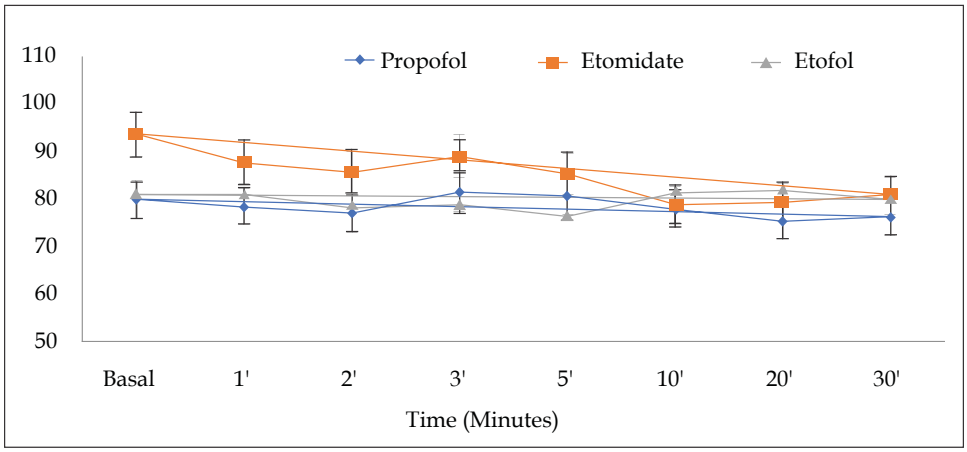

Fig. 1: Comparison of heart rate at different time interval in patients belongs to different groups

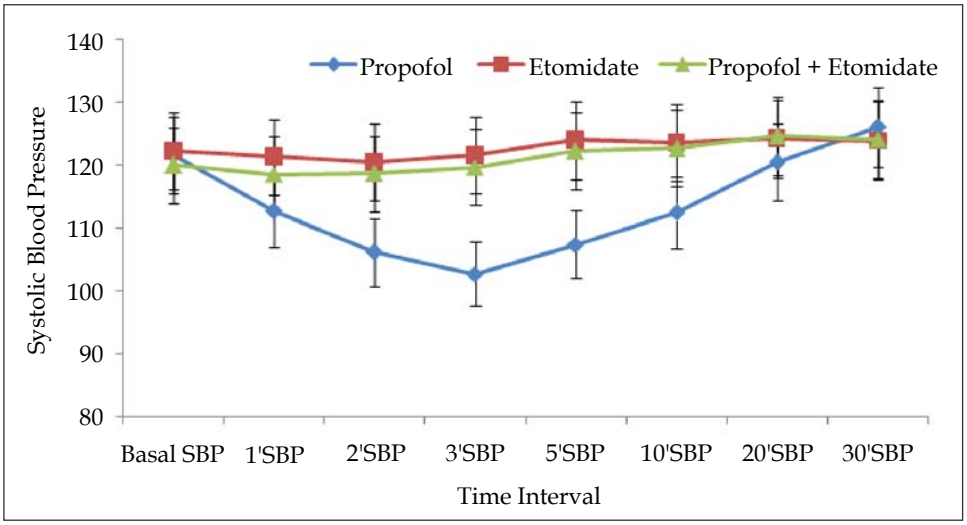

Fig. 2: Comparison of systolic blood pressure at different time interval of postinduction in patients belongs to different groups

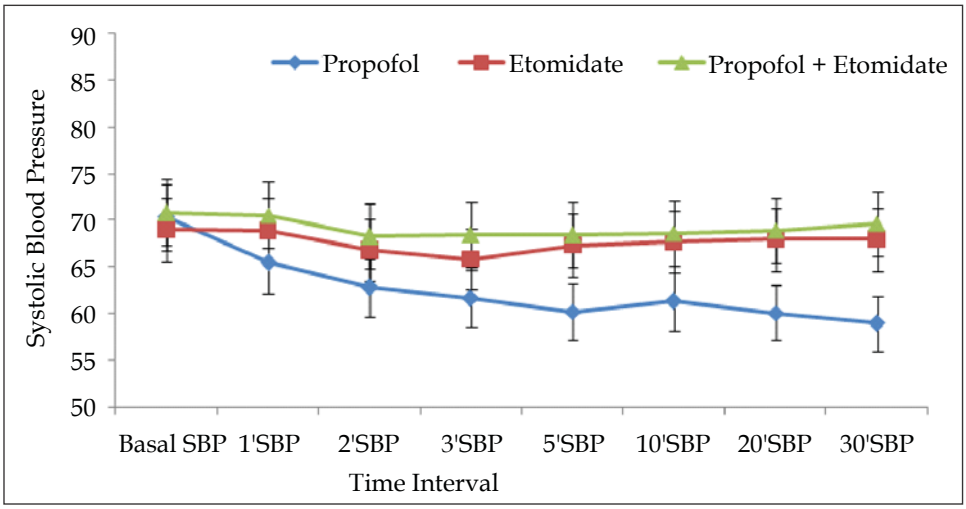

Fig. 3: Comparison of diastolic blood pressure at different time interval of postinduction in patients belongs to different groups

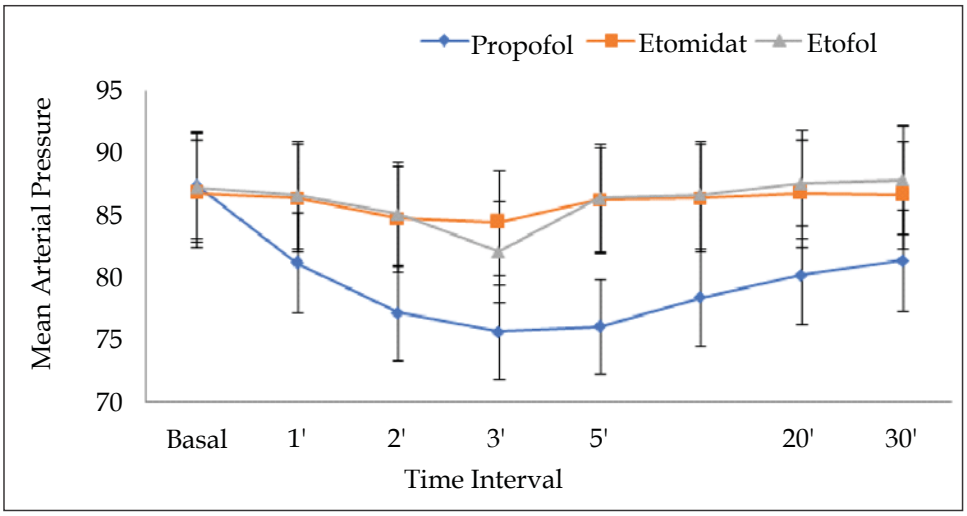

Fig. 4: Comparison of mean arterial blood pressure at different time interval of postinduction in patients belongs to different groups

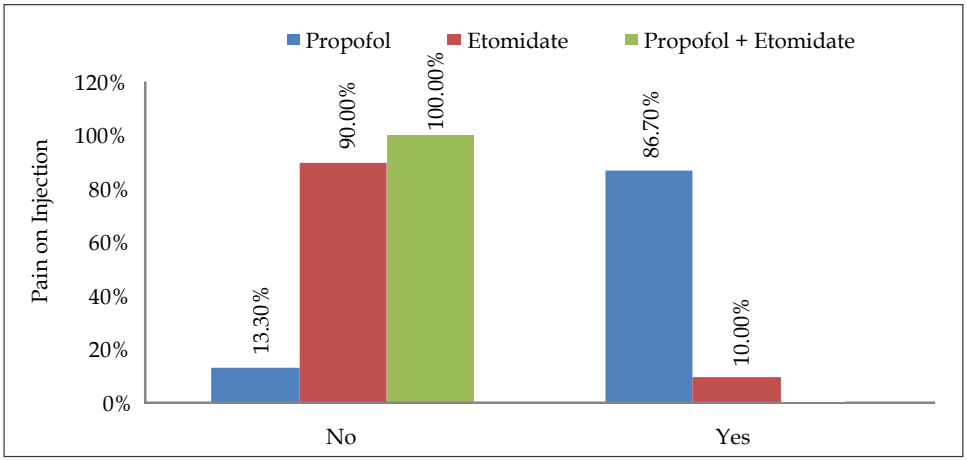

Fig. 5: Comparison of pain on injection at different time interval of postinduction in patients belongs to different groups

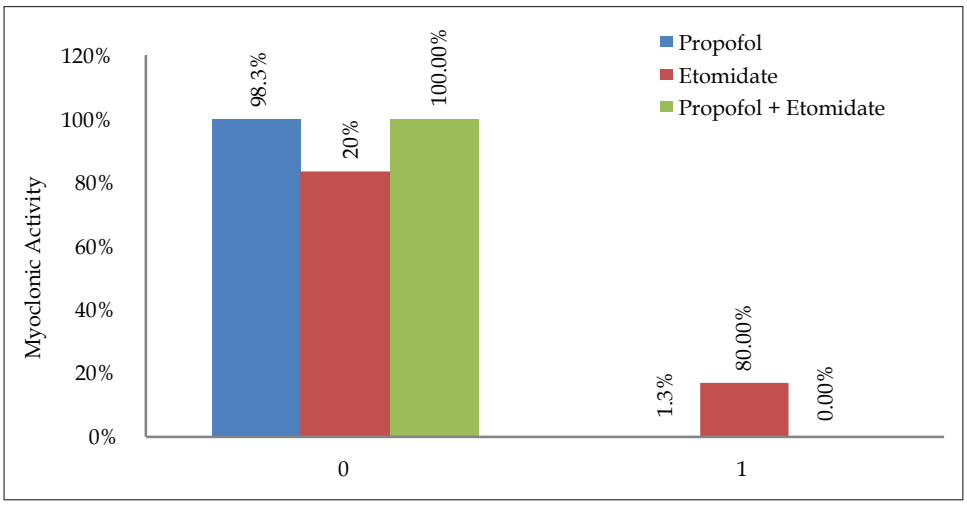

Fig. 6: Comparison of myoclonic activityat different time interval of postinduction in patients belongs to different groups

Discussion

Hemodynamic changes during perioperative period have become greater concern in modern day anesthesia. Hence, combinations of various anesthetic agents have been used for better hemodynamic stability and lesser adverse effects. In this study, we compared the hemodynamic effects of using combination of propofol & etomidate with each agent used separately for intravenous induction for general anesthesia. Pain on injection and presence of myoclonus were also observed.

Etomidate is an imidazoline group derivative known for its hemodynamic stability, had been widely used in various cardiac surgeries. It also causes pain on injection due to a solvent present in it. Propofol on the other hand is one of the commonest induction agents used in day care surgeries which also has pain on injection as a common side effect.

These two drugs were studied at Hacettepe University, Faculty of Pharmacy, Department of Pharmaceutical Technology for availability for admixture. They reported that these drugs can be mixed and physically available for an admixture, which they named this admixture etofopol.[9] In our study, we included 90 patients of ASA 1 & 2 physical status who were to undergo general anesthesia and divided into three groups of 30 each as described above.

VS Rathore et al.[10] in 2019 compared etomidate, propofol and an admixture of etomidate and propofol (PE) as induction agents and noted

hemodynamic stability and side effects with each agent and admixture. They observed that there was a significant decrease in mean arterial pressure and diastolic blood pressure in propofol group postinduction which concurs with our study. However, the heart rate in all the three-group remained stable. Additional advantages like reduction in pain on injection and myoclonus were also observed with admixture.

In 2016, Meena K et al.[8] compared hemodynamic profile of etomidate, propofol and an admixture of etomidate and propofol (PE) as induction agents among 90 patients. They observed that Heart rate and mean arterial blood pressure in all study groups decreases after induction and it was more in Group I (Propofol Group) compared to Group II (Etomidate) and III (Etomidate + Propofol). However, there were increase in heart rate and mean arterial blood pressures after intubation in Group 11 and Group 111 which returned to baseline. In our study, there is a statistically significant fall in heart rate in Group P from 2 to 5 minutes postinduction. They concluded that combination proved to be significantly better than either propofol or etomidate alone.

In a study by Hosseinzadeh et al.,[11] comparing hemodynamic changes during placement of Laryngeal Mask Airway (LMA) using propofol, etomidate and etomidate-propofol combination where group one was given Inj. Propofol 2.5 mg/kg, Group Two received Inj Etomidate 0.3 mg/kg and Group Three 1 mg/kg Propofol + 0.2 mg/kg Etomidate. LMA placement was done after loss of eyelash reflex and no response to verbal command. The main finding of the study was that more stable hemodynamics was provided by combination of propofol and etomidate, even though the dose of both drugs is reduced in the combination which was similar to observations of our study.

In a study, performed by Yagan Ö et al.,[12] patients were randomly divided into three groups as Group P (n = 30, Propofol 2.5 mg/kg), Group E (n = 30, Etomidate 0.3 mg/kg) and Group PE (n = 30, Propofol 1.25 mg/kg + Etomidate 0.15 mg/kg). They found that Etomidate-propofol combination may be a valuable alternative when extremes of hypotensive and hypertensive responses due to propofol and etomidate are best to be avoided. There was no statistically significant difference between the groups with respect to injection pain. A significant difference was determined between Group P and Group E in terms of myoclonus incidence ($p < 0.05$). But in our study, we observed that there is statistically lower incidence on pain on injection with combination of etomidate and propofol with comparison to individual agents. The observation of incidence was comparable to their study.

In 2011, Fatma et al.[9] compared propofol etomidate, and combination of etomidate and propofol as induction agents and noted hemodynamic stability and side effects. They concluded that mean and SBP were significantly decreased in the propofol group compared to the etomidate and PE groups. The incidence of injection pain was significantly lower in the PE Group, although higher incidence of myoclonus activity was seen in etomidate group compared with propofol and PE Groups. In our study, pain upon injection with the admixture group was significantly lower than PE alone, and the incidence of myoclonus and changes in hemodynamic parameters were consistent with above study.

The combination reduces the pain on injection which can be attributed to the reduction in the lipid solvent and propofol concentration. It can also be attributed to bradykinin release which is reduced when combination is given.

Etomidate was found to be associated with higher incidence of myoclonic activity than any other induction agent. Certain agents like fentanyl, midazolam, dexmedetomidine as premedication have found to reduce the incidence of myoclonus. Even priming with etomidate before induction is also found to be useful in reducing incidence of myoclonus. There were only two patients in combination group who had myoclonus while induction.

In our study, it was concluded combination of etomidate and propofol causes less pain on injection compared with other two agents, and considerably reduced the incidence of myoclonus when compared with etomidate alone. The combination provides better hemodynamic stability and hence can be considered as valuable alternatives as an induction agent.

Conclusion

We concluded from our study that combination of etomidate and propofol can be considered as valuable alternative to other induction agents in view of hemodynamic stability and added advantages like decreases incidence of pain on injection and myoclonus

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Conflict of Interest: There is no conflict of interest.

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Original Research Article

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A Comparative Study of Two Different Doses of Fentanyl 2mcg/kg and 4 mcg/kg in Attenuating the Hemodynamic Stress Response During Laryngoscopy and Endotracheal Intubation

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Abstract

Introduction: Direct laryngoscopy and endotracheal intubation induces cardiovascular stress response which in turn leads to increase in plasma catecholamine concentration and rise in blood pressure and heart rate. Fentanyl is a popular opioid used to attenuate a presser response to laryngoscopy and intubation. In this study, we compared two different doses of fentanyl 2 mcg/kg and 4 mcg/kg to asses maximum effectiveness and safety to prevent stress response during laryngoscopy and intubation. *Methods:* In this prospective comparative clinical study, 30 patients aged 18 to 50 years of ASA physical status I and II, scheduled for elective surgery under general anesthesia requiring endo tracheal intubation. Patients were randomized into two groups of 15 patients each: Group A: Received 2 µg/kg of fentanyl IV 5 minutes before induction. Group B: Received 4 µg/kg of fentanyl IV 5 minutes before induction. All groups were assessed for hemodynamic changes after premedication, during laryngoscopy and intubation, after intubation at 1, 3, 5 and 10 minutes, postoperative sedation and postoperative side effects. *Results:* Fentanyl in doses of 4 mcg/kg was effective in complete prevention of hemodynamic stress response during laryngoscopy and intubation. However, 4 mcg/kg of fentanyl produced a 15–20% decrease in hemodynamic variables from baseline compared to 5–10% with 2 mcg/kg of fentanyl. *Conclusion:* Fentanyl in dose of 4 µg/kg five minutes before induction is the most appropriate dose in terms of efficacy and safety for preventing hemodynamic stress response during laryngoscopy and intubation.

Keywords: Fentanyl; Pressor response; Endotracheal; Intubation; Hemodynamic.

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Introduction

Endotracheal intubation is an integral part of anesthetic management and critical care of patient and has been practiced following its description by Rawbo them and Magil in 1921.[1] Reild and Brace first

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described hemodynamic response to laryngoscopy and tracheal intubation.[2] Direct laryngoscopy and endotracheal intubation induces cardiovascular stress response which in turn leads to increase in plasma catecholamine concentration and rise in blood pressure and heart rate. This response is usually transient, variable and unpredictable. It occurs 30 seconds after starting the laryngoscopy and intubation and lasting for less than 10 mins.[3] These changes are well tolerated by healthy individual. But in patients with hypertension, coronary artery disease or left ventricular failure, arrhythmia, myocardial infraction, it may prove fatal.[4] This result suggests predominant sympathetic response during intubation and the need of prophylaxis in patients at risk.

Recommendations for attenuating reflex tachycardia and hypertension are manifold. The technique used should minimize these responses to anesthesia for patients at risk.

Drugs like Lidocaine, Esmolol, Fentanyl, Clonidine, Nitroglycerine, Verapamil and Nicardipine have been used to prevent pressor response to laryngoscopy and tracheal intubation.[5,6] Inhalational agents also do not have satisfactory effects and may need higher concentration which may cause serious hypotension, bradycardia and delayed recovery.

Opioid receptors are found in cardiovascular regulatory center, the sympathetic nervous system, the vagal nuclei, and the adrenal medulla. These precise locations of receptors enable fentanyl to significantly blunt the hemodynamic responses to hypopharyngeal noxious stimulation. Opioids are commonly used in perioperative period for their variety of desirable use. Fentanyl in particular has advantages over old opioids having rapid onset, short duration of action, cardio stability with no histamine release and broncho spasm. These are reasons fentanyl is being used now a days.[6] Fentanyl citrate, an opioid, is phenylpiperidine of the 4-aminopiperidine series controls both heart rate and blood pressure responses. It is an agonist at specific opioid receptors at presynaptic and postsynaptic sites in central nervous system as well as in periphery. The principle effect of opioid receptor activation is decrease in neurotransmission.[7] The present study was undertaken with an objective to compare the attenuation of the hemodynamic responses during laryngoscopy and intubation. In this study, we compared two different doses of fentanyl 2 mcg/kg and 4 mcg/kg to asses maximum effectiveness and safety to prevent stress response during laryngoscopy and intubation.

Materials and Methods

After approval from the hospital ethical committee and informed written consent, this study was carried out in Department of Anesthesiology, DY Patil Hospital and Research Centre, Pune. It was conducted in 60 adult patients belonging to American association of anesthesiologists (ASA) Grade I/II in age group of 18–60 years of age and posted for elective spine surgery under General Anesthesia.

Patients who were unwilling, or with respiratory of cardiac dysfunction or with renal or liver impairement were not included in the study. Also, patients with any coagulopathy or having known drug allergy were excluded from the study.

After detailed preanesthetic evaluation, routine and specific investigation, each patient was informed regarding nature, purpose of the study. Preoperative adequate fasting hours (6–8 hrs) were confirmed. The patients were randomized into two groups using the equal group random allocation method, that is, A and B groups. Patients were prepared by securing 20 gauge intravenous (IV) cannula, applying basic monitoring like plethysmography, standard 5-lead electrocardiography (ECG), noninvasive blood pressure. Patients in the A group received After detailed preanesthetic evaluation, routine and specific investigation, each patient was informed regarding nature, purpose of the study. Preoperative adequate fasting hours (6–8 hrs) were confirmed. The patients were randomized into two groups using the equal group random allocation method, that is, A and B groups. Patients were be prepared by securing 20 gauge intravenous (IV) cannula, applying basic monitoring like plethysmography, standard 5-lead Electrocardiography (ECG), noninvasive blood pressure.

After premedication with Inj. Glycopyrrolate 0.004 mg/kg Inj Ondansetron 0.1 mg/kg IV and Inj. Midazolam 0.0.2 mg/kg IV patients in Group A received Inj. Fentanyl 2 mcg/kg intravenously 5 minutes prior to induction and patients in Group B received Inj. Fentanyl 4 mcg/kg intravenously 5 minutes prior to induction. The vital parameters were recorded as (T1). Patient were preoxy genated with100% oxygen for 3 minutes. Induction was done with Inj. Propofol (2 mg/kg). The choice of muscle relaxant was injection succinylcholine (2 mg/kg) given after administering propofol once the patient is able to ventilate. Vital parameters were recorded as (T2). Patient were intubated with cuffed endotracheal tube. Oxygen and nitrous oxide

were started along with isoflurane. Loading dose of Vecuronium 0.1 mg/kg was given. Anesthesia was maintained with 65% nitrous oxide and 35% oxygen mixture along with isoflurane 0.8% -1% with controlled ventilation with intermittent doses of vecuronium (0.08 mg/kg) as and when required by patient. Postintubation vitals were recorded at 0, 1, 3, 5, 10 minutes.

During surgery, continuous pulse rate monitoring, SBP, DBP, Mean BP, SpO_2, respiratory rate was done, Patient was also be monitored for the side effects of the drug, if any during the course of intubation and in period following intubation. At the end of surgery patients were reversed with Inj. Glycopyrrolate 0.008 mg/kg along with Inj. Neostigmine methyl sulphate 0.05 mg/kg intravenously. Patient's after extubation were then be shifted to the recovery room.

All cases were completed in stipulated time. Data was compiled and tabulated. The statistical analysis was done using parametric test and the final interpretation was done based on 'Z' test (standard normal variant) with 95% level of significance.

Results

The patient characteristics shown in the Table 1, there was no significant differences in the two groups. (p value > 0.05).

Baseline HR was comparable in both the groups. Table 2 shows, changes in HR at various specific timings in both the groups. In both the groups, there was a significant decrease in HR within 5 minutes of fentanyl premedication. The extent of decrease was 5% in Group A, 10% in Group B. At the time of laryngoscopy and intubation, HR increased 17% from baseline in Group A while it remained below baseline with 10% decrease in Group B, (Fig. 1).

Table 1: Comparison of Patient Characteristics

	Group A Mean ± SD	Group B Mean ± SD	p - value
Sex (M/F)	9/6	11/4	0.438
Age	33.20 ± 4.74	32.67 ± 5.56	0.780
Weight	58.60 ± 4.87	58.60 ± 6.54	1.000
ASA score (I/II)	11/4	12/3	0.666

Table 2: Comparison of Heart rate

Timing	Group A		Group B		p - value
	Mean ± SD	% change	Mean ± SD	% change	
Baseline	87.87 ± 3.60	NA	89.00 ± 4.71	NA	0.465
After drug	83.07 ± 3.03	-5% ↓	80.13 ± 4.66	-10% ↓	0.052
After MR	84.87 ± 3.09	-3% ↓	79.87 ± 4.81	-10% ↓	0.002*
0 min	102.40 1.84±	17% ↑	75.53 ± 4.37	-15% ↓	0.000*
1 min	97.40 1.99±	11% ↑	76.00 ± 3.64	-15% ↓	0.000*
3 min	92.80 ± 2.70	6% ↑	73.67 ± 3.35	-17% ↓	0.000*
5 min	89.20 1.52±	2% ↑	73.00 ± 3.34	-18% ↓	0.000*
10 min	83.73 1.98±	-5% ↓	71.73 ± 2.91	-19% ↓	0.000*

* Statistically significant

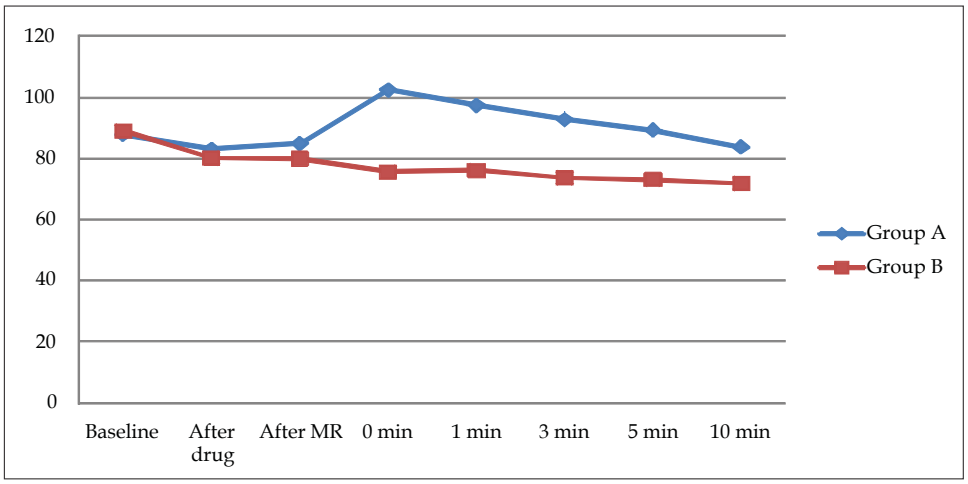

Fig. 1: Comparison of Heart rate

Table 3: Comparison of SBP

Timing	Group A		Group B		*p* - value
	Mean ± SD	% Change	Mean ± SD	% Change	
Baseline	128.20 ± 4.93	NA	121.87 ± 4.69	NA	0.001*
After drug	124.33 ± 4.51	-3% ↓	110.47 ± 4.64	-9% ↓	0.000*
After MR	126.73 ± 4.65	-1% ↓	111.67 ± 4.58	-8% ↓	0.000*
0 min	136.73 ± 3.37	7% ↑	109.00 ± 3.66	-11% ↓	0.000*
1 min	134.73 ± 3.06	5% ↑	106.93 ± 2.12	-12% ↓	0.000*
3 min	130.93±2.37	2% ↑	105.53 ± 3.78	-13% ↓	0.000*
5 min	127.20 ± 3.34	-1% ↓	104.40 ± 3.64	-14% ↓	0.000*
10 min	122.93 ± 4.03	-4% ↓	104.60 ± 3.25	-14% ↓	0.000*

* Statistically significant

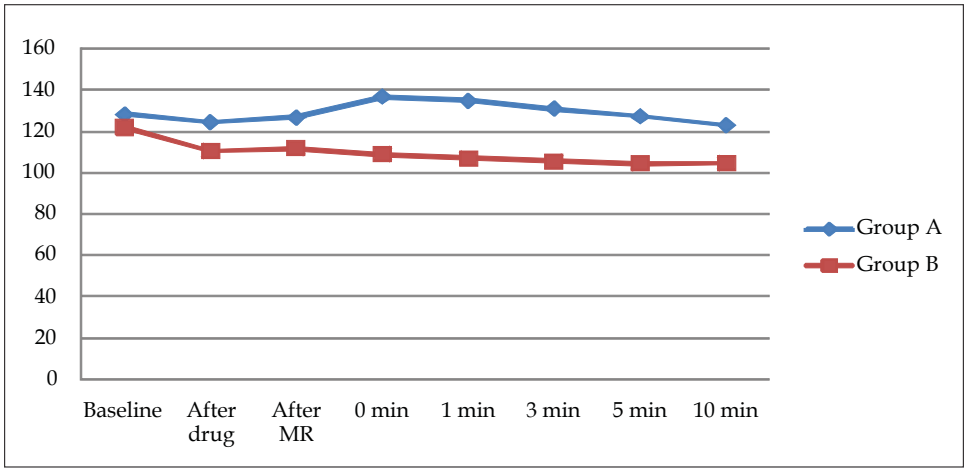

Fig. 2: Comparison of SBP

Table 4: Comparison of MAP

Timing	Group A		Group B		*p* - value
	Mean ± SD	% Change	Mean ± SD	% Change	
Baseline	97.58 ± 2.50	NA	94.31 ± 4.40	NA	0.020*
After drug	96.29 ± 2.32	-1% ↓	88.96 ± 4.60	-6% ↓	0.000*
After MR	96.73 ± 2.38	-1% ↓	88.60±3.28	-6% ↓	0.000*
0 min	101.44 ± 1.95	4% ↑	86.73 ± 2.98	-8% ↓	0.000*
1 min	99.44 ± 1.72	2% ↑	84.44 ± 1.66	-10% ↓	0.000*
3 min	98.13 ± 1.41	1% ↑	84.18 ± 1.92	-11% ↓	0.000*
5 min	96.00 ± 1.42	-2% ↓	79.60 ± 1.56	-16% ↓	0.000*
10 min	93.69 ± 1.67	-4% ↓	78.73 ± 1.35	-17% ↓	0.000*

* Statistically significant

Baseline SBP was comparable in all the three Groups. Table 3 shows, changes in SBP at various specific timings in both groups. In both groups, there was a significant decrease in SBP within 5 minutes of fentanyl premedication. The extent of decrease was 3% in Group A, and 9% in Group B. At the time of laryngoscopy and intubation, SBP increased 7% from the baseline in Group A while it remained below the baseline with 11% in Group B and III. The maximum decrease in SBP was in Group B of 14% at 10 mins after intubation as compared to baseline, (Fig. 2).

Baseline MAP was comparable in both the groups. Table 4 shows, changes in MAP at various specific timings in three groups. There was a significant decrease in MAP within 5 minutes of fentanyl premedication. The extent of decrease was 1 % in Group A and 6% in Group B. At the time of laryngoscopy and intubation MAP increased 4% from the baseline in Group A while it remained below the baseline with 8% decrease in Group B. There was maximum decrease in Group B in MAP of 17% at 10 minutes after intubation as compared to Group A which was only 4%, (Fig. 3).

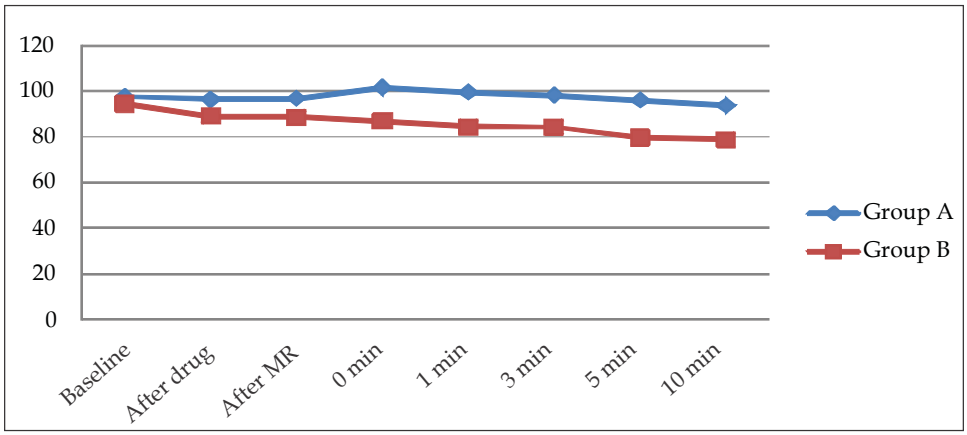

Fig. 3: Comparison of MAP

Discussion

This study compared the efficacy of 2 mcg/kg fentanyl and 4 mcg/kg fentanyl to attenuate pressor response to laryngoscopy and intubation. As compared to 2 mcg/kg fentanyl, 4 mcg/kg fentanyl attenuated the increase in systolic, diastolic, and mean arterial blood pressure after intubation.

Direct laryngoscopy and intubation is known to cause increase in heart rate and blood pressure. The mechanism behind this response is belived to be reflex sympathetic response due to catecholamines released when there is mechanical stimulation to upper respiratory tract i.e. larynx and trachea. There is significant elevation in serum levels of norepinephrine and epinephrine following laryngoscopy, with and without tracheal intubation.

Studies have shown that reflex changes in the cardiovascular system after laryngoscopy and intubation lead to an average increase in blood pressure by 40–50% and 20% increase in heart rate.[5]

Different doses of fentanyl have been used for the same in varying range of 1.5 to 6 mcg/kg in different studies. After observing results for different doses we choose doses of 2 mcg/kg and 4 mcg/kg in our study groups.[8] In our study, we choose to administer the study drug, that is fentanyl, 5 minutes prior to induction. This was done considering the pharmacological profile of fentanyl in different studies. As the onset of action starts within minutes and peak action is at 5 minutes for fentanyl.[9] In our study, there was a significant decrease in HR within 5 minutes of fentanyl premedication in both the study groups. The extent of decrease was more when 4 mcg/kg was used. At the time of laryngoscopy and intubation, HR increased 17% from baseline in group A while it remained below baseline with 10% decrease in Group B. Thus, there was attenuation to pressor resposnse with 4 mcg/kg of Inj. Fentanyl.

In a study, done by Sellamuthu Gunalan et al. (2015) [10], they concluded that Attenuation of rise in heart rate and blood pressure following laryngoscopy and endotracheal intubation was better with 1mcg/kg of dexmedetomidine when compared to fentanyl 2 mcg/kg. In our study too, 2 mcg/kg could not attenuate pressor response as compared to 4 mcg/kg of fentanyl.

In a study, done by Gurulingappa et al. (2012),[11] they concluded that attenuation of pressor response is seen both with lignocaine and fentanyl. Of the two drugs fentanyl 4 mg microgram IV bolus provides a consistent, reliable and effective attenuation as compared to lignocaine 1.5 mg/kg IV bolus. This result is similar to result in our study for 4 mcg/kg group.

In a study, conducted by Manoj kumar et al. (2017),[12] compared which of the three doses of fentanyl 2 mcg/kg, 3 mcg/kg and 4 mcg/kg is better to attenuate pressor response to laryngoscopy and intubation. They found that 2 µg/kg of fentanyl could not prevent the hemodynamic stress response to laryngoscopy and intubation and the hemodynamic variable like HR, SBP, DBP. Both the doses, 3 and 4 µg/kg of fentanyl were effective in complete prevention of hemodynamic stress response to intubation as patients in both the groups did not show any increase in hemodynamic parameters and were continuously below the baseline through the study period.

Although with 3 µg/kg of fentanyl, hemodynamic increased above preinduction level, while with 4 µg/kg of fentanyl, hemodynamic were still lower than preinduction level, showing a better efficacy of 4 µg/kg of fentanyl over 3 µg/kg in preventing the hemodynamic stress response to laryngoscopy and intubation.

In our study, we also found similar results on comparing between 2 mcg/kg and 4 mcg/kg for HR, SBP, MAP. In both groups, there was a significant decrease in SBP within 5 minutes of fentanyl premedication. The extent of decrease was 3% in Group A where 2 mcg/kg was given, and 9% in Group B with 4 mcg/kg fentanyl. At the time of laryngoscopy and intubation, SBP increased 7% from the baseline in Group A while it remained below the baseline with 11% in Group B and III. The maximum decrease in SBP was in patients with 4 mcg/kg of 14% at 10 mins after intubation as compared to baseline. There was a significant decrease in MAP within 5 minutes of fentanyl premedication. The extent of decrease was 1% in Group A with 2 mcg/kg of fentanyl and 6% in Group B that is with 4 mcg/kg fentanyl. At the time of laryngoscopy and intubation MAP increased 4% from the baseline in Group A while it remained below the baseline with 8% decrease in Group B. There was maximum decrease in Group B in MAP of 17% at 10 minutes after intubation as compared to Group A which was only 4%.

Conclusion

Fentanyl in dose of 4 µg/kg five minutes before induction is the most appropriate dose in terms of efficacy and safety for preventing hemodynamic stress response during laryngoscopy and intubation.

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Original Research Article

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To Study the Efficacy and Heamodynamic Response to Dexmedetomidine as Hypotensive Agent in Elective Spine Surgeries

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Abstract

Background: Spine surgeries require reduced intraoperative blood pressures to make better visualization of surgical site. Deliberate hypotension or controlled hypotension have been preferred technique used for many surgical procedures to attain clear surgical fields. *Aim:* The aim of our study is to evaluate the efficacy and hemodynamic response to IV Dexmedetomidine and placebo [Normal saline] as hypotensive agent in elective spine surgeries. *Methods:* Sixty patients between age group of 18–60 years were selected who were posted for elective spine surgeries. They were divided into two groups of 30 each i.e. Dexmedetomidine Group and Normal Saline Group and were be given their respective drug. Group D: Inj. Dexmedetomidine 100 mcg [diluted in 50 ml of 0.9% Normal saline]. Group N: 50 ml of 0.9% of normal saline. Patients in the D Group received 1 mcg/kg infusion (diluted in 50 ml of 0.9% normal saline) over a period of 10 min prior to premedication. After induction of anesthesia, patients in the D Group received a continuous infusion of Dexmedetomidine at 0.2 mcg/kg/h, whereas patients in the N Group received infusion of Normal saline at same dose as dexmedetomidine. The hemodynamic parameters Pulse Rate (PR), Systolic Blood Pressure, Diastolic Blood Pressure and Mean Arterial Blood Pressure (SBP, DBP, MAP), Respiratory Rate (RR), SpO_2 were studied in all the groups at baseline, after giving drug, after intubation, 15 minutes, 30 minutes and 45 minutes, 60 minutes, 75 minutes, 90 minutes, 105 minutes, 120 minutes, after stopping drug and after extubation. Postoperative sedation score was also measured. Patient were shifted to postanesthesia care unit and monitored for hemodynamic parameters, Ramsay sedation score and adverse effects if any. The statistical analysis was done based on Student's *t*-test for continuous variables and Chi-square test for categorical variables. Final interpretation will be based on *Z*-test with 95% level of significance. *Results:* Patients in D Group achieved desired MAP as compared to normal saline (placebo) group with good control over heart rate. With no significant difference in postoperative sedation score was found in patients with Dexmedetomidine group as compared to normal saline (placebo). *Conclusion:* Dexmedetomidine is an effective drug for achieving controlled hypotension and thus, can be used as hypotensive agent in spine surgery to maintain clear surgical field.

Keywords: Hypotension; Deliberate hypotension; Dexmedetomidine; Spine surgery; Surgical field.

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Introducton

Spine surgeries for traumatic spine fractures or tumors or other etiologies were known to cause tremendous blood loss during surgery. This resulted in severe complications to deal with intraoperative as well as postoperative. It also made surgical field visualization difficult. "Controlled hypotension or deliberate hypotension" is a commonly used technique to limit blood loss and improve visualization of the operative field during surgery. This involves reducing arterial pressure MAP to 65 mm Hg reversibly according to various literature and maintain the same throughout the surgery.[1,2] It reduces intraoperative blood loss which will facilitate good surgical field exposure also resulting in faster surgeries ultimately reducing intraoperative and postoperative need of blood transfusions. There are various anecdotal reports to describe this technique and have been published since the 1970s[3,4] Various types of trials have been undertaken mainly prospective type to demonstrate the efficacy of deliberate hypotension, which were aimed to decrease the blood loss and transfusion necessity during major spine or neurological surgery.[5,6] Dexmedetomidine is a potent and highly selective α2-adrenergic agonist, with a differential affinity for the α_2 : α_1 receptors in a ratio 1,620:1. It is a sedative, analgesic, and possesses anesthetic sparing effect and sympatholytic properties too. The central and peripheral sympatholytic action of Dexmedetomidine by binding to α2 adrenergic receptors brings about dose-dependent decrease in Mean Arterial Blood Pressure (MAP), Heart Rate (HR), cardiac output, and norepinephrine release.[7] In this study, the efficacy and hemodynamic response of Dexmedetomidine would be studied as hypotensive agent in elective spinal surgeries.

Materials and Methods

After approval from the hospital ethical committee and informed written consent, this study was carried out in Department of Anesthesiology, DY Patil Hospital and Research Centre, Pune. It was conducted in 60 adult patients belonging to American Association of Anesthesiologists (ASA) Grade I/II in age Group of 18–60 years of age and posted for elective spine surgery under General Anesthesia.

Patients who were unwilling, or with respiratory of cardiac dysfunction or with renal or liver impairement were not included in the study. Also, patients with any coagulopathy, heart rate < 65 beats/min prior to surgery or having known drug allergy were excluded from the study.

After detailed preanesthetic evaluation, routine and specific investigation, each patient was informed regarding nature, purpose of the study. Preoperative adequate fasting hours (6–8 hrs) were confirmed. The patients were randomized into two groups using the equal group random allocation method, that is, D and N Groups. The anesthesiologist loading the drugs and administering the premedication was different than the one conducting the case and managing patients in postanesthesia care unit. Thus, both the anesthesiologists were blinded to the assignment.

Patients were prepared by securing 20 gauge Intravenous (IV) cannula, applying basic monitoring like plethysmography, standard 5-lead Electrocardiography (ECG), noninvasive blood pressure. Patients in the D Group received 1 µg/kg infusion (diluted in 50 ml of 0.9% normal saline) over a period of 10 min prior to premedication. While patients on N Group received normal saline in the rate similar to Group D.

After premedication with injection ondansetron 4 mg IV, injection glycopyrrolate 0.2 mg IV, injection midazolam 0.05 mg/kg and injection fentanyl 2 µg/kg in both the groups, anesthesia induction was done with injection propofol 2 mg/kg. Tracheal intubation was facilitated by injection vecuronium bromide 0.1 mg/kg. The patients was then positioned prone on a Relton's frame. Necessary precautions were taken to protect pressure points and avoid nerve injury and limb ischemia. Patients in the D Group received a continuous infusion of Dexmdetomidine at 0.2 mcg/kg/h, whereas patients in the N Group received continous infusion of Normal saline at 0.2 mcg/kg/hr, similar to D Group.

Throughout the surgery heart rate, blood pressure [S.B.P, D.B.P., Mean B.P], Oxygen saturation, $EtCO_2$, Postoperative sedation, Urine output, Blood loss, Temperature were continulusly monitored.

The above parameters were measured at the following time points:

Baseline (Tb), at the start of the hypotensive agent - (Ts), immediately after intubation - (Ti), after 15 minutes (T15), after 30 minutes (T30), after 45 minutes (T45), after 60 minutes (T60), after 75 minutes (T75), after 90 minute (T90), after 105 minutes (T105), after 120 minutes after induction (T120), at the point of stoppage of administration of hypotensive agent (Tt) and at extubation (Te).

Target MAP was taken as 65–85 mm Hg and target HR was taken as more than 60 beats per minute.

Modified Ramsay sedation scale was used measure postoperative sedation.

Modified Ramsay sedation scale

Score	Characteristics
1	agitated, restless
2	cooperative, tranquil
3	responds to verbal commands while sleeping
4	brisk response to glabellar tap or loud noise while sleeping
5	Sluggish response glabellar tap or loud noise while sleeping
6	No sluggish response to glabellar tap or loud noise while sleeping

Adequate data was collected, compiled and tabulated in stipulated time. The statistical analysis was done based on Student's *t*-test for continous variables and Chi-square test for categorical variables. Final interpretation were done based on *Z*-test with 95% level of significance.

Results

The present study was conducted on 60 adult patients.

The demographic profile was comparable in both the study groups as given in Table I. The two groups were similar in age, weight, sex and ASA status.

Table 1: Demographic profile

	Dexmedetomidine	Normal saline	*p* - value
Age (in years)	34.63 ± 10.555	36.43 ± 10.464	5.10
Sex (male/ female)	16/14	18/12	0.79
Weight (kgs)	57.60 ± 7.295	54.27 ± 5.477	0.062
ASA Grade I/II	18/12	19/11	0.791

As shown in Fig. 1. All the patients in D Group achieved target MAP and maintained it throughout the surgery. 30 minutes after induction MAP was significantly low in Group D (86.73 ± 3.12 mm Hg) as compared to Group N (97.20 ± 2.49 mm Hg). It was also observed that mean Heart rate in Group D was sigmificantly lower than Group N (Fig. 2).

Table 2: Mean Arterial Blood Pressure distribution between Dexmedetomidine Group and the Normal Saline Group

Mean Arterial Blood Pressure (mm Hg)	Group	Mean	SD	*t* - test	*p* - value
Baseline	Dexmedetomidine	97.47	4.46	-1.73	0.08
	Normal saline	98.56	2.92		
After giving drug	Dexmedetomidine	97.09	3.58	-1.76	0.08
	Normal saline	98.13	2.70		
After intubation	Dexmedetomidine	99.42	3.58	-1.74	0.08
	Normal saline	100.87	2.70		
After 15 mins	Dexmedetomidine	96.64	2.40	-2.10	0.04
	Normal saline	97.84	2.64		
After 30 mins	Dexmedetomidine	86.73	3.12	-14.33	<0.001
	Normal saline	97.20	2.49		
After 45 mins	Dexmedetomidine	81.71	3.31	-20.89	<0.001
	Normal saline	96.76	2.10		
After 60 mins	Dexmedetomidine	77.56	3.63	-25.02	<0.001
	Normal saline	96.56	2.38		
After 75 mins	Dexmedetomidine	76.82	4.79	-20.19	<0.001
	Normal saline	96.73	2.10		
After 90 mins	Dexmedetomidine	76.42	5.19	-19.27	<0.001
	Normal saline	96.56	2.38		
After 105 mins	Dexmedetomidine Ondansetron	75.58	5.07	-20.31	<0.001
	Normal saline	96.42	2.41		
After 120 mins	Dexmedetomidine	75.31	5.30	-19.86	<0.001
	Normal Saline	96.44	2.42		
After stopping drug	Dexmedetomidine	75.40	5.10	-20.39	<0.001
	Normal Saline	96.44	2.42		
After extubation	Dexmedetomidine	97.16	3.23	-1.634	0.108
	Normal Saline	98.42	2.73		

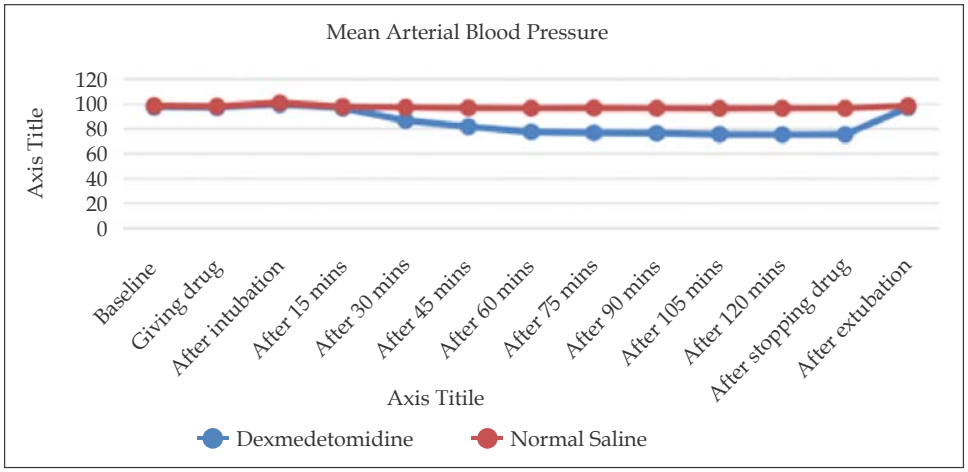

Fig. 1: Line diagram showing MAP in both the study groups

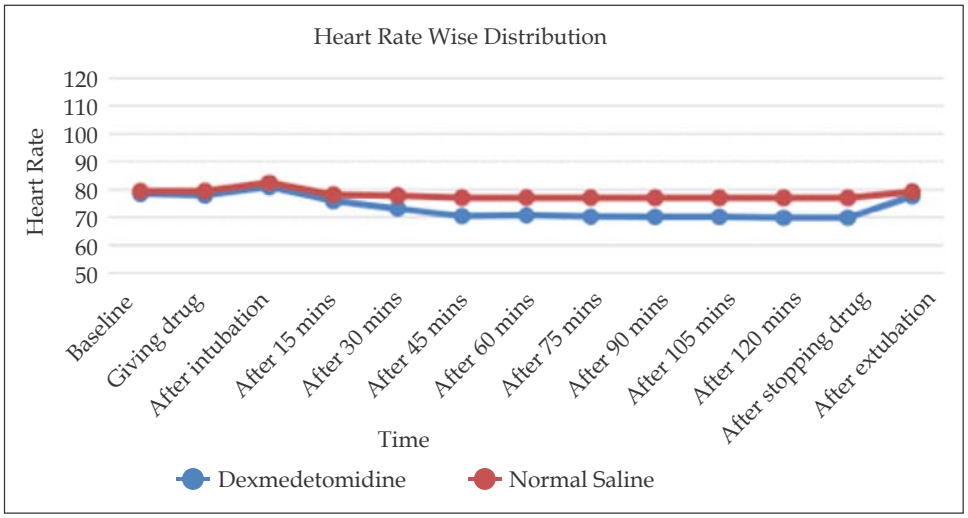

Fig. 2: Line diagram showing Heart rate in both the study groups

Table 3: Heart rate wise distribution between Dexmedetomidine group and the Normal Saline group

Heart Rate (beats/min)	Group	Mean	SD	*t* - test	*p* - value
Baseline	Dexmedetomidine	78.53	2.403	-1.407	0.165
	Normal Saline	79.47	2.726		
After giving drug	Dexmedetomidine	78.00	2.407	-2.209	0.312
	Normal Saline	79.47	2.726		
After intubation	Dexmedetomidine	81.00	2.407	-2.209	0.080
	Normal Saline	82.47	2.726		
After 15 mins	Dexmedetomidine	76.00	3.201	-2.111	0.39
	Normal Saline	78.20	2.644		
After 30 mins	Dexmedetomidine	73.20	3.263	-5.966	<0.001
	Normal Saline	77.87	2.776		
After 45 mins	Dexmedetomidine	70.73	4.653	-6.140	<0.001
	Normal Saline	77.13	3.309		
After 60 mins	Dexmedetomidine	70.73	4.653	-6.065	<0.001
	Normal Saline	77.13	3.309		
After 75mins	Dexmedetomidine	70.27	5.245	-6.026	<0.001
	Normal Saline	77.13	3.309		

(Contd.)

Heart Rate (beats/min)	Group	Mean	SD	*t* - test	*p* - value
After 90 mins	Dexmedetomidine	70.20	5.391	-6.026	<0.001
	Normal Saline	77.07	3.269		
After 105 mins	Dexmedetomidine	70.20	5.345	-5.952	<0.001
	Normal saline	77.07	3.269		
After 120 mins	Dexmedetomidine	69.87	5.823	0.852	<0.001
	Normal Saline	77.07	3.269		
After stopping drug	Dexmedetomidine	69.90	5.391	-6.026	<0.001
	Normal Saline	77.07	3.269		
After extubation	Dexmedetomidine	77.70	2.562	-2.260	0.28
	Normal Saline	79.27	2.803		

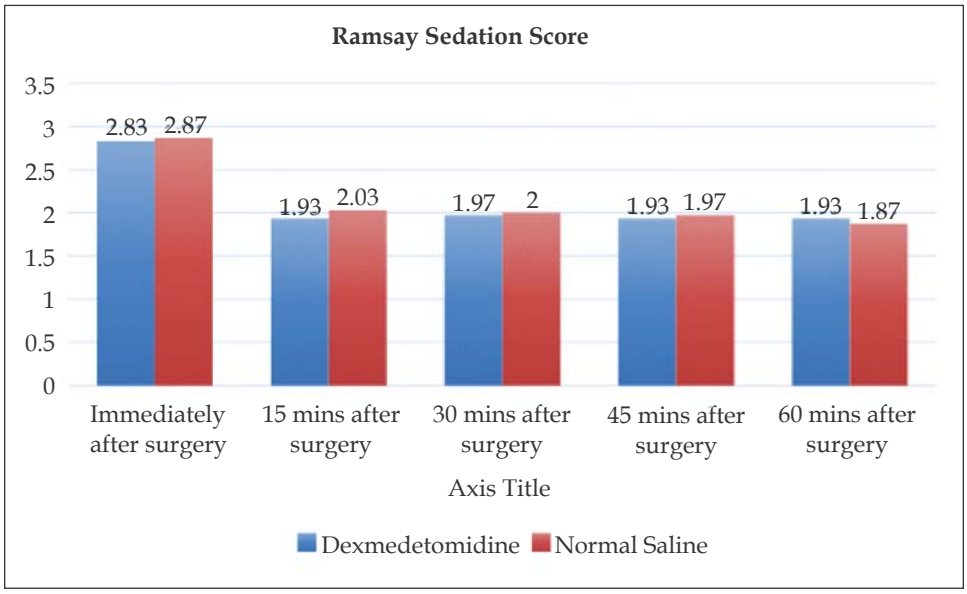

Fig. 3: Bar diagram showing Ramsay Sedation Score

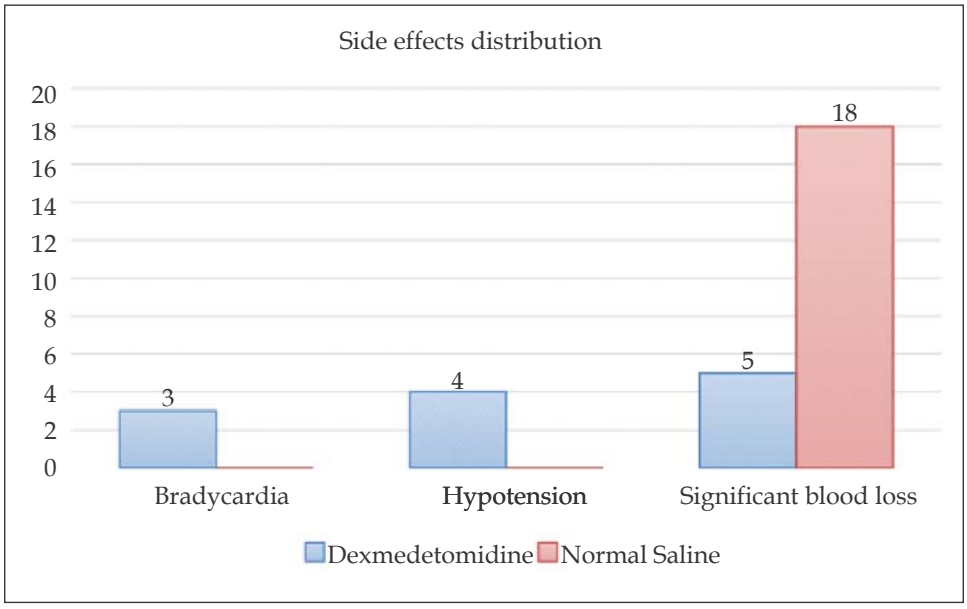

Fig. 4: Bar diagram showing distributon of side-effects between both the study groups

Table 4: Mean Ramsay Sedation Score distribution between Dexmedetomidine Group and the Normal Saline Group

Ramsay Sedation Score	Dexmedetomidine		Normal Saline		*t*-test	*p* - value
	Mean	SD	Mean	SD		
Immediately after surgery	2.83	0.461	2.87	0.507	-0.266	0.791
15 mins after surgery	1.93	0.254	2.03	0.183	-1.752	0.085
30 mins after surgery	1.97	0.183	2.00	0.263	-0.571	0.570
45 mins after surgery	1.93	0.254	1.97	0.183	-0.584	0.561
60 mins after surgery	1.93	0.254	1.87	0.346	0.851	0.398

The maximum decrease in heart rate in Group D was at 120 minutes (with mean 69.87 ± 5.823 beats/min). However, there was no significant changes in heart rate in Group N at start immediately after intubation and remained the same throughout the surgical duration. Clinically and statistically, there was no significant difference in the Ramsay Sedation Score (RSS) in the two groups, Fig. 2. As far as adverse events are concerned 3 patients with Dexmedetomidine had bradycardia which was treated with anticholinergics like Inj. Atopine or Inj. Glycopyrrolate. 4 patients in Dexmedetomidine Group had hypotension which was treated with vassopressors. In Normal Saline Group pateints there were no side effects like bradycardia or hypotension as seen in Dexmedetomidine Group (Fig. 3).

However, significant blood loss was seen in 18 patients with Normal Saline Group as compared to Dexmedetomidine where it was in only 5 patients (Fig. 4).

Disscusion

Anesthesia techniques for spine surgery is challenging to anesthesiologist. Many of the patients are of chronic pain complaints, of which mostly are of geriatric age group. These patients mostly have comorbidities with or with autonomic impairement. The main concerns during surgery which are challenging is to maintain hemodynamic stability without causing the intraoperative patient awareness to the surgery. This means keeping the plane of anesthesia deep enough yet no hemodynamic parameters to be affected.

This type of surgeries are often related to blood loss and large fluctuation in blood pressure during its course both intraoperative and postoperative. The main aim of anesthesiologist should be to maintain the blood pressure keeping in mind the blood less surgical site with adequate perfusion of end organs.

This practice of hypotensive anesthesia is being widely used for various types of surgeries using different anesthetic agents and drugs. As far as spine surgeries are concerned , various agents have been used till date. It includes drugs like propofol, esmolol, clonidine, inhalationals like isoflurane and sevoflurane etc. Alpha 2 adrenergic agonist are now-a-days being used and investigated in anesthetic practice as far as their sympatholytic, hemodynamic stabilizing, analgesic properties.

This study was done primarily, to compare the efficacy and hemodynamic response to intravenous Dexmedetomidine and placebo (Normal Saline) used as hypotensive agent in elective spine surgeries. Secondarily, to compare the sedation postoperatively in both the groups. And to study the side effects if any in both the groups. We choose mean arterial pressure as an important parameter to estimate the amount of hypotension. As MAP is a best indicator that reflects us the amount tissue perfusion. Baseline mean arterial pressure in both our study groups were comparable.

However, it was found that there was fall in mean arterial pressure at 30 minutes in dexmedetomidine group and continue to decrease throughout the surgery. The maximum decrease in MAP was seen after stopping drug in Dexmedetomidine Group (75.40 ± 5.10 mm Hg). For our study, we had considered lower-limit of MAP as 65 mm Hg. But it was observed that MAP did not fall below 65 mm Hg in any of the patients in our study group. For normal saline group there was no fall in mean arterial pressure throughout the surgery. There was increase in MAP in both the study groups at extubation. Similar observation was found in a study conducted by Ramila H Jamaliya et al. (2014).[8] they found that MAP was decreased from baseline values in dexmedetomidine group after induction, and remain low throughout the surgery and increased at the time of extubation. This finding is similar to our findings.

One more study, done by, Shams T, et al. (2013)[9] states that if dexmedetomidine infusion has been started 10 mins prior to surgery in dose of 1 mcg/kg/hr there is significant decrease in MAP and mean heart rate throughout the surgery. In our study, we also have similar finding with same loading dose of dexmedetomidine. These effects of dexmedetomidine are mainly due to its sympatholytic action on alpha-2 adrenergic

receptors present in blood vessels.

In our study, there was significant decrease in heart rate at 15 mins onwards in Group D with mean 76 ± 3.201 mm Hg SD and that persisted throughout the surgery and increased after extubation. The maximum decrease in heart rate in Group D was at 120 minutes with mean 69.87 ± 5.823 mm Hg. While there was no significant variation in heart rate from baseline in Group N from start of surgery and it remained same throughout the course of surgery.

In a study, by Sukhminder Bajwa et al (2016)[10], compared nitroglycerin, esmolol and dexmedetomidine as hypotensive agents in middle ear surgeries. They found that there was significant decrease in mean heart rate after giving the loading dose of the drug. They also found that heart rate increased after extubation . The mean heart rate remained low significantly through out the surgery compared to nitroglycerin and esmolol. They also stated that the cause of lower heart rate with dexmedetomidine is due to its sympatholytic properties.

This findings are similar to the findings found in our study. In our study, we used Ramsay Sedation Score to evaluate the postoperative sedation of patients from the study drugs used and compare the level of sedation in both the study groups. And we found that, there was no significant difference in both the study group for postoperative sedation using Ramsay Sedation Score**.** This findings are similar to the findings in a study conducted by Neamat I. Abel Rahman (2014)[11] where they found no significant difference in extubation or post operative sedation in dexmedetomidine group compared to placebo (normal saline). The limitations to our study was relatively small sample size, BIS monitoring or arterial line monitoring could not be done due lack of resources.

Conclusion

Thus, we conclude that, Dexmedetomidine in 1 mcg/kg loading dose given 10 minutes prior to induction and a continuous infusion at 0.2 mcg/kg/h intraoperatively maintains target mean arterial pressure and target heart rate to during the surgery. Dexmedetomidine thus helps in producing "deliberate or controlled" hypotension in spine surgeries. This helps in reducing the bloodloss during the surgery and helps in maintaining bloodless surgical site.

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Original Research Article

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Effects of Clonidine Versus Dexmedetomidine with Intrathecal Hyperbaric 0.5% Bupivacaine in Patients Posted for Elective Lower Abdominal Surgeries

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Abstract

Aims: To study and compare the efficacy of intrathecal dexmedetomidine 5 µg *versus* intrathecal clonidine 50 µg as an adjuvant to 0.5% bupivacaine heavy 12.5 mg for spinal anesthesia. *Materials and Methods:* The present study is prospective, controlled double blind comparative clinical study on spinal block characteristics in patients scheduled for elective lower abdominal surgeries was undertaken to evaluate the efficacy and the safety of dexmedetomidine or clonidine as adjuvant to intrathecal hyperbaric 0.5% bupivacaine. Ninety patients were randomly divided into three groups, each group consisting of thirty patients (n = 30). *Results:* Dexmedetomidine group and clonidine group there is an early onset of both sensory and motor blockade and a higher level of sensory blockade compared to control group and duration of sensory, motor blockade and duration of analgesia are significantly prolonged in the dexmedetomidine group and clonidine group compared to the control group. There was a small percentage of patients who developed significant fall *n* blood pressure and heart rate which were easily managed without any deleterious effect. Seven patients each in dexmedetomidine group and clonidine group and two patients in control group developed hypotension requiring treatment. Five patients in dexmedetomidine group, four patients in clonidine group and one patient in control group developed bradycardia requiring treatment. More number of patients in the dexmedetomidine group and clonidine group were sedated and easily arousable. *Conclusion:* Dexmedetomidine is a better neuraxial adjuvant compared to clonidine for providing early onset of sensory and motor blockade, adequate sedation and prolonged postoperative analgesia.

Keywords: Dexmedetomidine; Clonidine; Postoperative analgesia.

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Introduction

Regional anesthesia is the preferred technique for most of lower abdomen and lower limb surgeries. It allows the patient to remain awake, minimizes or completely avoids the problem associated with

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airway management. With spinal anesthesia, the technique is simple to perform, the onset of anesthesia is more rapid, avoids polypharmacy, allowing the surgical incision to be made sooner and also provides postoperative analgesia.

Hyperbaric bupivacaine 0.5% is extensively used in India for spinal anesthesia. Though the duration of action of bupivacaine is prolonged, it will not produce prolonged postoperative analgesia. Hence, another adjuvant is required for producing prolonged postoperative analgesia. The discovery of opioid receptors and endorphins in spinal and supraspinal regions soon led to the use of spinal opiates. Morphine was the first opioid administered intrathecally to augment neuraxial blocks. Opioid analgesic drugs produce intense, prolonged analgesic action without gross autonomic changes, loss of motor power or impairment of sensation other than pain when injected into subarachnoid or epidural space. Morphine can produce serious side effects like late and unpredictable respiratory depression, postoperative nausea and vomiting, pruritus and urinary retention.[1]

Clonidine has been shown to result in prolongation of the sensory blockade and reduction in the amount or concentration of local anesthetic required to produce postoperative analgesia. Clonidine also has the ability to prolong the motor blockade produced by bupivacaine. Large doses of intrathecal clonidine (as much as 450 µg) without local anesthetics provide sedation and intense and long lasting postoperative analgesia, are inadequate for surgical anesthesia and for this reason, clonidine has been used as an adjuvant to local anesthetics rather than used alone.[2]

While clonidine has been used as an adjuvant to local anesthetic agents for intrathecal purposes with successful results, there are only a few studies available for dexmedetomidine for such studies. Till recently dexmedetomidine was not available in India though it is being used in other countries since many years. Since, it has been recently introduced in India and not many studies have been done in India regarding its use as an adjuvant to local anesthetic agents for intrathecal purpose hence, there is a need to study its effectiveness for spinal anesthesia.

Hence, we have undertaken this study to evaluate and compare the effects of adding clonidine versus dexmedetomidine with intrathecal hyperbaric 0.5% bupivacaine in patients scheduled for elective lower abdominal surgeries.

Materials and Methods

The study entitled "Prospective, controlled double blind comparative clinical study of effect of adding 5 µg dexmedetomidine *versus* 50 µg clonidine to intrathecal 12.5 mg of 0.5% hyperbaric bupivacaine on spinal block characteristics in patients scheduled for elective lower abdominal surgeries" was undertaken in Alluri Sitarama Raju Academy of Medical Sciences, during the period November 2013 to July 2015. The study was undertaken after obtaining ethical committee clearance as well as informed consent from all patients.

Ninety patients in the age group between 20 years and 60 years of either sex belonging to ASA Grade-I and Grade-II posted for elective lower abdominal surgeries without any comorbid disease were grouped randomly into Three Groups (n = 30). Randomization was done using simple sealed envelope technique:

Group B (Control Group): Received 12.5 mg of 0.5% hyperbaric bupivacaine with 0.5 ml normal saline.

Group C (Clonidine Group): Received 12.5 mg of 0.5% hyperbaric bupivacaine with 50 µg clonidine.

Group D (Dexmedetomidine Group): Received 12.5 mg of 0.5% hyperbaric bupivacaine with 5 µg dexmedetomidine.

The doses of dexmedetomidine and clonidine were chosen according to a 1:10 ratio found to be equipotent and would produce similar effects on the characteristics of bupivacaine spinal anesthesia.

Inclusion criteria:

Adult patients of either sex, aged between 20 and 60 years, belonging to ASA Grade I and II without any comorbid disease scheduled for elective lower abdominal surgeries.

Exclusion criteria:

Age group less than 20 years and more than 60 years, Patients belonging to ASA Grade III, IV and V, Pregnant females, Patients posted for emergency surgeries, Patients with morbid obesity, Patients having any absolute contraindication for spinal anesthesia like raised intracranial pressure, severe hypovolemia, bleeding diathesis and local infection. and Patients with comorbid diseases.

Preoperative assessment was done for each patient and written informed consent was taken. Patients were kept NPO for solids 6 hrs and clear fluids 2 hrs before surgery. Patients were premedicated on the night before surgery with

Tablet Ranitidine 150 mg and Tablet Alprazolam 0.5 mg. Intravenous line was obtained with 18 guage cannula and preloaded with Ringer lactate 500 ml half an hour before anesthesia. Monitoring was done using multiparameter monitor having pulse oximetry, ECG and NIBP. Patients were placed in flexed lateral position. Under aseptic precautions spinal block was performed at level of L3-L4 through a midline approach using 25G Quincke spinal needle and study drug was injected with operative table kept flat. Patients were turned to supine posture immediately and supplemental oxygen given. The test drugs were prepared by the senior anesthesiologist who was not involved in the study, Clonidine (Cloneon; 150 µg/ml) was diluted to 1.5 ml with normal saline and 0.5 ml (50 µg) of it was added to 2.5 ml of 0.5% hyperbaric bupivcaine. Dexmedetomidine (Dexem 50 µg/0.5 ml) 0.5 ml was diluted to 5 ml with normal saline and 0.5 ml of this was added to 2.5 ml of 0.5% hyperbaric bupivacaine. The observer and the patient were blinded for the study drug.

The following parameters were noted:

- Onset of sensory blockade and motor blockade;
- Maximum level of sensory blockade attained and the time taken for the same was noted;
- Maximum level of motor blockade attained and the time taken for the same was noted;
- Two segments sensory regression time was noted;
- Total duration of analgesia was noted by VAS score;
- Total duration of sensory blockade and motor blockade was noted;
- Sensory blockade was tested using pinprick method with a blunt tipped 27G needle at every minute for first 5 mins and every 5 mins for next 15 mins and every 10 mins for next 30 mins and every 15 mins till the end of surgery and there after every 30 mins until sensory block is resolved;
- Quality of motor blockade was assessed by modified Bromage scale;
- Level of sedation noted by Ramsay Sedation Scale;
- Total duration of surgery and if any side effects were noted.

Hemodynamic monitoring was done during the block every 5 mins for first 15 mins and every 10 mins for next 30 mins and once in 15 mins till the end of surgery and postoperatively every hourly employing multi parameter monitor which displays Heart Rate (HR), Systolic Blood Pressure (SBP) Diastolic Blood Pressure (DBP), Mean Arterial Pressure (MAP), ECG and SpO_2 hourly.

Statistical Analysis:

Results are expressed as the means and standard deviations, medians and ranges, or numbers and percentages. The comparison of normally distributed continuous variables between the groups was performed using one-way analysis of variance (ANOVA) and, if appropriate, followed by the Bonferroni test for post hoc analysis. Nominal categorical data between study groups were compared using the Chi-squared test or Fisher's exact test as appropriate. Ordinal categorical variables and nonnormal distribution continuous variables were Dexmedetomidine or clonidine for supplementation of spinal bupivacaine compared using the Mann-Whitney *U*-test. $p < 0.05$ was considered to be significant.

Table 1: Demographic distribution in present study

	Groups					
	Group B		Group C		Group D	
	No. of Pts.	%	No. of Pts.	%	No. of Pts.	%
Age in years						
20–30	16	53.3	14	46.7	18	60
31–40	9	30	6	20	2	6.7
41–50	5	16.7	6	20	8	26.7
51–60	0	0	4	13.3	2	6.7
Total	30	100	30	100	30	100
Mean ± SD	31.17 ± 9.752		36.60 ± 11.082		33.07 ± 11.585	
Gender						
Male	15	50.0%	20	66.7%	24	80.0%
Female	15	50.0%	10	33.3%	6	20.0%
Total	30	100.0%	30	100.0%	30	100.0%

Results

There is no significant difference in the age of patients between the groups. All the three groups were similar with respect to age distribution (p > 0.05), shown in Table 1.

There is no significant difference in the sex distribution of the patients between the groups. (p > 0.05). 50%, 66.7%, 80% of the patients in Group B, Group C and Group D respectively are males and 50%%, 33.3% and 20% of the patients in Group B, Group C and Group D respectively are females.

There is no significant difference in the height and weight of patients between the groups (p > 0.05) (Table 2).

There is no significant difference in the type of surgical procedure in patients between the groups (p > 0.05). 73.3%, 53.3%, 63.3% of the patients in Group B, Group C and Group D respectively have undergone appendicectomy and 53.3%, 46.7% and 37.7% of the patients in Group B, Group C and Group D respectively have undergone inguinal hernia repair, (Fig. 1).

The mean duration of surgery is 53 ± 6.51 mins in Group B (Control Group), 57.66 ± 12.84 mins in Group C (Clonidine Group) and 51.166 ± 7.15 mins in Group D (Dexmedetomidine Group). There is no significant difference between mean duration of surgery between the groups (p > 0.05), Fig. 2).

There is no statistically significant difference between the groups (p = 0.24).

The mean time of onset of sensory blockade, mean time taken for attaining the maximum sensory blockade and taken for regression of sensory block by two segments is a statistically highly significant

Table 2: Height and weight distribution in present study

	Groups		
	Group B (n = 30)	**Group C (n = 30)**	**Group D (n = 30)**
Height in cm			
Mean	159.4 cm	161.03 cm	161.6 cm
Std. Deviation	4.76 cm	6.18 cm	5.14 cm
Minimum	152 cm	150 cm	150 cm
Maximum	168 cm	170 cm	170 cm
Weight in kg			
Mean	60.9 kg	61.33 kg	60.7 kg
Std. Deviation	4.62 kg	5.53 kg	5.74 kg
Minimum	50 kg	50 kg	50 kg
Maximum	68 kg	70 kg	70 kg

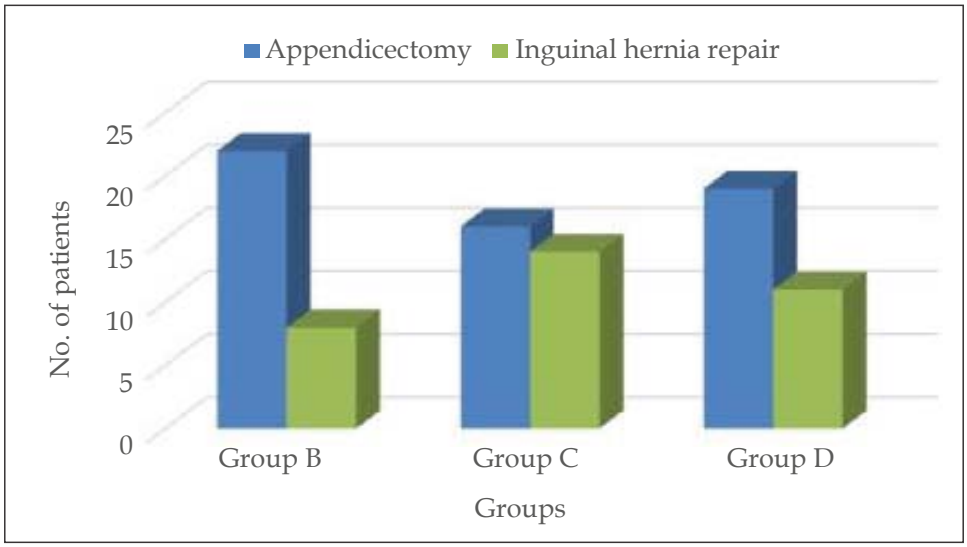

Fig. 1: Types of surgical procedures

difference when Group B was compared with Group C and with Group D (p = 0.000) and there is statistically significant difference between Group C and Group D (p = 0.024), Table 4).

The mean duration of analgesia is a statistically highly significant difference between Group B and Group C (p = 0.000) and between Group B and Group D (p = 0.000) and between Group C and Group D (p = 0.001), (Fig. 3).

The mean time taken for the onset of motor blockade, time taken for attaining maximum motor blockade and duration

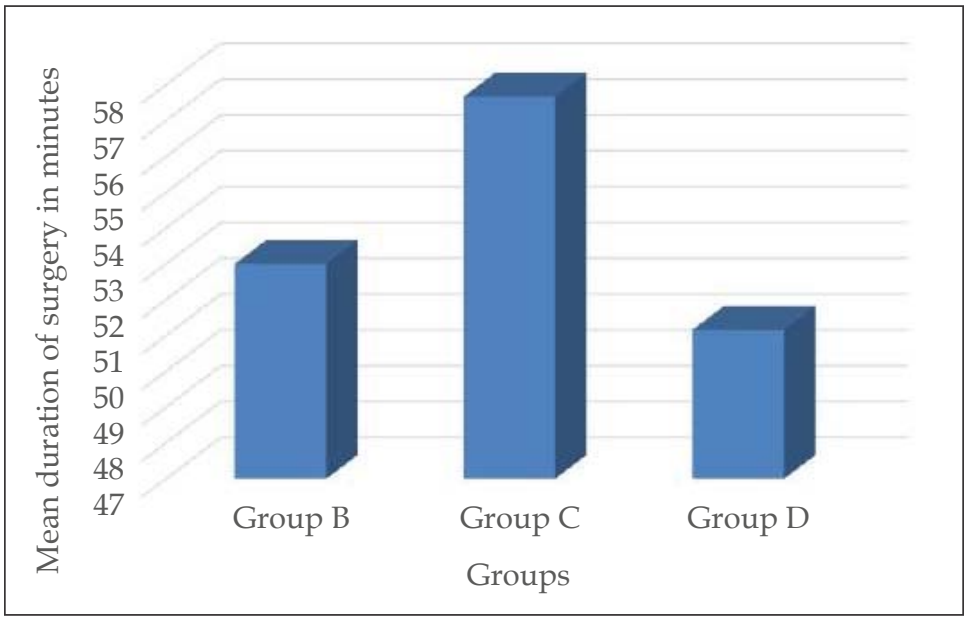

Fig. 2: Mean duration of surgery

Table 3: Maximum level of sensory block attained

Maximum level of sensory block attained	Groups					
	Group B		Group C		Group D	
	No. of Pts.	%	No. of Pts.	%	No. of Pts.	%
T4	2	6.70%	8	26.70%	12	40%
T5	4	13.30%	5	16.70%	2	6.70%
T6	24	80.00%	17	56.70%	16	53.30%
Total	30	100%	30	100%	30	100%

Table 4: Time taken for sensory onset in mins

	Group B	Group C	Group D	p - value B *vs* C	p - value B *vs* D	p - value C *vs* D
Time taken for sensory onset in mins						
Mean ± SD	2.80 ± .664	1.43 ± .504	1.13 ± .346			
Minimum	2	1	1	0.000	0.000	0.024
Maximum	4	2	2			
Time taken for maximum sensory block in mins						
Mean ± SD	7.4 ± 1.102	5.9 ± 0.803	5.2 ± 0.714			
Minimum	6	5	4	0.000	0.000	0.001
Maximum	9	7	7			
Duration of two segment sensory reg in mins						
Mean ± SD	79.46 ± 10.16	136.33 ± 10.90	136.33 ± 11.59			
Minimum	60	120	120	0.000	0.000	1.000
Maximum	95	155	150			

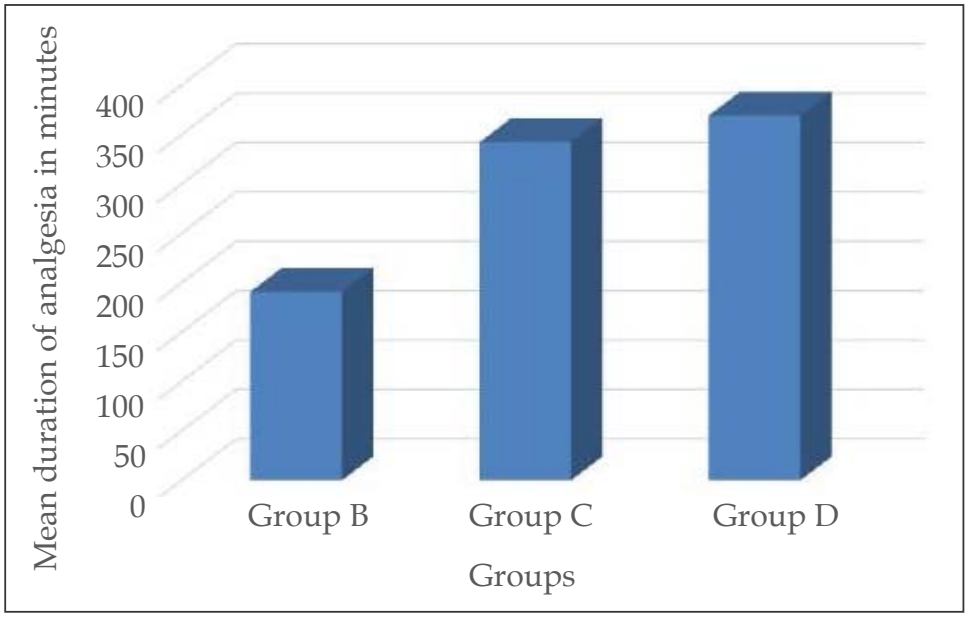

Fig. 3: Mean duration of analgesia

Table 5: Time taken for onset of motor blockade

	Group B	Group C	Group D	*p* - value B *vs* C	*p* - value B *vs* D	*p* - value C *vs* D
Time taken for Motor on set in mins						
Mean ± SD	4 ± 0.695	1.63 ± 0.49	1.17 ± 0.379			
Minimum	3	1	1	0.000	0.000	0.000
Maximum	5	2	2			
Time taken for Maximum motor block in mins						
Mean ± SD	6.57 ± 0.935	6.43 ± 1.04	5.5 ± 0.820			
Minimum	5	5	4	0.000	0.000	0.000
Maximum	9	8	7			
Duration of motor block in mins						
Mean ± SD	166.16 ± 20.95	279 ± 24.68	303.66 ± 35.95			
Minimum	135	240	240	0.000	0.000	0.003
Maximum	210	330	360			

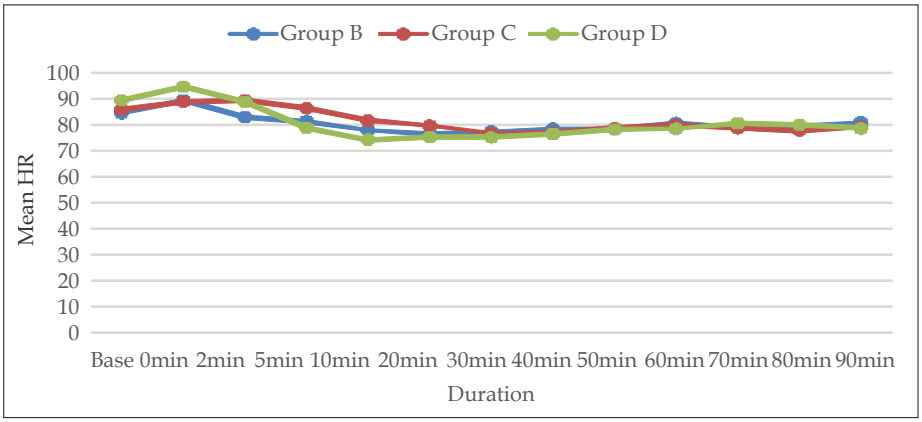

Fig. 4: Mean heart rate at various interval in bpm

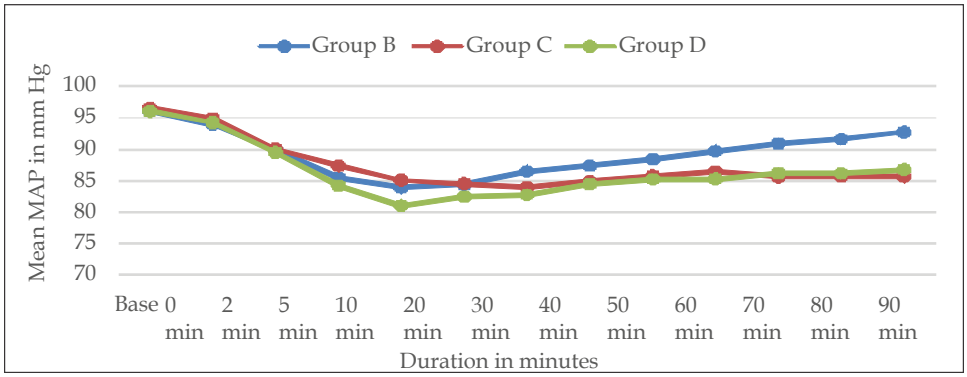

Fig. 5: Mean MAP at various intervals in mm Hg

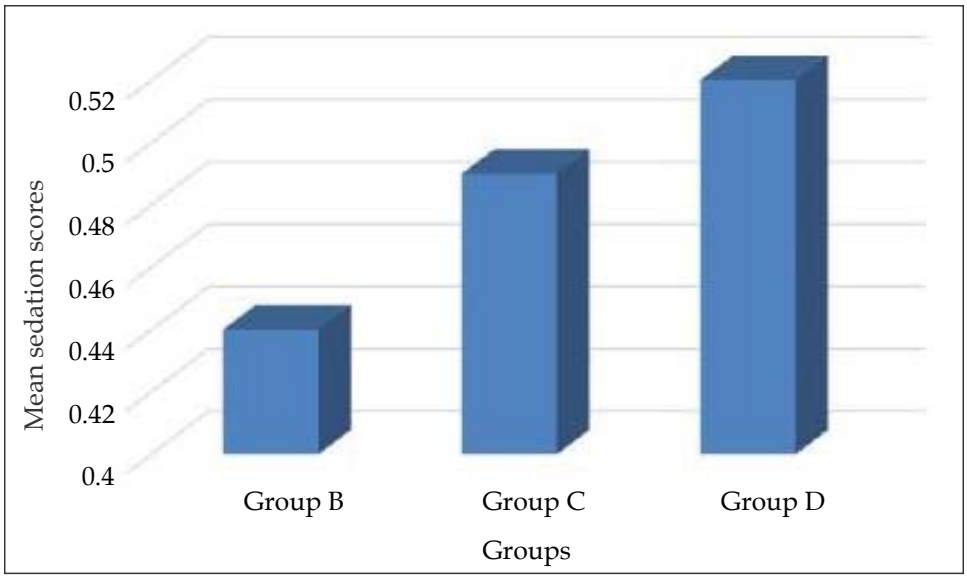

Fig. 6: Mean sedation scores

of motor blockis statistically highly significant difference between Group B and Group C and between Group Band Group D and between Group C and Group D. (p = 0.000), (Table 5).

The mean heart rate from basal to 90th minutes recording is statistically not significant between the groups, (Fig. 4).

The mean MAP from basal to 90th minutes recording is statistically not significant between Group C and Group D, (Fig. 5).

The mean sedation score is 0.4 ± 0.49 in Group B, 0.50 ± 0.682 in Group C, 0.53 ± 0.681 in Group D. There is a statistically highly significant difference between Group B and Group C and between Group B and Group D (p = 0.000). There is statistically no significant difference between Group C and Group D (p = 0.850), (Fig. 6).

In Group B, 2 out of 30 patients, in Group C, 7 out of 30 patients and in Group D, 7 out of 30 patients developed hypotension, which is statistically not significant ($p > 0.05$). All the patients who developed hypotension could be easily treated with intravenous fluids and vasopressor. In Group B (Control Group) 1 out of 30 patients, in Group C (Clonidine Group), 4 out of 30 patients and in Group D (Dexmedetomidine Group) 5 out of 30 patients developed bradycardia, which is statistically not significant ($p > 0.05$). All the patients who developed bradycardia were treated by single dose of 0.6 mg of atropine.

Discussion

In present study, demographic data comparing age, sex, height, weight shows no statistical difference

among the groups. Various authors have used different doses of clonidine for intrathecal blockade starting from 15 µg to 300 µg along with local anesthetics and doses of dexmedetomidine starting from 3 µg to 15 µg along with local anesthetics. More number of studies have used 5 µg as the dose hence, we selected a 5 µg of preservative free dexmedetomidine for our study.[2,3]

Asano T et al. showed that binding affinity to spinal alpha-2 receptors of dexmedetomidine compared with clonidine is approximately 1:10.[3] Hence, in our study we selected 10 times the dose of dexmedetomidine as clonidine that is 50 µg.

In our study, the mean time taken for onset of sensory block is 2.8 ± 0.6 mins in the Control Group, 1.43 ± 0.5 mins in the Clonidine Group and 1.13 ± 0.346 mins in the Dexmedetomidine Group. There is a statistically highly significant decrease in the onset of sensory blockade in Clonidine Group and in the Dexmedetomidine Group compared to the Control Group.

In a study, conducted by Saxena H et al. authors observed the onset of sensory blockade to be 6.57 ± 0.49 mins in control group and 2.58 ± 0.33 mins, 2.54 ± 0.34 mins and 2.09 ± 0.89 mins in clonidine group (15 µg, 30 µg and 37.5 µg respectively) and in this study there was a significant reduction in the onset time which concurs with our study.[2] But compared to our study the onset time of sensory block is higher and this could be possibly due to the dose of clonidine used being less than compared to our study in which we used 50 µg.

In a study, conducted by Al-Mustafa MM et al. in which dexmedetomidine was added to spinal isobaric bupivacaine for urological procedures authors observed the onset of sensory blockade to be 9.5 ± 3 mins in control group and 6.3 ± 2.7 mins and 4.7 ± 2 mins in dexmedetomidine group (5 µg and 10 µg respectively) and in this study there was a significant reduction in the onset time of sensory block.[4] But compared to our study the onset time of sensory block is higher and this could be possibly due to the isobaric bupivacaine used compared to our study in which we used hyperbaric bupivacaine.

In a study, conducted by Shukla D et al. authors observed that the duration of onset of sensory blockade in dexmedetomidine group was 2.27 ± 1.09 mins and in control group was 4.14 ± 1.06 mins which showed significant reduction in the onset time of sensory blockade.[5]

The mean time taken for maximum sensory blockade in the present study is 7.4 ± 1.1 mins in the control group, 5.9 ± 0.8 mins in the clonidine group and 5.2 ± 0.71 mins in dexmedetomidine group. There is a statistically significant decrease in the mean time taken for the maximum sensory blockade in the clonidine group and dexmedetomidine group compared to the control group.

In a study, conducted by Saxena H et al. authors observed the mean time to achieve maximum sensory level was 6.8 ± 1.20 mins, 7.4 ± 1.31 mins and 6.7 ± 1.12 mins in clonidine groups (15 µg, 30 µg, 37.5 µg respectively) which is more than our study in clonidine group and this may be due to less mass of clonidine used in the study.[2]

In our study, the maximum level of sensory blockade achieved was T4. Two out of 30 patients in control group, 8 out of 30 patients in clonidine group and 12 out of 30 patients in dexmedetomidine group had T4 level of sensory blockade. There is no statistical significant difference in the maximum level of sensory blockade in the clonidine group and dexmedetomidine group compared to the control group. In studies conducted by Kanazi GE et al., Al-Ghanem SM et al. in dexmedetomidine group the maximum level of sensory blockade achieved was T4 and there was no statistically significant difference in the maximum level of sensory blockade which concurs with our study.[6,7]

The time taken for regression of sensory block by two segments in the present study is 79.46 ± 10.1 mins in the control group, 136.33 ± 10.90 mins in the clonidine group and 136.33 ± 11.590 mins in dexmedetomidine group. There is a statistically significant increase in the mean time taken for regression of sensory block by two segments in clonidine group and dexmedetomidine group compared to the control group.

In a study, conducted by Kanazi GE et al. authors observed the time taken for regression of sensory block by two segments to be 80 ± 28 mins in control group, 101 ± 37 mins in clonidine group and 122 ± 37 mins in dexmedetomidine group, which shows a significant prolongation of two segment regression compared to the control group and it compares with our study.[6] Our study is also consistent with the study done by Sethi BS et al. in clonidine group where it was 136 mins in control group and 218 mins in clonidine group and study done by Eid HEA et al. in dexmedetomidine group where it was 76.9 ± 26.8 mins in control group, 103 ± 28.7 mins in D1 (10 ug) group and 200.6 ± 30.9 mins in D2 (15 ug) group.[8,9] Here authors observed a statistically significant increase in the mean time taken for regression of sensory block by two segments.

The time taken for sensory block to regress to S1 in the present study is 203.33 ± 42.41 mins in the control group, 365.0 ± 24.6 mins in the clonidine group and 396.16 ± 30.61 mins in the dexmedetomidine group. There is a statistically significant increase in the mean time taken for regression of sensory block to S1 in clonidine group and dexmedetomidine group compared to the control group.

This compares with the study conducted by Kanazi GE et al. where the time taken for regression of sensory block to S1 to be 190 ± 48 mins in control group, 272 ± 38 mins in clonidine group and 303 ± 75 mins in dexmedetomidine group which is less than the value in our study.[6] This could be due to the less doses of clonidine and dexmedetomidine used. In a study, conducted by Al-Ghanem SM et al. the mean time taken for regression of sensory block to S1 in dexmedetomidine group was 274.8 ± 73.4 mins compared to fentanyl Group F (179.5 ± 47.4 mins) and in the study conducted by Al-Mustafa MM et al. it was 338.9 ± 44.8 mins in D10 (10 ug) group and 277.1 ± 23.2 mins in D5 (5 ug) group compared to 165.5 ± 32.9 mins in control group and in study conducted by Eid HEA et al.[4,6,7] It was 320 ± 65.8 mins in D1 (10 ug) group and 408.7 ± 68 mins in D2 (15 ug) group compared to 238 ± 57 mins in control group. Authors observed a statistically significant increase in the mean time taken for regression of sensory block to S1 dermatome in dexmedetomidine groups which concurs with our study.

The mean duration of analgesia in our study is 191 ± 22.9 mins in control group, 342.33 ± 28.12 mins in clonidine group and 369.33 ± 34.13 mins in dexmedetomidine group. There is a statistically highly significant increase in the duration of analgesia in dexmedetomidineand clonidine group compared to the control group.

Our study concurs with the study conducted by Grandhe RP et al., where authors observed the mean duration of analgesia of 228 ± 42 mins in the control group and 378 ± 48 mins when using clonidine of 1 µg/kg with a mean weight of 60.6 ± 19.4 kg.

In our study, the mean time for onset of motor block is 4 ± 0.69 mins in control group, 1.63 ± 0.49 mins in clonidine group and 1.17 ± 0.379 mins in dexmedetomidine group. There is a statistically highly significant decrease in the mean time for onset of motor blockade in the dexmedetomidine group and clonidine group compared to the control group.

In a study, conducted by Al-Mustafa MM et al., the duration of onset of motor blockade in Group D10 (10 µg) was 10.4 ± 3.4 mins, Group D5 (5 µg) was 13.0 ± 3.4 mins and Group N (Control Group) was 18.0 ± 3.3 mins and in a study conducted by Shukla D et al. it was 3.96 ± 0.92 mins in Group D and 4.81 ± 1.03 mins in control group which showed a significant decrease in the mean time for onset of motor blockade.[4,5] In the study, done by Saxena H et al. in the clonidine group authors observed a significant decrease in the mean time for onset of motor blockade which was 7.41 ± 0.55 mins in control group and 2.67 ± 0.45 mins, 2.30 ± 0.45 mins, 2.20 ± 0.50 mins in clonidine group (15 µg, 30 µg, 37.5 µg respectively) which concurs with our study.[2]

The mean time taken for maximum motor blockade in our study is 6.57 ± 0.9 mins in control group, 6.43 ± 1.04 mins in clonidine group and 5.5 ± 0.820 mins in dexmedetomidine group. There is a statistically significant decrease in the time taken for maximum motor blockade in dexmedetomidine and clonidine groups compared to the control group. But the grade of motor blockade in the study groups did not differ. All the groups had a motor blockade of Bromage Grade 3.

This compares with the study conducted by Kanazi GE et al. where the time taken for maximum motor blockade is significantly shorter in dexmedetomidine group (13.2 ± 5.6 mins) compared to the control group (20.7 ± 10.3 mins).[6] This is consistent with the studies done by Sethi BS et al. and Saxena H et al. who observed the complete motor blockade of the lower extremity in all patients in clonidine group.[2,8] In a study, conducted by Dobrydnjov I et al. authors found a better quality of block in all the three clonidine groups, where no supplementation with general anesthesia for relaxation request from surgeons was needed intraoperatively.[10]

In our study, the mean duration of motor blockade was 166.16 ± 20.95 mins in control group, 279 ± 24.68 mins in clonidine group and 303.66 ± 35.95 mins in dexmedetomidine group. There is a statistically highly significant increase in the duration of motor blockade in dexmedetomidine group and clonidine group compared to the control group.

This compares with study conducted by Kanazi GE et al. where the mean duration of motor blockade is 163 ± 47 mins in control group, 216 ± 35 mins in clonidine group and 250 ± 76 mins in dexmedetomidine group which is less than the value in our study.[6] This could be due to the less doses of clonidine and dexmedetomidine used. Our study almost concurs with the study

conducted by Kaabachi O et al. who observed the mean duration of motor blockade to be 252 ± 79 mins when using clonidine of 1 μg/kg.[11]

In the control group, we observed a maximum fall in MAP of 12.2 mm Hg from basal MAP at 10th min, in the clonidine group it was 12.56 mm Hg at 30th min and in the dexmedetomidine group it was 14.96 mm Hg at 30th min. There was no statistically significant difference in any of the three groups regarding fall in MAP. However, it was found that there was a delay in maximum fall in MAP in the clonidine group and the dexmedetomidine group compared to the control group.

Two patients in control group, seven patients in clonidine group and seven patients in dexmedetomidine group developed hypotension and were easily managed with intravenous fluids and vasopressor.

In a study, conducted by Sethi BS et al. authors observed lowest MAP (70 mm Hg) in clonidine group (1 μg/kg, mean weight 57.93 ± 4.75 kg) which is less than that in our study (76.05 ± 2.54 mm Hg). In a study, conducted by Grandhe RP et al. the incidence of hypotension (fall in MAP of > 20% of preinduction value) was 10/15 patients in clonidine group (clonidine 1 μg/kg, mean weight 60.6 ± 19.4 kg) and 8/15 patient in clonidine group (clonidine 1.5 μg/kg, mean weight 62.7 ± 18 kg).[8,12] In a study, conducted by Al-Ghanem SM et al. authors observed that the hypotension (fall in MAP of > 30% of preinduction value) was mild to moderate in both dexmedetomidine and fentanyl group.[7] 4/38 patients in dexmedetomidine group and 9/38 patient in fentanyl group had hypotension but it did not reach a significant difference.

Hemodynamic disturbances resulting from intrathecal Alpha 2 agonists depends upon other factors like segmental site of injection, patient position, preloading and baricity of local anesthetic employed.

In the control group, we observed a maximum decrease in the mean heart rate of 7.8 bpm from basal value at 20th min, in the clonidine group it was 9.26 bpm at 30th min and in the dexmedetomidine group it was 15.33 bpm at 10th min. There was no statistically significant difference in any of the three groups regarding decrease in the mean heart rate. However, it was found that there was a delay in maximum decrease in the mean heart rate in the clonidine group compared to the dexmedetomidine group and the control group. Five patients in dexmedetomidine group, four patients in clonidine group and one patient in control group had bradycardia which is statistically not significant. Bradycardia was easily reversed with 0.6 mg intravenous atropine in all the patients. In a study, conducted by Kaabachi O et al. the authors observed the incidence of bradycardia to be 30% in clonidine (2 μg/kg) group which is higher compared to our study and this may probably due to larger dose of clonidine (2 μg/kg) used compared to our study (17.77%).[12]

In our study, sedation is assessed using a sedation scale according to the study done by Al-Ghanem SM et al. at the end of surgery.[7] In our study, in the dexmedetomidine group 10% of patients had Grade 2 sedation, 33.33% had Grade 1 sedation and remaining 56.7% had Grade 0 sedation and in the clonidine group 36% of patients had Grade 2 sedation, 30% had Grade 1 sedation and remaining 60% had Grade 0 sedation compared to 40% of patients in control group having Grade 1 sedation and 60% having Grade 0 sedation. No patients in control group had Grade 2 sedation and there was a statistical significance in mean sedation scores between control group and clonidine group and between control group and dexmedetomidine group. There was no statistical significance between clonidine group and dexmedetomidine group.

In our study, we did not observe any evidence of respiratory depression, episodes of nausea, vomiting, shivering in any of the groups. None of the patients came back to us with backache, buttock pain or leg pain or any neurological deficit. This was conformed with most of the studies.

Conclusion

Dexmedetomidine and clonidine when used intrathecally along with Bupivacaine significantly prolonged the duration of analgesia and there was also clinically significant difference between clonidine and dexmedetomidine on spinal block characteristics, intrathecal dexmedetomidine was better than clonidine with regards to onset and duration of both sensory and motor blockade as well as duration of analgesia. Hence, dexmedetomidine is a better neuraxial adjuvant compared to clonidine for providing early onset of sensory and motor blockade, adequate sedation and prolonged postoperative analgesia.

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Original Research Article

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A Comparative Study on Ultrasound- Guided Supraclavicular Brachial Plexus Block Vs Ultrasound Guided Nerve Stimulated Supraclavicular Brachial Plexus Block

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Abstract

Background: The brachial plexus block can be performed by the landmark nerve technique, nerve stimulator guided (NS) or (ultrasound (US)-guided technique. A patient need not be subjected to the discomfort of paresthesia when the nerve is stimulated to produce a motor twitch, because motor fibers have a lower electrical threshold than sensory fibers. The use of the NS technique, however, did not reduce the complication rates. Therefore, the combined nerve stimulator and ultrasound-guided approach are much preferred. For supraclavicular brachial plexus block. *Aim of the Study:* Targeting the individual nerve bundles using a nerve stimulator would obtain a higher success rate for ultrasound-guided supraclavicular brachial plexus block. *Materials and Methods:* 66 patients presenting for upper limb surgeries under USG guided Supraclavicular brachial plexus block were randomly assigned into 2 Groups. Group USG NS– Ultrasound-guided, nerve stimulated Supraclavicular block group USG – Ultrasound-guided Supraclavicular block patients received a mixture of 23 ml of a local anesthetic containing 2% Lignocaine 11.5 ml and 0.75% Ropivacaine 11.5 ml. Group USG NS– (n = 33) – half the volume of drug is injected into 'corner pocket' guided by USG, confirmed by nerve stimulation and remaining half the volume is injected into main neural cluster under USG guidance, confirmed by nerve stimulation. Group USG – Under USG guidance half the volume was deposited in 'corner pocket' and half the volume was injected in the main neural cluster. Sensory and motor blockade of ulnar nerve, median nerve, musculocutaneous nerve, and radial nerve was recorded at different time intervals. Surgical anesthesia, number of needles passes, performance time and complications were also recorded. *Results:* Compared with Group USG, Group USG NS had higher success rate of combined sensory-motor block within 15 min (79% *vs* 52%, $p < 0.001$). The success rate of sensory block of 4 nerves within 15 min is higher in Group USG NS (Ulnar nerve-91 *vs* 70%, Median nerve – 91 *vs* 73%, radial nerve-88 vs 67%, Musculocutaneous nerve 88 *vs* 64%, $p < 0.001$). The performance time is increased by 4 min in USG NS Group (14.3 ± 2.88 *vs* 10.33 ± 5.69 min, $p < 0.001$). ***Conclusion:*** USG guided nerve stimulated supraclavicular brachial plexus block provides higher success rate and complete sensory-motor blockade of all four nerves within 15 minutes of local anesthetic injection.

Keywords: Ultrasound; Nerve stimulator; Supraclavicular; Brachial plexus block.

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Introduction

The Supraclavicular approach to the Brachial Plexus Block (SBPB) is preferred in upper extremity surgeries because it has the anatomical advantage of the blockade at a level where the trunks and divisions are tightly grouped.[1,2] State of the art ultrasound technology for supraclavicular blocks helps localize the brachial plexus accurately and improve success rates.[3,4] With the use of nerve stimulators, the needle tip can be positioned adjacent to a nerve by eliciting an appropriate motor response.[5] The aim of the study was to compare the success rate of the block between the ultrasound-guided technique and the combined ultrasound-guided, nerve stimulated technique. The region innervated by the ulnar nerve is often spared as this nerve originates entirely from the inferior trunk of the brachial plexus. In the classical double injection technique described by Tran,[6] the ultrasound is used to block the inferior trunk (the ulnar nerve) and the first increment of local anesthetic is given lateral to the subclavian artery and superior to the first rib (the corner pocket). In the Modified Double Injection Technique (MDI) described by Quechua Luo,[7] in addition to the Ultrasound, a nerve stimulator was used to identify the ulnar nerve by eliciting motor response and the local anesthetic was deposited lateral to the subclavian artery and superior to the first rib (the 'corner pocket').[8] We assumed that a modification of the double – injection technique by combining ultrasound guidance with nerve stimulator would improve the onset and effectiveness of the blockade and used this technique to block all the four nerve including the ulnar nerve.

Materials and Methods

The study was conducted at the Rajiv Gandhi Government General Hospital, Madras Medical College from July 2018 to November 2018. After obtaining written informed consent, patients belonging to ASA physical status I and II, aged 18–60 years posted for elective orthopedic procedures of the upper extremity were included in this study. Patients who refused consent and Patients with a difficult airway, coagulopathy, neuropathy, infection at the needle insertion site, allergy to the local anesthetic drugs used were excluded from this study. Randomization was done, dividing patients into one of two groups. Ultrasound-guided supraclavicular brachial plexus block using a classical double-injection technique (Group USG) or Ultrasound-guided supraclavicular brachial plexus block combined with nerve stimulator using a modified double-injection technique. (Group USG-NS).

Technique

On arrival in the operating room, patients were connected to the standard monitors. Oxygen supplementation was given through nasal cannula at 3-4L/min. The patients were premedicated with Inj. Midazolam 1 mg and inj. Fentanyl 50 µg. A high-resolution ultrasound machine (Sonosite) with a Linear array probe with a 6-13 Hz frequency was used for visualization of the brachial plexus. A 22G, 10 cm stimulating needle with a peripheral nerve stimulator (Braun, Messenger, Germany) was used. All blocks were performed by experienced anesthesiologists.

Group USG

The classical double-injection technique described by Tran et al.[6] was followed with ultrasound guidance. A 90 mm, 23-G Quincke Spinal needle was inserted in-plane after obtaining a short-axis view of the subclavian artery and the neural clusters close to the artery, (Fig. 1). The needle tip was directed towards the "corner pocket which lies in the angle between the first rib and subclavian artery in a lateral to medial direction. Half the volume (11.5 ml) of a local anesthetic mixture of 0.75% Ropivacaine and 2% lignocaine was injected in the corner pocket after confirming negative aspiration, (Fig. 2). The needle was withdrawn and redirected towards the main neural cluster which was visualized by ultrasound. Here, the remaining Local anesthetic mixture of 11.5 ml was injected.

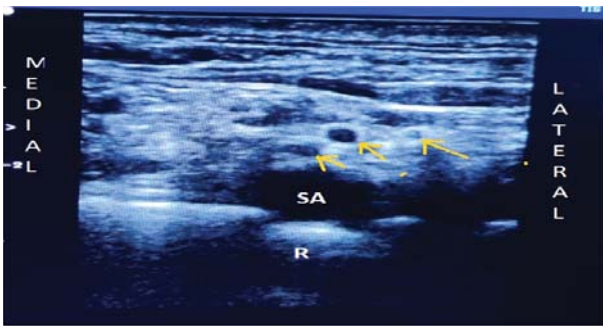


Fig. 1: Transverse Sonogram showing the main neural cluster (arrows) of the brachial plexus which are visualized as hypoechoic circular structures SA-Subclavian Artery, R-First Rib.

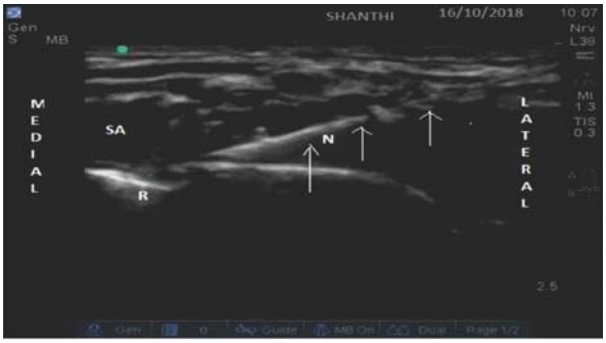


Fig. 2: Transverse sonogram of the needle (arrows) with the needle tip in the corner pocket N-Needle, R-First Rib, SA-Subclavian Artery.

Group-USG-NS

A modification of the double-injection technique was followed for this group. The nerve stimulating needle was directed towards the corner pocket. After obtaining a real-time ultrasound image of the same, the nerve stimulator was turned on and the electric current of 0.4 mA (2 Hz frequency, pulse width 0.1 ms) was used to stimulate the nerve. Muscle twitch response for ulnar nerve was observed i.e. flexion or paresthesia of fourth or fifth finger or thumb adduction. 11.5 ml of the same local anesthetic mixture as described previously was injected at the location after eliciting the desired motor response. The needle was then redirected and repositioned near the main neural cluster. Muscle twitch response was elicited for any one of the following nerves: Flexion of 2^{nd} or 3^{rd} finger for median nerve, an extension of fingers or wrist extension for radial nerve, flexion of forearm for musculocutaneous nerve. The remaining volume (11.5 ml) was deposited in the neural cluster after obtaining adequate muscle twitch with the same level of electric current, (Fig. 3).

Measurements

The sensory-motor blockade of the four nerves (median, radial, ulnar and musculocutaneous nerves) was evaluated at 3, 6, 9, 12, 15 and 30 min after local anesthetic injection. The primary outcome measure was the sensory and motor block success rate of all four nerves. Both sensory and motor blockade of the median, radial and ulnar and musculocutaneous nerves were assessed using a 3-point scale. An ice bag was used for the sensory testing, this was 0 = normal cold sensation 0 = no block, 1= partially block of cold sensation and 2 = complete anesthesia. No cold sensation: For motor this was 0 = Normal power, 1= Partial paresis, 2 = Paralysis Sensory block was evaluated in the innervated area of the four nerves as follows: Musculocutaneous (lateral forearm), median (palmar aspect of the second finger), radial (dorsum of the hand between the thumb and second finger) and ulnar (fifth finger). Motor blockade was assessed by elbow flexion (musculocutaneous), wrist flexion (median nerve), wrist extension (radial nerve) and flexion of the fourth and the fifth finger (ulnar nerve). A sensory-motor block score of 16 was considered satisfactory. This was possible when sensory and motor block scores of all four nerves reach point 2 (complete anesthesia). The secondary outcomes were the performance time, number of needle passes and success rate of surgical anesthesia. We also recorded the incidence of vascular puncture, paresthesia during the procedure and Horner's syndrome. The performance time was defined as the time from the start of initial scanning to the removal of the needle, for both techniques. Needle pass was defined as the need for the needle tip to be withdrawn and redirected at least 10 mm. Surgical anesthesia is the ability to proceed with surgery without the use of analgesics or general anesthesia. When patients complained of pain during surgery, the block was considered inadequate and general anesthesia was administered.

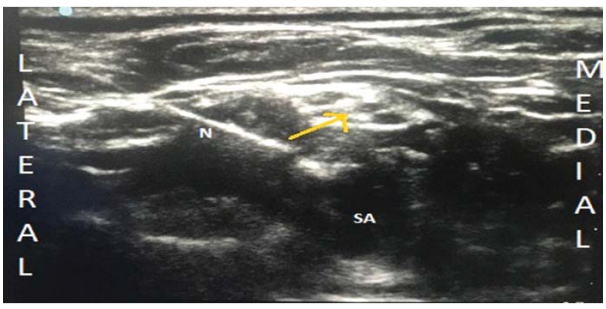


Fig. 3: Transverse sonogram showing the needle targeting the neural cluster which is pushed up by the local anesthetic spread. N-Needle, SA-Subclavian Artery

Statistical Analysis:

A pilot study was performed with ultrasound-guided supraclavicular brachial plexus block to estimate the percentage of complete sensory block at 15 min. The rate was 50% at 15 min by this approach. We assumed that combining ultrasound with nerve stimulator would increase this proportion to 80%, with a 95% level of significance and 80% power. Thus, a sample size of 33 in each group was required to accomplish this goal. SPSS Window 16.0 was used for statistical analysis. The normality of the data was tested using the Kolmogorov – Smirnov test and then the Student "*t*" test was used to compare continuous variables. Sensory block at different times was compared by using Friedman Repeated Measures Analysis of Variance on Ranks for

within-group comparisons and Kruskal – Wallis one-way analysis of variance on ranks for intergroup comparisons, and the P-value was calibrated. Categorical data were analyzed using the Chi-square test. We considered *p* - values of less than 0.05 to be statistically significant.

Results

There was no statistical difference between groups with respect to age, sex, BMI, ASA-PS classification and the surgical site. In the USG-NS group, the performance time was 4 minutes longer compared to USG Group (14.3 ± 2.88 *Vs* 10.33 ± 5.69, $p < 0.001$). surgical anesthesia in both groups was similar. Although 3 patients in USG Group required general anesthesia, it was not statistically significant. There was no difference found in terms of number of needle passes, paresthesia during procedure, vascular puncture and Horner's syndrome, (Fig. 4).

A complete sensory block of all four nerves block was achieved within 15 minutes in > 90% of patients in the USG-NS Group in comparison with the USG Group. (Ulnar nerve-91% *Vs* 70%, Median nerve-91% *Vs* 73%, Radial nerve-88% *Vs* 67%, Musculocutaneous nerve-88% *Vs* 64%, $p < 0.001$), shown as in Figs. 5 and 6. Although significant proportions of patient had achieved complete sensory block at 6 min, 9 min, (2 min respectively in USG-NS Group. No difference was found in success rate of Sensory Block between USG-NS Group and USG Group at 30 min.

Complete motor block of all 4 nerves is significant in > 80% of patients within 15 min in the USG-NS Group compared to the USG Group. (Ulnar nerve-91% *Vs* 61%, Median nerve-88% *Vs* 64%, Radial nerve-85% *Vs* 52%, Musculocutaneous nerve-82% *Vs* 52%, $p < 0.001$), shown in Fig. 7. The significant motor blockade was achieved in 6, 9, and 12 min in the USG-NS Group ($p < 0.001$), also

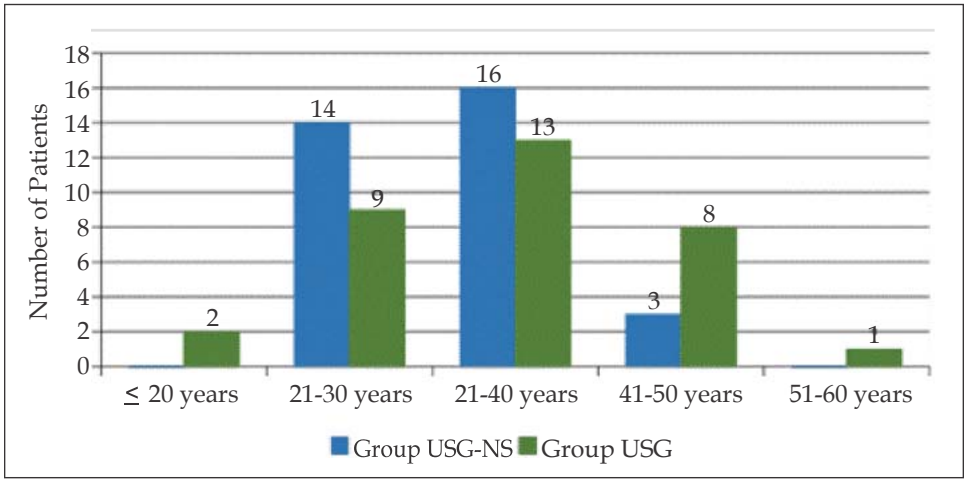


Fig. 4: Age

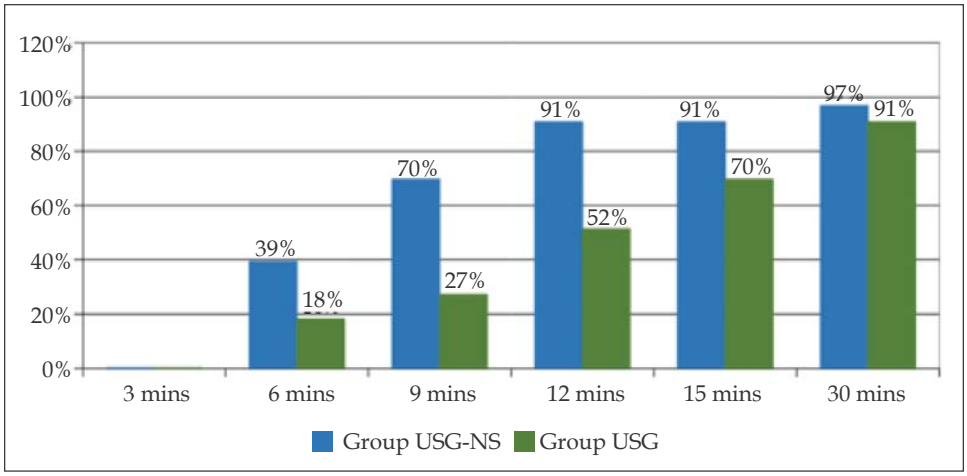


Fig. 5: Sensory Block

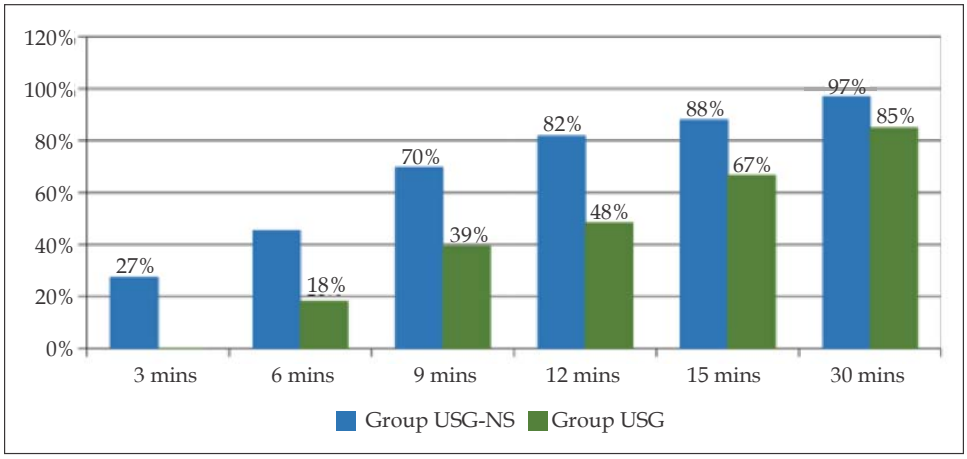
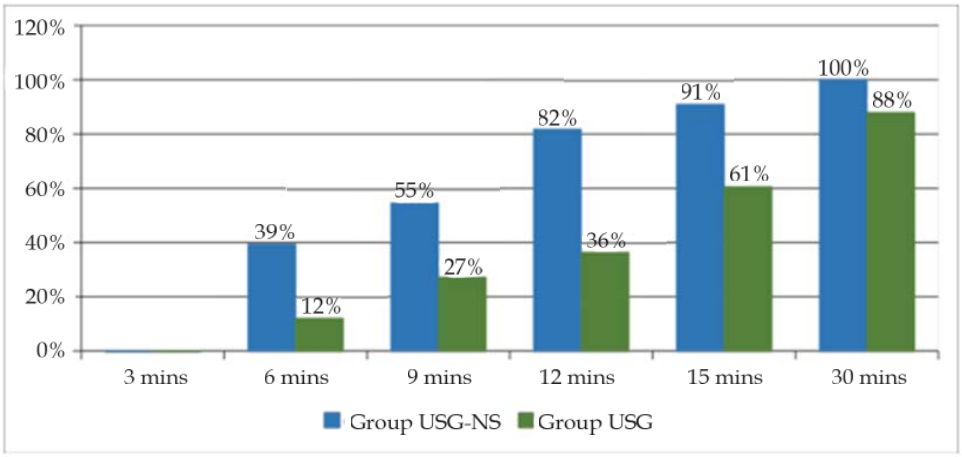
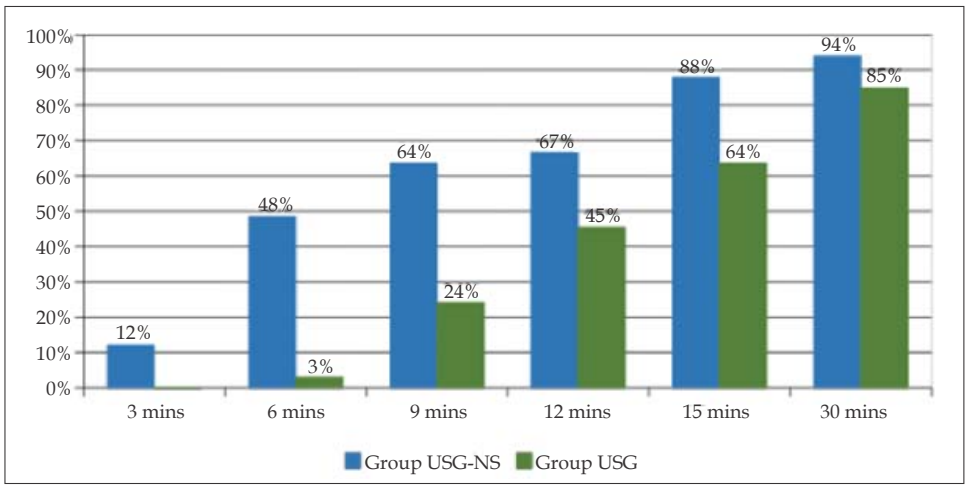
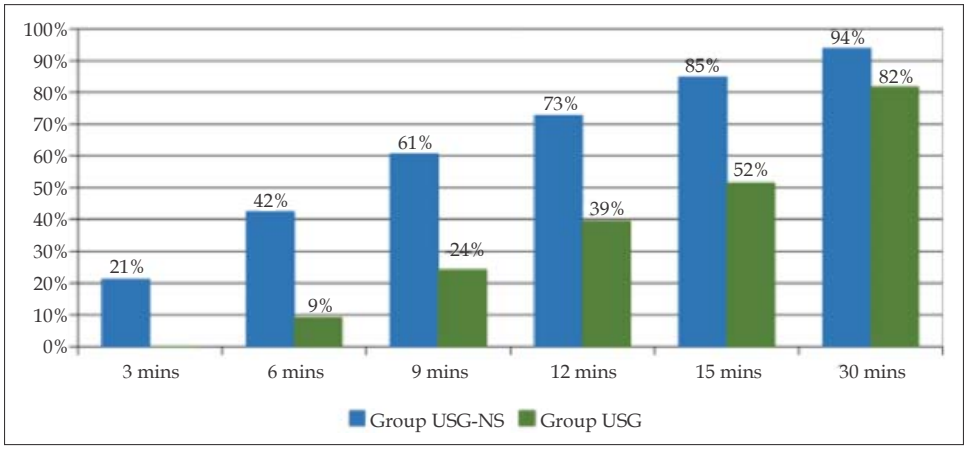
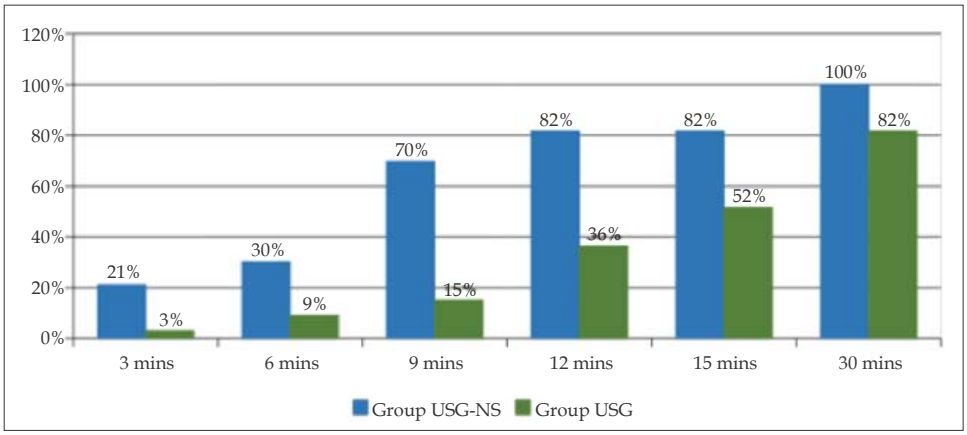


Fig. 6: Showing complete Sensory Block









Figs. 7–10: Complete Motor Block

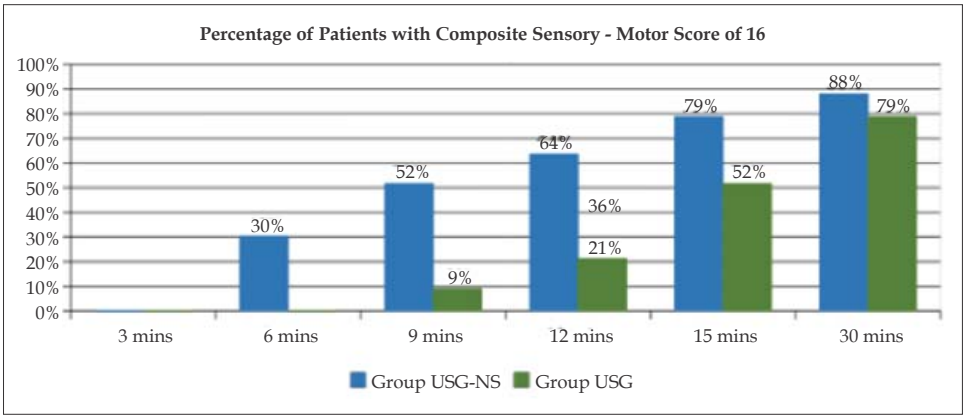


Fig. 11: Combined Sensory and Motor Block

shown as in Figs. 8 and 9. However, there was no statistical difference found in success rate of motor block between USG-NS Group and USG Group in 30 min.

The Combined Sensory and Motor Block Score was significantly high in the USG-NS Group compared to the USG Group at 6, 9, 12 and 15 min time intervals ($p < 0.001$). However, no significant difference in Sensory-motor Block was found between Two Groups at 3 min. (p -0.329), (Fig. 11).

Discussion

In this study, we demonstrated that the USG-NS Group (ultrasound guidance with nerve stimulation) technique is associated with a faster onset of supraclavicular brachial plexus block than the USG Group. The success rate of both sensory and motor blockade of all four nerves was similar at 30 minutes in both groups. We also found that the performance time was slightly longer in the USG-NS Group than the USG Group. In Quechua Luo's study, the time needed to perform the block was about 1 minute longer than the traditional technique. Quechua Luo et al.[7] used the stimulating needle to target only the ulnar nerve. Our performance time was longer by 4 minutes as we targeted and stimulated both the ulnar nerve and the main neural cluster. The success rate of complete blockade was higher in our study in USG-NS Group than the rate that has been shown in a similar study by Quechua Luo et al.[7] Luo et al. modified the classical double injection technique by stimulating the ulnar nerve specifically so, that the ulnar nerve is not spared during the block. Arab et al.[9] showed that the combined sensory block success rate with triple injection technique was 72% as opposed to single-injection technique which had a success rate of 47%. In our study, the success rate of combined sensory and motor block was 90% with double injection technique Haleem et al.[5] used a landmark technique in which the subclavian artery was palpated to locate the injection site. We used state-of-the-art ultrasound technology in which supraclavicular block was performed after obtaining real-time images with high-resolution ultrasound. In addition, complications such as accidental intravascular injection and pneumothorax which are associated with landmark technique can be easily avoided with the use of ultrasound.[15] There were conflicting results with study by Beach et al.[10] which reported that there was no significant increase in the success rate with nerve stimulator technique. But Haleem et al.[5] showed that there is a strong association between the pattern of motor response and the successful nerve block. In Beach's study,[10] local anesthetic was deposited under ultrasound guidance regardless of the motor response. Compared with Beach, in our USG-NS Group, blocks were given after identifying the brachial plexus with ultrasound guidance and then confirming the needle position by eliciting motor response. Quechua Luo et al.[7] used a modified double injection technique in which only ulnar nerve was identified with ultrasound guidance and muscle twitches were elicited in its distribution. Compared with Quechua, we identified both the ulnar nerve and main neural cluster with ultrasound and injected local anesthetic after obtaining appropriate motor responses. Thus, we were able to obtain a higher success rate of combined sensory-motor block of all the nerves mentioned above.

The success of the nerve block not only depends on the site of injection but also on the effective volume of local anesthetic injected.[16] Although a volume as high as 30 to 35 ml of local anesthetic solution is commonly used for landmark technique, we used 23 ml for our study. A minimum effective volume of 17 ml is sufficient to produce reliable sensory-motor blockade (with 95% confidence interval) determined by Song et al.[11] However, Song et al. determined this local anesthetic volume by single injection technique into corner pocket. We used a double injection technique, in which a total volume of 23 ml was used, of which half the volume was injected at corner pocket and the remaining volume into the main neural cluster. This allowed us to produce similar results under the same conditions. The ideal position of needle tip under ultrasound guidance is the connective tissue matrix between neural elements, determined by Franco et al.[12] Intraneural injection of local anesthetic resulted in higher transient postoperative numbness using double injection technique. Hence, extra fascial technique was determined safer by Bigeleisen et al.[13] The stimulation threshold of 0.4 mA for eliciting motor response in extraneural plane was determined by Bigeleisen et al. We used stimulating current in USG-NS Group, which allowed us to place the needle tip within the brachial plexus sheath but not into the neural cluster. Thus, neural injury and postoperative numbness were totally avoided in our study. The speed of onset of corner pocket supraclavicular brachial plexus block under ultrasound guidance as evaluated by Fredrickson et al.[14] was 22 minutes. In our study, with the modified double injection technique, complete blockade of all four nerves was possible as early as 15 minutes.

Conclusion

In summary, combining ultrasound with nerve stimulator for supraclavicular brachial plexus block resulted in a complete sensory-motor blockade within 15 minutes after local anesthetic injection. Although the performance time was longer by 4 minutes in this group, higher success rate and early blockade were achievable than the technique in which ultrasound alone was used. The precise location of the brachial plexus with real-time ultrasound imaging and nerve stimulation with desired muscle twitches almost eliminated the possibilities of undesired complications such as inadvertent intravascular and intraneural injections and Horner's syndrome.

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Original Research Article

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Postoperative Analgesia in Tympanomastoid Surgery with Great Auricular Nerve Block

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Abstract

Background: Great auricular nerve block provides better postoperative analgesia than systemic analgesics in tympanomastoid surgery, henceforth reduces chances of systemic side effects like nausea and vomiting as systemic analgesics used being minimized. This prospective randomized clinical study was carried out to evaluate the efficacy of great auricular nerve block, to compare the total number of analgesics required in 24 hours period postoperatively and to look for complications if any. *Methods:* In this prospective randomized clinical study, 60 patients of ASA Grade I or II, aged 18 to 65 years, undergoing tympanomastoid surgery were randomly allocated in Two groups. Group G (n = 30) patients received great auricular nerve block, and Group C (n = 30) as control Group. All patients were premedicated with Inj. Nalbuphine (0.15 mg/kg), and general anesthesia was given using conventional method. In Group G great auricular nerve block was given using 0.25% Inj. bupivacaine 7 ml with Injection Epinephrine 5 µg/ml 1:200000 prior to reversal of general anesthesia.and Group C (Control Group) didn't receive the block. *Results:* Duration of postoperative analgesia was 20.67 ± 4.54 hours in Group G and 2.13 ± 4.18 hours in Group C ($p < 0.001$). Total number of rescue analgesics required in 24 hours in postoperative period less in Group G compared to Group C. *Conclusions:* The Great auricular nerve block provides prolonged duration of action and decreased number of rescue analgesic in postoperative period for patients posted for mastoidectomy.

Keywords: Bupivacaine; Great auricular nerve block; Postoperative analgesia; Tympanomastoid surgery.

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Introduction

The great auricular nerve block has been used in patients for all acts on external ear, in cosmetic surgeries, emergency wound repair and other painful procedures of the ear.[1–5] Systemic analgesics are routinely used for postoperative analgesia in tympanomastoid surgeries,[9] which adds to nausea and vomiting, that generally follows middle ear surgeries.[8] There have been nominal studies of the particular block as a sole modality for postoperative analgesia in tympanomastoid surgery.[1] In children, the use of block as analgesic in tympanomastoid surgery has been studied and found comparable

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to systemic analgesics and incidence of vomiting events was found less.[1,5] Our aim of study was to evaluate the efficacy of the Great auricular nerve block for postoperative analgesia following tympanomastoid surgery in adults and observe for any complications.

Materials and Methods

The present study was carried out in the Department of Anesthesiology, tertiary care hospital from October 2011 to October 2012. It was a prospective randomized controlled study of total 60 patients. Sample size was calculated using *n*-master 2.0 software, and total duration of analgesia as main parameter and minimum 26 per group patients required so, we have studied 30 patients in each of the group.[1]

We have included 60 patients between the ages of 18 and 65 year; with American Society of Anesthesiologists (ASA) physical status I & II of either gender; who were scheduled to have tympanomastoid surgery in this prospective randomized comparative clinical study. Patients on anticoagulant drugs or with bleeding disorders; facial or other nerve palsy; infection, trauma, scar or sinuses at the site of block; patient with known hypersensitivity to local anesthetic drug; pregnant and lactating women; patients unable to speak or understand the verbal command and Visual Analog Score (VAS); patients unwilling to participate in the study; patient with any psychiatric illness were excluded from the study.

All the patients underwent a thorough preanesthesia check-up and routine investigations were carried out for all patients. Special investigations like ECG, Chest *X*-Ray or others were done depending upon the history and examination. Patients were explained in detail about the objective of study, methodology, advantage and likely complications. Written informed consent was taken from those patients who were ready to participate in the study. In the preoperative room, they were explained about VAS score and to request pain relief as and when required following anesthesia. All the patients were kept nil by mouth for at least six hours. All patients received oral Ranitidine 150 mg and oral Diazepam 10 mg orally on night prior to surgery. Injection Glycopyrrolate 5 mcg/kg intramuscularly was given 45 min before induction and Injection Nalbuphine 0.15 mg/kg was given intravenously three min before induction. After giving Injection Ranitidine 50 mg intravenously and Injecton Ondansentron 4 mg intravenously, conventional general anesthesia was given.

The anesthetic technique was standardized for both the groups. After preoxygenation with 100% oxygen for 5 min, general anesthesia was induced with injection Propofol 2 mg/kg intravenously, injection Suxamethonium 1.5 mg/kg intravenously. Anesthesia was maintained with 50% N_2O in O_2 with Isoflurane and Inj. Vecuronium Bromide. Patients were randomly allocated in Two Groups. Group G (n = 30) patients received great auricular nerve block with 0.25% Inj. Bupivacaine 7 ml with Injection Epinephrine 5 mcg/ml 1:200000, using distilled water as diluent whereas Group C (n = 30) Control Group did not receive block.

The block was performed at the end of surgery prior to reversal of general anesthesia. Distilled water was taken as diluent. Patient's head was turned towards the side opposite to the block to be given. After all aseptic and antiseptic precautions, two reference marks were identified first mastoid process and second lateral edge of sternocleidomastoid muscle on cricoid level. The block was given on the line joining the two marks. The puncture was done with 24G 1.5 inch needle over second mark, a wheal was raised by Infradermic Injection of 1 ml anesthetic solution (as mentioned above) after negative aspiration test. The needle was then advanced towards mastoid in the infradermic plane; and anesthetic solution was administered after negative aspiration test while gradually withdrawing the needle, very slowly. A discrete massage was then given towards mastoid to support the diffusion of the solution.[6] After arrival of respiratory effort, Injection Neostigmine 50 mcg/kg and Injection Glycopyrrolate10 mcg/kg were given intravenously. Patients were extubated after fulfillment of criteria for extubation.

Vital parameters including pulse rate, blood pressure and SpO_2 measured at basal, at induction, intraoperative, before block and after block in Group G), before extubation, after extubation every 5 min upto 30 minutes, were observed. Effectiveness of sensory block was assessed by pinprick test in comparison with the contralateral area. Visual analog score was noted every hourly up to 8 hours, then 2 hourly for the first 24 hours postoperatively. When VAS was more than or equal to 4, Injection Diclofenac sodium 1.5 mg/kg intravenously was given as rescue analgesic. Time interval from extubation to the time at which VAS 4 or more, being considered as total duration of postoperative analgesia and also total number of analgesics required within 24 hours were noted. Patients were observed for complications if any.

The results of the study were statistically analyzed by using Fischer test, Manu whitney test, Chi-square test (for qualitative data-Gender, ASA Grade) , paired *t*-test (for quantitative Data-Heart-rate, Blood pressure, SpO_2, Respiratory-rate) and unpaired *t*-test for rest of quantitative data. Results were expressed as Mean ± SD. ($p > 0.05$ not significant, $p < 0.05$ significant and $p < 0.001$ is highly significant).

Results

The present study was carried out in the Department of Anesthesiology, Medical College and SSG Hospital, Vadodara from March 2011 to January 2012 to evaluate postoperative analgesia in tympanomastoid surgery with great auricular nerve block.

The numbers of patient in either group were 30. The mean age of patients was 26.7 ± 10.04 years in Group G and 27.8 ± 12.74 years in Group C. The ratio of Male to Female was 17:13 in Group G and 18:12 in Group C. The mean weight of patients was 56.43 ± 7.6 kg in Group G and 59.03 ± 6.91 kg in Group C. 76.66% of patients in Group G and 70% in Group C were of ASA class I while rest of the patients were of ASA II. Thus, both the groups were comparable to each other with regards to the demographic data of the patient. ($p > 0.05$), (Table 1).

On intragroup comparison, fall in mean blood pressure was statistically highly significant intraoperatively in both the groups and showed no significant change before or after block in Group G. The rise in mean blood pressure was statistically highly significant after extubation and statistically significant at 5 and 10 min after extubation & statistically insignificant after 20 min of extubation in both the groups, thus, attained near preoperative values in both the groups 15 minutes after extubation. On intergroup comparison, a change in mean blood pressure was statistically insignificant perioperatively.

On intragroup comparison, fall in mean pulse rate was statistically highly significant intraoperatively in both the groups and showed no significant change before or after block in Group G. The rise in mean pulse rate was statistically highly significant after extubation and statistically significant at 5 and 10 min after extubation & statistically insignificant after 15 min of extubation in both the groups, thus attained near preoperative values in both the groups 15 minutes after extubation. On intergroup comparison, a change in mean pulse rate was statistically insignificant perioperatively.

The mean duration of tympanomastoid surgery was 182.16 ± 32.10 minutes in Group G and 194.33 ± 33.34 minutes in Group C. Thus, nature and duration of surgery was comparable amongst both the groups. There was no significant inter or intragroup difference in mean oxygen saturation perioperatively ($p > 0.05$).

The mean duration of postoperative analgesia was 20.67 ± 4.55 hours in Group G and 2.126 ± 4.18 hours in Group C as checked using pinprick method, the *p* - value being < 0.001, shown in Table 2. Thus, total duration of postoperative analgesia was significantly longer in Group G patients compared to Group C patients ($p < 0.001$). Requirement of rescue analgesic was much earlier in Group C compared to Group G. In Group G, 15 patients required no analgesics 24 hours postoperatively while 12 patients required 1 analgesic, 2 patients required 2 & 1 patient required 3 analgesics postoperatively. In Group C, 17 patients required 2 analgesics and 13 patients required 3 analgesics, (Fig. 1).

In Group G, mean VAS score continued to be low up to 16 to 20 hours postoperatively. While in Group C, mean VAS score gradually increased

Table 1: Demographic data

Parameters	Group G	Group C	*p* - Value
Number of patients	30 (100%)	30 (100%)	$p > 0.05$
Age (in years, Mean ± SD)	26.7 ± 10.04	27.8 ± 12.74	$p > 0.05$
Sex (Male : Female)	17:13	18:12	$p > 0.05$
Weight (in kg, Mean ± SD)	56.43 ± 7.6	59.03 ± 6.91	$p > 0.05$
ASA (I : II)	23 (76.66%):07 (23.33%)	21 (70%):09 (30%)	$p > 0.05$

Table 2: Postoperative analgesia

Parameters	Group G	Group C	*p* - value
Duration of analgesia (Mean ± SD) (hrs)	20.67 ± 4.55	2.12 ± 4.18	< 0.001

up to 1 to 2 hours postoperatively and gradually decreased at 3 to 4 hours and continued to be low up to 8 to 10 hours, then gradually increased up to 20 hours.

On comparing the mean VAS score between two groups, shown in Fig. 2, the mean VAS score were significantly lower in Group G compared to Group C ($p < 0.001$) up to 18 hours postoperatively. And later the mean VAS score difference between two groups was not significant ($p > 0.05$). One patient in Group G failed to achieve analgesia, as evidenced by presence of pin prick sensation at the area of block. There was no other block related complications in any patients. Nausea and vomiting was reported in 2 cases in each of group, which was comparable.

Discussion

Controlling pain after tympanomastoid surgeries is important for patient comfort and well-being,

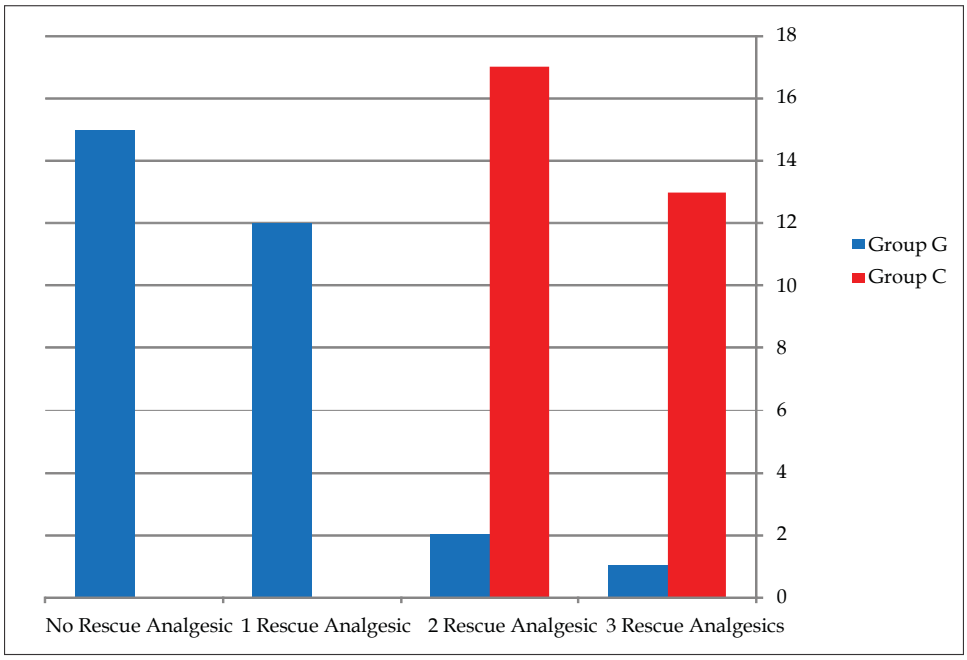

Fig. 1: Total number of rescue analgesics needed in total number of patients postoperatively

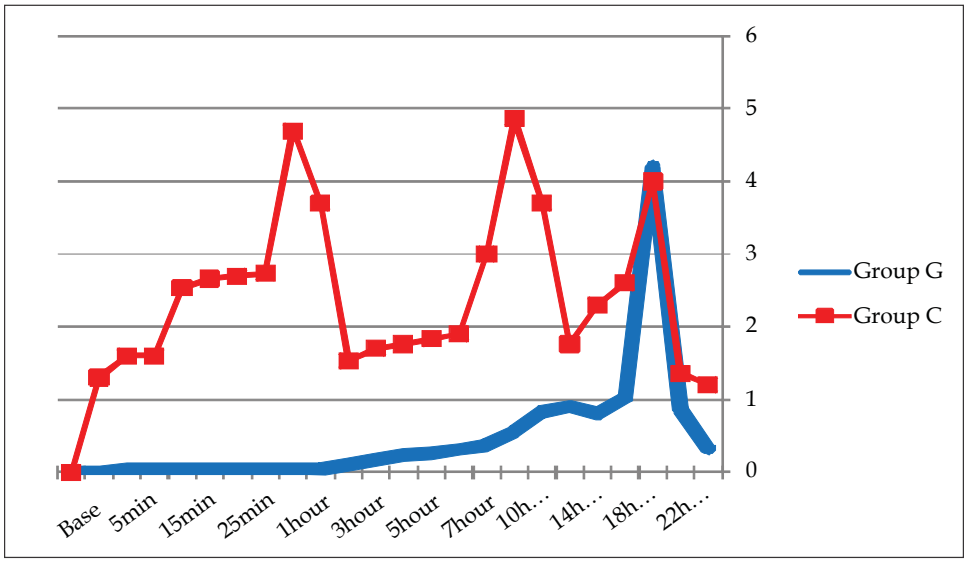

Fig. 2: Mean VAS (Visual Analogue Scale) score at different time intervals postoperatively

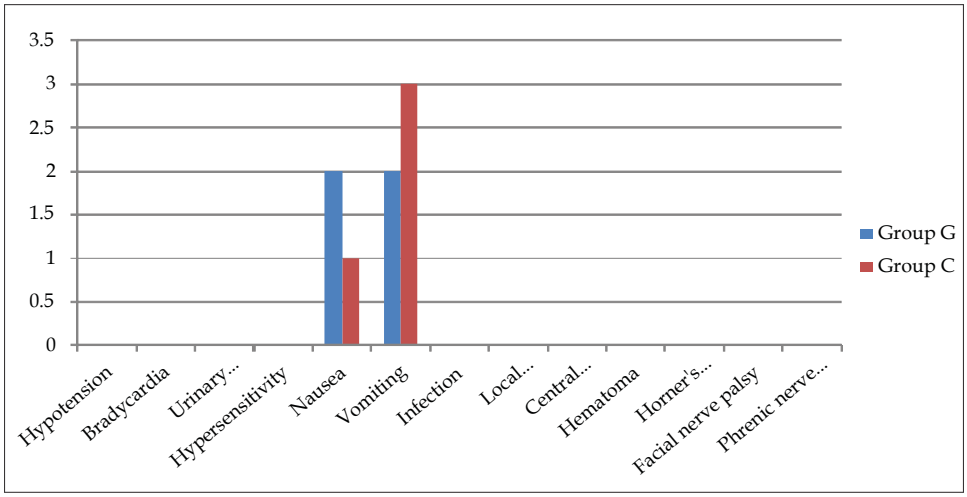

Fig. 3: Incidence of perioperative complications

especially in successful day care surgeries where one of the key elements is effectiveness of control of postoperative pain along with minimizing postoperative nausea-vomiting. Regional anesthetic techniques score over systemic medication by abolishing primary hyperalgesia due to tissue damage thus blocking central sensitization which prevents secondary hyperalgesia altogether. They block the volley of nerve impulses conducted by the unmyelinated C and Aδ fibers which carry it from peripheral somatic and visceral nociceptors to the dorsal horn of spinal cord. Peripheral nerve blocks has always been skillfully applied as part of analgesics with general anesthesia and has expanded its role from operating suite into the area of postoperative and chronic pain management.[11–14] Great auricular nerve a branch of superior cervical plexus supplies the sensory innervation to the mastoid area and the external ear.[7] Postoperative pain hampers the daily activity of patient and may cause embarrassment. Great auricular nerve block for analgesia following tympanomastoid surgery is now-a-days found to be one of the most effective means of perioperative pain relief.

In this study, 60 patients (30 in each group), aged between 18 and 60 years, of either sex were included. The mean age and sex of patients was comparable in both the groups. Elderly patients being more vulnerable to adverse effects of drug were excluded. Pediatric patients were excluded due to difficulty in assessing pain. The mean weight and ASA physical status was also comparable in both the groups. Patients were randomly allocated in two groups.

Group G patients received great auricular nerve block with 0.25% Inj. Bupivacaine 7 ml with Inj. Epinephrine 1:200000 (n = 30) . The block was performed at the end of surgery prior to reversal of general anesthesia. Group C was considered Control Group, whom block was not given (n = 30). We preferred the use of block prior to extubation so, as to prevent the onset of pain, which helps in psychological well-being, comfort and improvement in the general condition of the patient.[6,11,12] Technique of great auricular nerve block used in our study was by classical method.[1,5,6] Santhanam Suresh et al. also stated that the anatomic location of this nerve and the ease with which this nerve block can be performed does not significantly increase the procedure time.[15,16] In our study, we have used Bupivacaine 0.25%, as it has a long-duration of action and low-tissue toxicity. At this concentration sensory effects are seen predominantly. We have added Adrenaline 5 µg/ml (1:200000) to Inj. Bupivacaine so, as to decrease the peak plasma levels of bupivacaine.[1,5] The volume of drug used in our study was 7 ml 0.25% Inj. Bupivacaine HCl.[6] Rescue analgesia was given when VAS ≥ 4, in the form of Injection Diclofenac sodium 1.5 mg/kg. Failure of procedure in one case was observed. Nausea and vomiting were seen in 2 cases in both the groups, (Fig. 3).

On comparing the mean VAS score between two groups, the mean VAS score were significantly lower in Group G compared to Group C ($p < 0.001$) until 18 hours postoperatively, and later the mean VAS score between two groups was not significant. ($p > 0.05$). The mean duration of postoperative analgesia was 20.67 ± 4.55 hours in Group G and 2.12 ± 4.18 hours in group C ($p< 0.001$). Thus

total duration of post operative analgesia was significantly longer in Group G patients compared to Group C patients. A study by A Pulcini and JP Guerin also mentioned that a local anesthetic of long duration, with an additive drug, allows a very good quality of postoperative analgesia during at least ten hours. The mean duration of postoperative analgesia in the control group was around 2.12 ± 4.18 hour which might be due to long elimination half life of Inj. Nalbuphine (5 hours) given as premedication.

In Group G, patients required 0 to 1 dose of rescue analgesia in 24 hours postoperatively, while in Group C all patients required two to three doses of rescue analgesia.

Because the neck is very vascular, intravascular Injection of local anesthetic solution may occur, care should be taken while performing nerve block. Likely complications with great auricular nerve block include local anesthetic toxicity, hypersensitivity, inadvertent arterial puncture, hematoma, horner's syndrome, transitory facial nerve palsy, ipsilateral phrenic nerve paresis or central neuraaxial block.[7] All these complications can be avoided if injection of anesthetic solution is being done strictly in infradermal plane, that too, very slowly after aspiration.[6] Addition of Adrenaline to Bupivacaine decreases the peak plasma concentration of Bupivacaine thus decreases the chances of potential adverse effects.[1] The recurrent laryngeal nerve can sometimes be blocked during cervical plexus blockade. This usually occurs if the injection is performed deep at the posterior border of the sternocleidomastoid. Deep injection should be avoided as it can block the cervical sympathetic ganglia leading to Horner's syndrome (ptosis, miosis, and anhydrosis) or phrenic nerve paresis. Failure of procedure in one case was observed. Nausea and vomiting were seen in 2 cases in both the groups. Shown in Fig. 3, Rescue analgesia was given when VAS ≥ 4, Injection Diclofenac sodium 1.5 mg/kg and inspite of injection if patient does not have pain relief Inj. Tramadol 1 mg/kg intravenously was given.

Conclusion

We conclude that *The Great auricular nerve block* provides prolonged duration of action and decreased number of rescue analgesic in postoperative period for patients posted for mastoidectomy. We have not observed any complications.

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Original Research Article

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Comparative Study of Three Techniques of Proseal Laryngeal Mask Airway (PLMA) Insertion In Patients Undergoing Elective Surgeries

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Abstract

Background: The LMA has revolutionized airway management and its use are now standard practice in General Anesthesia. The rationale behind the study was to compare three techniques of Proseal Laryngeal Mask Airway (PLMA) insertion. *Objectives:* To assess the superiority of placement with three techniques of Proseal Laryngeal Mask Airway insertion with respect to 1. Number of attempts to successful placement 2. Insertion time 3. Oropharyngeal leak pressure 4. Fiber Optic Bronchoscopy (FOB) Grading. *Materials and Methods:* A randomized prospective comparative study was done for a period of 1 year. The study was carried out at Saveetha Medical College and Hospital. The study was conducted on 90 adult patients of either sex, in the age of 18–65years, belonging to ASA I and II with Modified Mallampati Score I & II posted for elective surgeries. Systemic sampling was used. All patients were kept on fasting for 8 hrs. SPSS version 20 was used for analysis. One-way ANOVA and Chi-square test was used for analysis. *p* - value of < 0.05 is considered statistically significant. *Results:* There was no significant difference between the three groups in terms of age, weight, ASA, MMS. The insertion time for Group-G was 22.5 ± 5.0 sec and Group-IT was 14.2 ± 3.3 sec which were significantly higher than Group D (11.37 ± 2.7 sec). GEB guided PLMA insertion was successful in 30/30 (100%) and IT guided insertion was also successful in 30/30 (100%) in the first attempt. Oropharyngeal leak pressure in Group IT (26 ± 3.3) and Group G (27.8 ± 2.3) was significantly higher when compared to Group D. *Conclusion:* We conclude that GEB-guided insertion and Introducer technique is comparable to digital technique in successful placement of PLMA. However, GEB and IT technique provides better airway seal compared to digital technique.

Keywords: Proseal LMA; General anesthesia, Oropharyngeal leak pressure; Fiber-optic grading; Gum elastic bougie.

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Introduction

The LMA has revolutionized airway management and its use are now standard practice in General Anesthesia.[1,2] Since, the introduction of LMA in 1988, it has challenged the supposition that tracheal intubation is the only acceptable way to maintain clear airway and provide positive

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pressure ventilation. Widespread use of LMA was restricted due to its risk of gastric distension, pulmonary aspiration of gastric contents and fear of inadequate ventilation.[3] PLMA insertion with digital technique/IT was successful in 87% and 84% patients in first attempt, while 10% of insertions required second attempt in most of the studies.[4–6] The principle cause of failed and/or delayed insertion with the digital and IT techniques were impaction of the PLMA at the back of the mouth, which resulted in failed passage into the pharynx, or folding over of the distal cuff, or the distal cuff being directed into the glottis inlet rather than the hypopharynx.[6] To overcome these problems of digital technique, Insertion techniques like IT and Gum Elastic Bougie (GEB) aided placement were introduced. These newer techniques have better placement.[7] GEB-guided PLMA insertion was successful in 100% patients in first attempt. Insertion was more frequently successful with the GEB-guided technique at the first attempt than the digital or IT techniques. The GEB-guided technique is more frequently successful because it reduces impaction at the back of the mouth, prevents folding over of the distal cuff, and guides the distal cuff directly into the hypopharynx.[6,7] The Purpose of this study was to evaluate if GEB and IT technique would offer better placement than Digital technique.

Materials and Methods

This study was a randomized, prospective, comparative study. After obtaining institutional Ethical committee clearance and patient's written informed consent, the study was carried out at Saveetha Medical College and Hospital. The study was conducted on 90 adult patients of either sex, in the age of 18–65 years, belonging to ASA I and II with Modified Mallampati Score I & II posted for elective surgeries. The study was conducted from July 2015–July 2016 (12 months).

Inclusion criteria:

Includes age group of 18–65yrs who were Posted for elective surgeries, belonging to ASA I and II with Modified Mallampati Score I/II. Patients willing to participate and giving informed consent were included.

Exclusion criteria:

Age group below 18 and above 65 were excluded Patients posted for Emergency surgery Belonging to ASA III, IV, V Patients with increased risk of aspiration (e.g.: Hiatus hernia, Gastro Esophageal Reflux Disease, obesity, pregnancy, etc.). Patients with anticipated difficult airway (e.g.: inter incisor distance < 2 cm, Modified Mallampatti Score III and IV).

Patients were randomly allocated into Three Groups by computer based randomization:

1. Group D - PLMA insertion by Digital technique-30 patients;
2. Group IT - PLMA insertion by Introducer tool technique-30 patients;
3. Group G - PLMA insertion by Gum Elastic Bougie guided technique-30 patients.

All patients were kept on fasting for 8 hrs. They were given aspiration prophylaxis with Tab. Ranitidine 150 mg Per Oral and Tab. Metoclopromide 10 mg PO at 6 am on the Day of surgery. Patients were premedicated with Inj. Glycopyrolate 0.2 mg IV one hour before surgery. After the placement of standard minimum monitoring ECG, Pulse oximetry, NIBP, Capnography, the patient was kept in Sniffing position. All the patients were premedicated with Inj. Fentanyl 2 mcg/kg and Preoxygenated for 3 min with 100 percent oxygen. Anesthesia was induced with Inj. Propofol 2–3 mg/kg IV given over 30 sec and maintained with 1–2% Isoflurane in oxygen and N_2O (50% : 50%) with facemask ventilation & PLMA was inserted when there was adequate jaw relaxation. In patients weighing between 30 and 50 kg size 3 PLMA (TELEFLEX TM, United States) was used and in patients weighing between 50 and 70 kg size 4 PLMA was used. An experienced anesthetist who was well-trained in using PLMA, performed the PLMA insertion.

Group-A: (*Digital Technique*) Digital insertion technique was performed according to manufacturer's instruction. The Digital technique involved the use of the index finger to press the PLMA into and advance it around the Palatopharyngeal curve.

Group-B: (*Gum Elastic Bougie guided insertion*) – The drain tube of the PLMA was primed with lubricated 60 cm long, (16F) Gum elastic bougie with its straight end first, leaving the 5 cm bent portion protruding from the proximal end (for the assistant to grip), and the maximum length protruding from the distal end (for anesthetist to manipulate) was 30 cm.

Group-C: (*Introducer tool Technique*) – The IT technique involved attaching the Introducer tool using a single-handed rotational Technique to press

the PLMA into oropharynx and advance it around the palatopharyngeal curve and removing the IT.

Primary Outcome Measures:

1. *Insertion time*: The Insertion time is defined as the time taken since taking PLMA/ Laryngoscope in hand till time taken to obtain effective airway as a spontaneous movement of the breathing system (shown by square wave capnography).
2. *No. of attempts*: (Number of attempts taken for a successful placement of PLMA)
3. *Oropharyngeal leak pressure*: (The oropharyngeal leak was determined by closing the Adjustable Pressure Limiting (APL) valve of the circle system at a fixed gas flow of 3 liters/min and recording the airway pressure at which equilibrium was reached (maximum allowed was 40 cm H_2O). Equilibrium was taken as the point at which an audible leak could be heard from the mouth. The Dragger anesthesia machine was used for recording airway pressure.)
4. *Grading of placement* (FOB Grading) After recording the above observations, a 5.5 mm fiber Optic Bronchoscope was passed through the LMA till its tip lies 1 cm proximal to the end and the view was assessed by a standard score devised by Brimacombe and Berry.

Sample Size Calculation:

Assuming the oropharyngeal leak pressure in previous studies, the sample size was estimated to be 20 in each group for a Type I error of 0.05 & power of 90 at 5% significance level. To make the study more precise, we took sample size of 30 in each group.

Statistical Analysis:

All data were collected, tabulated and expressed as Mean ± Standard deviation. The analysis of variance (One way ANOVA) test was used to compare the groups for parametric data (age, weight, OLP, insertion time) while the qualitative parameters such as ASA, ease of insertion, number of attempts were analyzed using the Pearson Chi-square test or Fisher exact test (whichever applicable). The statistical analysis was carried out using SPSS software version 20. The p - value < 0.05 was taken as significant.

Results

As per Table 1, The three groups were comparable with respect to the demographic characteristics. There was no significant difference between the three groups in terms of age, weight, ASA, MMS. ($p > 0.05$).

As per Table 2, the insertion time for Group-G was 22. 5 ± 5.0 sec and Group IT was 14. 2 ± 3. 3 sec which were significantly higher than Group D (11. 37 ± 2.7 sec). One-way Anova reveals p - value of 0. 001 which was significant. Hence, GEB guided and Introducer guided insertion of PLMA took longer time than digital technique for the successful placement.

Table 1: Demographic details of the patient

Parameters		Digital	Introducer	GEB	p - value
Age (yrs)		36.17	35.53	34.03	0.82
Weight (kg)		59.17	60.93	59.43	0.75
ASA	I	16	19	23	0.61
	II	14	11	7	
MMS	I	4	2	6	0.31
	II	26	28	24	

Table 2: Insertion time of PLMA with three techniques

Method	Insertion time	p - value
Digital	11. 37 ± 2.7	0.00
Introducer	14. 20 ± 3.3	
GEB	22. 57 ± 5.0	

Table 3: Comparison data of number of attempts between three groups in Insertion of PLMA

No. of Attempts	Group			Total (*n*)	*p* - value
	Digital	Introducer	Bougie		
1st Attempt	28 (93.3%)	30 (100%)	30 (100%)	88 (97.8%)	
2nd Attempt	2 (6.7%)	0	0	2 (2.2%)	
Total (*n*)	30	30	30		0.12

Table 4: Comparison of Oropharyngeal Leak Pressure between three groups

Method	Oropharyngeal leak pressure (cm of H_2O)	*p* - value
Digital	23 ± 2. 4	0.00
Introducer	26.5 ± 3.3	
GEB	27.8 ± 2.3	

Table 5: Comparison of Fiberoptic Grading between three groups

Grading of placement FOB		Group			Total	*p* - value
		Digital	Introducer	Bougie		
1	Count	3	3	1	7	0. 6
	% within Group	(10.0%)	(10.0%)	(3.3%)	(7.8%)	
2	Count	15	10	7	32	0. 4
	% within Group	(50. 0%)	(33.3%)	(23.3%)	(35.5%)	
3	Count	10	15	14	39	0. 4
	% within Group	(33.3%)	(50.0%)	(46.7%)	(43.3%)	
4	Count	2	2	8	12	0.04
	% within Group	(6.7%)	(6.7%)	(26.7%)	(13.3%)	
Total	Count	30	30	30	90	
	% within Group	(100%)	(100%)	(100%)	(100%)	
Clinically accepted		30	30	30		1. 00

According to Table 3, GEB guided PLMA insertion was successful in 30/30 (100%) and IT guided insertion was also successful in 30/30 (100%) in the first attempt. Insertion with digital technique was successful in 28/30 (93.3%) at the first attempt and it was placed successfully at the 2nd attempt by lateral technique in 2/30 (6.7%) patients. These data was not statistically significant (p = 0. 12).

As per Table 4, Oropharyngeal leak pressure in Group IT (26 ± 3. 3) and Group G (27.8 ± 2.3) was significantly higher when compared to Group D (23 ± 2.4). One Way Anova revealed p - value of 0.001 which was significant. Hence, better airway seal was achieved with GEB guided and IT guided technique when compared to Digital technique.

As per Table 5, in the grading of placement of FOB, significance level was seen only in Grade 4. (p < 0.05) which shows fiberoptic grading is comparable in all groups except in Grade 4 although it was clinically acceptable.

Discussion

The Proseal LMA provides an acceptable way to maintain a clear airway & positive pressure ventilation. It also reduces the risk of gastric insufflation, regurgitation and aspiration of gastric contents. Various insertion techniques have been developed by authors to overcome misplaced PLMA leading to ineffective ventilation. Previous studies with bougie guided technique have shown that the use of laryngoscope for Proseal Laryngeal Mask airway insertion helps to maintain intubation skills, improves placement and prevents folding of distal cuff. This technique also improves the success rate of gastric tube insertion compared with other techniques, hence indicating lesser incidence of cuff malpositioning. The disadvantages of this technique could be the hemodynamic response associated with the Laryngoscopy and airway trauma due to bougie insertion. However, studies have supported and denied the above findings. In our study, the first

attempt success rate for bougie guided technique (100%), Introducer Technique (100%), digital (93%) were similar in all the groups. The two failed cases by the digital technique was successfully placed by lateral technique in the second attempt. Our study was similar to a randomized control study done by Savita Saini[8] et al. where the 1st attempt success rate with bougie guided technique (100%) Introducer Tool 98%) and digital technique (90%). Maclean et al.[9] also had similar results with bougie guided technique (96%), Introducer

Technique (93%). J Brimacombe et al.[4] reported significant higher first attempt success rate with the GEB technique (100%) over other techniques [digital (88%), IT (84%)] and the success after 3rd attempt was similar in all the techniques. We noted a higher insertion time in bougie guided technique (22.57 ± 5.0 sec) than Introducer Technique (14.20 ± 3.3 sec) and Digital technique (11.37 ± 2.7 sec). This was comparable to savita et al.[8] (G 24 ± 5.4/ IT 20.6 ± 4.8/D 20 ± 8 sec). The longer insertion time noticed in bougie guided technique was due to laryngoscopic handling and removal of Bougie after insertion.

However, Brimacombe[4] and colleagues found lesser insertion time (G25 ± 14/IT 28 ± 14/D 27 ± 12) in GEB guided technique than digital and introducer tool technique. The authors noted that the difference in the study was due to the skill with which all anesthetists are conversant, was used in the GEB guided group and this might have contributed to the shorter time taken to insert the PLMA using GEB guidance[10] Oropharyngeal leak pressure indirectly indicates airway seal, higher the oropharyngeal leak pressure, better the airway seal. In our study, Oropharyngeal leak pressure was higher with bougie guided technique (27.8 ± 2.3) and Introducer technique (26.5 ± 3.3) than Digital technique (23 ± 2.4) which was comparable to Kuppusamy et al.[11] (D 23 ± 3.6/G 30 ± 4.7). However, few other studies[4,5,7,12] found higher Oropharyngeal Leak Pressure with bougie guided technique. Nileshwar et al.[12] and Maclean et al.[9] were other studies which showed similar results in fiberoptic grading. This explains the reason for the significant decrease in oropharyngeal leak pressure with Digital technique.

Conclusion

We conclude that GEB-guided insertion and Introducer technique is comparable with digital technique in successful placement of PLMA. GEB and IT technique provides better airway seal compared to digital technique. We suggest that GEB and IT technique can be used as a backup technique when digital technique fails.

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Conflict of Interest: None declared.

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Original Research Article

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The Effects of Intravenous Propofol and Intravenous Etomidate as Induction Agents on Blood Glucose in Elective Surgeries Under General Anaesthesia: A Randomized Control Trail

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Abstract

*Introduction***:** Acute hyperglycemia is known to occur during major surgeries, its occurrence even for a brief period may lead to immune suppression. Surgeries which require general anesthesia are more susceptible for stress mediated immune response and intraop rise in blood glucose levels. Drugs used during induction and maintenance of anesthesia are also known to cause plasma glucose derangement along with surgical stress response, which can lead to adverse postoperative morbidity. *Aim:* To study the effect of blood glucose level at specified time intervals with intravenous Propofol and Etomidate. *Materials and Methods:* Sixty cases requiring general anesthesia, belonging to class 1 and 2 of American Society of Anesthesiology were selected. Patients were preoxygenated and premedication drugs were given and induced with either Propofol 2 mg/kg or Etomidate 0.3 mg/kg. Blood glucose was measured before premedication, at 5^{th} minute and at 15^{th} minute respectively. Statistical analysis done using Student *t*-test for parameters on continuous scale and Chi-square test for parameters on categorical scale. *p* - value of less than 0.05 was considered statistically significant. *Results:* The blood glucose in Etomidate Group increased compared to premedication value (84.7 ± 15.37 to 92.5 ± 17.09) and was statistically significant (*p - value 0.0167*). In Propofol Group, variation in blood glucose level was not significant (88.26 ± 15.47 to 87.0.5 ± 12.84). There was no significant increase in Heart rate, SBP, DBP & MAP at T5 & T15 in both the groups. *Conclusion:* In the current study, increase in blood glucose in nondiabetic patients following induction was found to be significantly high with Etomidate when compared with Propofol.

Keywords: Blood Glucose; Nondiabetic patients; Diabetes mellitus; Hemodynamic parameters.

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Introduction

The induction of anesthesia in patients undergoing any surgery has concerns including hemodynamic stability and attenuation of stress response. Of many metabolic reactions by the body during surgery the most important is resistance to insulin and hyperglycemia.[1] Hyperglycemia in the perioperative period is due to stress leading to release of many hormones such as epinephrine,

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cortisol and other inflammatory mediators. The immediate perioperative problems faced by the diabetic patients are: (i) Surgical induction of the stress response with catabolic hormone secretion; (ii) Interruption of food intake, which may be prolonged following gastrointestinal procedures; (iii) Altered conscious masks the symptoms of hypoglycemia and necessitates frequent blood glucose estimations; and (iv) circulatory disturbances associated with anesthesia and surgery, which may alter the absorption of subcutaneous insulin and is associated with significantly increased infectious complications associated with patient mortality.[2] Acute hyperglycemia in the perioperative period is associated with significantly increased complications and worsens prognosis even in the patients who had normal glucose tolerance test.[3,4] Hyperglycemia provokes numerous deleterious effects even on myocardium subjected to ischemia–reperfusion process. High blood glucose concentration abolishes ischemic preconditioning and amplifies reperfusion injuries and intraoperative glycemic control may be rendered difficult despite insulin therapy.[5]

The ADA specified that the diagnosis of diabetes mellitus should be made if a random plasma glucose value in an asymptomatic individual is > 11.1 mmol litre^{-1}. If a fasting plasma glucose is > 7.0 mmol litre^{-1} (6.1 mmol litre^{-1} blood glucose) in an asymptomatic individual, the test should be repeated on a different day and a diagnosis to be made if the value remains above this limit.[6] The ADA defines fasting plasma glucose concentrations between 6.1 and 7.0 mmol litre^{-1} (5.6–6.1 mmol litre^{-1} blood glucose) to represent 'impaired fasting glycemia.[6] WHO has also recommends the diagnosis of diabetes mellitus would be made if a random plasma glucose concentration is > 11.1 mmol litre^{-1} (venous whole blood > 10.0 mmol litre^{-1}).[6] It can also be diagnosed with a fasting plasma glucose concentration of > 7.0 mmol litre^{-1} and a second similar test or an oral glucose tolerance test producing a result in the diabetic range.

Lattermann R et al.[7] inferred that Combined spinal epidural technique can prevent hyperglycemia compared to GA in the patients undergoing any surgery, but surgeries which mandates the use of General anesthesia including Head and neck surgeries, Cardio-thoracic surgeries etc. requires intense monitoring of blood glucose and more so in diabetic individuals. Several intravenous anesthetic agents are used during induction including Ketamine which is associated with change in blood glucose levels and hemodynamics.

Propofol is an alkyl phenol, substituted with two isopropyl groups. The induction dose of propofol in healthy adults is 1.5 to 2.5 mg/kg, with blood levels of 2 to 6 μg/ml producing unconsciousness depending on the concomitant medications (e.g., opioid analgesics), patient's age, physical status and surgical stimulation.[8] It has been reported to inhibit phagocytosis and to reduce proliferative response of lymphocytes in critically ill.[9] Because fat emulsions are known to support the growth of micro-organisms, contamination can occur with long-term use of propofol.[10] Diabetic patients show a reduced ability to clear lipids from the circulation but with usage of propofol as an induction agent or during short anesthetic procedures for maintenance lipid accumulation is not seen.

Etomidate is a carboxylated imidazole which penetrates brain rapidly, reaching peak level within 1 min after intravenous injection. Etomidate transiently depresses adrenocortical function by dose dependent inhibition of conversion of cholesterol to cortisol. Etomidate blocks adrenal steroidogenesis and hence cortisol synthesis, by its action on 11 β-hydroxylase and cholesterol cleavage enzymes, and consequently decreases the hyperglycemic response to surgery by approximately 1 mmol litre^{-1} in nondiabetic subjects.[11]

There are several studies which have compared the effect of blood glucose using Propofol and other inhalational agents.[12–15] In current literature, there are no studies which have compared the effect of Propofol and Etomidate as induction agentson blood glucose in elective surgeries on nondiabetic patients. Hence, this study was conducted to compare the effect of Propofol and Etomidate as induction agents on blood glucose and hemodynamic parameters at specified time intervals.

Materials and Methods

This study was a double blind, prospective, randomized comparative study. The study was conducted at Adichunchanagiri Institute of Medical Science between 08.08.2018 and 25.02.2019. An approval by the Institutional Ethical Committee (AIMS/IEC/2197/2018–19) was obtained. Oral and informed consent was taken from all patients included in the study group.

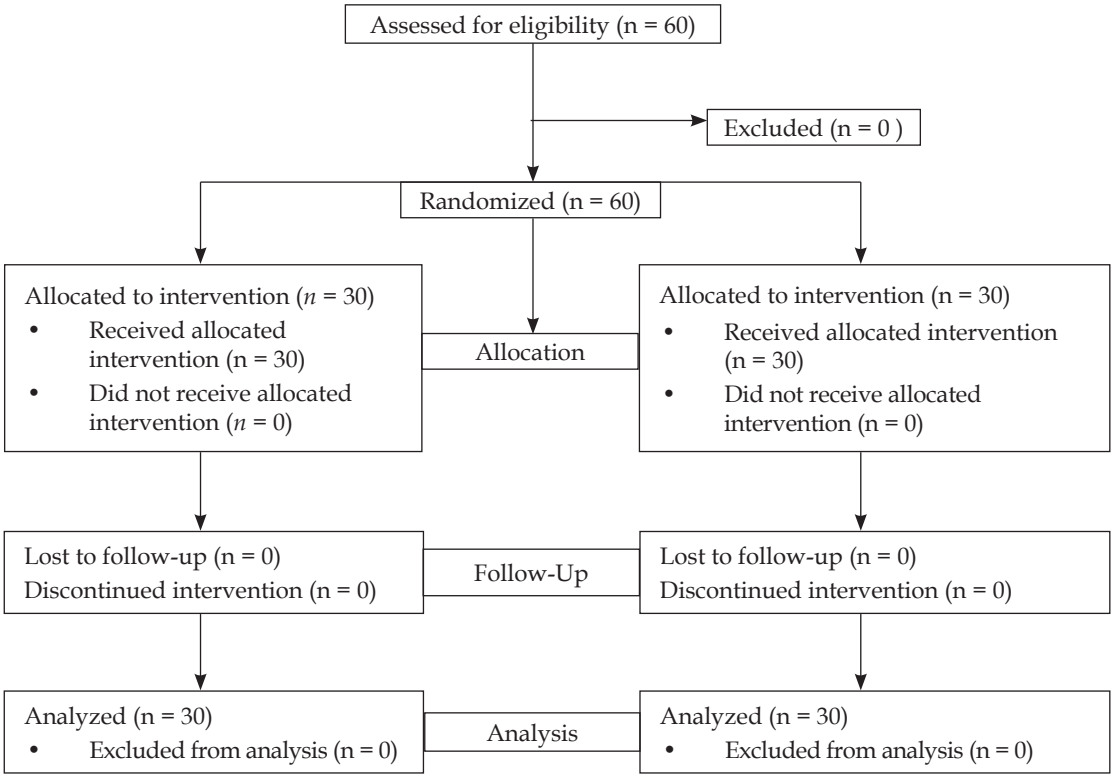

Fig. 1: Data-flow Diagram (DFD)

The necessary sample size was calculated to detect a 25% change in blood glucose level. Minimum number of patients required in each group was 30 and there were no dropouts in the study group. All patients between the age of 20 and 60 years with no associated comorbidities posted for elective surgeries were included in the study group. Standard deviation of the study was 33% of the mean, power of study was 80% with Alpha error being 0.005.

Patients with associated comorbidities, belonging to ASA Grade of more than II, cases posted for Emergency surgeries, patients with previously diagnosed Diabetes, patients with psychiatric illnesses, metabolic diseases, endocrine dysfunction, known allergy to study drugs, impaired coagulation profile and on medications which affects blood glucose at least one week before surgery like steroids, β blockers etc. were excluded from the study. Randomization was done according to random number table and study sample were divided into 2 Groups:

Group P: Where Propofol 2 mg/kg was used as induction dose (n = 30);

Group E; Where Etomidate 0.3 mg/kg was used as induction dose (n = 30).

A thorough preanesthetic check-up was done and all relevant investigations including complete hemogram, Renal function test, Serum Electrolytes, Bleeding time and Clotting time, Electrocardiogram and Random blood glucose assessment was done for all patients. Those patients who were accepted under ASA 1 and ASA 2 were included in the study. Patients were kept nil per oral for 8 hours prior to surgery. On arrival to the operating room monitors including ECG, NIBP, Pulse oximeter were connected for continuous monitoring of Pulse, Saturation, Systolic BP, Diastolic BP and Mean Arterial Pressure. All patients were premedicated with Inj. Midazolam 1 mg intravenously and preoxygenated with 100% oxygen for 5 minutes. Blood glucoses checked prior to induction, at 5 minutes and 15 minutes following induction with study drug. Group P patients were induced with Inj. Propofol 2 mg/kg and Group E patients with Inj. Etomidate 0.3 mg/kg. After administration of induction agent succinylcholine of 1.5 mg/kg was administered. Direct laryngoscopy done and tracheal intubation was performed by the senior

faulty to reduce the intubation response. Blood glucose levels with Pulse, Heart rate, Systolic Blood Pressure, Diastolic Blood Pressure were measured continuously and noted down at 5th and 15th minute after giving study drug. Blood glucose checked by glucometer - Optimum Exceed. With the data collected Blood glucose levels were compared between 2 Groups.

Stastistical Analysis:

Student *t*-test was used for parameters on continuous scale. Chi-square test was used for parameters on categorical scale. P - value of less than 0.05 was considered significant. Statistical software: SAS 9.2, SPSS 15.0, stata 10.1, Medcalc 9.0.1, Systat 12.0 & R environment ver. 2.11.1 was used.

Results

The demographic data showing age, sex, weight and ASA grading of the study groups has been shown in Table 1. The average age group in our study is 33.36 ± 14.33 for Group P and 34.36 ± 11.85 for Group E which is statistically comparable. Similarly the weight among the patients in two groups were comparable where the average weight in group P was 55.88 ± 9 and in group E was 57 ± 10.52.

There was no significant increase in Heart rate at different time intervals when compared to premedication value among the Groups P (*p* - value 0.73) and E (*p* - value 0.05). Change in MAP values were comparable and statistically insignificant when compared to premedication value among the Groups P (*p* - value 0.73) and E (*p* - value 0.05), as shown in Table 2.

The blood glucose in Group E was increased compared to premedication value & was statistically significant (*p* - value 0.0167), whereas in Group P the blood glucose variation at 5th and 15th minute was not statistically significant (*p* - value 0.7470) as compared to premedication value which is shown in Table 3. There were no major adverse effects seen during the study.

Discussion

On the basis of the collected evidence regarding ASA I–II status of the cases posted for surgeries requiring general anesthesia in nondiabetic patients, it is statistically significant that use of Etomidate as induction agent caused an increase in blood glucose level (*p* - value 0.0167), while the

Table 1: The demographic data showing age, sex, weight and ASA grading of the study groups

Variable	Group P	Group E	*p* - value
Age (years)	33.36 ± 14.33	34.36 ± 11.85	0.76
Sex (male/female)	14/16	19/11	-
Weight (kgs)	55.88 ± 9	57 ± 10.52	0.65
ASA I	14	17	-
ASA II	16	13	-

Table 2: Tabular column showing Hear Rate (HR) variation and Mean BP (Blood Pressure) variation in Group P and Group E before premedication, at 5th minute (T5) and at 15th minute (T15) respectively with its *p* - value. P-Propofol, E-Etomidate.

Group	Hr variation in Group P	Hr variation in Group E	Group	Mean BP variation in Group P	Mean BP variation in Group E
Premeds	88.92± 12.06	95.2 ±16.78	Premeds	88.92 ± 12.06	95.2 ± 16.78
T 5	91.66± 16.29	95 ± 13.92	T 5	91.66 ± 16.29	95 ±13.92
T 15	90.07± 13.72	87.53±12.62	T 15	90.07 ±13.72	87.53±12.62
p - value	0.73	0.05	*p* - value	0.73	0.05

Table 3: Blood glucose values which were measured following usage of Propofol and Etomidate at different time intervals. P-Propofol, E-Etomidate.

Group	Group P	Group E
Premedication value	88.26 ± 15.47	84.7 ± 15.37
5 Minutes	83.61 ± 14.55	88.13 ± 15.29
15 Minutes	87.05 ± 12.84	92.5 ± 17.09
p - value	0.7470	0.0167

same did not occur with the use of Propofol as induction agent (*p* - value 0.7470).

The reason for hyperglycemia during surgery may be surgical pain and metabolic response to surgical stress that even deeper plane of anesthesia cannot block the response. But with enough analgesia we can maintain blood glucose in normal limits and prevent hyperglycemia.

Jeong JS et al.[12] studied on the effects of propofol and enflurane on blood glucose. This study showed that propofol maintains normal glycemia during surgery compared to enflurane which supports our study.

Shekoufeh Behdad et al.[13] studied the effects of Propofol and Isoflurane on Blood glucose during Abdominal Hysterectomy in Diabetic patients in a study group of 30 women undergoing Abdominal hysterectomy. Blood glucose was measured during 60^{th} and 90^{th} minute of surgery and they concluded that Isoflurane caused an increase in blood glucose during maintenance of anesthesia as compared with Propofol where there was no rise in blood glucose levels which is similar to our study.

In the study by Diltoer M and Camu[14] the effect of isoflurane anesthesia on glucose tolerance test was evaluated with or without surgical stress. This study concluded that growth hormone and norepinephrine concentrations increases during surgical stress in turn causing insulin secretion in response to hyperglycemia impaired during isoflurane anesthesia without surgical stress, but during surgery under isoflurane anesthesia cortisol, growth hormone, norepinephrine, and epinephrine concentrations increases and due to insulin resistance and/or increased production of glucose, glucose tolerance impaired further[14] the effect of propofol or etomidate in our study for maintenance was not assessed and further research is required for the same.

Kitamura T et al.[15] in their study on Comparison of the changes in blood glucose levels during anesthetic management using sevoflurane and propofol implied that the effect on glucose metabolism of propofol was significantly less than that of sevoflurane. This study was performed on a study group of about 154 for Sevoflurane and 63 for Propofol. The study size is comparably larger than our study but the inference in the study is similar to ours showing the beneficial effects of propofol in glucose metabolism.

Zhu M et al.[16] study showed that propofol protects endothelial cells against hyperglycaemia induced insult. Kaushal RP et al.[17] in their study on the effect of etomidate and propofol as induction agent on hemodynamic andendocrine response in patients undergoing major cardiac surgeries including coronary artery bypass grafting, mitral valve and aortic valve replacement surgery on cardiopulmonary bypass showed that etomidate provided morestable hemodynamic response as compared to Propofol while Propofol caused vasodilation and resulted in fall of systematic BP. Thus, they concluded saying Etomidate could therefore be safely used for induction in patients with good LV functionfor CABG/MVR/AVR on CPB without serious cortisol suppression whose effect lasted for more than twenty-four hours. The hemodynamic stability has been similarly shown in our study as well where the Heart rate and Blood pressure did not alter for the induction dose in both the inducing agents as shown in Table 2.

Limitations

This study was conducted in nondiabetic patients and further studies are required to analyze the effects of the induction agents on blood glucose level in diabetic patients. Also, this study has considered the blood glucose variation only during induction of anesthesia while it has not taken into consideration the blood glucose variation during maintenance of anesthesia.

Conclusion

From the observations & results of the study we conclude that intravenous propofol prevents hyperglycemia compared to intravenous etomidate when values were compared to basal readings. Hemodynamic parameters were not statistically significant in both the groups. There were no significant adverse effects during the study.

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