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Comparison of Ondensetron & Dexamethasone Alone and Combination as Prophylaxis in Post Operative Laparoscopic Surgeries

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Abstract

Background: Post-operative nausea and vomiting is very much prevalent and unpleasant complaints with laparoscopic surgeries that leads to numerous emergencies so antiemetic prophylaxis reduced complications associated with nausea and vomiting. *Aim and Objectives*: To compare an efficacy of ondansetron & dexamethasone singly as well as a combination of both dexamethasone & ondansetron in the patients for those who undergoes laparoscopic surgeries and have a requirement of rescue anti-emetics. *Methods*: Sample size of the study was 150 patients (50 patients per group) which was between the age group of 20 years to 50 years of ASA I, II for those who chiefly requires a general anesthesia for laparoscopic surgeries in an arbitrary clinical trial. Therefore, 150 patients was divided into 3 group of 50 each of name Ondensetron group (O), Dexamethsone group (D)and OD group and respective drugs was administered 10 minutes before induction, and post-operative patients were evaluated at time interval of 0 to 6 hours (early vomiting category), 6 to 24 hours (delayed vomiting) to check the degree of nausea, vomiting along with the requirements of antiemetic drug. *Results*: Nausea was the bottom-most in Combination Group OD (considered as 6%) when compared to Ondansetron Group O (considered as 20%) & Dexamethasone Group D (considered as 12%). For vomiting incidence, results were opposite. It was less in OD Group (i.e. 4% only) when compared to O Group (i.e. 12%) & D Group (i.e. 16%). The requirement for antiemetic drug in the above-mentioned groups of O, D and OD was 26, 20 and 6 respectively. Last but not the least, incidence of vomiting & failure in prophylaxis was observed and analyzed in D Group during initial to 6 hours of duration. Also requirement was more for anti-vomiting drug of post-operation within 6 to 24 hours observed in O Group compare to OD Group. *Conclusion*: Combination therapy of ondansetron (Group O) & dexamethasone (Group D) shows adequate control of PONV with delayed PONV which was being better controlled than early PONV (as and when compared to ondansetron & dexamethasone one singly). The need of adjunct antiemetics was emphatic reduced in initial 24 hours of duration.

Keywords: Ondansetron; Dexamethasone; PONV; Laparoscopic Surgery.

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Introduction

Post-operative nausea as well vomiting was very frequent, common and well identified irritating complications along with anesthesia and surgery activities. It guides to several emergencies such as wound dehiscence, bleeding, delayed discharge process of hospitals [1], aspiration of gastric contents, hospitalization unexpectedly, shows less satisfaction among the patients. There were several explanations for post-operative nausea & for vomiting during the process of laparoscopic surgery which includes pharyngeal stimulation due to peritonial distension, Anesthetic agents, opioids, CO_2 insufflations, pain.

Contributing factor for above mentioned causes are Hypertension, Hypoxia, Psychological factors (Age/ Gender/ Medical history of earlier nausea & vomiting), Vestibular disturbances, Rough handling, Duration of operation, Diaphragmatic irritation, Visceral organ irritation etc.

Now-a-days, use of combination of anti-emetics that measures at different receptors and acquisition of multi-modal approach has been prescribed to handle such problem.

The current study was designed in such a manner to assess an efficacy of dexamethasone & ondansetron single as well combination of both ondansetron and dexamethasone for prevention of post-operative nausea as well as vomiting [2]. Furthermore, fluid & electrolyte loss accompanying vomiting can cause dehydration and life-threatening electrolyte imbalance. Following were at least 3 kinds of vomiting:

- Attributed to anesthetics
- Reflex responses
- Opioids

Our next investigation unfolded spectrum of non-anesthetics factors in the pathogenesis of Post operative nausea and vomiting. It was a general trend to decrease in the incidence & intensity of the problem due to

- Modifications in anesthesia practice from opioid
- Use of less emetic anesthetic agents
- Anesthesia to non-opioid or supplemented opioids to lighter & non ether anesthesia
- Refinement of operative techniques and identification of patient predictive factor
- Improved pre & post-operative medication

Even after several medical advancements still nausea & vomiting continue within acceptable frequency with surgery & anesthesia which also known to be a big little problem [3]. Persistence nausea/ vomiting might have some serious medical consequences as well as financial implication in delayed discharge process of hospitals.

Earlier, pharmacological efforts for removal of incidence or reduction in the risk of emesis have included to administered anti-histaminics, anti-cholinergics and dopamine antagonists. Physical maneuvers were also included to impose the following

- Nothing per os regimens
- Application of cricoid pressure
- Ingestion of antacid solutions
- Pre-anesthetic suctioning of gastric contents
- Avoiding inflation of stomach during ventilation by mask

As a result, nothing was entirely successful either a combination or alone in mitigating the distressing occurrence of emesis & its potential sequel. Our study was conducted to analyse efficacy of ondansetron and dexamethasone single as well as combination of both of these and then to compare efficacy for prevention of post-operative nausea & vomiting in laparoscopic surgeries so that we can observe or compare the requirements of rescue antiemetic in the study group mentioned.

Methodology

This comparative study was conducted in 150cases (50 per group) with age groups starting from 20 years to 50 years with physical status as ASA I & II those who adopted for elective laparoscopic surgeries for example laparoscopic cholecystectomy, laparoscopic sterilization etc. Patients were randomized here by computer generated blocks according to below 3 groups:

- Group O (n=50) which was as receiving ondansetron alone
- Group D (n=50) which was as receiving dexamethasone alone
- Group OD (n=50) which was as receiving combination of dexamethasone & ondansetron

The following were excluded exceptionally:

- Patients who denied for the study
- Patients who received opioids, NSAIDS or

antiemetic agents 24 hours prior to surgery

- Patients with physical status of ASA III/ IV
- Pregnant/ lactating females
- Patients under ASA I/ II with history of motion sickness or migraine
- Patients where laparoscopy was converted to laparotomy

Methods

For the purpose of pre-operative evaluation, visit was conducted on a very previous day of surgery along with detailed history & current complaints noted. Following were done

- General & Systemic examination of cardio vascular, respiratory & central nervous system
- Bleeding & clotting time
- Routine laboratory investigations for hemoglobin (HB) level, total count/ differential count, routine urine, blood urea nitrogen & serum creatinine
- ECG

Pre-operative order: All sufferers for this were advised to remain NIL orally after mid night.

*On the operation day intravenous cannulation with 18G catheter was established.

- Study medication Ondansetron 4 mg to group O, Dexamethasone 8 mg to group D & both Ondansetron + dexamethasone to group OD was administered to patients 10 min before induction of anesthesia.
- Patient were pre-medicated with inj. Glycopyrrolate 0.2 mg + 1 mg midazolam + Fentanyl 2 µg/kg & induced by inj. propofol 2 to 2.5 mg/kg. Tracheal intubation was facilitated by inj. vecuronium 0.1 mg/kg. Baseline NG tube was placed for emptying the gastric contents. Anesthesia was maintained by N_2O + O_2 + Isoflurane / sevoflurane. (0.6 to 0.8%). Intermittent doses of vecuronium were given during anesthesia to maintain adequate muscle relaxation.
- Intra operative monitoring HR, BP, SpO_2, ECG, $EtCO_2$ & urine output was carried out. During laparoscopic surgery abdomen was insufflated with CO_2 at a pressure of 8 to 12 mm Hg. On the completion of operation the abdomen was deflated by the surgeon. At the end of surgery the patient was extubated by reversing the patient with 0.05 mg/kg Neostigmine & 0.2 mg

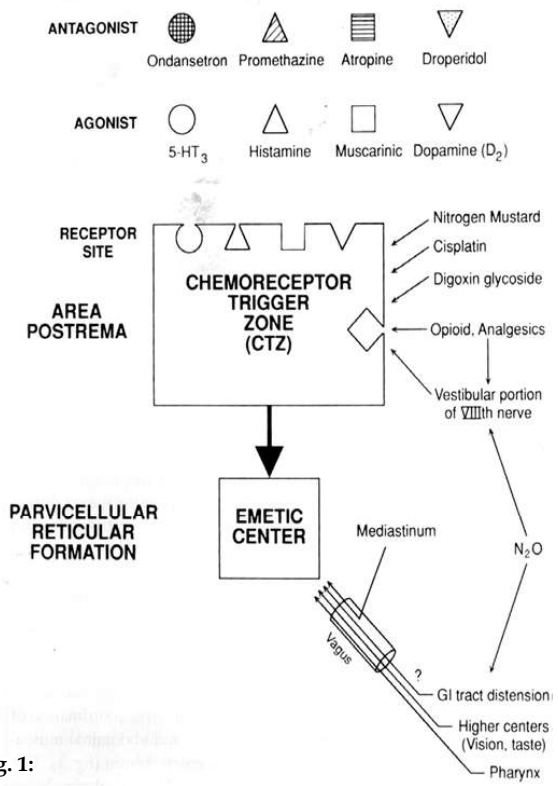


Fig. 1:

Glycopyrrolate. Duration of anesthesia was noted.

In post-operative period, monitoring of patient's vitals were done. All post-operative cases were followed up from 0 to 6 hours, then 6 to 24 hours for the purpose of post-operative nausea & vomiting. The requirements of anti-emetic drug in several patients were also recorded and noted from initial to 6 hours and then 6 to 24 hours in post-operative period.

Statistical Analysis

The analysis was performed with the help of SPSS trial version 23 tool for Windows statistical software package (SPSS inc., Chicago, il, USA) and Primer tool for the generation of descriptive and inferential statistics. The categorical data were presented as numbers (or in percent) and the quantitative data were presented as mean and standard deviation values. The difference in proportion was analyzed by using chi square test for which statistical significance was set to $p < 0.05$.

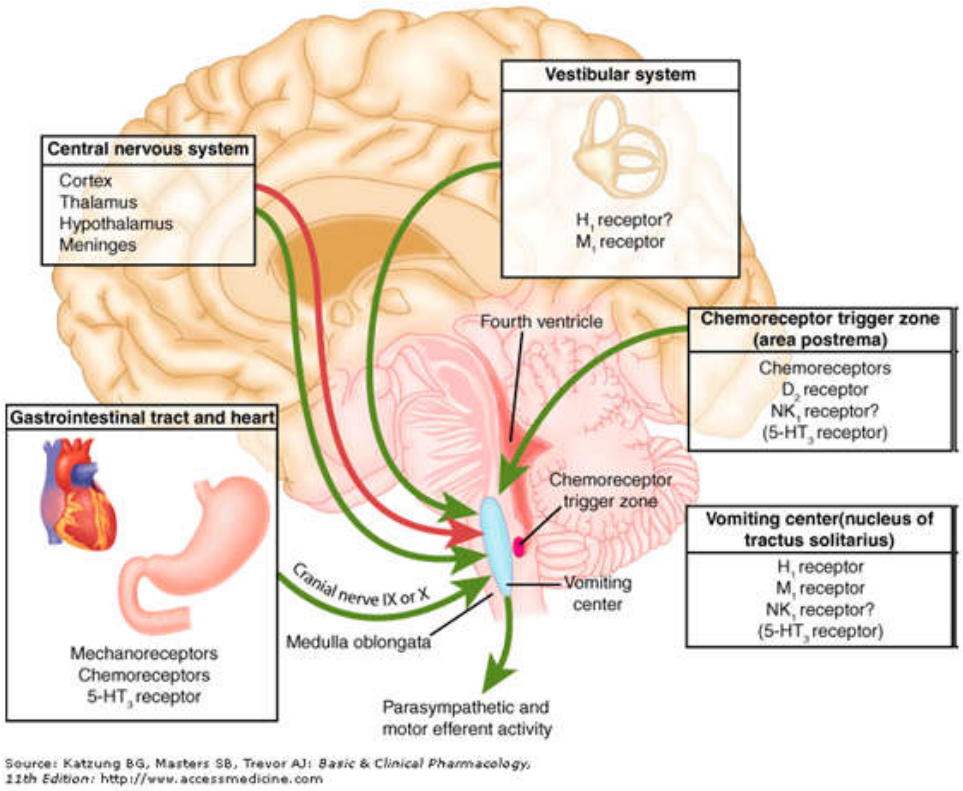


Fig. 2:

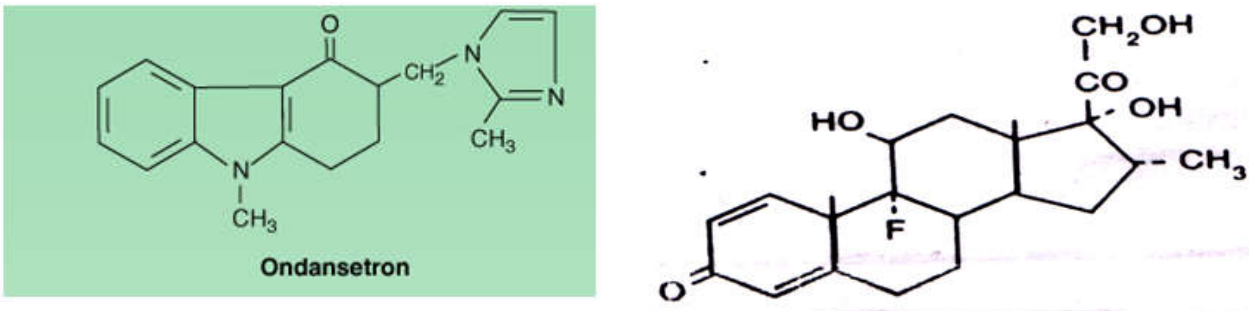
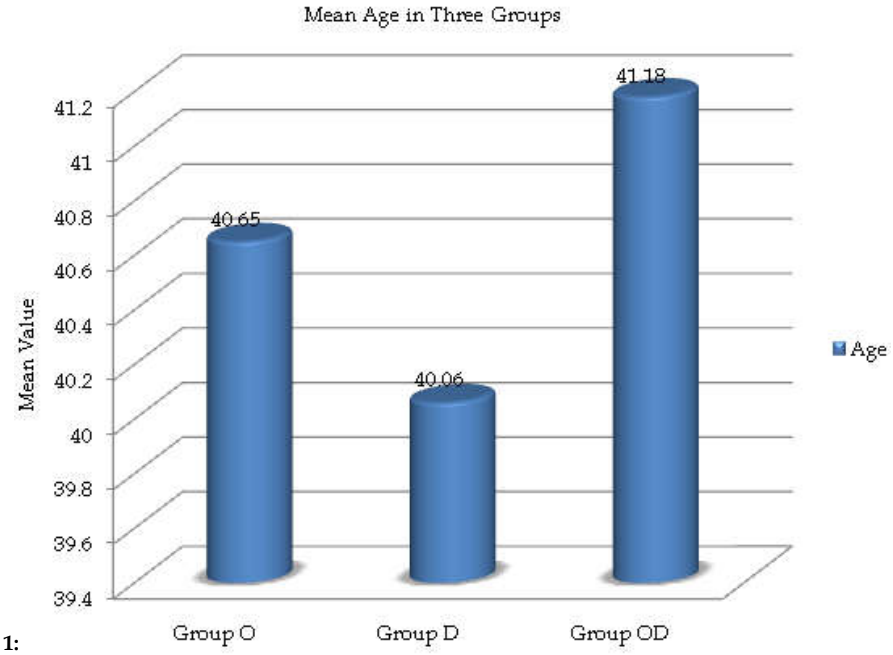


Fig. 3:

Observations and Results

Table 1: Description of characteristics of the cases among the groups (Age)

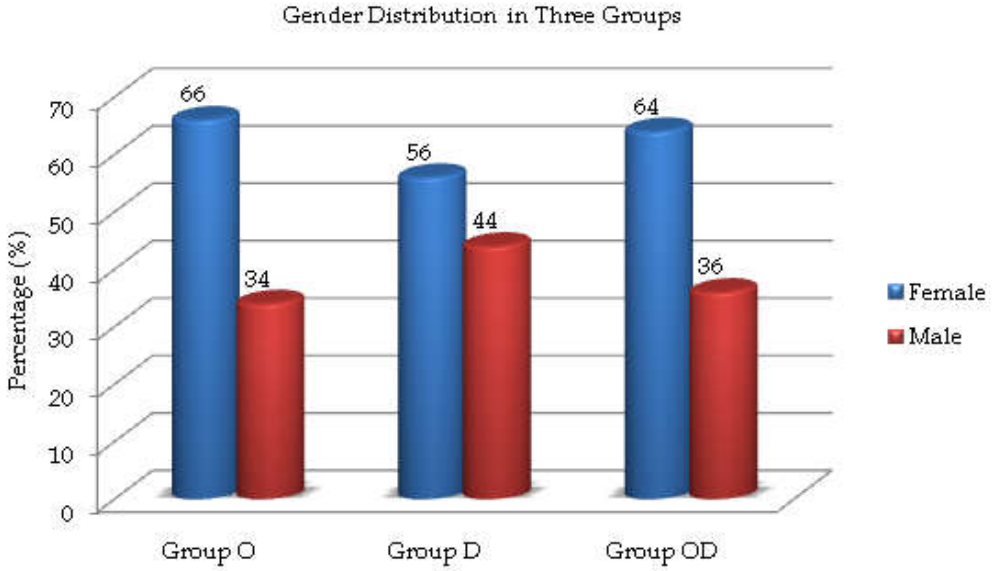
Parameter	Group O (mean ± SD)	Group D (mean ± SD)	Group OD (mean ± SD)	p value
Number of Patients	50	50	50	
Age	40.65 ± 9.0	40.06 ± 8.2	41.18 ± 7.51	0.81, NS



Graph 1:

Table 2: Description of characteristics of the cases among the groups (Gender)

Gender	Group O		Group D		Group OD		P value
	No.	%	No.	%	No.	%	
Female	33	66.00	28	56.00	32	64.00	0.81, NS
Male	17	34.00	22	44.00	18	36.00	
Total	50	100.00	50	100.00	50	100.00	



Graph 2:

Table 3: Incidence of Nausea (3 groups) for initial 6 hours & then 6 to 24 hours

Time Interval	Group O (N=50)		Group D (N=50)		Group OD (N=50)	
	No.	%	No.	%	No.	%
0-6 hours	2	4.00	4	8.00	1	2.00
6-24 hours	8	16.00	2	4.00	2	4.00
Total	10	20.00	6	12.00	3	6.00

Table 4: Statistical Analysis

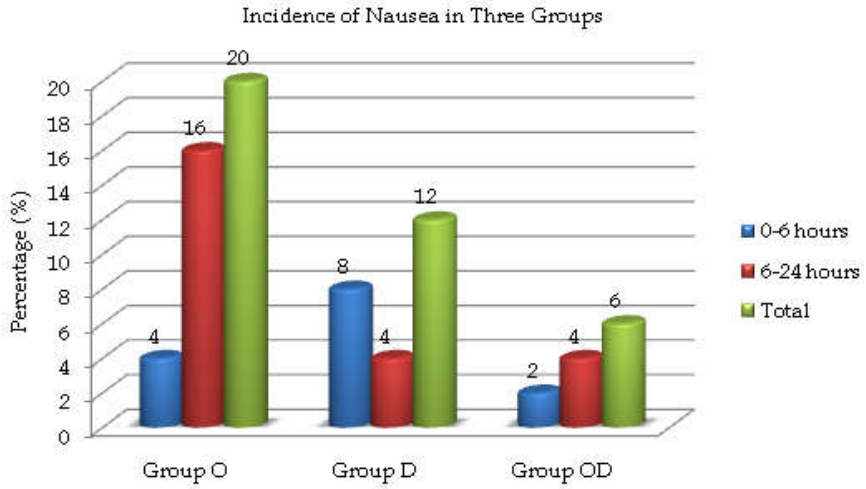
a. In 0-6 hours

Group	P value	Significance
Group O Vs. Group D	0.42	Not significant
Group O Vs. Group OD	0.60	Not significant
Group D Vs. Group OD	0.18	Not significant

b. In 6-24 hours

Group	P value	Significance
Group O Vs. Group D	0.09	Not significant
Group O Vs. Group OD	0.046*	Significant
Group D Vs. Group OD	1.00	Not significant

* Significant (p value < 0.05)



Graph 3:

Table 5: Incidence of Vomiting (Groups at 0 to 6 hours & 6 to 24 hours)

Time Interval	Group O (N=50)		Group D (N=50)		Group OD (N=50)	
	No.	%	No.	%	No.	%
0-6 hours	2	4.00	6	12.00	0	0.00
6-24 hours	4	8.00	2	4.00	2	4.00
Total	6	12.00	8	16.00	2	4.00

Table 6: Statistical Analysis

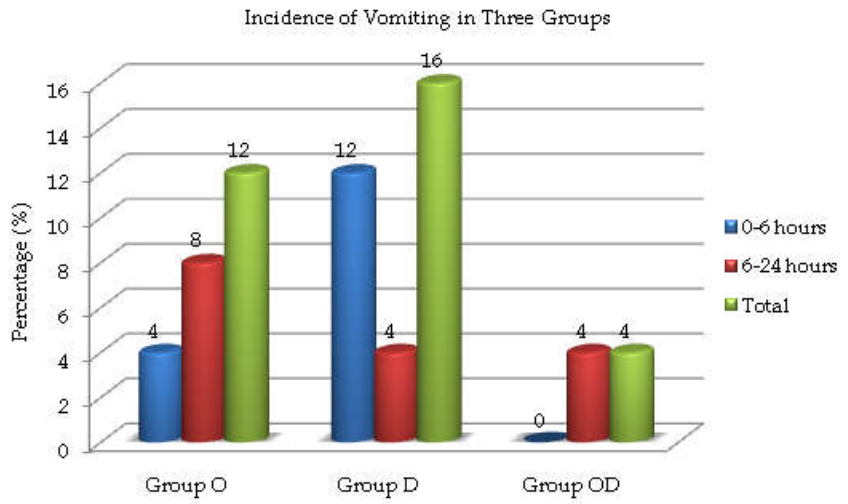
a. In 0-6 hours

Group	P value	Significance
Group O Vs. Group D	0.26	Not significant
Group O Vs. Group OD	0.23	Not significant
Group D Vs. Group OD	0.01*	Significant

b. In 6-24 hours

Group	P value	Significance
Group O Vs. Group D	0.60	Not significant
Group O Vs. Group OD	0.40	Not significant
Group D Vs. Group OD	1.00	Not Significant

* Significant (p value < 0.05)



Graph 4

Table 7: Comparative analysis of Incidence of PONV in 3 Groups (Duration 0-6 & 6-24 hours)

Time Interval	Group O (N=50)		Group D (N=50)		Group OD (N=50)	
	No.	%	No.	%	No.	%
0-6 hours	4	8.00	10	20.00	1	2.00
6-24 hours	12	24.00	4	8.00	4	8.00
Total	16	32.00	14	28.00	5	10.00

Table 8: Statistical Analysis

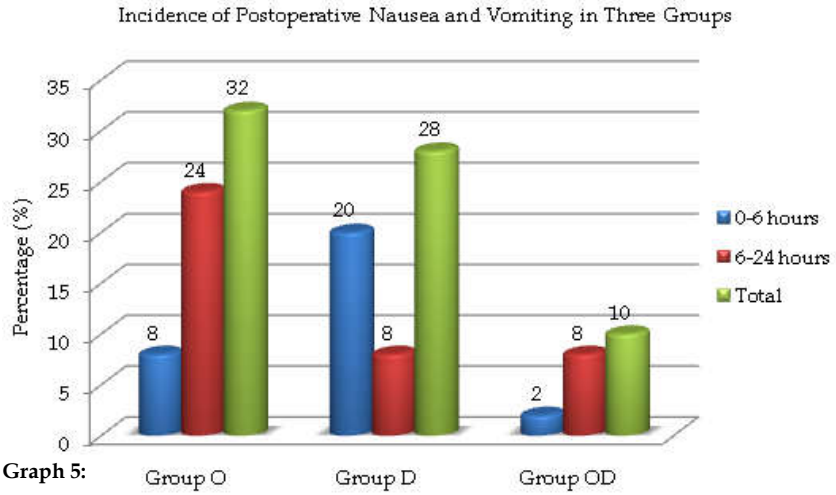
a. In 0-6 hours

Group	P value	Significance
Group O Vs. Group D	0.08	Not significant
Group O Vs. Group OD	0.19	Not significant
Group D Vs. Group OD	0.003*	Significant

b. In 6-24 hours

Group	P value	Significance
Group O Vs. Group D	0.09	Not significant
Group O Vs. Group OD	0.025*	Significant
Group D Vs. Group OD	0.7	Not significant

* Significant (p value < 0.05)



Graph 5:

Table 9: Comparative analysis of use of Antiemetic in 3 Groups (0-6 & 6-24 hours)

Time Interval	Group O (N=50)		Group D (N=50)		Group OD (N=50)	
	No.	%	No.	%	No.	%
0-6 hours	3	6.00	8	16.00	1	2.00
6-24 hours	10	20.00	2	4.00	2	4.00
Total	13	26.00	10	20.00	3	6.00

Table 10: Statistical Analysis

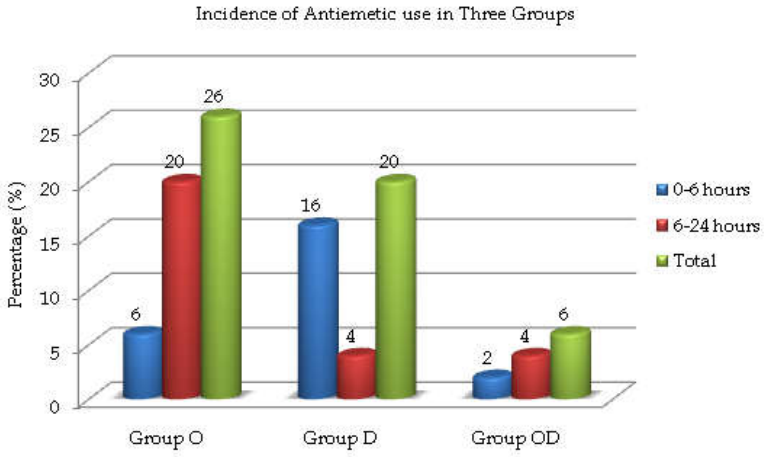
a. In 0-6 hours

Group	P value	Significance
Group O Vs. Group D	0.047*	Significant
Group O Vs. Group OD	0.60	Not significant
Group D Vs. Group OD	0.01*	Significant

b. In 6-24 hours

Group	P value	Significance
Group O Vs. Group D	0.056	Not significant
Group O Vs. Group OD	0.012*	Significant
Group D Vs. Group OD	1.00	Not significant

* Significant (p value < 0.05)

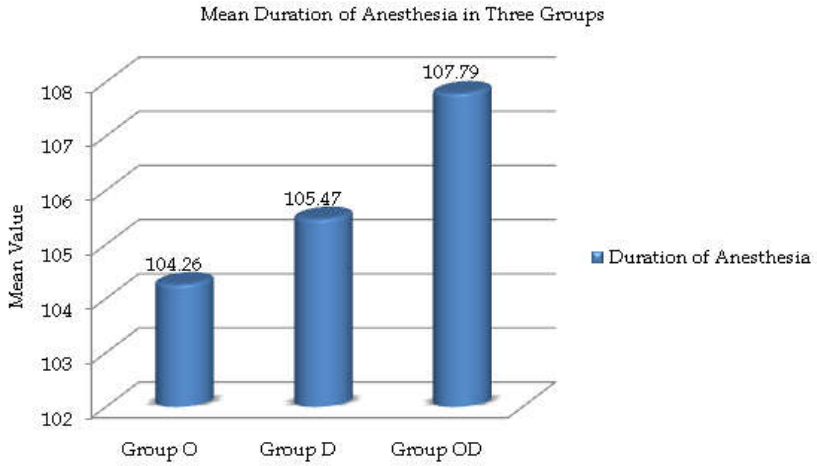


Graph 6:

Table 11: Duration of Anesthesia in these patients

Duration of Anesthesia	Group O (mean ± SD)	Group D (mean ± SD)	Group OD (mean ± SD)	P value
Duration	104.26 ± 7.97	105.47 ± 9.83	107.79 ± 9.58	0.169, NS

NS: Not significant



Graph 7:

Table 11 shows mean duration of anesthesia in group O 104.26 ± 7.97 min, group D 105.47 ± 9.83 min and group OD is 107.79 ± 9.58 min.

Discussion

Our comparative study observed that the post-operative nausea as well as vomiting were the most common complaints after laparoscopic surgery. There is also a high incidence of PONV in patients undergoing general anesthesia for laparoscopic surgeries which is due to many reasons as listed including prolonged CO_2 insufflations, gallbladder surgery, residual pneumoperitoneum, isoflurane & glycopyrrolate, history of movement disorders, hypotension during the operation and PONV [4] (Dexamethasone acts as an antiemetic [5])

- Reducing level of 5-hydroxytrptophan in neural tissue by depleting its precursor tryptophan.
- Dexamethasone potentiates main effect of ondansetron as an antiemetic by sensitizing its receptor.
- Anti-inflammatory properties of dexamethasone prevent release of serotonin in the gut.
- Prolonged antiemetic effect of dexamethasone can be attributed to the prolonged half-life of this drug (36 to 72 hr)[6].
- After 24 hours post operation we observed that the incidence of PONV & the need to antiemetic drug in patients who used combination of dexamethasone & ondansetron was significantly less than the patients who use alone of these drugs. The use of either one of these drugs had similar antiemetic effect. In a study conducted by McKenzie & associates [8], similar results were found.
- Ondansetron is selective 5-HT_3 antagonist that is used for its effect in nausea & vomiting due to chemotherapy & radiotherapy in addition to surgery [7]. This medicine has minor side effects such as headache, flushing, vertigo & constipation.
- In the current study during the first six hours post operation, the incidence of vomiting & the need for antiemetic drug in the group that received dexamethasone was significantly higher than the group that received either ondansetron or a combination of dexamethasone & ondansetron with no significant difference was observed in incidence of PONV. This result indicates that the use of dexamethasone is not sufficient to prevent the premature vomiting in patients who undergo surgery. Rajeeva *et al.* [9] showed that the combination of ondansetron – dexamethasone controls the late PONV more effectively than the premature PONV.
- In this study, within the 6 to 24 hours post operation, the patients who used ondansetron after the operation needed more antiemetic drug than the patients who received the combination dose (p = 0.012), however, no significant difference was found between the group that received dexamethasone compared to the patients who received ondansetron (p^2= 0.05). The shorter duration of effectiveness for ondansetron compare to dexamethasone is an indication of late prophylaxis failure for ondansetron. The half-life of ondansetron is between 4 to 9 hours 46.

Last but not the least, forget about the advancements in medical sciences & anesthesiology, still PONV remains a challenge.

Conclusion

The following were the conclusion that we have observed:

- Nausea level was lower in combination Group OD (i.e. 6%) as compared to Group O of ondansetron (i.e. 20%) & Group D dexamethasone (i.e. 12%). Incidence of vomiting was too less in Group OD (i.e. 4%) as compared to Group O (i.e. 12%) & Group D (i.e. 16%).
- The need for the antiemetic drug in groups O, D, & OD was 26, 20 & 6% respectively. The incidence of vomiting & failure in prophylaxis was observed in D-group during the first 6 hrs. The requirement of anti-emetic drug within 6 hours to 24 hours of post-operation observed higher in Group O in comparison to Group OD.
- In our study we have concluded that ondansetron & dexamethasone used single was less effective in control of early PONV compared to combination of all two. Hence we concluded that combination therapy of ondansetron & dexamethasone gives adequate control of PONV along with delayed PONV being better controlled as compared to early PONV in patients who undergoes elective laparoscopic surgeries under general anesthesia.

Limitations: The following were the key limitation of our study:

- Avoided counting frequency, length, severity and time duration of nausea or vomiting to follow-up recording of variables of interest (i.e. after 24 hours of operation)
- Length of hospitalization & expected side effects were not examined
- Result of our study shows that patients faced PONV were treated by combined drug prophylactic approach which required less antiemetic drug as compared to patients who receive 1 drug only

References

1. Saeeda Islam, P.N. Jain. Post-operative nausea & vomiting (PONV): A review article. Indian J. Anaesth. 2004;48(4):253-58.
2. P.L.R. Andrews, Physiology of nausea/ vomiting. Br. J. Anaesth. 1992;69(S):2-19.
3. Patricia A. Kapur, Editorial: The big "little problem". AnesthAnalg. 1991;73:243-45.
4. Koivuranta MK, Laara E, Ryhanen PT. Antiemetic efficacy of pro phylactic ondansetron in laparoscopic cholecystectomy. A randomized, double-blind, placebo-controlled trial. Anaesthesia. 1996;51(1): 52-5.
5. Henzi I, Walder B, Martin R, Tamer. Dexamethasone for the prevention of PONV- A quantitative systematic review. Aquatitative systemic review. Anaesth Analog. 2000;90(1):186-94.
6. Thune A, Appelgren L, Haglind E. Prevention of postoperative nausea and vomiting after laparoscopic cholecystectomy. A pro spective randomized study of metoclopramide and transdermal hyoscine. Eur J Surg. 1995;161(4):265-8.
7. Gautam B, Shrestha BR, Lama P, Rai S. Antiemetic prophylaxis against postoperative nausea and vomiting with ondansetron-dexamethasone combination compared to ondansetron or dexamethasone alone for patients undergoing laparoscopic cholecystectomy. Kathmandu Univ Med J (KUMJ). 2008;6(23):319-28.
8. Hill RP, Labarsky DA, Fortney JT, Phillips-Bute B, Creed MR, Class PSA *et al*. Cost effectiveness of prophylactic antiemetic therapy with ondansetron, droperidol or placebo. Anaesthesiology. 2000; 92:958-67.
9. Evertt LL. Can the risk of postoperative nausea and vomiting be identified and lowered during the preoperative assessment. Int Anaesthesiology Clic. 2002;40:47-60.

Original Research Article

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A Study to Compare the Effects of Low Dose Intrathecal Fentanyl and Low Dose Intrathecal Tramadol Combined with 0.5% Bupivacaine (Heavy) in Patients Undergoing Orthopaedic Surgeries

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Abstract

Introduction: Relief of pain during operation and postoperative period is one of the main stay of balanced anaesthesia. Bupivacaine Hydrochloride is known for long procedures due to prolonged action. The addition of opioids has been opted as a method to reach these goals. *Aims:* To compare the intra-operative effects of a single low dose of intrathecal tramadol and fentanyl with hyperbaric bupivacaine hydrochloride. *Materials and Methods:* Fifty patients posted for various elective orthopedic procedures were studied in a randomized prospective double blinded manner. Patients will be randomly divided into two following groups. Group A: SAB with addition of 25 µg fentanyl to 3 ml of 0.5% Bupivacaine. Hydrochloride (hyperbaric), Group B: SAB with addition of 25 mg tramadol to 3 ml of 0.5% Bupivacaine Hydrochloride (hyperbaric). *Results:* During Intraoperative period no significant differences in BP, heart rate and respiratory rate were noted. There was no delay in time to full motor recovery in both the groups of patients. The mean duration of analgesia did not differ in both groups. Mean duration of analgesia in Group A was 565.4 minutes and in Group B was 551 min.Time for two segment regression did not differ in both the groups. The patients showed minimal side effects, like nausea, Vomiting, shivering and pruritis in both groups which was statistically insignificant. *Conclusions:* Both intrathecal tramadol and fentanyl act synergistically to potentiate bupivacaine induced sensory spinal block. Excellent surgical anaesthesia and an extended analgesia were observed in post-operative period with minimum side effects among both the groups.

Keyword: Intrathecal tramadol; Bupivacaine; Orthopedic procedures.

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Introduction

Relief of pain during operation and postoperative period is one of the main stay of balanced anaesthesia, so any experience acquired in this field should be extended to the postoperative period also. Postoperative pain relief is a growing concern for an anaesthesiologist, as an uneventful postoperative period makes surgery a comfortable proposition for surgical patients [1]. The choice between regional anaesthesia and general anaesthesia for orthopaedic procedures has been extensively debated. Many studies have found a lower incidence of morbidity and mortality in the early postoperative period, following regional anaesthesia [2]. If we can provide post-operative analgesia in a simple and inexpensive manner, it may go a long way in alleviation of pain and suffering. Spinal anaesthesia with hyperbaric.

Bupivacaine Hydrochloride is mostly used for longer procedures due to its prolonged action. But there is a need to intensify and increase duration of sensory blockade without increasing the intensity and duration of motor blockade, and thus prolong the duration of postoperative analgesia. The addition of opioids has been suggested as a method to accomplish these goals.This study is designed to quantitatively examine the effects of adding fentanyl and tramadol to Hyperbaric Bupivacaine Hydrochloride for spinal anaesthesia on duration and recovery of sensory and motor blockade.

Materials and Methods

This study was conducted in the Department of Anaesthesiology at GSL Medical College & Hospital over a period of 24 months from October 2015 to September 2017. Approval was obtained from the ethical committee of the institution. Fifty patients posted for various elective orthopedic procedures were studied in a randomized prospective double blinded manner at GSL General Hospital and Medical College, Rajahmundry. Patients will be randomly allocated into two following groups.

Group A: SAB with addition of 25 µg fentanyl to 3 ml of 0.5% Bupivacaine Hydrochloride (hyperbaric)

Group B: SAB with addition of 25 mg tramadol to 3ml of 0.5% Bupivacaine Hydrochloride (hyperbaric).

The selection of patients were carried out randomly, depending on the lists of operations submitted by the surgical team on the previous day. A written informed consent was obtained from all these patients.

Inclusion criteria

1. Patients between the age 20-80 years of both sexes
2. Patients belonging to ASA physical status I/II
3. Patients posted forelective lower limb surgery from orthopedics

Exclusion Criteria

1. Patients with a history of known sensitivity to the drugs used.
2. Patients with gross spinal deformity.
3. Patients with Peripheral neuropathy or having any contraindication to neuraxial block- local/Systemic infections, coagulation disorders, hypovolemia, signs of raised intra cranial tension, uncontrolled hypertension.
4. Patient refusal.
5. Patients with history of valvular heart diseases with fixed cardiac output states like mitral stenosis.

Pre-anaesthetic evaluation included general examination, systemic examination of respiratory, cardiovascular, CNS systems and examination of the spine for any diseaseor deformity, airway examination, local examination at the site proposed for lumbar puncture (LP).

Investigations carried out were Haemoglobin, Bleeding and Clotting time, Random or fasting blood sugar, Viral Markers, Blood urea, Serum Creatinine, Urine analysis for albumin, sugar and microscopy and Electrocardiogram and Chest X-ray as and when required.

Anaesthetic procedure was briefly explained to the patients and informed written consent was obtained from the patient and his/her relatives.

Premedication was standardized with medications. All patients were instructed about the visual analogue scale for pain. 0- no pain and 10- worst ever pain. All patients were given injection Ondansetron 4 mg I.V prior to SAB.

After shifting the patients to the operation theatre, intravenous access was secured with 18 G cannula. NIBP, ECG, Pulse oximeter monitors were connected & baseline pulse rate, blood pressure, ECG, respiratory rate and SPO_2 were recorded. Under strict aseptic precautions LP was

performed using 25 guage disposable Quinke type of spinal needle after local infiltration of skin using 2% Xylocaine, at L2–L3 spinal intervertebral space by midline approach. LP was performed in sitting position. Patients were made to lie supine immediately after the completion of injection. The time of injection of the drug was recorded as 0 minute. All patients were given intravenous fluids-Isotonic saline and ringers lactate for maintenance. After spinal anaesthesia all the patients were turned supine, pulse rate and blood pressure was recorded immediately and at 5,10, 15, 30, 60, 120, 180 minutes, End of surgery. Time intervals at which hypotension, bradycardia or other complications occurred were noted. Oxygen 4L/min via face mask was administered to all patients throughout the procedure. Respiratory rate was monitored.Level of sensory blockade was checked with a 23G hypodermic needle immediately after SAB and at 5, 10, 15, 30, 60, 120, 180 minutes.

Assessment of sensory blockade

Sensory blockade was assessed by pinprick and time noted for the block to reach different dermatomal level

a) Onset of sensory block – Time from the deposition of drug to the loss of pin prick Sensation
b) Duration of analgesia – Time when patient first complains of pain after the spinal block
c) Time for two segment regression – Time (counted in minutes) taken for the recovery of sensory level to two dermatomal segments below the highest level.

Level of motor blockade was also assessed by using the Bromage scale immediately after SAB and at 5, 10,15,30,60,120,180 minutes. (Bromage scale 0-full flexion of kneed and feet; 1 – just able to flex knees, full flexion of feet; 2-unable to flex knees, but some flexion of feet possible, 3-unable to move legs or feet).Onset of Motor Blockade – Time interval (counted in minutes) between injection of drug in to Subarachnoid space to Patients inability to lift the straight extended legs.

The following side effects due to intrathecal administration of fentanyl were noted down during the perioperative and postoperative period. Nausea, vomiting, pruritis, shivering, desaturation or hypoxaemia ($SpO_2 < 90\%$), respiratory depression (RR < 10), hypotension, sedation. Hypotension was defined as decrease in systolic blood pressure more than 30% of base line and was treated with Inj. Ephedrine 6 mg increments IV. Inj. Atropine was given when heart rate decreases greater than 20% of base line.

Duration of post-operative analgesia

The duration was calculated from the time when the block was given. The patients were followed up for 24 hours after surgery. They were asked to point out the intensity of their pain on the linear visual pain scale. VAS score along with heart rate and blood pressure was recorded in the recovery room (3 hours after SAB), evening of surgery (6 hours after SAB) and on the first post-operative day (24 hours after SAB).

During the post-operative period the injections of analgesics or opioids were avoided until demanded by the patients due to pain. The time at which supplementation given was noted down along with drug and dosage. This point corresponded to poor analgesia on the scale. Total dose of analgesics administered to the patients in 24 hours was noted. Pain assessment was conducted by a single observer. The time taken for complete motor and sensory recovery was noted. The duration of motor blockade was taken from the time of injection of the drug to the time when the patient was able to move his ankle.

Statistical methods

The data were analyzed as follows. First, the descriptive statistics were computed. These included the range, mean and standard deviation (SD) for quantitative variables, and category frequency counts for qualitative variables.

The independent sample (Student's) t test was employed to compare the means of two independent groups. Alpha for significance for all inferences was set at $p < 0.05$. All tests of hypotheses, wherever applicable, were two-tailed.

Results

Table 1: Age and gender distribution in study

		Group A	Group B
Age	Range	20-70	20-65
	Mean	42.88	39
	S.D	16.89	12.71
Sex	Male	15	14
	Female	10	11

The two groups did not differ significantly in age and gender (Table 1).

Table 2: Baseline heart rate

		Group A	Group B	Significance
Base line Heart Rate	Range	71-114	66-109	T=1.47
	Mean	88.4	83.8	Df=48
	S.D	12.44	9.43	p=0.14
Baseline systolic blood pressure	Range	110-150	105-160	T=0.82
	Mean	126.64	123.6	Df=48
	S.D	12.78	13.33	p=0.41
Baseline diastolic blood pressure	Range	55-105	70-104	T=0.16
	Mean	81.16	81.60	Df=48
	S.D	10.29	9.08	p=0.87

Baseline heart rate, systolic blood pressure, and diastolic bloodpressure are not significant in both groups and comparable with each other (Table 2).

Even though there was significant difference in heart rate over time among both the groups but there was no significant difference in the pattern of decrease in heart rate between the Groups (Fig. 1).

Even though there was significant difference in systolic blood pressure over time among both the groups but there was no significant difference in the pattern of decrease in heart rate between the Groups except in first five minute reading which showed a significant fall in blood pressure in Group B. (Fig. 2).

Even though there was significant difference in diastolic blood pressure over time in both groups but there was no significant difference in the pattern of decrease in diastolic blood pressure between Groups. (Fig. 3).

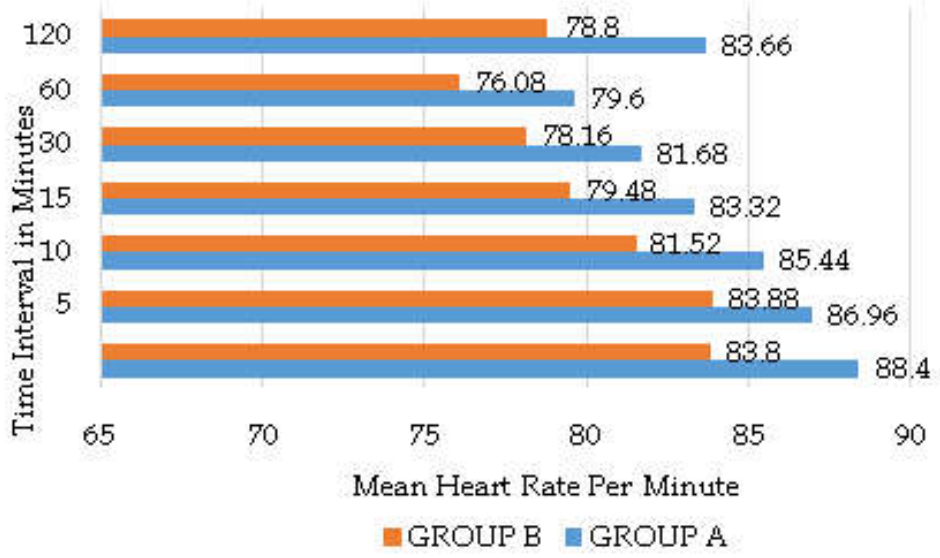

Fig. 1: Heart rate at different intervals of time

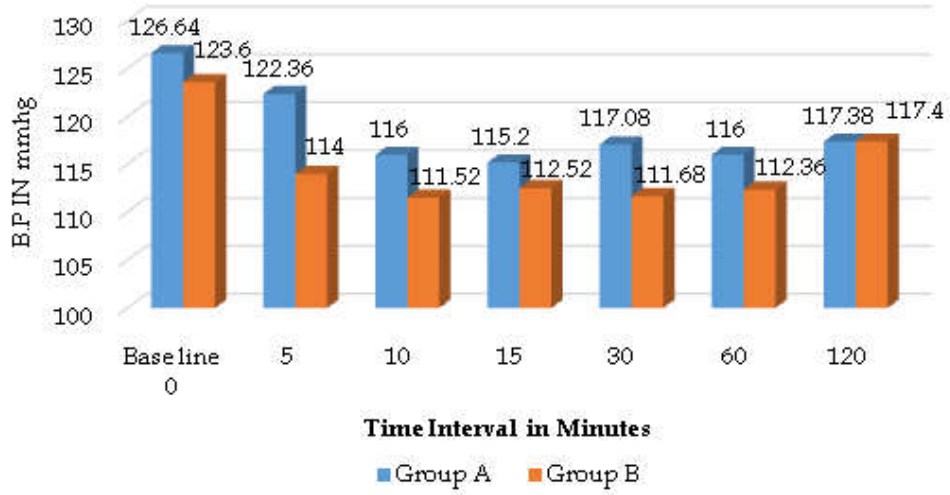

Fig. 2: Systolic blood pressure at different intervals of time

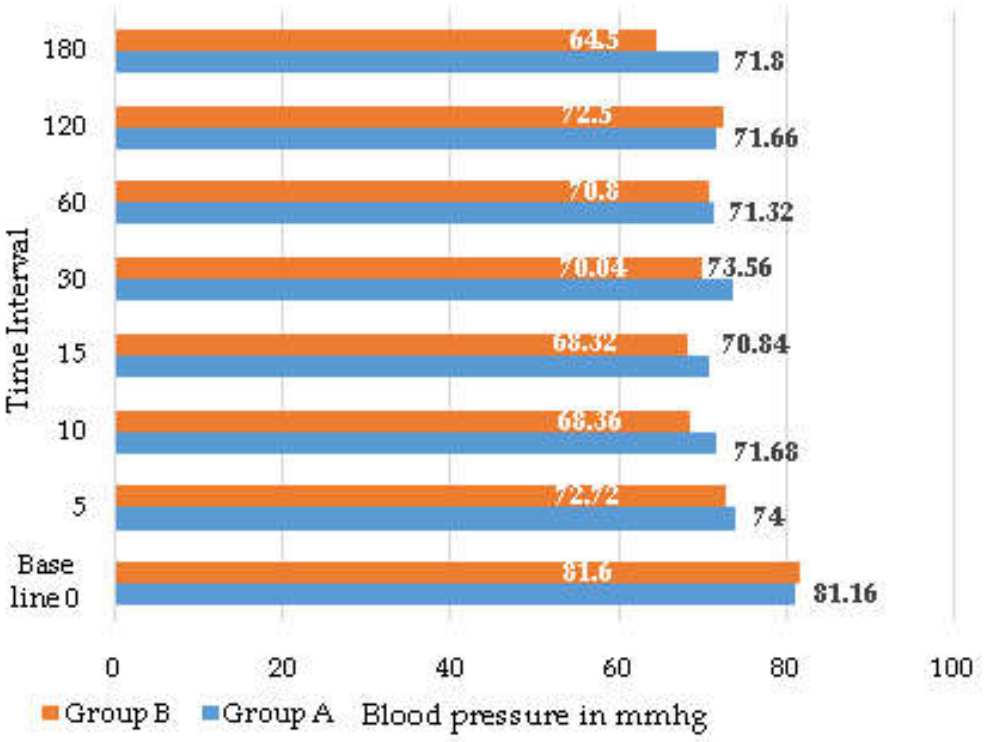

Fig. 3: Diastolic blood pressure at different time intervals

Table 3: Visual analogue scale at different time intervals post operatively.

Visual analogue scale	Group A Mean (SD)	Group B Mean (SD)
0	0 (0)	0.12 (0.43)
6 hours	0.4 (0.64)	0.64 (0.85)
24 hours	1.88 (1.2)	1.68 (1.35)

Visual analogue scale 6 hours post operatively was significantly more likely to be greater than 0 in Group B as compared to Group A.Visual analogue scale 24 hours post operatively was significantly greater than 1 in both the groups (Table 3).

Table 4: Time of first request of analgesic and dose

Variable		Group A	Group B	Significance
Time of first request for analgesic	Mean	565.4	551	T=0.38
	SD	150.4	112.64	P=0.70
Dose	Mean	108.6	100.2	T=1.10
	SD	29.5	23.8	P=0.27

There was no significant difference with respect to time of first request for analgesic between the two groups. There was no significant difference in total analgesic dose required between both the groups (Table 4).

Table 5: Motor recovery and 2 segment regression of sensory level

Variable		Group A	Group B	Significance
Time to full motor recovery	Mean	230	226.8	T=0.38
	SD	28.9	29.5	P=0.70
Time to 2 segment regression of sensory level	Mean	94	97.4	T=0.595
	SD	23.0	16.9	P=0.55
Motor Sensory recovery	Mean	245	241.4	T=0.42
	SD	27.48	32.53	P=0.67

There was no significant difference with respect to time to full motor recovery, time to 2 segment regression of sensory level and time for complete motor sensory recoverybetween both the groups (Table 5).

Table 6: Side effects in both the groups

Side Effects	Group A	Group B
Nausea	Nil	Nil
Vomiting	Nil	Nil
Pruritis	2	2
Shivering	2	0
Desaturation or hypoxaemia (SpO2 < 90%)	Nil	Nil
Sedation	Nil	Nil

Sedation score was recorded every 10 minutes first hour and every 30 minutes next till end of

surgery (Table 6).

0 = wide awake, 1 = Sleeping comfortably, responding to verbal commands

2 = Deep sleep but arousable, 3 = Deep sleep, not arousable.

Discussion

Effective pain control is mandatory for optimal care of patients in the pre and postoperative period. With advancements in the knowledge of pain pathophysiology development of more effective techniques even then patients continue to experience considerable pain after surgery. To become a successful method of analgesia it should be available to large number of patients, and it must be suitable for use in a general surgical ward with simple routine monitoring of nurse. Most commonly drugs used for spinal subarchnoid block are lignocaine and bupivacaine. One disadvantage with spinal anesthesia using local anesthetics is that analgesia ends with the regression of the block, which means that there is an early post-operative need of analgesia post-operative pain, apart from causing discomfort.

In modern era, the use of intrathecal narcoticsis increasing even there is risk for respiratory depression. Tramadol, in contrast, is a centrally acting analgesic that has minimal respiratory depressant effects, by virtue of its 6000 fold decreased affinity for μ receptors compared to morphine. Thought it would be appropriate to study the effects of intrathecally administered tramadol and compare it with a commonly used intrathecally administered opioid like fentanyl.

Fentanyl has rapid onset and shorter duration of action following intrathecal administrations. It prolongs the duration of bupivacaine induced sensory blockade. This suggests a potential synergism between fentanyl and bupivacaine as reported in an animal study by Wang *et al.* [3]. and Gielen MJM *et al.* [4] in 1993 reported that fentanyl is one of the safest opioids. The principal advantage of intrathecal opioids over systemic is that the former produces 'segmental analgesia' resulting in localised nociception without motor, sensory, autonomic or systemic side effects. In order to reduce the side effect profile the use of 'low dose' intrathecal opioids have been advocated, but it is a relative concept.

The main reason for selecting orthopaedic patients was, most of the procedure can be done under regional anaesthesia like spinal anaesthesia. Oue prospective study was conducted to compare intrathecal bupivacaine with low dose tramadol and bupivacaine with low dose fentanyl in orthopaedic lower limb surgeries.

Patient characteristics across the groups

The patients studied across the group which is not significant in respect to age or sex. In group A the range of age was 20-70 years and in group B was 20-65 years which is almost similar. There were 15 male patients and 10 female patients in group A and 14 male patients and 11 female patients which is almost similar in present study. Base line heart rate (HR), systolic blood pressure (SBP), diastolic blood pressure (DBP) were also similar in both the groups with standard deviations of 12.44 (HR), 12.78 (SBP), 10.29 (DBP) for group A and 9.43 (HR), 13.33 (SBP), 9.08 (DBP) for group B respectively.

Changes in the perioperative cardiovascular parameters

In the present study, the incidence of hypotension was equal in both groups but in first five minutes there was significant hypotension in group B with a 'p' value of 0.023, indicating 98% confidence levels. But this effect has to be studied further weather the hypotension is due to bupivacaine alone or contemplating with tramadol.Hypotension was corrected by giving iv fluids and administration of injection mephentermine 6mg iv in incremental doses.

Wong C *et al.* [5] in their experimental work found that the decrease in sympathetic efferent activity after spinal anesthesia is does related to bupivacaine and not to the intrathecal opioid which was added. In the present study, the significant fall in blood pressure is probably the effect of 3 ml of bupivacaine rather than the low dose of the intrathecal opioid. Heart rate, systolic blood pressure and diastolic blood pressure in the both groups did not vary significantly. Jagtap S *et al.* [6] concluded Intrathecal RF provided satisfactory anaesthesia with haemodynamic stability for major lower limb orthopaedic surgery. It provided similar sensory but shorter duration of motor block compared to BF which is a desirable feature for early ambulation, voiding and physiotherapy. This concludes that fentanyl adds prolonged analgesic duration when added with local anaesthetics, and this supports current study. Li Z *et al.* [7] conducted a four group study which included Group A –Bupivacaine with Fentanyl (gBF), Group B–Bupivacaine with Clonidine (gBC),

Group C – Bupivacaine with Dexmedetomidine (gBD), Group D – Bupivacaine (gb), which were administered intrathecally. This study found that onset of blockade was significantly faster in group gBD and group gBC, than group with fentanyl. But group gBD, gBC had more sedation than group with fentanyl, suggesting that fentanyl causes less sedation than other medication. They concluded that addition of dexmedetomidine and clonidine as adjuvants to hyperbaric bupivacaine provided adequate anesthesia and postoperative analgesia compared to fentanyl adjuvant without causing any significant side effects.

Alsheshmi J. A *et al.* [8] in 2003 found that intrathecal tramadol did not influence the intra operative hemodynamic parameters. Idowu OA, Sanusi AA, Eyelade [9] concluded that 25 microg of fentanyl to bupivacaine intrathecally for elective Caesarean section increases the duration of complete and effective analgesia thereby reducing the need for early postoperative use of analgesics, supporting the present study.

In study done by Yaddanapudi C.N. *et al.* [10] in 2000 with epidurally administered tramadol. Reuben S.S. *et al.* [3] studied different dosages from 0 to 50 mcg of fentanyl and observed that not a single patient had respiratory depression.

Changes in the onset and duration of sensory and motor blockade:

The total mean duration of analgesia in group A was 565.4 minutes and in group B 551 minutes. This was significantly longer duration compared with bupivacaine alone. The two groups did not differ significantly in total analgesic dose requirement. Binay Kumar *et al.* [11] conducted a study on 80 patients undergoing orthopedic surgeries. This study concluded that both 25-µg fentanyl and 25-µg butorphanol given intrathecally with 12.5 mg of hyperbaric bupivacaine provide effective and safe anesthesia for lower limb surgeries with minor side effects.

Neeta S, Upadya M, Gosain A, Manissery JJ [12] conducted a study concluding that Fentanyl with bupivacaine produced prolonged analgesia and delayed two-segment regression and demonstrated reduced incidence of complications as compared with intrathecal sufentanil. As the quality of analgesia was complete and comparable, fentanyl emerges as a better option for analgesia and it is much economical too when compared to sufentanil. Thus inferring that opioids provide prolonged analgesia when used along with local anaesthtetics which strongly supports the current study.

Visual analogue scale 6 hours post operatively was significantly more likely to be greater than 0 in Group B as compared to Group A. Visual analogue scale 24 hours post operatively was significantly greater than 1 in both the groups.

Afolayan JM *et al.* [13] Conducted a study on 186 patients undergoing emergency open appendicectomy under spinal anaesthtesia. showed that intrathecal tramadol (25 mg) can safely replace intrathecal fentanyl (25 µg) in the management of visceral pain and discomfort during subarachnoid block for appendicectomy.

Brijesh Jain *et al.* [14] in 2000 found that intrathecal tramadol 25 mg added to bupivacaine provided a mean duration of post-operative pain relief of about eight hours, which is similar to our finding. Frikha N *et al.* [15] concluded that 2.5 micrograms of intrathecal sufentanil combined with 2.5 mg bupivacaine provides rapid-onset and profound analgesia during the first stage of labor without adverse maternal or fetal effects. 25 mg intrathecal tramadol with 2.5 mg bupivacaine had longer-lasting analgesia. The major side effect was vomiting.

Inanoglu K, Ozcengiz D, Gunes Y, Unlugenc H, Isik G. [16] aimed to compare the effects of ropivacaine (R) alone and ropivacaine plus tramadol (RT) administered epidurally for postoperative analgesia in children. The duration of analgesia was significantly longer in group RT than in group R (298.6 ± 28 and 867.9 ± 106.8 min in group I and II, respectively) ($p < 0.05$). CHEOPS scores were significantly lower in group RT at 30 min, 45 min, and 3 h postoperatively than in group R ($p < 0.05$). Turker G *et al.* [17] study revealed that the quality of analgesia achieved with repeated doses of lumbar epidural tramadol after muscle-sparing thoracotomy is comparable to that achieved with repeated doses of lumbar epidural morphine. Compared with morphine, lumbar epidural tramadol results in less sedation and a less-pronounced decrease in oxygenation.

Mean Time for full motor recovery in the current study was 230 minutes in group A, and 226 minutes in group B, Mean Time for 2 segment regression of sensory level in group A was 94 minutes and in group B was 97.4 minutes which shows there was no significant difference between the two groups. Mean time for complete motor sensory recovery in groupA 245 minutes and in group B was 241.4 minutes which showed no significant difference between the groups.Gauchan S, Thapa C, Prasai A, Pyakurel K, Joshi I, Tulachan J. [18] conducted a study on parturients undergoing

caesarean section electively and this study found that duration of sensory block was prolonged in fentanyl group ($p < 0.05$). Duration of complete analgesia (97 ± 8.23 minutes vs 153 ± 7 minutes; p value = 0.00) and effective analgesia (134 ± 5.6 minutes vs 164 ± 9; p value = 0.00) were also found to be prolonged in fentanyl group. There was not much difference in the occurrence of side effects in both the groups. Addition of fentanyl to intrathecal bupivacaine for cesarean section increases the duration of postoperative analgesia without increasing maternal or neonatal side effects. This strongly supports the current study saying that less side effects with addition of fentanyl despite of prolonged analgesic effect.

Roussel JR, Heindel L. [19] conducted a study on fifty patients. This study found no differences in onset and duration of sensory or motor block. This study concluded that fentanyl does not enhance the onset and duration of sensory or motor block produced by 12 mg of intrathecal bupivacaine. Fentanyl, however, prolongs postoperative analgesia and increases the risk of pruritis. Yaddanapudi LN *et al.* [10] study shows that epidural tramadol can provide adequate postoperative analgesia comparable to that of epidural morphine in patients undergoing laminectomy.

In present study there are minimal side effects. In group A 3 patients developed pruritis, two patients developed shivering. In group B 2 patients developed vomiting, 3 patients developed pruritis, 1 patient developed shivering. Bruce-Ben David *et al.* [20] found significant pruritis with of intrathecal opioids. The prophylactic use of ondansetron in both groups would explain the incidence of minimal pruritis and nausea in our study.

Conclusion

Addition intrathecal tramadol or fentanyl to bupivacaine hemodynamic changes, post-operative analgesia, and sensory blockade without prolonging motor recovery showed no significance in groups. Addition of both opioids produced minimal intraoperative and postoperative side effects.

References

1. Vaswani RK, Raiger LK, Purohit R, Bajaj P. The effect of intrathecal midazolam on postoperative pain relief in orthopedic surgery. Hospital Today. 2002;7(4):150-53.
2. Valentine N, Lomoholt B, Jeusen JS, Hejgarrd N, Kreiner S. Spinal or general anesthesia for surgery of the fractured hip? Br J Anaesth. 1986;58:284-91.
3. Wang CY. Respiratory depression after extradural fentanyl (Letter). Br J Anaesth. 1992;69:544.
4. Gielen MJM. Spinal anesthesia. Current opinion in Anaesthesiology. 1993;6:803-7.
5. Benzon HT, Wong HY, Belavic AM, Goodman I, Mitchell D, Lefheit T, Locicero J. A randomized double-blind comparison of epidural fentanyl infusion versus patient-controlled analgesia with morphine for postthoracotomy pain. Anesth Analg 1993;76:316-22.
6. Jagtap S, Chhabra A, Dawoodi S, Jain A. Comparison of intrathecal ropivacaine-fentanyl and bupivacaine-fentanyl for major lower limb orthopaedic surgery: A randomised double-blind study. Indian J Anaesth. 2014;58:442-6.
7. Li Z, Tian M, Zhang CY, Li AZ, Huang AJ, Shi CX, Xin DQ, Qi J, Li KZ. A randomized controlled trial to evaluate the effectiveness of intrathecal bupivacaine combined with different adjuvants (fentanyl, clonidine and dexmedetomidine) in caesarean section. Drug Res. 2014;65:581–86.
8. Alhashemi JA, Kaki AM. Effect of intrathecal tramadol administration on postoperative pain after trans urethral resection of prostate. British Journal of Anaesthesia. 2003 Oct;91(4):536-40.
9. Idowu OA, Sanusi AA, Eyelade OR. Effects of intrathecally administered fentanyl on duration of analgesia in patients undergoing spinal anesthesia for elective caesarean section. Afr J Med Med Sci. 2011;40:213–9.
10. Yaddanapudi LN, Wig J, Singh B, Tewari MK. Comparison of efficacy and side effects of epidural tramadol and morphine in patients undergoing laminectomy : a repeated dose study. Neurol India 2000;48:398-400s.
11. Kumar B, Williams A, Liddle D, Verghese M. Comparison of intrathecal bupivacaine-fentanyl and bupivacaine-butorphanol mixtures for lower limb orthopedic procedures. Anesth Essays Res. 2011;5(2):190–95. doi:10.4103/0259-1162.94775.
12. Neeta S, Upadya M, Gosain A, Manissery JJ. A prospective randomized controlled study comparing intrathecal bupivacaine combined with fentanyl and sufentanil in abdominal and lower limb surgeries. Anesth Essays Res. 2015 May-Aug;9(2):149-54.
13. Afolayan J M, Olajumoke T O, Amadasun F E, Edomwonyi NP. Intrathecal tramadol versus intrathecal fentanyl for visceral pain control during bupivacaine subarachnoid block for open appendicectomy. Niger J Clin Pract 2014;17:324-30.
14. Brijesh Jain, V.K. Sarasawat. Efficacy of intrathecal Tramadol for post operative pain relief in cases of L.S. C.S, and major gynaecological surgeries – a

clinical evaluation. Indian Journal Anesthesia. 2001; 45(4):282.

15. Frikha N, Ellachtar M, Mebazaa MS, Ben Ammar MS. Combined spinal-epiduralanalgesia in labor--comparison of sufentanil vs tramadol. Middle East J Anaesthesiol. 2007 Feb;19(1):87-96. PubMed PMID: 17511185.
16. Inanoglu K, Ozcengiz D, Gunes Y, Unlugenc H, Isik G. Epidural ropivacaine versus ropivacaine plus tramadol in postoperative analgesia in children undergoing major abdominal surgery: a comparison. J Anesth. 2010 Oct;24(5):700-4.
17. Turker G, Goren S, Bayram S, Sahin S, Korfali G. Comparison of lumbar epiduraltramadol and lumbar epidural morphine for pain relief after thoracotomy: a repeated-dose study. J Cardiothorac Vasc Anesth. 2005 Aug;19(4):468-74.
18. Gauchan S, Thapa C, Prasai A, Pyakurel K, Joshi I, Tulachan J. Effects of intrathecal fentanyl as an adjunct to hyperbaric bupivacaine in spinal anesthesia for elective caesarean section. Nepal Med Coll J. 2014 Sep;16(1):5-8.
19. Roussel JR, Heindel L. Effects of intrathecal fentanyl on duration of bupivacaine spinal blockade for outpatient knee arthroscopy. AANA J. 1999 Aug;67(4):337-43.
20. Nieuwenhuij SD, Bruce J, Drummond GB, *et al.* Influence of oral tramadol on the dynamic ventilatory response to CO_2 in healthy volunteers. Br.J.Anaesth. 2001;87:860-865.

Original Research Article

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A Comparative Study of Intubating Condition and Hemodynamic Responses Using Propofol or Thiopentone without Muscle Relaxants

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Abstract

Introduction: Muscle relaxants are frequently used to facilitate endotracheal intubation during the induction of anesthesia. However, the administration of short-acting depolarizing muscle relaxants is associated with postoperative myalgias, malignant hyperthermia, hyperkalemia and increased intracranial or intraocular pressure. *Aim:* To compare the intubating condition and haemodynamic response to induction, laryngoscopy and intubation in patients induced with lignocaine, fentanyl and propofol or lignocaine, fentanyl and thiopentone and intubated without muscle relaxants. *Methods:* 40 patients were randomly allotted in P group [Propofol group] and T group [Thiopentone group]. Patients with the predicted difficulty of intubation, history of hypertension, history of asthma, drug or alcohol abuse, significant cerebrovascular disease and cardiovascular disease, BMI more than 30 kgm^{-2} were excluded from the study. The results were compared between both the groups. Jaw relaxation, vocal cord position, patient's response to laryngoscopy and intubation were assessed and graded as excellent, good, and poor. *Results:* In this study higher incidence of ideal and acceptable intubating conditions were observed in 95% of patients in P group when compared with T group in which the acceptable intubating conditions were observed in 30% of the patients which is statistically significant ($p < 0.05$). The mean heart rate was decreased in both the groups after induction, but immediately after intubation, mean heart rate was high in group T, when compared with group P. *Conclusion:* We conclude that induction with Propofol, Fentanyl and Lignocaine provides better intubating conditions with less haemodynamic response to laryngoscopy and intubation than induction with Thiopentone, Fentanyl and Lignocaine.

Keywords: Propofol; Thiopentone; Intubation without muscle relaxants.

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Introduction

Induction of anaesthesia is now commonly facilitated by the administration of a combination of short-acting hypnotic drugs, depolarizing or non-depolarizing muscle relaxant drugs. Nevertheless muscle relaxants have their limitations. The use of succinylcholine is controversial because of its side effects which include hyperkalemia, muscle rigidity, malignant hyperthermia, myoglobinuria increased intracranial pressure, increased intraocular pressure, the prolonged neuromuscular blockade in patients with plasma choline esterase deficiency, anaphylaxis, etc. They may cause

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serious complications and even death in patients with concurrent diseases.

And the use of long-acting muscle relaxants is disadvantageous in intubating the patients with unpredicted airway difficulty where there is a dangerous possibility of getting into a cannot ventilate, cannot intubate situation. The other complications of non-depolarizing neuromuscular blocking agents include Histamine release, vagolytic, Ganglion blockade, anaphylaxis, nephrotoxicity etc.

So, there is a need for an optimal technique that provides acceptable intubating conditions with reasonable haemodynamic stability without using muscle relaxants particularly in patients with severe burns, hyperkalemia, spinal cord injury where the muscle relaxants are contraindicated or in cases where tracheal intubation is necessary but not prolonged muscle relaxation, such as short ENT and Gynaecological procedures.

The commonly used hypnotic drugs are propofol, thiopentone and etomidate etc. Thiopentone an ultrashort-acting barbiturate was introduced into clinical practice in 1934 became a gold standard induction agent.

However thiopentone produced side effects in some patients like bronchospasm, analgesia etc [1,2]. Etomidate first described by *Paul Janssen* came into clinical practice in 1974 was often used as a drug of choice for anesthetizing hemodynamically unstable patients. Nevertheless it produced pain on injection, myoclonus, and inhibition of Steroidogenesis etc. Propofol is the recent addition which was first synthesized and clinically tested in 1977. It was found that it produces hypnosis quickly and prompt recovery when the drug was discontinued, suppresses pharyngeal reflexes without a need for either muscle relaxants or potent inhaled anaesthetics [3].

To obtain better haemodynamic stability while intubating the trachea without using muscle relaxants the untoward cardiovascular responses during laryngoscopy and intubation itself has to be prevented. For this intravenous lignocaine [4], narcotics, β Blockers, calcium channel blockers, ACE inhibitors, vasodilators, clonidine etc have been used.

Since the advent of short-acting opioids [5], intubating trachea without muscle relaxants has been successful when they are used in combination with the induction agents. In this study propofol and thiopentone were used as induction agents to intubate the trachea without using muscle relaxants [6].

In this study the intubating condition and haemodynamic response of both the drugs were compared. Fentanyl and lignocaine were used as adjuvants to blunt the pressor response to laryngoscopy and intubation [7,8].

Aim

To compare the intubating condition and haemodynamic response to induction, laryngoscopy and intubation in patients induced with lignocaine, fentanyl and propofol or lignocaine, fentanyl and thiopentone and intubated without muscle relaxants.

Materials and Methods

After approval of the study by our institutional Ethics Committee, the study was undertaken in a total of 40 ASA grade I patients of age between 16-65 years, undergoing elective surgery under general anaesthesia. Informed written consent was obtained from all the patients. In all patients weight, pulse rate, blood pressure were recorded. The preoperative investigation included blood hemoglobin, blood sugar, urea, creatinine, urine albumin and sugar, ECG and chest X-ray. All the patients were on overnight fasting. Patients with the predicted difficulty of intubation, history of hypertension, history of asthma, drug or alcohol abuse, significant cerebrovascular disease and cardiovascular disease, BMI more than 30 kg m-2 were excluded from the study. All patients were premedicated with, Tab. Diazepam 5 mg and Tab. Ranitidine 150 mg the previous day night and morning of the surgery and were prehydrated using 0.9% saline 5 ml per kilogram. Out of the total of 40 patients 20 were randomly included in the P group [Propofol group] and the other 20 were included in the T group [Thiopentone group]. In the operating room intravenous access was established by inserting 18 gauge cannula. Patients were connected to NIBP, ECG, Pulse oximetry monitors and preoperative baseline values of heart rate, blood pressure, and SpO_2 were recorded. The patients were preoxygenated with 100% O_2 for 3 min and were administered Inj.Glycopyrollate 0.2 mg intravenously. All the patients received Inj.Fentanyl 2.5 microgram per kilogram intravenously, 2 minutes after the administration of fentanyl, Inj lignocaine 1.5 milligrams per kilogram was administered. One minute after administration of lignocaine, patients in the Propofol (P) group was induced with 3 mg per kilogram of propofol

intravenously and with thiopentone 6mg per kilogram intravenously in the Thiopentone (T) group. When the patient became unconscious, his or her respiration was assisted through a mask with 100% O_2. Ninety seconds after propofol or thiopentone administration, laryngoscopy and tracheal intubation was attempted using appropriate size Macintosh laryngoscope blade and appropriate size endotracheal tubes. Intubation was performed by another experienced anaesthesiologist who was blinded to the drugs used. Measurements of heart rate, mean arterial pressure, and SpO_2. 40 sec after induction (Post Induction), immediately after laryngoscopy (Post Laryngoscopy) and placement of endotracheal tube (Post Intubation) were recorded. The results were compared between both the groups. Jaw relaxation, vocal cord position, patient's response to laryngoscopy and intubation were assessed and graded as excellent, good, and poor. This scoring is assessed by the intubating anaesthesiologist. Patients who could not be intubated at the first attempt were given succinylcholine 1.5 milligrams per kilogram and intubation was completed.

Results

The present study was undertaken in 40 ASA grade I Patients of both genders between the age group of 16-65 years scheduled for elective surgeries under general anaesthesia. The patients were categorized into 2 groups (Propofol (P) group and Thiopentone (T) group). 17 patients [85%] showed complete jaw relaxation in P group when compared with the T group in which 15 patients (75%) showed complete jaw relaxation. 14 patients (70%) had fully opened vocal cord in P group in comparison with T group where only 2 patients (10%) had fully opened vocal cords. There was no response to laryngoscopy and intubation in 8 patients (40%) and less than 2 bucking was observed in 11 patients (55%) in P group when compared with T group where only 6 patients had less than 2 bucking (30%). In this study higher incidence of ideal and acceptable intubating conditions were observed in 95% of patients in P group when compared with T group in which the acceptable intubating conditions were observed in 30% of the patients which is statistically significant ($p < 0.05$). Not even a single patient in the T group had an excellent intubating condition. Considering the haemodynamic response it is observed that the mean heart rate was decreased in both the groups after induction, but immediately after intubation, mean heart rate was high in group T, when compared with group P. Both groups showed a decrease in mean arterial pressure after induction. Whereas the increase in mean arterial pressure was observed in group T immediately after laryngoscopy and intubation ($p < 0.0001$).

Table 1: Patient characteristics

Variables	Group P (n=20)	Group T (n=20)	p value
Mean age (yr)	42.95 ± 14.48	36.80 ± 11.86	0.15
Mean weight (kg)	57.35 ± 6.71	52.70 ± 8.04	0.054
Mean HR (min)	78.50 ± 8.05	80.00 ± 7.57	0.752
Mean MAP (mmHg)	91.88 ± 3.98	89.97 ± 5.18	0.547

Table 2: Jaw Relaxation

Group	Fully relaxed	Slight tone	Stiff
P group	85%	15%	0%
T group	75%	15%	10%

Table 3: Position of vocal cords

Group	Open	Moving	Closed
P group	70%	25%	5%
T group	10%	65%	25%

Table 4: Response to laryngoscopy

Group	No response	Less than 2 Bucking	Persistent bucking or Peripheral limb movement or Use of succinylcholine
P group	40%	55%	5%
T group	0	30%	70%

Table 5: Overall intubating condition

Group	Ideal		Acceptable		Poor	
	No of patients	%	No of patients	%	No of patients	%
P group	6	30%	13	65%	1	5%
T group	0	0	6	30%	14	70%

Table 6: Percentage deviation from the baseline level

Heart Rate	Group P (n=20) (Mean ± SD)	Group T (n=20) (Mean ± SD)	p value
Post induction	-16.60 ± 6.56	-6.59 ± 6.90	0.000*
Post laryngoscopy	-6.27 ± 16.28	0.81 ± 8.60	0.094
Post intubation	-3.21 ± 17.11	8.83 ± 8.46	0.008*

Table 7: Percentage deviation from the baseline level.

MAP	Group P (n=20) (Mean ± SD)	Group T (n=20) (Mean ± SD)	p value
Post induction	-12.00 ± 6.23	-4.91 ± 4.76	0.000*
Post laryngoscopy	-10.84 ± 4.48	2.49 ± 6.96	0.000*
Post intubation	-7.81 ± 4.62	6.97 ± 7.77	0.000*

Discussion

Various other methods to intubate the trachea without the use of muscle relaxants include high dose opioids, and using thiopentone and propofol as sole agents. The technique of intubation without using muscle relaxants offers a useful alternative when neuromuscular blocking drugs are undesirable. The example in patients with hyperkalemia, burns, renal failure or in an anticipated difficult airway. Although intubation without muscle relaxants is considered safe in some patients, this technique is not without complications.

While attempting tracheal intubation without using muscle relaxants, it is mandatory to prevent pressor response, coughing, and laryngospasm produced by laryngoscopy and intubation itself as these unwanted side effects place the anaesthesiologist in a critical situation like an increase in intracranial pressure, cardiac events due to an increase in heart rate and mean arterial pressure in susceptible patients.

Our study is aimed at comparing the intubating conditions and the associated haemodynamic changes following induction and tracheal intubation in the propofol group and thiopentone group without using muscle relaxants in adult patients.

In our study the complete jaw relaxation was observed in 17 patients (85%) in the Propofol group when compared with Thiopentone group in which it was observed in 15 patients (75%).

In a study done by Andel H *et al.* in which he used 3 micrograms per kilogram of fentanyl in combination with Propofol observed complete jaw relaxation in 93% of the patients [9].

The lower incidence of complete jaw relaxation observed in our study when compared with that of Herald Andel et al is probably due to the lower dose of fentanyl used in our study.

Baker P *et al.* assessed the vocal cord movement after induction of anaesthesia with either propofol and thiopentone and observed that the vocal cords adducted to a greater extent with thiopentone than propofol [10].

In our study 14 patients (70%) had fully opened vocal cord in the Propofol group in comparison with Thiopentone group where only 2 patients (10%) had fully opened vocal cords.

McKeating *et al.* investigated the depressant effect of induction doses of thiopentone and propofol on airway integrity and reactivity. They found that when no muscle relaxant was given laryngoscopy was easier to perform after propofol than after an equipotent dose of thiopentone, and that pharyngeal and laryngeal reactivity during laryngoscopy without attempting intubation was more depressed after propofol than after thiopentone [11].

Moreover Eames WO *et al.* found that respiratory resistance after tracheal intubation was lower after induction with propofol than after induction with thiopentone [12]. In our study there was no response to laryngoscopy and intubation in 8 patients (40%) and less than 2 bucks were observed in 11 patients (55%) in p group when compared with T group where only 6 patients had less than 2 bucking (30%).

The results of this study suggests that propofol 3 milligram per kilogram administered with lignocaine 1.5 milligram per kilogram and fentanyl 2.5 microgram per kilogram provides ideal and acceptable intubating conditions in 95% of premedicated patients with favorable airway anatomy whereas thiopentone 6 milligram per kilogram provides acceptable intubating conditions in only 30% of patients which is statistically significant ($p < 0.05$).

In a similar study done by Samar Taha *et al.*, who compared propofol (2 milligram per kilogram) and thiopentone (5 milligram per kilogram) in combination with remifentanil (2 microgram per kilogram) and lignocaine (1.5 milligram per kilogram), observed ideal intubating condition in 50% of patients induced with thiopentone and in 84% of patients induced with propofol [13].

The decreased incidence of ideal intubating condition with propofol group in Samar taha study may be due to the reduced dose of propofol used in that study [13].

In our study none of the patients in the thiopentone group showed ideal intubating condition when compared with Samar taha study which may be due to the fact that fentanyl is less potent when compared with remifentanil [13].

The decreased incidence of severity of bucking and decreased vocal cord movement, but not complete jaw relaxation contributed much to the high percentage of the patients with the ideal and acceptable intubating conditions in the propofol group.

This is attributed to the fact that propofol itself and the synergism with lignocaine in decreasing the muscle tone and abolishing the laryngeal response to tracheal intubation.

When laryngoscopy, intubation and skin incision are considered, tracheal intubation is the strong stimulus. It is important to produce adequate conditions for laryngoscopy, but preventing subsequent coughing or haemodynamic response after tracheal intubation may be even more important.

Addition of lignocaine at induction of anaesthesia has been shown to be beneficial in improving the intubating conditions. This may be attributed to a decrease in the incidence and severity of coughing following insertion of the tracheal tube. It is likely the antitussive effect of lignocaine is caused by at least partially by an increase in the depth of anaesthesia.

Woods AW *et al.* suggested that the combination of lignocaine and propofol may have a synergistic effect [14].

In our study all patients were prehydrated with 0.9% saline before induction of anaesthesia and were premedicated with an anticholinergic agent (Glycopyrollate 0.2 mg intravenously).

Considering haemodynamic response both Propofol and Thiopentone produced a decrease in mean arterial pressure and heart rate immediately after induction. (Mean ± SD -16.60 ± 6.56 and -6.59 ± 6.90) respectively. While doing laryngoscopy and intubation, propofol had blunted the pressor response effectively by maintaining the decrease in mean arterial pressure and heart rate below the baseline values when compared with thiopentone group where an increase in mean arterial pressure and heart rate above the baseline values was observed.

The cardiovascular depressant effects of propofol may be attributed to direct myocardial depression and decreased systemic vascular resistance. Also propofol alters the baroreflex mechanism, resulting in a smaller increase in heart rate for a given decrease in arterial blood pressure as described by Cullen *et al.* in 1987 [15].

The decrease in mean arterial pressure and heart rate following propofol may be well tolerated in healthy, well-hydrated patients, but can be hazardous in elderly patients and in patients with clinically significant cardiovascular disease.

In our study no patient was treated with vasopressor, a decrease in mean arterial pressure was not less than 70 mmHg in both the groups. No patient had a fall in heart rate of fewer than 60 beats per minute.

Peripheral oxygen saturation remained at the preinduction level, 97-99%, in all groups throughout the procedure.

Conclusion

We conclude that induction with Propofol, Fentanyl and Lignocaine provides better intubating conditions with less haemodynamic response to laryngoscopy and intubation than induction with Thiopentone, Fentanyl and Lignocaine. So when intubation is to be done without the use of muscle relaxants propofol will be a better drug than thiopentone for induction.

References

1. Avram MJ, Sanghvi R, Henthron TK. Determinants of thiopental induction dose requirements. Anesth Analg. 1993;76:10-17.
2. Barker P, Langton JA, Wison IG, Smith G. Movement of vocal cords on induction of anaesthesia with thiopentone or propofol. Br. J Anaesth. 1992;69:23-25.
3. Erhan E, Ugur G, Gunusen I, Alper I, Ozyar B. Propofol – not thiopental or etomidate with remifentanil provides adequate intubating conditions in the absence of neuromuscular blockade. Can J Anaesth. 2003 Feb;50(2):108-15.
4. Davidson JAH, Gillespie JA, Tracheal intubation after induction of anesthesia with propofol, alfentanil and intravenous lignocaine. Br J Anesth 1993;70:163-66.
5. Joo HS, Salasidis GC, Kataoka MT, Mazer CD, Naik VN, Chen RB, Levene RG. Comparison of bolus remifentanil versus bolus fentanyl for induction of anesthesia and tracheal intubation in patients with cardiac disease. J Cardiothorac Vasc Anesth. 2004 Jun;18(3):263-8.
6. Hovorka J. Honkavaara P. Kortilla K. Tracheal intubation after induction of anaesthesia with thiopentone or propofol without muscle relaxants Acta Anaesthesiol scand. 199;35(4):326-328.
7. Ko SH, Kim DC, Han YJ, Song HS. small dose fentanyl; optimal time of injection for blunting the circulatory responses to tracheal intubation. Anesth Analg. 1998 Mar;86(3):658-61.
8. Lev R, Rosen P. Prophylactic lignocaine use preintubation: a review. J Emerg Med. 1994;12: 499-506.
9. Andel H, Klune G, Andel D, Felfernig M, Donner A, Schramm W, *et al.* Propofol without muscle relaxants for conventional or fiberoptic nasotracheal intubation: A dose-finding study. Anesth Analg. 2000;90:458-61.
10. Barker P, Langton JA, Wilson IG, Smith G. Movements of the vocal cords on induction of anaesthesia with thiopentone or propofol. Br J Anaesth. 1992 Jul;69(1):23-5.
11. Mc Keating K, Bali IM,Dundee JW. The effects of thiopentone and propofol on upper airway

intergrity. Anesthesia. 1988;43:638-40.

12. Eames WO, Rooke GA, Wu RS, Bishop MJ. Comparison of the effects of etomidate, propofol, and thiopental on respiratory resistance after tracheal intubation. Anesthesiology. 1996 Jun;84(6):1307-11.
13. Taha S, Siddik-Sayyid S, Alameddine M, Wakim C, Dahabra C, Moussa A, Khatib M, Baraka A. Propofol is superior to thiopental for intubation without muscle relaxants. Can J Anaesth. 2005 Mar;52(3):249-53.
14. Woods AW, Grant S, Harten J, Noble JS, Davidson JA. Tracheal intubating conditions after induction with propofol, remifentanil and lignocaine. Eur J Anaesthesiol. 1998;15:714–8.
15. Cullen PM, Turtle M, Prys-Roberts C, Way WL, Dye J. Effects of propofol anesthesia on baroreflex activity in humans. Anesth Analg 1987; 66: 1115–20.

Original Research Article

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Randomized Control Trial Using Bupivacaine in Spinal Anaesthesia with and without Intravenous Dexmedetomidine in Lower Abdominal Surgeries

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Abstract

Introduction: Commonly we use 0.5% hyperbaric bupivacaine in spinal anaesthesia. Adjuvants to spinal anaesthesia have been used to improve quality of analgesia and in prolongation of anaesthetic duration. Dexmedetomidine has been studied and shown to have synergism with bupivacaine and other local anesthetics. Recently, in a few studies, intravenous (IV) dexmedetomidine has been shown to improve analgesic quality. In this study we aimed at finding the efficacy of (IV) dexmedetomidine in improving the analgesia quality and duration of subarachnoid blockade in our hospital scenario. *Materials and Methods:* Ninety patients were divided into two groups of 45 each. In Group A - 3.5 mL of 0.5% hyperbaric bupivacaine was used for spinal anesthesia. In Group B - 3.5 mL 0.5% hyperbaric bupivacaine used for spinal anaesthesia, thirty minutes later a loading dose of IV dexmedetomidine 1 mcg/Kg was infused over 30 min followed by maintenance dose of 0.3 mcg/kg/hr IV dexmedetomidine infused till the end of surgery. In Group A, isotonic saline was used instead of dexmedetomidine preparation. Duration of motor block, sensory block, analgesia, hemodynamic changes, sedation levels, complications and side effects were noted and compared between the study groups in patients undergoing lower abdominal surgeries. *Results:* The duration of motor block in Group A was 149.38 ± 21.32 minutes vs.189.13 ± 31.18 minutes in Group B ($p< 0.05$), duration of sensory block in Group A was 166.79 ± 33.12 minutes vs. 248.13 ± 48.32 minutes in Group B ($p< 0.05$), and duration of analgesia in Group A was 198.69 ± 41.38 minutes vs. 298.57 ± 34.65 minutes in Group B ($p< 0.05$). *Conclusion:* Use of IV dexmedetomidine improves analgesia quality and prolongs anaesthesia duration in subarachnoid block with 0.5% hyperbaric bupivacaine without any hemodynamic instability and with optimum sedation.

Keywords: Spinal anaesthesia; Bupivacaine; Dexmedetomidine; Postoperative analgesia.

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Introduction

Spinal anaesthesia is a very common procedure carried out in the operation theatre and is accomplished by injecting local anaesthetic solution into the cerebrospinal fluid in the region of lower lumbar intervertebral spaces which creates an intense sensory, motor and sympathetic block and provides excellent operating conditions for surgeries below the umbilicus. Spinal anaesthesia also provides good operating conditions for lower abdominal and lower limb surgeries [1]. However; one of the major limitations is the anesthesia duration in subarachnoid block. To

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overcome this, many additives and adjuvants have been tried. Intrathecal adjuvants like morphine, fentanyl, sufentanyl, neostigmine, ketamine, midazolam, magnesium sulphate, clonidine and dexmedetomidine, have been used to improve analgesia quality and anaesthesia duration in spinal anaesthesia [2-13].

Use of IV dexmedetomidine premedication in general anaesthesia has been shown to provide sedation preoperatively, reduces intraoperative inhalational anaesthetic requirements, intraoperative and postoperative analgesia with good hemodynamic stability [14]. In central nervous system highest number of alpha2 adrenoreceptor receptors are present in locus ceruleus, presynaptic activation of theses in locus ceruleus leads to inhibition of noradrenaline release resulting hypnotic and sedative effects. In the spinal cord, activation of alpha$_2$ adrenoreceptor receptors at substantia gelatinosa leads to inhibition of nociception and release of substance P. [15].

Materials and Methods

Ethical committee approval was taken. After written informed consent, ninety patients between 20 and 60 years of age, of ASA Class I and II, scheduled for elective lower abdominal surgery were enrolled in the study. Computer based randomization was done. Investigator and the patient were blinded to the study. Infection at the site of spinal anaesthesia, patients with uncontrolled hypertension and diabetes, any neurological or psychiatric diseases and patients with bleeding or coagulation disorders were excluded from the study.

Preoperatively all study patients were advised 8 hours nil by mouth. All patients received Tab. Ranitidine 150 mg orally on the night before surgery at 10 pm with a sip of water as premedication. The patients were transferred to the operation theatre at 8.30 AM. Intravenous access was achieved with 18G cannula. All patients were preloaded with Ringer's Lactate 10 mL/Kg, 15 minutes prior to the surgery. In operating theatre, standard monitoring viz. oxygen saturation (SpO_2) heart rate (HR), non – invasive blood pressure (NIBP), electrocardiogram (ECG) were attached and baseline hemodynamic parameters were recorded. Under aseptic precautions, using 25G Quincke spinal needle, subarachnoid block was performed at L_3–L_4 inter-space in the midline with 0.5% hyperbaric bupivacaine (Neon Pharmaceuticals, India) was administered at the rate of 0.2 mL/sec.

Group A received 3.5 mL of 0.5% hyperbaric bupivacaine and normal saline infusion. Group B received 3.5 mL 0.5 % hyperbaric bupivacaine for spinal anaesthesia, thirty minutes later loading dose of dexmedetomidine 1 mcg/Kg was infused over 30 min followed by maintenance dose of 0.3 mcg/kg/hr IV dexmedetomidine infused till the end of surgery (AKAS Syringe Pump). SpO_2, HR, Systolic blood pressure (SBP), Diastolic blood pressure (DBP) and Mean arterial pressure (MAP) were recorded preoperatively and after performing the subarachnoid block, every 5 minutes till the end of surgery.

Modified Bromage Scale was used to assess level of motor block. Time taken for regression of motor block to Modified Bromage Scale 1 was considered. Using pinprick bilaterally at mid – clavicular line, time of onset of sensory block, level of sensory block and sensory block duration were recorded. Time taken to reach L5/S1 dermatome was considered as recovery time for sensory block. Postoperatively, the Modified Bromage Scale and the sensory level were recorded every 15 minutes till the patients were discharged from the postanaesthesia care unit. The level of pain was assessed by The Visual Analog Scale (VAS). VAS greater than 4 was considered as cut off point to treat pain. IV Paracetamol 1 gram was considered for rescue analgesia [16,17]. Level of sedation was assessed by The Ramsay Sedation Score. Score greater than 4 was considered as excessive sedation.

Any decrease in MAP of 20% from the baseline was treated with bolus dose of 6 mg IV ephedrine and infusion of intravenous fluids. HR less than 50/min was treated with IV 0.6 mg atropine. The baseline, intraoperative and postoperative hemodynamic changes at various time intervals were compared between the study groups using *Chi square test* and *unpaired t test*. Data validation and analysis was carried out by SPSS Version 11.0. All the p values < 0.05 were considered significant statistically.

Results

The study groups were comparable in terms of demographic data (Table 1), baseline hemodynamic parameters (Table 2) and mean duration of surgery (Table 3). Both the duration of motor block and sensory block were prolonged in Group B compared to Group A ($p < 0.001$) (Table 4). The two segment regression in Group A was 87.9 ± 9.64 minutes whereas in Group B it was 119.0 ± 11.79 minutes ($p < 0.001$) (Table 5). The time taken for rescue

analgesia was prolonged in Group B compared to Group A ($p < 0.001$) (Table 6).

In Group A, the mean sedation score was 2 at the beginning of postoperative period and 1 at the end of 90 minutes whereas in Group B, the mean sedation score was 2.18 at the beginning of postoperative period and 2.08 at 90 minutes. The Ramsay sedation score was higher in Group B ($p < 0.05$). However, respiratory depression was not observed in any of the patients of either group.

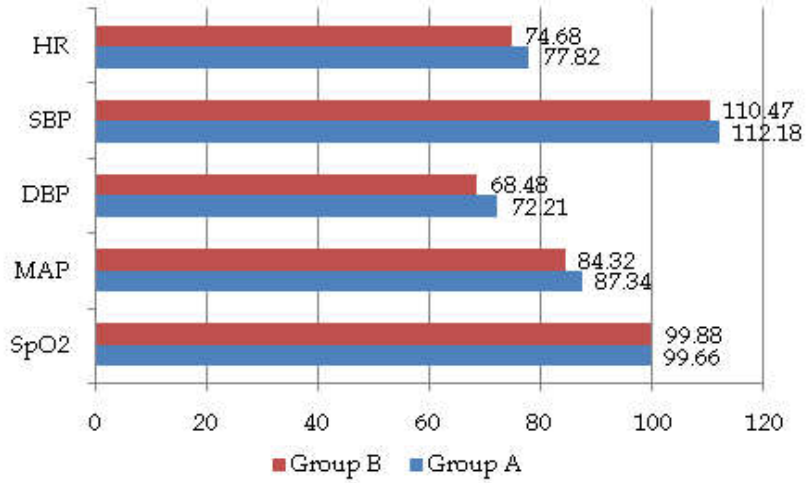
In Group A, the VAS score was 2.13 at the beginning of post – operative period and gradually increased to 4.93 at 90 minutes whereas in Group B, the VAS score was 0.71 at the beginning of post – operative period and 2.97 at 90 minutes. The pain scores were higher in Group A ($p < 0.05$). Hence, it is evident from the above observations that intravenous dexmedetomidine provides adequate sedation and analgesia even in the post – operative period without causing any respiratory depression.

Intraoperatively, 9 patients had bradycardia and hypotension in 13 patients in Group A, whereas in Group B, 4 patients had bradycardia and 4 patients had hypotension. The two groups did not differ significantly with respect to intraoperative hemodynamics at any interval of time and SpO_2 at any interval of time ($p > 0.05$) (Graph 1).

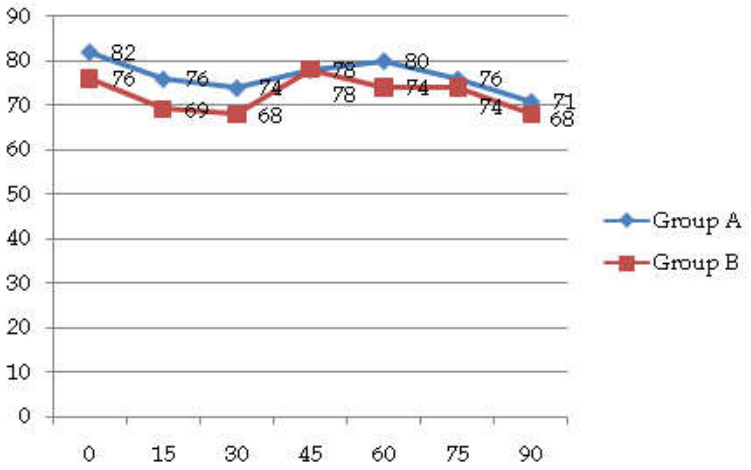
In Group A, 1(2%) patient had vomiting whereas in Group B, none were observed. It was treated with IV Ondansetron 4 mg. In Group A, 1(2%) patient experienced shivering in the postoperative period. It was treated with IV Pheniramine Maleate 45.5 mg whereas in Group B, none was observed.

Table 1: Demographic data

Parameter	Group A	Group B	p value
Age (Years)	45.44 ± 7.60	46.20 ± 8.36	0.658
BMI (kg/m^2)	20.44 ± 1.82	19.98 ± 2.01	0.269
Sex (Male/Female)	14:31	13:32	



Graph 1: Intraoperative Hemodynamics at various intervals



Graph 2: Postoperative HR at various intervals

Table 2: Baseline Hemodynamic Parameters

Parameter	Group A	Group B	p Value
HR	81.88	86.08	<0.05
SBP	129.73	127.07	<0.05
DBP	79.75	81.44	<0.05
MAP	98.33	97.17	<0.05
SpO_2	100	99.88	<0.05

Table 3: Duration of Surgery

Group A	Group B	p value
97.11 ± 24.79	97.44 ± 26.19	0.95

Table 4: Comparison of sensory and motor blockade

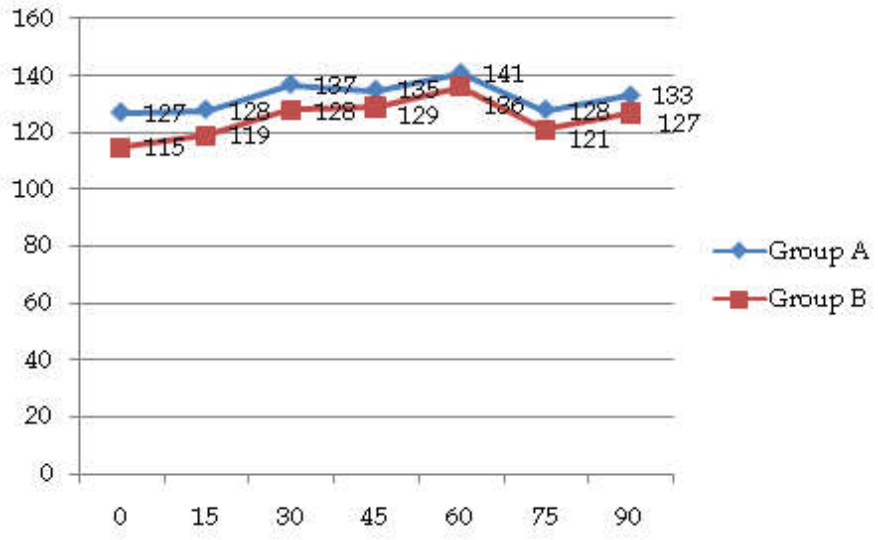
Parameter	Group A	Group B	p value
Sensory Blockade	166.79 ± 33.12	248.13 ± 48.32	< 0.001
Motor Blockade	149.38 ± 21.32	189.13 ± 31.18	< 0.001

Table 5: Two segment regression

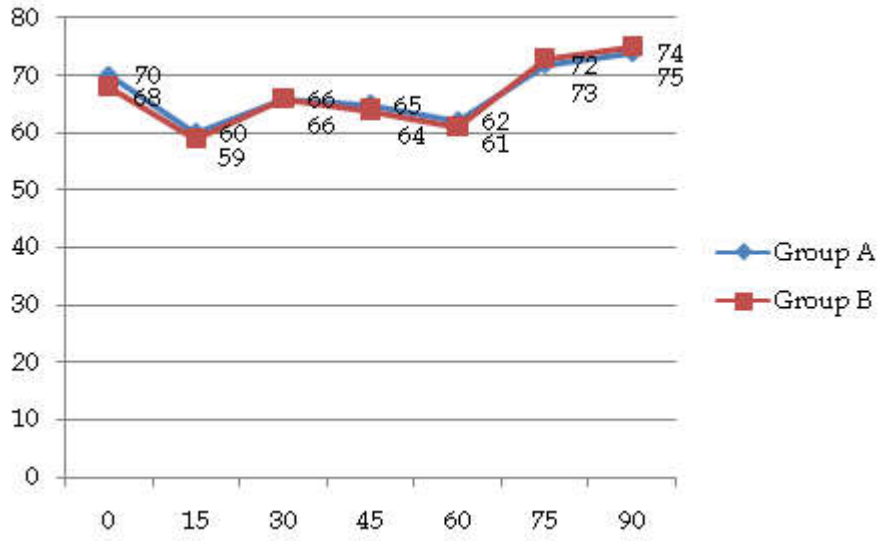
Group A	Group B	p value
87.9 ± 9.64	119.0 ± 11.79	< 0.001

Table 6: Rescue Analgesia

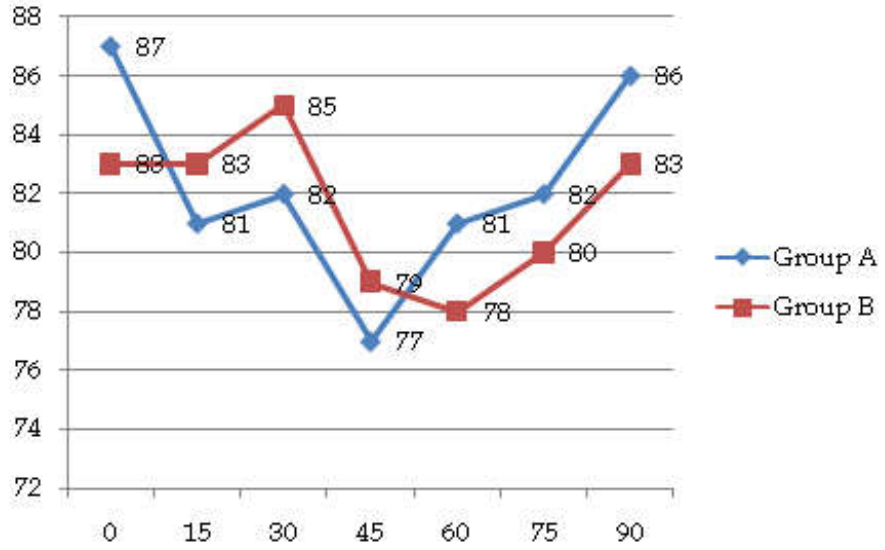
Group A	Group B	p Value
198.69 ± 41.38	298.57 ± 34.65	< 0.001



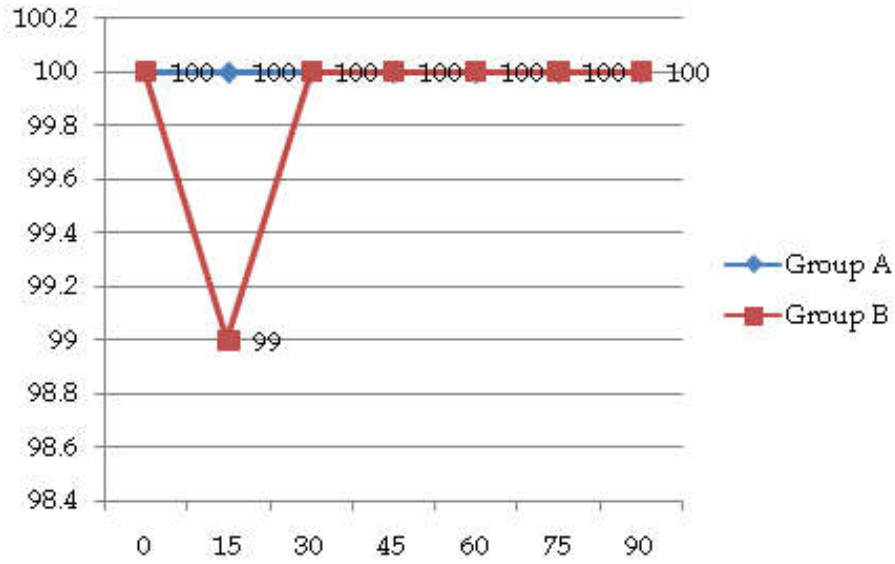
Graph 3: Postoperative SBP at various intervals



Graph 4: Postoperative DBP at various intervals



Graph 5: Postoperative MAP at various intervals



Graph 6: Postoperative SpO_2 at various intervals

Discussion

Dexmedetomidine is a boon in the present day practice of anaesthesia. It has wonderful properties such as hemodynamic stability, sedation, anxiolysis and reduced postoperative requirements of parenteral analgesics owing to its supraspinal action. It reduces the release of neurotransmitters and hyperpolarization of neurons. Neuroprotection is another added benefit. Dexmedetomidine mainly acts on the locus ceruleus by causing disinhibition of nociception. It reduces the release of noradrenaline and blocks its sympathetic activity. In the intensive care it is blessing in disguise owing to its affinity for $alpha_2$ receptors and routinely used by many clinicians.

In a study done by Mahmoud M al Mustafa showed that when dexmedetomidine was administered there was statistically significant prolongation of sensory and motor blockade (p <0.05) [18]. Similarly, SS Harsoor et al. concluded that the duration of effective analgesia was prolonged in subjects who received dexmedetomidine intravenously (p < 0.001) [19]. First analgesic requirement was increased by more than 50% in a clinical study done by Abdallah FW

($p < 0.00001$) [20]. In a clinical study done by Reddy VS showed that the level of sensory blockade level was greater with dexmedetomidine and also the time to first analgesic requirement was higher ($p < 0.0001$) [21]. The 2 segment regression of sensory blockade was increased by 42.33 minutes in a clinical study by Jyotsana Kubre and the duration of analgesia was increased by 70.50 minutes in the group of subjects who received dexmedetomidine ($p < 0.05$) [22]. The duration of analgesia was prolonged levobupivacaine was administered caudally along with concurrent dexmedetomidine intravenously in the study done by Yao Y [23]. In a clinical study conducted by Vatsalya T concluded that dexmedetomidine shortened the time taken to reach dermatome level of T10 along with significant prolongation the duration of regression of sensory and motor blockade. Analgesia was prolonged significantly by 34.38 minutes ($p = 0.0001$). The profile of side effects and its treatment were comparable with incidences of bradycardia and hypotension [24]. In a study done by Kavya UR showed that sensory block was significantly higher by 83.4 minutes. Motor blockade recovery also showed significant prolongation by 88.2 minutes. Subjects who received dexmedetomidine were adequately sedated and were easily arousable [25]. Hemodynamic responses are in direction relation to dose and speed of infusion of dexmedetomidine. Transient hypertension with reflex bradycardia is often followed by hypotension when dexmedetomidine is infused rapidly.

Conclusion

Dexmedetomidine when infused in the loading dose of 1 mcg/kg followed by 0.3 mcg/kg/hr prolongs the action of hyperbaric bupivacaine in subarachnoid block along with improved quality of analgesia, adequate sedation and hemodynamic stability.

Conflicts of interest: None

References

1. Barnards C.M Epidural and Spinal Anaesthesia Barash. P. G, Cullen B. F and Stoelting. R. K. Clinical Anaesthesia, 4th *ed*. Philadelphia, Lippincott William and Wilkins. 2001.pp.689-709.
2. Cousins M.J and Bidenbaugh P.O. Neural blockade in clinical Anaesthesia and management of pain, 3rd ed. Philadelphia, Lippincott – Raven publisher, 1998.pp.203-24.
3. Henneberg SW *et al.* Epidural morphine for postoperative pain relief in children. Acta Anaesthesiol Scand. 1993;37:664–67.
4. Krane EJ *et al.* Caudal morphine for postoperative analgesia in children: a comparison with caudal bupivacaine and intravenous morphine. Anesth Analg. 1987;66:647–53.
5. Liu S *et al.* Fentanyl prolongs lidocaine spinal anesthesia without prolonging recovery. AnesthAnalg. 1995;80:730–734.
6. Korhonen AM *et al.* Intrathecal hyperbaric bupivacaine 3 mg + fentanyl 10 microg for outpatient knee arthroscopy with tourniquet. Acta Anaesthesiol Scand. 2003;47:342–46.
7. Demiraran Y et al: Intrathecal sufentanil (1.5 mcg) added to hyperbaric bupivacaine (0.5%) for elective caesarean section provides adequate analgesia without need for pruritus therapy. J Anesth. 2006; 20:274–78.
8. Kumari Vasantha NS, Madhusudhana R: Intrathecal Bupivacaine with neostigmine and bupivacaine with normal saline for postoperative analgesia: A cost – effective additive. Anesth Essays Res. 2018; 12:328-32.
9. Hawksworth C, Serpell M. Intrathecal anesthesia with ketamine. Reg Anesth Pain Med. 1998; 23:283–88.
10. Prochazka J. Intrathecal midazolam as an analgesic – 10 years experience. Eur J Pain. 2006;10:S202.
11. Buvanendran A *et al.* Intrathecal magnesium prolongs fentanyl analgesia: a prospective, randomized, controlled trial. Anesth Analg. 2002; 95:661-66.
12. Thakur A *et al.* Intrathecal clonidine as an adjuvant to hyperbaric bupivacaine in patients undergoing inguinal herniorrhaphy: A randomized double-blinded study. J Anaesthesiol Clin Pharmacol. 2013; 29:66-70.
13. Al Mustafa MM *et al.* Effect of dexmedetomidine added to spinal bupivacaine for urological procedures. Saud Med J. 2009;30:365–70.
14. Niu XY *et al.* Effects of intravenous and intrathecal dexmedetomidine in spinal anaesthesia: a meta-analysis. CNS Neurosci Ther. 2013;19:897–904.
15. Joseph A. Giovannitti *et al.* Alpha-2 Adrenergic Receptor Agonists: A Review of Current Clinical Applications. Anesth Prog. 2015 Spring; 62(1): 31–38.
16. Alireza Kamali *et al.* A comparative study on the prophylactic effects of paracetamol and dexmedetomidine for controlling hemodynamics during surgery and postoperative pain in patients with laparoscopic cholecystectomy. Medicine (Baltimore). 2018 Dec;97(51):e13330.
17. Ridhima Sharma *et al.* Postoperative Analgesia with Intravenous Paracetamol and Dexmedetomidine in Laparoscopic Cholecystectomy Surgeries: A

Prospective Randomized Comparative Study Int J Appl Basic Med Res. 2017 Oct-Dec;7(4):218–22.

18. Mahmoud M al Mustafa *et al.* Intravenous dexmedetomidine prolongs bupivacaine spinal anaesthesia. MEJ Anaesth. 2009 Jun;20(2):225-31.
19. SS Harsoor *et al.* Low dose intravenous dexmedetomidine for spinal anaesthesia. IJA. 2013; 57(3):265-69.
20. Abdallah FW *et al.* The Facilitatory Effects of Intravenous Dexmedetomidine on the Duration of Spinal Anaesthesia: A Systematic Review and Meta – Analysis. Anesthesia Analgesia. 2013;117(1):271-8.
21. Reddy VS *et al.* Intravenous dexmedetomidine versus clonidine for prolongation of bupivacaine spinal anesthesia and analgesia: A randomized double-blind study. Journal of Anesthesiology and Clinical Pharmacology. 2013 Jul;29(3):342-7.
22. Jyotsna Kubre *et al.* Single dose intravenous dexmedetomidine prolongs spinal anesthesia with hyperbaric bupivacaine. Anesth Essays Res. 2016 May-Aug;10(2):273-77.
23. Yao Y *et al.* Caudal and intravenous dexmedetomidine similarly prolong the duration of caudal analgesia in children: A randomized controlled trial. Paediatr Anaesth. 2018 Oct;28(10):888-96.
24. Vatsalya T, Waikar C. Comparison of intravenous bolus and infusion of dexmedetomidine on characteristics of subarachnoid block, Anesth Essays Res. 2018;12:190-3.
25. Kavya UR *et al.* Effect of intravenous dexmedetomidine administered as bolus or as bolus-plus-infusion on subarachnoid anesthesia with hyperbaric bupivacaine. Journal of Anesthesiology and Clinical Pharmacology. 2018;34:46-50.

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Comparison of Laryngoscopic View Obtained by Conventional 10 cm Head Rise to that Obtained by Horizontal Alignment of External Auditory Meatus and Sternal Notch

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Abstract

Objectives: The aim of this study was to determine the effect of position (Sniff / HELP) during laryngoscopy on the extent of change/ improvement in laryngoscopic view of glottis. *Materials and Methods:* This prospective, observational study was conducted on 245 patients who were scheduled to undergo elective surgeries, age 18-60 years, of either sex and ASA physical status I and II. Patients were positioned in HELP at first, following standard anaesthesia induction laryngoscopy was done to evaluate CL grade (HELP score). Patients were then positioned to sniff position and CL grade was reassessed (SNIFF score) and intubated. SNIFF score and HELP score were then compared. Chi-square, Fisher's exact, Student's t-test were used for analysis. *Results:* In 163 cases (66.5%) HELP and Sniff showed equal CL grades. In 67 cases (27.34%) HELP showed improved CL grades in comparison to Sniff. 47 cases (19.2%) of CL grade II by SNIFF position showed grade I view in HELP. Out of total 22 cases (9%) showing C & L grade III in SNIFF position, 15 cases (6.1%) showed grade I and 5 cases (2%) showed grade II in HELP. HELP provided equal/improved view in 230 cases (93.8%) of our study population which was statistically significant. *Conclusion:* HELP provides better glottic visualization and it should be the ideal intubating position for all patients (both obese and non obese) irrespective of age and sex. Neck circumference serves as more accurate predictor of poor glottic visualization during direct laryngoscopy as compared to BMI.

Keywords: HELP; Sniffing position; Laryngoscopic view; Cormack & Lehane grade.

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Introduction

The anticipated difficult intubation led to position the patient in such a way that we get optimal glottic view during laryngoscopy for tracheal intubation. Inadequate positioning may result in protracted or failed tracheal intubation attempts because of the inability to visualize the larynx.

The sniffing position described by Sir Ivan Magill [1] by causing lower cervical flexion and atlanto-occipital extension aligns the oral, pharyngeal and laryngeal axes, thus facilitates laryngoscopic visualization for tracheal intubation. In 1944, Bannister and Macbeth [2] introduced the

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three axis alignment theory (TAAT) to explain the anatomical reasoning behind the superiority of sniffing position.

HELP (Head Elevated Laryngoscopic Position) brings sternal notch and external auditory meatus at one level. Keith Greenland *et al.* [3] by using magnetic resonance imaging (MRI) showed that external auditory meatus reflects the position of clivus (external auditory meatus overlies the clivus) and sternal notch reflects the glottis opening. Clivus lies immediately behind the nasopharynx. So when the patient is placed in HELP, nasopharynx comes to lie above glottic opening (line between glottis and nasopharynx is sloping upwards). This rotates the pharyngeal and laryngeal axes anticlockwise and thereby aligning with oral axis. With head extension, laryngoscopic blade insertion and elevation, glottic opening will come to lie along the line of vision. This is suited in both obese and non-obese.

Cormack RS, Lehane J *et al.* [4] in 1984 scored the laryngoscopic views into four grades for the purpose of making comparisons easier.

We tried to compare Cormack Lehane grade in both Sniff and Head Elevated Laryngoscopy position with respect to parameters like BMI and neck circumference. The aim of this study was to determine the effect of position (Sniff/HELP) during laryngoscopy on the extent of change/ improvement in laryngoscopic view of glottis.

Materials and Methods

Study design: This was a prospective observational study.

Sample size calculation: Sample size was calculated using Right-Size (China-Uganda-Zimbabwe, version 2.0.0.0.2 1/19/2002) statistical software where (N=1700) i.e. total number of patients attending Anaesthesia Department of hospital taking expected frequency of the disease presumed to be at least 20% with 95% confidence level, considering confidence interval of 5%, a total of 245 patients will be required.

Study population: Total 245 patients, of age group 18–60 years, with American Society of Anaesthesiologists (ASA) physical status I and II, who were scheduled to undergo elective surgical procedures under general anaesthesia with endotracheal intubation were enrolled in this study. Exclusion criteria were patients with connective tissue disorders, diseases in which bones are prone to fracture example renal osteodystrophy in chronic kidney disease, metabolic disorders like diabetes mellitus with possibility of cervical spine involvement and decreased atlanto-occipital movement, acromegaly, tonsillar hypertrophy, pregnancy, epiglottitis, craniofacial abnormality, burn patients with neck contracture, buck teeth, thyromental distance <6.5 cm, hyomental distance <6 cm, sternomental distance <12.5 cm, interincisor distance <5 cm, receeding mandible, micrognathia, loose teeth, head extension <70 degrees, Samsoon & Young scores III & IV.

Study protocol: The study was started following Institutional Ethics Committee approval. Written informed consent was taken from the patients. Preoperative assessment was done and BMI, neck circumference at the level of thyroid cartilage, Samsoon and Young scores, thyromental distance, hyomental distance, sternomental distance, interincisor distance, head extension and mobilility of atlanto-occipital joint were noted.

After all standard preparations, routine monitors such as ECG, non invasive blood pressure cuff, pulse oximeter were connected to the patient. An intravenous access was secured.

Patients were kept in HELP at first. HELP was achieved by placing a firm pillow of 10 cm size underneath the head and then making necessary arrangements with the help of multiple drapes and table tilt to align external auditory meatus and sternal notch. Idea behind this approach was, when we try to shift the patient to sniff position, we needed only drapes to be removed from underneath of the patient.

Patients were preoxygenated with 100% O_2 for 3 minutes with a close fitting mask in HELP at first. After administration of fentanyl (2 mcg/kg i.v), intravenous induction was done with propofol (2-3 mg/kg body weight) and muscle relaxation with vecuronium (0.1 mg/kg body weight). Patients were ventilated for 3 minutes. The anaesthesiologist then did laryngoscopy with Macintosh 3 or 4 size blade and assessed the Cormack Lehane grade. For the purpose of comparison we called it as "HELP SCORE".

After that anaesthesiologist sprayed 10% lignocaine between vocal cords into trachea. The patients were then placed in sniff position following which the anaesthesiologist with the same laryngoscope blade reassesssd the Cormack Lehane grade (it was called as SNIFF SCORE) and the trachea was intubated.

In this way both the anaesthesiologist and the patient served themselves as his/her own control.

Anaesthesia was maintained with isoflurane 1–2% with O_2-air mixture on controlled ventilation. HELP SCORE and SNIFF SCORE were then compared.

For ease of comparison and to standardize a common reference point for all laryngoscopists, the pictures of Cormack Lehane grades (Figure 1) were shown to them during laryngoscopy. The laryngoscopist ticked on the appropriate picture of Cormack Lehane grade based on glottic visualization during HELP positioning (HELP score) and sniff positioning (SNIFF score).

The laryngoscopy view was graded according to the CL grade as follows:

Grade I - Visualization of entire laryngeal aperture.

Grade II - Visualization of just the posterior portion of laryngeal aperture

Grade III - Visualization of only the epiglottis

Grade IV - Visualization of just the soft palate

Statistical analysis: The data of the present study was recorded and fed into the computer and after its proper validation, checked for error; coding & decoding was compiled and analyzed with the help of SPSS 20 software for windows. Appropriate univariate and bivariate analysis and the descriptive statistics carried out. Other statistical tests such as Student's t-test for continuous data and Fishers Exact Test or χ^2 test for categorical data were applied to support the hypothesis. All means are expressed as mean ± standard deviation and the proportion as in percentage (%). The p value of less than 0.05 is considered as significant for the results.

Results

There was no statistically significant difference between mean age of male and female group (p value > 0.05, t = 0.237). (Table 1)

From table 2 it was found that in sniffing position 56.7% cases had grade 1, 34.3% cases grade 2 and 9% cases grade 3 CL score. While in HELP 75.9% cases had CL grade 1, 23.3% cases grade 2 and only. 8% cases had grade 3 CL scores. By applying McNemar Chi-square test, we got t value of 36.51 and p value of less than 0.0001 which was highly significant.

The table 3 compares HELP and SNIFF scores according to neck circumference. For the purpose of comparison we took the median value of neck circumference (which came out to be 35 cm) and then divided total cases into two groups (<35 cm group and >35 cm group).

In <35 cm group, by applying Mantel Haenszel Chi-square test for linear trend we got a p value of 0.06251 which indicated that there was a positive and significant linear trend of improvement of laryngoscopic view in HELP as compared to sniff position. In >35 cm group, by applying Mantel Haenszel Chi-square test for linear trend we found a very highly significant linear trend of improvement of CL grade (p value of 0.0000001) in HELP.

Though HELP caused statistically significant improvement of glottic view in both these groups, the linear trend of improvement of glottic visualization became more statistically significant in higher neck circumference patients as compared to patients with lower neck circumference.

The table 4 compares HELP and SNIFF scores according to BMI. For the purpose of comparison, we formed two groups (<25 BMI group, >25 BMI group).

In <25 BMI group, Chi-square test for linear trend showed a p value of 0.002972 which indicated a significant linear trend of improvement of glottic view in HELP as compared to Sniff position. In >25 BMI group, Chi-square test for linear trend

Table 1: Age and sex distribution

Age (in years)	M (n=162)	F (n=83)	Total (n=245)
<20	8 4.9%	1 1.2%	9 3.7%
20-29	35 21.6%	19 22.9%	54 22.0%
30-39	44 27.2%	23 27.7%	67 27.3%
40-49	34 21.0%	25 30.1%	59 24.1%
50-59	41 17.3%	15 12.0%	56 15.5%
Mean ± SD	38.48 ± 12.855	38.08 ± 11.420	38.35 ± 12.365

showed a p value of 0.000000729 which indicated a significant linear trend of improvement of glottic view in HELP as compared to sniff position.

Though HELP caused statistically significant improvement of view in both these groups, the linear trend of improvement of glottic visualization became more statistically significant in higher BMI patients as compared to patients with lower BMI.

The regression model using logistic regression analysis (Table 5, Figure 2), taking SNIFF Score as dependent variable and neck circumference (in cm), BMI as predictors showed a significant F ratio ($F=13.092$; $p<0.0001$, $R^2=0.098$) and it was observed that neck circumference compared to BMI was significantly correlated with increased CL Grade ($t=3.875$; $p<0.05$ for neck circumference and $t=0.720$; $p>0.05$ for BMI). The results of regression analysis strongly recommend that the neck circumference is statistically more accurate in predicting poor glottic visualization as compared to BMI.

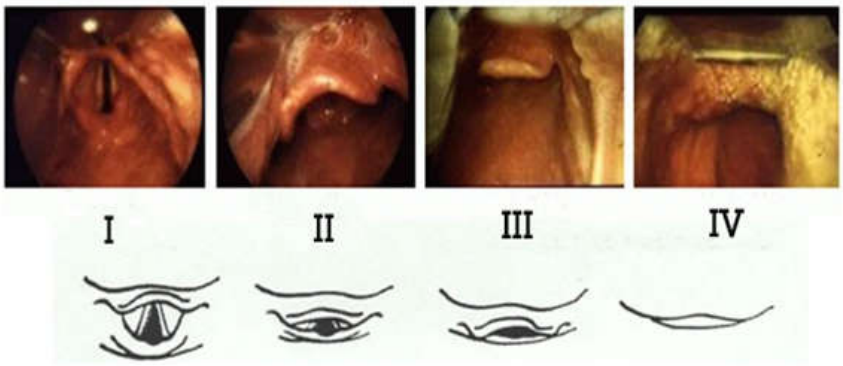

Fig. 1: Cormack Lehane Grades

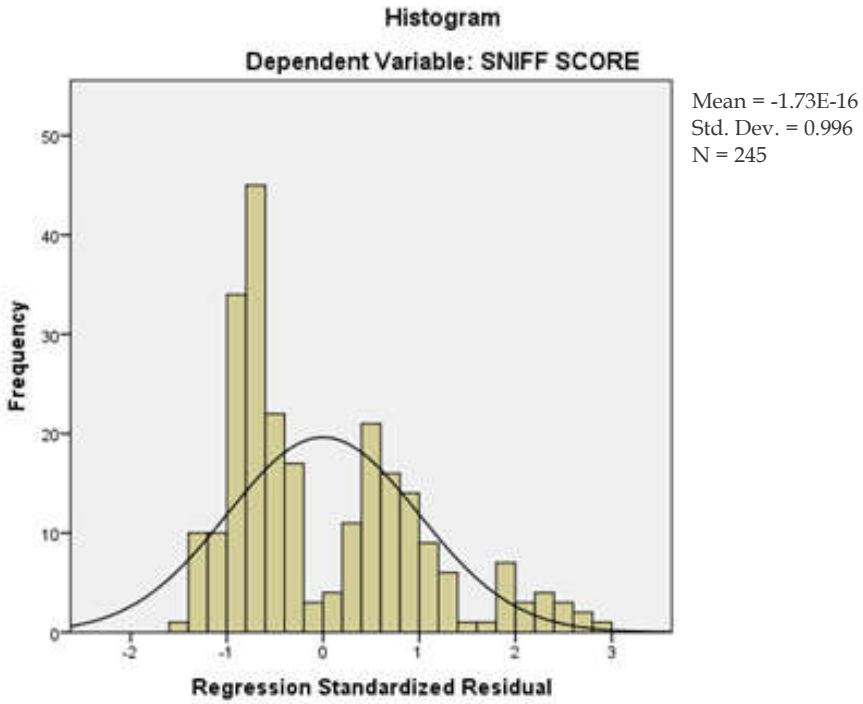

Fig. 2: Histogram- SNIFF score dependent variable

Table 2: Comparison of HELP score and SNIFF score

1		Help Score 2	3		Total
Sniff Score	1	124 50.6%	15 6.1 %	0 0.0%	139 56.7%
	2	47 19.2%	37 15.1%	0 0.0%	84 34.3%
	3	15 6.1%	5 2%	2 0.8%	22 9.0%
Total		186 75.9%	57 23.3%	2 0.8%	245

McNemar Chi-square t value = 36.516; p<0.0001

Table 3: HELP and SNIFF score comparison according to neck circumference

Cormack Lehane Grade	<35 CM		>35 CM	
	HELP	Sniff Position	HELP	Sniff Position
1	93 76.9%	84 69.4%	93 75.0%	55 44.4%
2	27 22.3%	31 25.6%	30 24.2%	53 42.7%
3	1 0.8%	6 5.0%	1 0.8%	16 12.9%
Total	121	121	124	124
	t value=3.47; p=0.06251		t value=31.31; p=0.0000001	

Table 4: HELP and SNIFF score comparison according to BMI

Cormack Lehane Grade	BMI <25kg/m^2		BMI >25kg/m^2	
	HELP	Sniff Position	HELP	Sniff Position
1	125 74.0%	104 61.5%	61 80.3%	35 46.1%
2	42 24.9%	55 32.5%	15 19.7%	29 38.2%
3	2 1.2%	10 5.9%	0 0.0%	12 15.8%
Total	169	169	76	76
	T value =8.82; p=0.002972		T value =24.54; p=0.000000729	

Table 5: Comparison between neck circumference and BMI for predicting poor glottic visualisation

Variables	t value	p value
BMI	0.720	0.472
Neck Circumference	3.875	0.0001

Dependent Variable: SNIFF SCORE

Discussion

In our study we compared the laryngoscopic view of glottis between two positions Sniff and HELP. Results showed that HELP was better in laryngoscopic view for both obese and non obese patients.

Positioning the patient to HELP improves jaw mechanics during laryngoscopy by achieving greater mouth opening and the more thyromental space. So the increased thyromental space means more place for tongue to get displaced making better glottic visualisation.

The tension in anterior cervical muscles created by extending head provides a counterforce on laryngoscope blade during lifting. As face plane remains parallel to ceiling in HELP position, there is less tension on anterior cervical muscles. By de-tensing anterior cervical muscles, HELP facilitates laryngoscopy.

HELP by elevating head and shoulder decreases pressure exerted on thorax by abdominal contents.

It simplifies ventilation leading to increased functional residual capacity and tidal volume. Thus extends the duration of safe apnea period.

In 2004, Collins *et al.* [5] showed that arranging blankets underneath a morbidly obese (BMI>40 kg/m^2) patient's upper body and head until horizontal alignment was achieved between the external auditory meatus and sternal notch, significantly improved laryngoscopic view in comparison to a separate similar group of morbidly obese patients whose head was supported only by a 7 cm cushion. Working from the findings of Collins *et al.*, P.W. Lebowitz *et al.* tried to evaluate direct laryngeal visualization in anaesthetized adult patients in the HELP position and using each patient as his/her own control, compare it with laryngeal visualization in sniff position.

We did our study based on the protocols followed by P.W. Lebowitz *et al.* [6] Main difficulty associated with this study was to create a protocol that did not give an advantage to either of the two positions. The ideal study design would have had patients selected at random to receive either the "HELP" or the "sniff" position first and the other second. The logic behind this approach is that an anaesthesiologist who performs laryngoscopy on a given patient get to know the landmarks and feel for that patients' airway and will have an easier time attempting a second laryngoscopy on that patient. This logic then would seem to favor the sniff position in our study since it was always performed after HELP. We accepted this limitation because moving an anaesthetized patient, particularly an obese one into HELP would have required several assistants and increased injury chances to the patient which was not encountered simply by removing the HELP.

Different patients have different airway anatomy. By studying the effect of two positions on laryngeal view in same patient, we had eliminated the bias that might have occurred in the study because of different airway anatomies in different patients.

Since the senior anaesthesia residents served as laryngoscopists, the variability in laryngoscopic skills and interpretation of resultant laryngoscopic views among the participants provided another limiting variable in assessing our results. To standardize a common reference point for all the anaesthesiologists participating in the study, each anaesthesiologist was shown pictures of different grades of Cormack Lehane scale before laryngoscopy. Furthermore, the study required the anaesthesiologist to perform both laryngoscopies in each study patient so as to standardize the grading. Hence, while there was variability among the laryngoscopists, each anaesthesiologist served as his/her own control.

Collins *et al.* enrolled 60 morbidly obese patients undergoing elective bariatric surgery and randomly assigned them into two groups. First group patients were intubated in HELP and second group of patients in SNIFF position. They found improved laryngeal view in HELP when compared to sniff (p value of 0.037). Our study was in agreement with the study of Collins et al. with respect to the superiority of HELP. The two studies had difference with respect to sample size (60 cases in Collins et al. study versus 245 cases in our study) and also we included both non obese and obese patients while Collins et al. included only morbidly obese patients.

Levitan *et al.* [7] did laryngoscopy in 7 fresh human cadavers at first in head lying flat on the table and then in HELP. They found that HELP provided better view than head flat. Our study also found that HELP provided superior view but on contrary to 7 cases studied in Levitan *et al.* study we included 245 live anaesthetized patients (not human cadavers) in our study.

We did our study based on the protocol followed by P.W. Lebowitz *et al.* Our study was in unison with the study of P.W. Lebowitz *et al.* and showed that HELP was superior in improving laryngoscopic view than sniff position in both obese and non obese patients. The difference in two studies was sample size (189 cases in P.W. Lebowitz *et al.* study versus 245 patients in our study). They had taken into account only BMI for comparing CL grades in different patients but we compared CL grades in different patients with respect to both BMI and neck circumference.

The studies [8,9,10] supported the sniffing position as optimal laryngoscopic position. Sahay N *et al.* [11] in their meta-analysis showed that sniffing position provides better glottis exposure, therefore should be used as initial position when attempting intubation. But these studies did not made any comparison of sniff position to HELP.

Our secondary objective was to compare between neck circumference and BMI in accuracy of predicting poor glottic visualization. Our study showed that neck circumference was statistically more accurate in predicting poor glottic visualization as compared to BMI. The study results were congruent with the results of Brodosky *et al.* [12], Ezri T, G. Gewurtz *et al.* [13] and Gonzalez *et al.* [14] and showed that neck circumference is a better predictor of poor glottic visualization as

compared to BMI.

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Conflicts of interest: There are no conflicts of interest.

References

1. Hagberg CA Benumof's Airway management Principle & Practice 2nd ed Preparation and positioning. p.381.
2. Bannister FB, Macbeth RG. Direct laryngoscopy and tracheal intubation. Lancet 1944;2:651-4.
3. Greenland KB, Edwards MJ, Hutton NJ.External auditory meatus-Sternal notch relationship in adults in the sniffing position:a magnetic resonance imaging study.Br J Anaesth. 2010;104(2):268-69.
4. Cormack RS, Lehane J. Difficult tracheal intubation in obstetrics. Anaesthesia. 1984;39:1105–11.
5. Collins JS, Lemmens HJ, Brodsky JB, Brock-Utne JG, Levitan RM. Laryngoscope And morbid obesity: a comparison of the "sniff" and "ramped" positions. Obes Surg. 2004 Oct;14(9):1171-5.
6. Lebowitz PW. Shoulder and head elevation improves laryngoscopic view for tracheal intubation in nonobese as well as obese individuals. J Clin Anaesth. 2012;24:104-8.
7. Levitan RM, Mechem CC, Ochroch EA, Shofer FS, Hollander JE. Head-elevated laryngoscopy position: improving laryngeal exposure during laryngoscopy by increasing head elevation. Ann Emerg Med. 2003 Mar;41(3):322-30.
8. Hochman II, Zeitels SM, Heaton JT. Analysis of the forces and position required for direct laryngoscopic exposure of the anterior vocal folds. Ann Otol Rhinol Laryngol. 1999;108:715–24.
9. Adnet FA, Borron SW, Dumas JL, Lapostolle F, Cupa M,Lapandry C. Study of the "sniffing position" by MRI. Anesthesiology. 2001;94:83– 6.
10. Isono A. Common practice and concepts in anesthesia: time for reassessment—is the sniffing position a "gold standard" for laryngoscopy? Anesthesiology. 2001;95:825–7.
11. Sahay N, Samaddar DP, Chatterjee A, Sahay A, Kant S, Ranjan A. Sniff to see. Comparing sniffing position versus simple head extension position for glottic exposure-A prospective, randomized cross over study. J Health Spec. 2016 Jul 1;4(3):212.
12. Brodsky JB, Lemmens HJM, Brock-Utne JG, Vierra M, Saidman.Morbid obesity and tracheal intubation. Anesth Analg. 2002;94:732– 6.
13. Ezri T, Gewurtz G, Sessler DI, Medalion B, Szmuk P, Hagberg CA, Susmallian S. Prediction of difficult laryngoscopy in obese patients by ultrasound quantification of anterior neck soft tissue. Anaesthesia. 2003;58:1111-4.
14. Gonzalez H, Minville V, Delanoue K, Mazerolles M, Concina D, Fourcade O. The importance of increased neck circumference to intubation difficulties in obese patients. Anesth Analg 2008 Apr 1;106(4):1132-6.

Original Research Article

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A Comparative Study of Efficacy of Bupivacaine and Ropivacaine with Fentanyl in Epidural Labour Analgesia

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Abstract

Introduction: Labour is a highly complex and personal process for every woman. Analgesic intervention is a matter of personal choice for delivery. Local anesthesia given as an epidural injection along with an opioid gives quicker analgesia without impeding motor activity. Bupivacaine and Ropivacaine are commonly employed drugs to provide efficient epidural analgesia in labour. *Aims:* To compare the efficacy of ropivacaine with fentanyl and bupivacaine with fentanyl given as continuous infusion in labour epidural analgesia. *Materials and Methods:* This was a prospective randomized control trial wherein 70 women in labour were studied. These 70 parturients were randomly put into two groups. Group A (n=35) received 12 ml of 0.125% ropivacaine as the initial bolus followed by 8 ml/hour infusion of 0.125% ropivacaine with 2 µg/ml fentanyl. Group B (n=35) received 12 ml of 0.125% bupivacaine as initial bolus followed by 8ml/hour infusion of 0.125% bupivacaine with 2 µg/ml fentanyl. Various parameters like duration of labour, mode of delivery, neonatal outcome and complications were noted and compared for both the groups. *Results:* Both the groups showed minimal fluctuations in pain that were clinically and statistically insignificant. The spontaneous deliveries were similar in both groups. The rate of instrument assisted delivery and caesarean delivery was similar in both groups. No adverse neonatal outcome (because of the drugs used) in the form of low APGAR scores or admission to NICU were noticed in both the groups. Motor block was not statistically significant. The incidence of complications was minimal and comparable in both groups. *Conclusion:* Ropivacaine used at lower concentration (0.125%) offers good pain relief equivalent to that of bupivacaine. Both the drugs give similar results as regards the duration of labour, mode of delivery, neonatal outcome and complications. Though ropivacaine is less potent than bupivacaine, its safety and efficacy is equivalent to bupivacaine.

Keywords: Epidural analgesia, Ropivacaine, Bupivacaine, Motor blockade

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Introduction

Labour is a natural and physiologic process with a happy outcome for most of the women. But it can be a very painful and unpleasant experience for some. Analgesic intervention during delivery is a matter of personal choice for an individual. All the antenatal women should be provided with information regarding the process of labour and the means available to ease the process. Whether a woman opts for analgesia during labour is her own decicion. Many religious and cultural factors influence the patient's thought process regarding analgesia during labour. An ideal analgesic should

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be safe for the mother and newborn, should not affect the progress of labour, and should be adaptable to changing conditions.

The analgesia should last for a sufficient time period, should be titratable as per patient requirements, without any undue adverse effects in the mother or new-born. Also it should be physician and cost friendly. At present to achieve this end, many modalities are available. Extensive research has made way for use of neuraxial techniques that are safe and effective.

Current neuraxial labour analgesia focusses not only on pain relief but also on the overall quality of analgesia [1].

Central neuraxial analgesia is considered the gold standard method for pain control in the present day practice of obstetrics. This method also gives a better and satisfying birth experience to women [2]. This technique can be used as a subarachnoid or as an epidural block. Between the two, epidural block is considered to be better for labour as it can provide continuous analgesia for longer time period and also is amenable to conversion to anesthesia if at all a surgical intervention is required.

Epidural injection of a local anaesthetic combined with an opioid provides a more rapid onset of analgesia with little motor blockade. The onset of pain relief is faster and also lasts longer if both the drugs are used. As two drugs are being used each has a lower concentration, which reduces the risk of systemic toxicity by local anesthetic and also reduces the side effects of opioids [3]. Bupivacaine and Ropivacaine are widely used to provide efficient epidural analgesia in labour. Bupivacaine has increased risk of motor blockade thereby leading to increased rates of forceps/instrument use and also it has some cardiac toxicity. On the other hand, Ropivacaine is advantageous in having more sensory motor differential blockade and also less systemic toxicity. Various authors have reported contrasting results of ropivacaine and bupivacaine for labour analgesia [1]. Some studies observed less motor block by ropivacaine as compared to bupivacaine while others observed no difference between the two. To prevent or lessen unwanted motor block, dilute solutions of epidural local anesthetics combined with opioids have been recommended.

In the present study, we attempted to evaluate whether ropivacaine offers any significant advantage over bupivacaine with regard to obstetrical outcome and whether changing over from bupivacaine to ropivacaine is warranted. Both the drugs were evaluated and compared for pain relief, motor block, and labour characteristics.

Materials and Methods

This was a prospective randomized control trial carried out in the Department of Obstetrics and Gynaecology, Dr. PSIMS and RF, Chinnaoutpalli over a period of 13 months from1st October 2012 to 31st October 2013. Approval was taken from Institutional ethics committee and scientific committee.

The study had 70 women who were due for labour. They were informed and counselled regarding facility of labour analgesia. The procedure was explained to all the patients and informed consent was obtained from willing patients. Complete clinical history of the patient was recorded. Routine investigations like blood grouping and typing, hemoglobin estimation, and platelet count were done as per our hospital labour protocol. Only those patients who fulfilled the inclusion criteria and who gave consent were selected and were then randomly allocated to one of the study groups.

Inclusion Criteria

1. Normal singleton pregnancies.
2. Age between 18 to 35 years
3. ASA status: I and II
4. Patients in active labour with cervical dilatation of 3-5 cm.

Exclusion Criteria

1. Contraindications to epidural block
2. Pre-term pregnancy
3. Multiple gestations.
4. Previous cesarean section.

The patients were cannulated with 18G IV cannula and infused with Ringer lactate solution. The patient was asked to be in sitting position with the back aligned with the edge of the bed. Under all aseptic precautions, cleaning and draping of the skin in the lower thoracic and lumbar region was done. The best interlumbar space between L_2 and L_4 was selected and infiltrated with 2 ml of 2% lignocaine.

Epidural catheterization was done and a length of 5 cm of catheter was kept in the epidural space. Care was taken not to aspirate CSF or blood at any time during the procedure.

After the catheter was satisfactorily in situ, the puncture site was cleaned and an occlusion dressing was applied. A bacterial filter was attached to the hub of the catheter. The catheter was secured by adhesive tape by fixing it against the dorsum. First a small test dose of local anaesthetic (3 ml of 2% Lignocaine with Adrenaline) was given through the catheter to rule out intravascular or intrathecal placement of catheter. Signs of motor block suggest intrathecal placement and tachycardia suggests intravascular placement so these were looked for. In absence of these signs (after 5 minutes) the patient was put in a supine position. Then the test drug was given as bolus dose followed by the infusion.

If there was any breakthrough pain then patient was given 6 ml of either 0.125% Ropivacaine or 0.125% Bupivacaine based on the subject's study group. Various maternal parameters were continuously monitored and noted every 15 minutes in the first hour, every 30 minutes in the second hour and every hourly thereafter. Continuous fetal heart monitoring was also done. Duration of first stage of labour was taken from insertion of epidural catheter (3-5 cm of cervical dilatation) to full dilatation of cervix.

Parameters monitored: Maternal Heart rate, Maternal Blood pressure, Maternal respiratory rate and oxygen saturation, Pain relief by 11 point verbal numerical rating scale (VNRS) and Motor block by Bromage score (0-3).

Clinical outcome studied: The following parameters were noted: Pain relief, Motor block, Duration of labour, Mode of delivery and Neonatal outcome.

The statistical analysis was performed using SPSS (Statistical package for social sciences) version 17 for windows. The profile of the cases was compared with the treatment allocation in order to check if there was any significant imbalance. Descriptive statistics are presented as mean ± SD. Chi-square test for association was used to compare categorical variables between treatment allocations

Results

Total number of cases was 70.

Table 1: Demographic details and profile of the cases

Mean	Group A (Ropivacaine with Fentanyl)	Group B (Bupivacaine with Fentanyl)
Age (in years)	25.37	25.23
Weight (in Kgs)	68	64.29
Gravida and parity		
Gravida 1	19	26
Gravida 2	15	8
Gravida 3	1	1
Parity 0	21	27
Parity 1	14	4.4
ASA Grade		
ASA Grade I	94.3	91.4
ASA Grade II	5.7	8.6
Mode of delivery		
Cesarean	11.4	8.6
Vaginal Assisted	25.7	37.1
Vaginal Spontaneous	62.9	54.3
Level of epidural catheter placement		
L2-L3	22.9	40
L3-L4	68.6	51.4
L4-L5	8.6	8.6

The patient demographics of age (p=0.874), weight (p=0.843), Gravida (p=0.200) and parity (p=0.122) were statistically insignificant between the two groups.

Also the ASA grade II distribution of patients was statistically insignificant. (p=0.643).

There were more spontaneous vaginal deliveries in Group-A (62.9%) compared to group-B (54.3%). Assisted vaginal deliveries were less in group- A (25.7%) compared to group-B (37.1%). Four patients in group-A (11.4%) and three patients in group-B (8.6%) had cesarean deliveries.

More than 50% of the patients in both the groups received epidural in the L3-4 interspace. The distribution of level of epidural catheter placement among both the groups did not have any statistical significance. (p=0.287).

Comorbid conditions

Gestational diabetes mellitus (GDM) was present in one woman (2.9% in each group). PIH Pregnancy Induced Hypertension (PIH) was present in one woman (2.9%) in group-A and in two (5.8%) women in group-B. Their distribution among groups was statistically insignificant. (p=0.840).

Vaginal dilatation

The average vaginal dilatation of all 70 subjects was 3.44 ± 0.65 cm. The mean for group-A was 3.37 ± 0.54 cm and for group-B it was 3.51 ± 0.74 cm. The difference was statistically insignificant. (p=0.206)

Outcome measured

Hemodynamics

All the 70 patients had continuous monitoring of their hemodynamic parameters. The baseline values were noted before giving epidural analgesia, then at 15 minutes, at 30 minutes, at 45 minutes, and at the end of 1, 1.5, 2, 3, 4, 5, 6, 7 hours. All 70 individuals had minimum monitoring time around 3 hours.

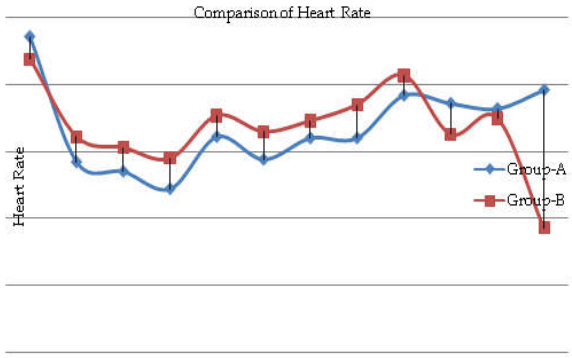

Fig. 1: Comparison of heart rate in both groups

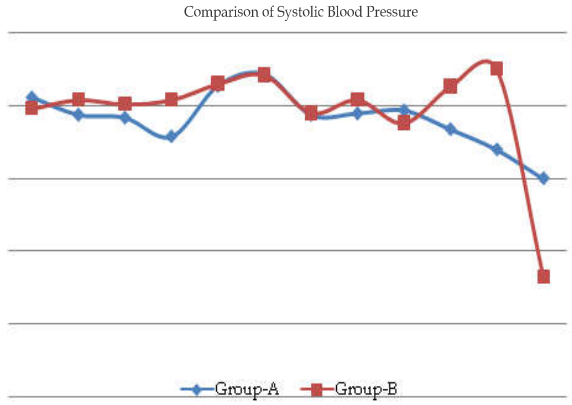

Fig. 2: Comparison of systolic blood pressure in both groups

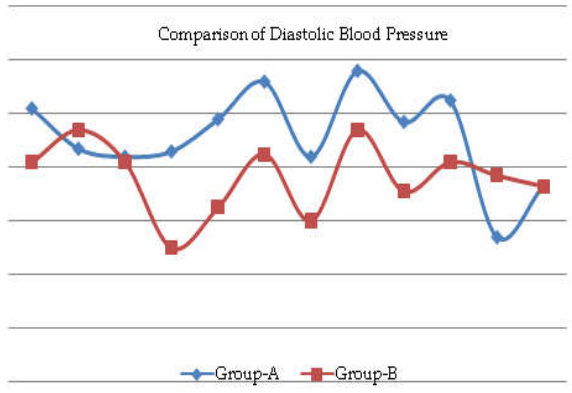

Fig 3: Comparison of diastolic blood pressure in both groups

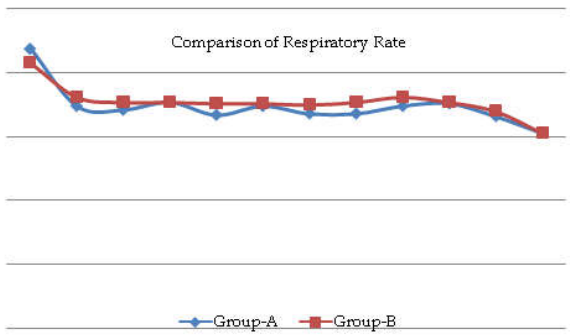

Fig. 4: Comparison of respiratory rate in both groups

The hemodynamic parameters did not show any statistically significant difference between the two groups. The oxygen saturation (SpO_2) among both groups also did not vary significantly.

Table 2: Comparison of pain score in both groups

Time	Group-A	Group-B	t Value	p Value
Baseline	7.88 ± 0.7	7.65 ± 0.8	1.170	0.246
15 mins	0.31 ± 0.4	0.17 ± 0.3	1.393	0.168
30 mins	0.02 ± 0.1	0.08 ± 0.2	-1.023	0.310
45 mins	0.02 ± 0.1	0.05 ± 0.2	-0.583	0.562
1 hr	0.02 ± 0.1	0.08 ± 0.2	-1.023	0.310
1.5 hr	0.11 ± 0.5	0.05 ± 0.2	-1.358	0.179
2 hr	0.08 ± 0.2	0.02 ± 0.1	1.023	0.310
3 hr	0.20 ± 0.6	0.08 ± 0.3	1.041	0.302
4 hr	0.28 ± 0.8	0.09 ± 0.3	1.235	0.221
5 hr	0.42 ± 0.9	0.52 ± -.2	-0.289	0.774
6 hr	0.00 ± 0	0.38 ± 1.1	-1.127	0.276
7 hr	0.00 ± 0	0.00 ± 0		

The pain levels immediately after bolus were reduced. The pain levels did not go above VNRS (verbal numerical rating scale) of 3 during infusion in both the groups. Most of the increase in pain scores occurred during the second stage of labour. But the pain score variation was statistically insignificant.

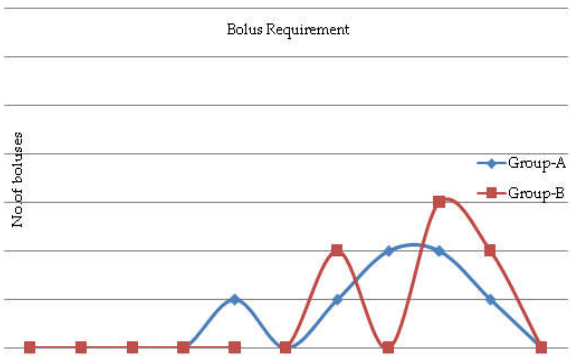

Fig. 5: Bolus Requirement for both groups

For both the groups an equal number of patients (7 women in each group) required boluses during their labour.

Table 3: Duration of labour for both groups

Duration (in minutes)	Group-A	Group-B	t Value	P Value
Stage-I	467.4 ± 95.8	467.6 ± 87.8	-0.007	0.995
Stage-II	33.5 ± 8.5	31.1 ± 8.9	1.116	0.269
Stage-III	6.8 ± 1.7	6.1 ± 1.2	1.769	0.082

All 3 stages of labour were comparable for both groups without much variation.

The standard APGAR score was used to rate the neonatal outcome which was taken at 1 and 5 minutes. At the end of 1 minute the average APGAR score was 7.65 ± 0.59 and 7.68 ± 0.47 in group-A and group-B respectively. At 5 minutes, the APGAR score was 8.94 ± 0.23 and 9 in group-A and B respectively. There was no statistically significant difference in the mean values 1 minute (p-0.460) and 5 minutes (0.221) for both groups.

NICU admission

NICU care and admission was required in 5 neonates (14.3%) in group-A and in 3 neonates (8.6%) in group-B. The difference was not statistically significant (p-0.845). The indications for admission in NICU in group-A, and group B were cord around the neck, respiratory distress and meconium stained liquor. The remaining two neonates in group A had IUGR.

Motor block

Motor blockade of Bromage score-1 was seen in 3 persons in group-B. This was observed during the 5th hour in all 3 patients. There was no clinically observable motor blockade in Group-A. However this statistically insignificant (p-=0.071).

Numbness

In group-B, 2 patients had numbness that was seen in the 6th and 7th hour. In group A, no patient had numbness. The numbness rate was statistically insignificant.

Pruritus

No patient from either group complained of pruritus.

Discussion

In the recent Cochrane review it was concluded that epidural analgesia offered better pain relief as compared to non-epidural methods. Also it obviated the need for additional pain relief and had reduced risk of acidosis. In the present study we have compared bupivacaine and ropivacaine for labour epidural analgesia. Bupivacaine is an established drug and is often used for labour analgesia. We compared bupivacaine with ropivacaine, (levo-enantiomer) as ropivacaine gives better sensory-motor differentiation. Also it

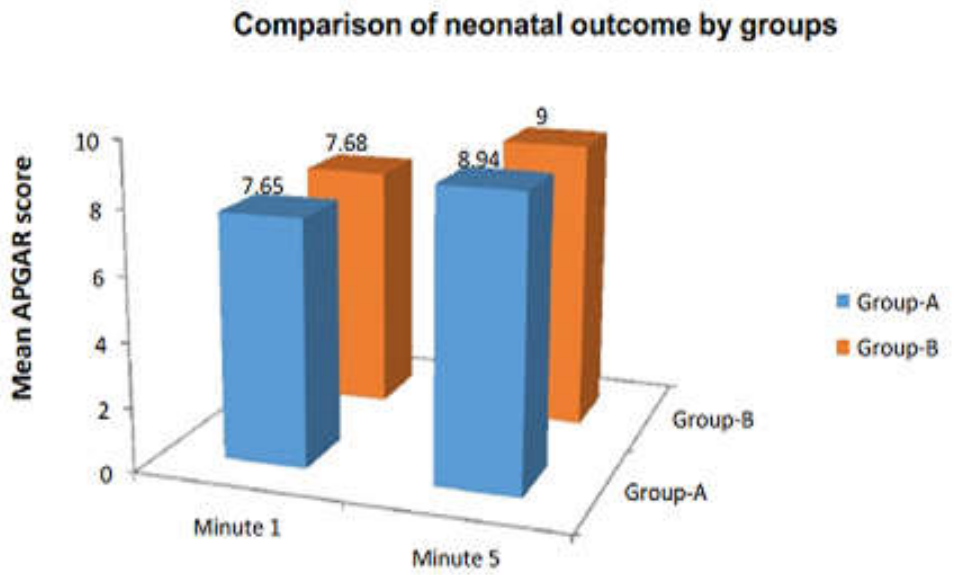

Fig. 6: Neonatal Outcome for both groups

has less cardiotoxic potential than bupivacaine.

Ropivacaine is only 60% potent as compared to bupivacaine [4]. Some of the studies have compared both drugs in equal concentrations [5] (i.e. 0.125% bupivacaine versus 0.125% ropivacaine) while some have compared equi-potent concentrations of both drugs [6] (i.e 0.1% bupivacaine versus 0.15% ropivacaine). Most of the authors have concluded that both drugs are more or less equally effective and that ropivacaine has a slight advantage as it causes less motor block on prolonged infusion. The recommended dose of bupivacaine and ropivacaine in labour epidural analgesia is 0.0625%-0.125% (8-15 ml/hour) and 0.125%-0.25% (6-12 ml/hour) respectively [7].

We used 12 ml of 0.125% ropivacaine for initiation and 8 ml/hour of 0.125% ropivacaine with 2 μg/ml fentanyl for maintenance. There is a synergistic action when neuraxial local anesthetics and opioids are used together and better neuraxial analgesia is achieved. This combination decreases the minimal local analgesic concentration (MLAC) of local anaesthetics used. We used fentanyl in a concentration of 2 μg/ml as many previous studies have used it at this concentration. We used ropivacaine at 0.125% concentration (with fentanyl) since it has less incidence of motor blockade at this concentration which is important during labour analgesia. Also as we wanted to compare the analgesic effect of two drugs it was reasonable to use them at same concentrations. The other factors like the age, weight, gravida, parity, vaginal dilatation were similar in both the groups.

Pain relief

It is difficult to measure pain as it is subjective and depends on the individual's pain perception. Various scales are in vogue to measure pain and the popular ones are verbal rating scale, numerical rating scale (NRS) and visual analog scale (VAS). We used the NRS in our study due to its ease and better patient compliance. We observed that the mean pain level was 7.8 ± 0.7 in ropivacaine group and 7.6 ± 0.8 in bupivacaine group. After epidural analgesia it came down to 0.31 in ropivacaine and 0.17 in bupivacaine group. At the end of 5 hours the pain score went up to 0.42 and 0.52 in ropivacaine and bupivacaine group respectively. The onset of pain relief was similar in both the groups. Our findings agree well with those of Meister *et al.* 2000 [5]. In their study, they compared equal concentrations of bupivacaine and ropivacaine (0.125%) along with fentanyl in both groups. They observed mean NRS scores of 9 in bupivacaine and 8 in ropivacaine group which came down to 0.4 and 0.3 post epidural analgesia. Similar observations were reported by Fernandez *et al.* 2001 [8] when they compared 0.0625% bupivacaine with fentanyl and 0.1% ropivacaine and fentanyl.

The onset of pain relief was similar in both groups. Also the patient satisfaction was more or less same in both groups. Inspite of using a less potent ropivacaine, the pain relief was almost equal in both groups with insignificant statistical difference.

Motor blockade

Halpern *et al.* 2003 [9] did a meta-analysis and compared ropivacaine (0.05-0.2%) and bupivacaine (0.05-0.125%). In this meta-analysis 19 out of 23 studies concluded that ropivacaine has minimal motor block and 5 of these studies were statistically significant. In our study, only 2 patients in bupivacaine group had demonstrable Bromage score-I motor block. There was no clinically demonstrable motor block in the ropivacaine group. This difference was not clinically significant. In this study the incidence of motor block was low in bupivacaine and it was absent in ropivacaine group which is consistent with other studies [5].

Duration of labour

Duration of 1st stage of labour

The first stage of labour includes good uterine contractions, the dilatation of cervix and the descent of the presenting part of fetus. In our study the first stage of labour was taken from the insertion of epidural catheter (at 3-5 cms) of cervical dilatation to the full dilatation of cervix. The duration of first stage of labour was 467.7 ± 95.8 minutes in ropivacaine group and 467.6 ± 87.8 minutes in the bupivacaine group. The mean duration for both groups was not statistically significant. Various authors have compared varying concentrations of bupivacaine with ropivacaine. They observed similar duration of first stage of labour with both the drugs. (Feranandez 2001, Owen 2002, Boselli 2003) [8,10,11]. Our findings agree well with the above studies. In contrast, Lee *et al.* [12] in their study found longer first stage of labour in the bupivacaine group as compared to ropivacaine group. They felt that though this difference was statistically significant, it was clinically insignificant.

Duration of 2nd stage of labour

According to ACOG guidelines, if the second stage of labour takes more than 3 hours in case

of a primipara and more than 2 hours in case of a multipara with regional analgesia, then it is called prolonged second stage. Halpern *et al.* [9] did a meta-analysis which had 2400 parturients who received either epidural analgesia or parenteral opioid analgesia. He observed that those who received any medication had a slightly longer (14 minutes more) second stage of labour. A recent Cochrane review found that women in labour who had epidural analgesia had slightly longer second stage of labour [13].

In our study there was no difference in the duration of second stage of labour in both groups. The mean duration was 33.5 min in ropivacaine group and 31.1 min in bupivacaine group. This difference was not statistically significant. Our result coincides well with the meta-analysis done by Halpern *et al.* in 2003 [9] which took into account 23 studies comparing ropivacaine and bupivacaine for labour epidural analgesia. They found that neither bupivacaine nor ropivacaine group had any difference in the duration of second stage of labour.

Mode of delivery

Instrumental vaginal delivery

Halpern *et al.* 1988 [9] in their meta-analysis found higher possibility of instrumental vaginal delivery in women who received epidural analgesia. Cambic and Wong 2010 [14] in their review also observed higher rate of instrumental vaginal delivery while using epidural analgesia. In our study we had an instrumental delivery rate of 25.7% and 37.1% in ropivacaine and bupivacaine group respectively, which was not statistically significant. In majority of cases, maternal failure was the cause of instrumental delivery. Finegold *et al.* [15] in their study reported instrumental vaginal delivery rate of 18% in ropivacaine and 28% in bupivacaine group respectively. In their study also the difference was statistically insignificant.

Halpern *et al.* [10] also did not find any difference in the mode of delivery between the two drugs. However a meta-analysis of 6 studies comparing 0.25% ropivacaine and 0.25% bupivacaine done by Writer *et al.* [16] in 1998 found that there were fewer instrumental vaginal deliveries in the ropivacaine group. This may be because of the higher concentration of bupivacaine used and difference in the motor blocking potency of ropivacaine.

Caesarean delivery

In general, the process of normal labour converting to caesarean delivery is never attributable to epidural anaesthesia. In the present study, the ropivacaine group had a cesarean delivery rate of 11.4% and bupivacaine group had a rate of 8.6%. However, the indications for the cesarean delivery were failure to progress, cord around the neck and meconium stained liquor leading to fetal distress.

In the study done by Beilin *et al.* in 2007 [17] they observed a cesarean rate of 33% and 30% in bupivacaine and ropivacaine group respectively. Halpern *et al.* [10] also in their meta-analysis did not find any difference in cesarean delivery rates between the two groups when epidural analgesia was used.

Fetal and neonatal outcome

It was observed in the Cochrane review that women who had opted for epidural analgesia during labour, their new borns had less acidosis and lesser requirement for naloxone as compared to women who received inhalational and intravenous, mainly opioid analgesics [13]. In the present study, the fetal heart rate monitoring during labour analgesia was regular without much variations and post epidural fetal bradycardia was not evident. The mean APGAR scores were 7.65 and 7.68 in ropivacaine and bupivacaine groups respectively. At 5 minutes it averaged to 8.94 and 9 respectively. Both the groups had similar NICU admission rates. Beilin and Halpern in 2010 [9] in their review observed that there was no adverse outcome in neonates when the said drugs were used for labour analgesia.

Writer *et al.* [16] observed a difference in the neurologic and adaptive capacity score, favoring ropivacaine, at 24 hours after birth, but not at 2 hours after birth. However, a later study by Halpern SH *et al.* [9] suggested that these scores were unreliable. The incidence of low APGAR scores at 5 minutes is approximately 2% for both drugs. Also the umbilical artery and vein pH are well maintained irrespective of the drug used as observed by Lee BB *et al.* [12] Wang *et al.* [17] observed that the need for neonatal resuscitation is low and similar with both drugs. The incidences of complications were very minimal in both groups.

Conclusion

Obstetric analgesia aims at making childbirth a smooth and painless procedure. Epidural analgesia is one such method that bestows excellent analgesia that is safe for the mother and baby and also does not have any side effects. From this study we conclude

that ropivacaine used at lower concentration (0.125%) offers good pain relief equivalent to that of bupivacaine. Both the drugs give similar results as regards the duration of labour, mode of delivery, neonatal outcome and complications. Motor blockade was not seen with ropivacaine group. From this study it can be concluded that though ropivacaine is less potent than bupivacaine, its safety and efficacy is equivalent to bupivacaine.

References

1. Owen MD, D' Angelo R, Gerancher JC. 0.125% ropivacaine is similar to 0.125% Bupivacaine for labour analgesia using patient controlled epidural infusion. Anesth Analg. 1998;86:527-31.
2. Hawkins JL. Epidural analgesia for Labour and delivery. N Engl J Med. 2010;362:1503-10.
3. Polley LS, Columb MO, Wagner DS, Naughton NN. Dose-dependent reduction of the minimum local analgesic concentration of bupivacaine by sufentanil for epidural analgesia in labour. Anesthesiology. 1998;89(3):626-32.
4. Owen MD, D' Angelo R, Gerancher JC. 0.125% ropivacaine is similar to 0.125% Bupivacaine for labour analgesia using patient controlled epidural infusion. Anesth Analg. 1998;86:527-31.
5. Wong CA. Advances in labour analgesia, Int J Womens Health. 2009;1:139-54.
6. Meister GC, D' Angelo R, Owen M, Nelson KE, Gaver R. A comparison of epidural analgesia with 0.125% Ropivacaine with Fentanyl versus 0.125% Bupivacaine with Fentanyl during labour. Anesth Analg. 2000;90:632-37.
7. Clément HJ, Caruso L, Lopez F, Broisin F, Blanc-Jouvan M,Derré-Brunet E, Thomasson A, Leboucher G, Viale JP. Epidural analgesia with 0.15% ropivacaine plus sufentanil 0.5 microgram ml-1versus 0.10% bupivacaine plus sufentanil 0.5 microgram ml-1: a double-blind comparison during labour. Br J Anaesth. 2002 Jun;88(6):809-13.
8. Obstetric anaesthesia, Wylie and Churchill-Davidsons, A practice of Anaesthesia, 7th Edition, 2003.p.927.
9. Fernández-Guisasola J, Serrano ML, Cobo B, Muñoz L, Plaza A, Trigo C, Del Valle SG. A comparison of 0.0625% bupivacaine with fentanyl and 0.1% ropivacaine with fentanyl for continuous epidural labour analgesia. Anesth Analg. 2001 May;92(5):1261-5.
10. Halpern SH, Walsh V. Epidural ropivacaine versus bupivacaine for labour: a meta-analysis. Anesth Analg. 2003 May;96(5):1473-9.
11. Owen MD, Thomas JA, Smith T, Harris LC, D'Angelo R. Ropivacaine 0.075% and Bupivacaine 0.075% with Fentanyl 2 µg/m Lare Equivalent for Labour Epidural Analgesia. Anesth Analg. 2002;94:179-83.
12. Boselli E, Debon R, Duflo F, Bryssine B, Allaouchiche B,Chassard D.Ropivacaine 0.15% plus sufentanil 0.5 microg/mL and ropivacaine 0.10% plus sufentanil 0.5 microg/mL are equivalent for patient-controlled epidural analgesia during labour. Anesth Analg. 2003 Apr;96(4):1173-7.
13. Lee BB, Ngan Kee WD, Lau WM, Wong AS. Epidural infusions for labour analgesia: a comparison of 0.2% ropivacaine, 0.1% ropivacaine, and 0.1% ropivacaine with fentanyl. Reg Anesth PainMed. 2002 Jan-Feb;27(1):31-6.
14. Anim-Somuah M, Smyth R, Howell C. Epidural versus non-epidural or no analgesia in labour. Cochrane Database Syst Rev. 2005 Oct; 9(4):CD000331. Review. Update in: Cochrane Database Syst Rev 2011;(12).
15. Cambic CR, Wong CA. Labour analgesia and obstetric outcomes. Br J Anaesth. 2010;105 Suppl 1:i50-60.
16. Finegold H, Mandell G, Ramanathan S. Comparison of ropivacaine 0.1%-fentanyl and bupivacaine 0.125% -fentanyl infusions for epidural labour analgesia. Can J Anesth. 2000;47(8):740-45.
17. Writer WD, Stienstra R, Eddleston JM, Gatt SP, Griffin R, Gutsche BB, Joyce TH, Hedlund C, Heeroma K, Selander D. Neonatal outcome and mode of delivery after epidural analgesia for labour with ropivacaine and bupivacaine: a prospective meta-analysis. Br J Anaesth. 1998;81(5):713-7.
18. Wang Li-zhong, CHANG Xiang-yang, LIU Xia, HU Xiao-xia andTANG Bei-lei. Comparison of bupivacaine, ropivacaine and levobupivacaine with sufentanil for patient-controlled epidural analgesia during labour: a randomized clinical trial. Chin Med J. 2010;123(2):178-83.

Original Research Article

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Efficacy of intrathecal Buprenorphine a Sole Method of Analgesia in Labour : A Randomized Clinical Trial

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Abstract

Background: Parturients are often not prepared for labour analgesia in advance. They demand it when they are already in labour with unbearable pain; many a times an hour or two before the delivery. This study was done to evaluate the efficacy of medicine in analgesia during labour. *Objective:* To assess the efficacy of intrathecal Buprenorphine as a sole method for analgesia in labour. *Methods:* Double blind, randomized controlled trial, 30 parturients in active labour were studied. Labour ward, Department of Obstetrics and Gynaecology, Dr. Balabhai Nanavati Hospital, Vile Parle, Mumbai, during 1st January 2006 to 31st December 2006. Epi-info 7 was used for analysis and student t-test was used. *Results:* There was no significant difference in age, weight, height and gestational age between two groups. ($p > 0.05$). There was significant change in duration of analgesia in both the groups ($p < 0.001$). Mean Pulse rate At 0 minutes and 2 minutes p value was < 0.05 – significant when compared in both groups. *Conclusion:* Addition of buprenorphine to intrathecal fentanyl and bupivacaine provides early onset and prolonged duration of analgesia during labour.

Keywords: Randomized control trial; Blinding; Labour analgesia; Intrathecal Buprenorphine.

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Introduction

In Indian setup, Parturients are often not prepared for labour analgesia in advance. They demand it when they are already in labour with unbearable pain; many a times an hour or two before the delivery. In such conditions, other pharmacological interventions such as intravenous narcotics or inhaled nitrous are much less effective, have short duration and many have unwanted maternal or fetal sedation as potential side effects [1]. Many studies have been done using intrathecal morphine as a sole method of analgesia in labour [2,3,4] specially in advanced labour. However, technique of intrathecal narcotics is limited in duration [5]. Fentanyl (25 mcg) lasts 1-3 hours and morphine (0.25 mg) may last 4-7 hours. Intrathecal morphine alone has a slow onset

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(40–60 min). So, it is best used in combination with fentanyl, which has a rapid onset (3-5 min). The literature supports use of intrathecal narcotics as a safe and effective alternative to epidural analgesia. Intrathecal narcotics provide a selective blockade of pain transmission without significant sympathetic or motor blockade. Literature supports the use of intrathecal buprenorphine for surgical anaesthesia as well as post-operative analgesia. Buprenorphine is 33 times more potent than morphine [6]. The onset of Buprenorphine effect occurs in about 30 minutes and duration of action is at least 8 hours. The affinity of Buprenorphine for mu receptors is 50 times greater than that of morphine and subsequent slow dissociation from these receptors' accounts for its prolonged duration of action and resistance to antagonism with naloxone. Since there is paucity of literature comparing intrathecal Buprenorphine and its quality of analgesia to other narcotics used by intrathecal route for labour analgesia. On this basis, we designed a double-blind study to evaluate efficacy and duration of intrathecal Buprenorphine for obstetric pain relief.

Material & Methods

Study Area- Labour ward, Department of Obstetrics and Gynaecology, Dr. Balabhai Nanavati Hospital, Vile Parle, Mumbai.

Study type- double blind, randomized control study

Study population- 30 parturients of the age group between 20 and 32 years who presented for full term normal delivery in the labour room

Study duration- 1st January 2006 to 31st December 2006.

Sampling technique- Purposive Sampling Technique.

Inclusion criteria- Parturients in the age group of 20 and 32 years in active labour, cervix 3 to 4 cm dilated. ASA I and II. Gravida I and II. Cephalic, Singleton pregnancy – 36 to 42 weeks.

Exclusion criteria- Age below 20 years and above 35 years. Foetal distress, fetal anomalies. Cephalopelvic dispraportion, Preecelamcia, Diabetes Mellitus, Preterm labour, Placenta previa, Heart Disease, Coagulation disorders, Socliosis, Morbid Obesity, Neurological disorders, Severe anaemia. Gross spinal deformity. Local Infection. Patients with known drug allergies were excluded.

Methodology: 30 Parturients of age group 20 to 32 years undergoing normal vaginal delivery, belonging to ASA grade I and II were considered for this study. The Parturients were randomly divided in to two groups of 15 each.

Group A: 15 Parturients of this group received 1.25 mg Bupivacaine + 12.5 mcg fentanyl.

Group B: 15 Parturients of this group received 1.25 mg Bupivacaine + 12.5 mcg fentanyl + 30 mcg Buprenorphine.

Study solution was prepared as follows.

Group A : 0.5 ml of 0.5% Bupivacaine +0.5 ml Fentanyl (diluted to 2 ml with NS).

Out of 2 ml only 1 ml solution was injected so that Bupivacaine becomes 1.25 mg (0.125%) and fentanyl 12.5 mcg.

Group B : 0.5 ml of 0.5% Bupivacaine +0.5 ml Fentanyl + 0.2 ml Buprenorphine (diluted to 2 ml with NS).

Out of 2 ml only 1 ml solution was injected so that Bupivacaine becomes 1.25 mg (0.125%), Fentanyl 12.5 mcg and Buprenorphine 30 mcg. Final concentration of Bupivacaine was 0.125% Drugs aspirated with the help of insulin syringe. All agents were introduced intrathecally and total volume of agents administered was 1 ml. Demographic variables like age, weight, height and gestation age were recorded from the case sheet.

Duration of analgesia or pain relief was taken as time after spinal injection to time of rescue analgesic administered or VAS was more than 40. Study ended at 240 minutes but duration of analgesia for episiotomy pain was considered even after delivery and data collected from sister's record.

Study tool- In order to compare the data and to draw conclusions; the mean and standard deviation of heart rate, Bromage scale and duration of analgesia were calculated.

Consent Type- Informed consent

Statistical Analysis- Data will be consolidated and entered a Microsoft Excel spreadsheet and then transferred to Epi info version (7.1.3.0. centre for disease control and prevention, Atlanta, Georgia, USA, 2013) software for analysis. student t- test was used.

Results

Table 1: Comparison of baseline characteristics of the two study groups.

Characteristics	Group A	Group B	p Value
Age (Years) (Mean + SD)	27. 73 + 6.8	27.33 + 6.3	p = 0.31
Weight (kgs) (Mean + SD)	67.0 + 12	61.8 + 10.8	p = 0.15
Height (cms) (Mean + SD)	153 + 3.3	156 + 5.1	p = 0.09
Gestational Age (Weeks) (Mean + SD)	39.6 + 1.0	39.2 + 1.3	p = 0.23

As per table 1 there was no significant difference in age, weight, height and gestational age between two groups (p > 0.05). Though weight, age and Gestational age was higher among Group A compared to B.

Table 2: Mean time of duration of Analgesia in Group A and Group B.

	Group A	Group B	p Value
On set of Analgesia in Minutes.	5.793 + 1.66	5.16 + 1.34	0.756
Duration of Analgesia (Minutes)	148.06 + 15.56	328.06 + 28.56	0.000

As per table 2 there was significant change in duration of analgesia in both the groups (p<0.001. It was 148.06 (± 15.56) minutes in group A, were as 328.06 (+ 28.56) minutes in group B. However, quality of analgesia was same in both the groups.

Table 3: Mean pulse rate between Group A and Group B

Time after Intrathecal Injection (Minutes)	Mean Pulse Rate + SD		p Value
	Group A	Group B	
T0	99.60 + 12.12	86.00 + 7.47	0.001
T2	96.66 + 13.17	87.40 + 8.07	0.028
T4	94.53 + 12.08	87.07 + 9.91	0.075
T6	89.47 + 10.37	85.80 + 9.81	0.359
T8	85.73 + 12.26	81.40 + 10.91	0.315
T10	84.00 + 14.36	81.33 + 11.51	0.663
T20	84.93 + 14.56	82.33 + 13.40	0.615
T30	86.40 + 12.88	81.73 + 8.39	0.249
T40	87.00 + 12.67	81.13 + 5.77	0.114
T60	89.20 + 10.08	80.80 + 5.95	0.010
T90	92.93 + 10.69	80.33 + 8.14	0.001
T120	93.33 + 11.51	79.53 + 8.11	0.001
T150	94.53 + 11.48	79.57 + 8.47	0.000
T180	94.93 + 9.79	78.80 + 9.58	0.000
T210	96.27+ 8.58	80.53 + 10.155	0.000
T240	103.7 + 9.16	81.80 + 9.79	0.000

Mean pulse rate was compared between Group A and Group B at different time interval after intrathecal injection. At 0 minutes and 2 minutes P value was <0.05 – significant. At 4,6,8,10,20,30 and 40 minutes after intrathecal injection, p value > 0.05 – not significant. At 60,90,120,150,180,210 and 240 minutes after intrathecal injection, p value <0.05 – significant.

As per figure 1 Mean APGAR score at 1 min and 5 minutes was higher in Group A and was found to be significant. (p<0.05).

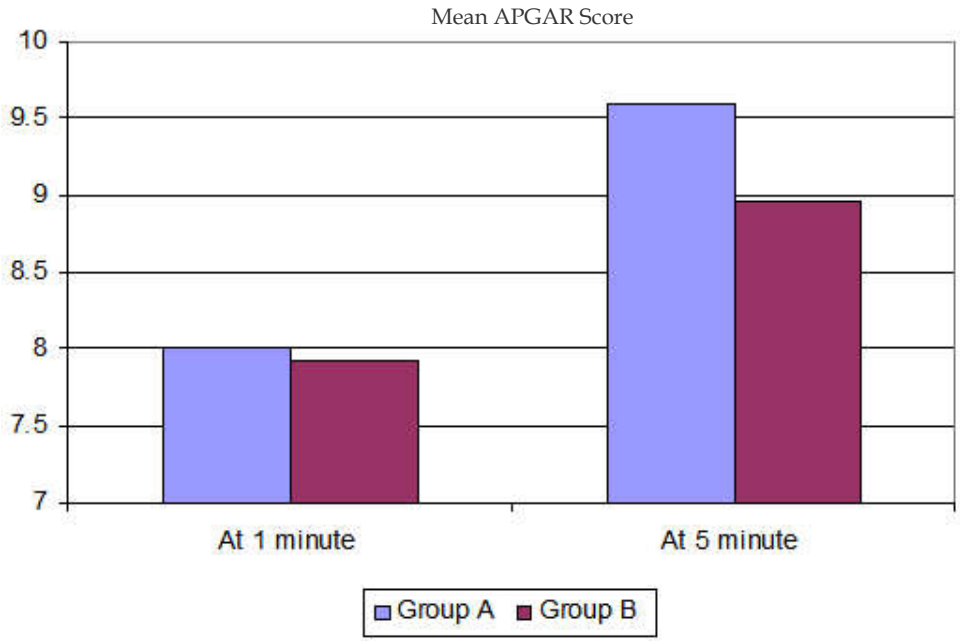

Fig. 1: Mean APGAR score

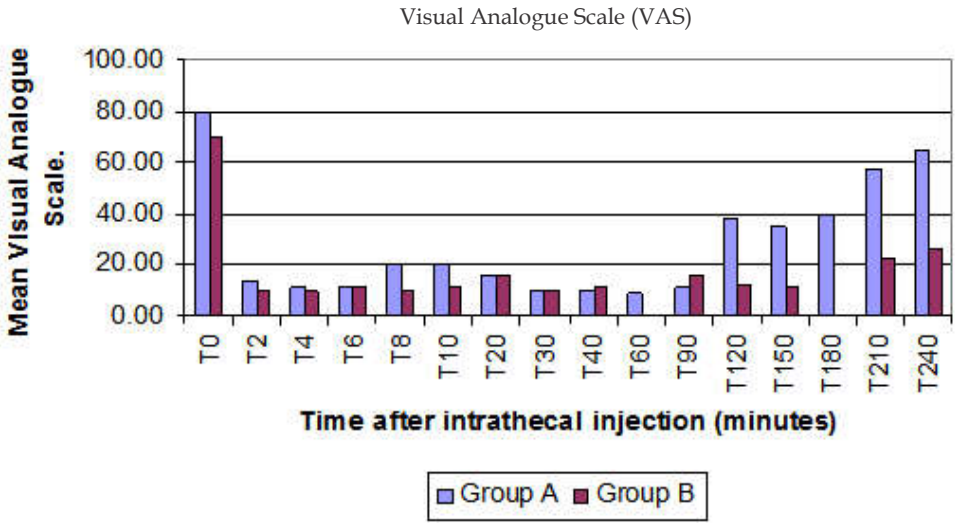

Fig. 2: Mean VAS among the groups

In figure 2 mean visual analogue scale after intrathecal injection was significantly higher in group A as compared to group B in different duration. At T_0, VAS was between 70 to 80. But within 2 minutes of intrathecal injection, VAS reduced significantly to around 20 in both the groups. VAS was between 16 to 20 in both the groups till 90 minutes of intrathecal injection.

Discussion

Intrathecal administration of opioids for labour analgesia is becoming increasingly popular because of potential savings in cost and manpower [4]. Intrathecal morphine provides prolonged analgesia, but is associated with increased risk of nausea, vomiting, pruritus and respiratory depression [7]. Short acting narcotics like fentanyl and sufentanyl have been shown to provide adequate pain relief, but of short duration [8]. Buprenorphine, a mu receptor agonist with low intrinsic activity can also be administered safely in the subarachnoid space [9]. It has a high molecular weight and lipophilicity which may prevent its rostral spread. When used intrathecally in combination with bupivacaine, it has improved the quality and duration of analgesia compared to bupivacaine alone [10]. Very few studies are done using intrathecal buprenorphine for labour analgesia. But more studies have been done using intrathecal buprenorphine for post-operative analgesia. In the present study there was no significant difference in demographic and anthropometric variables like age, height, weight and gestational age. Among the vital parameters only pulse rate was recorded in both the groups at the time intervals. As parturients were in pain, basal pulse rate was high in both the groups, but after giving intrathecal injection, within 5 to 6 minutes Pulse rate came down by 8-10 beats/ min. This was probably due to pain relief. After 90 minutes pulse rate started increasing in group A Whereas it was stable in Group B. There was no significant difference in number of partutients experiencing fall in pulse rate in both Group A and Group B. This study is consistent with the study done by Fauzia A Khan *et al.* [11]. Where it was found that there was no incidence of fall in heart rate in either groups. There was significant change in duration of analgesia in both the groups ($p < 0.001$). It was 148.06 (±15.56) minutes in group A, were as 328.06 (+28.56) minutes in group B. However, quality of analgesia was same in both the groups [4]. Parturients in Group A required rescue analgesics versus only one in Group B. This was consistant with the study done by Fauzia A Khan *et al.* [11], were the duration of sensory block was significantly longer in buprenorphine – bupivacaine group. The mean time from spinal injection to the first requirement of analgesia was 534 + 35 min in Fentanyl group and 834 ± 59 min ($p < 0.01$) in buprenorphine group. 6 patients in buprenophine group did not require any analgesic for 24 hrs (study period). There was no difference in neonatal APGAR score among the groups. However according to studies done by Zap J [12], significant differences were seen. At T_0, VAS was between 70 to 80. But with in 2 minutes of intrathecal injection, VAS reduced significantly to around 20 in both the groups. VAS was between 16 to 20 in both the groups till 90 minutes of intrathecal injection. But after that the number in group A started increasing and that of in group B was which is like the study

conducted by Lestie [1].

Conclusion

The present study was performed to evaluate the efficacy of intrathecal buprenorphine for pain relief during labour. Addition of buprenorphine to intrathecal fentanyl and bupivacaine provides early onset and prolonged duration of analgesia during labour.

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References

1. Neil G. Lestie, Intrathecal narcotics for labour analgesia: The poor man's epidural, GJRM. 2005; 5(4):226-29.
2. Edward RD, Hansel N K, Pruessner H T, Barton B, Intrathecal Morphine as analgesia for labour pain. J AM Board fam pract. 1988;1(4);245-50.
3. Stephens M B, Ford R E. Intrathecal narcotics for labour analgesia A M fam physician. 1997;56(2):463 -70.
4. Rust LA, Waring RW, Hall GL, Nelson EL, Intrathecal narcotics for obstetrics analgesia in a community hospital AM J ObstelGynecol. 1994; 170(6):1643-46.
5. Practice guideline for obstetrical anaesthesia. A report by the American Society of anaesthesiologist Task Force on Obstetrical anaesthesia. Anaesthesiology. 1999;90(2):600-11.
6. Kazuhiko Fukuda, Ronald D Miller. Intravenous opioid analgesics. Millers Anaesthesia, 6th edition 2005.p.418-19.
7. Chaney M A. Side effects of intrathecal and epidural opioid can J Anaesthesia. 1995;42:891-903.
8. Fournier R, Van Gessel F, Weber A, Gamulin Z. A comparison of intrathecal analgesia with fentanyl or sufentanyl in hip replacement. AnesthAnalg 2000;90:918-22.
9. Cousins JM, Bridenbough PO. Spinal narcotics and pain relief in acute care, In cousins MJ, Philips JD, EDS. Acute pain management New York; Churchill Livingstone, 1986.pp.156-7.
10. Celleno D, Capogna G, Tagariello V, Loffreda – Maniculli C. Intrathecal buprenorphine for post-operative analgesia in the elderly patient. Anaesthesia. 1988;43:128-30.
11. Fauzia A Khan, Gauhar A Hamadi. Comparison of intrathecal fentanyl and buprenorphine in urological surgery. JPMA. 2006 Jun;56(6):277-81.
12. Zap J, Thorne T. Comfortable labour with intrathecal narcotics mill med. 1995;160(5):217–9.

Original Research Article

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A Comparative Study of Hyperbaric Ropivacaine (0.5% in Glucose 5%) with Hyperbaric Bupivacaine (0.5% in Glucose 8%) for Spinal Anaesthesia for Lower Abdominal Surgery

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Abstract

Background: Spinal anaesthesia is well established technique in which several local anaesthetic drugs are used. These drugs have their own advantages and disadvantages regarding safety profile, onset and duration of action. The continuous search is going on to find safer drugs with having lesser side effects. *Material and Method:* This study was planned with an aim to compare Ropivacaine 0.5% in 5% glucose solution with the commercially available Bupivacaine 0.5% in glucose 8% (heavy) given in spinal anaesthesia regarding stability; onset and duration of sensory block; onset and duration of motor block and associated side effects like nausea/vomiting and pruritus. This was a prospective randomized double blind clinical control trial in which total 80 patients of either sex were enrolled and divided into two groups (Group A-Ropivacaine and Group B- Bupivacaine) using envelope method. *Data Analysis:* Data of both the groups were recorded and compared statistically. To compare the means, independent t-test was applied and to compare categorical data chi-square test was used. *Result:* As a result of the study it was found that hemodynamic parameters were comparable in both the groups; Onset of sensory as well as motor block were faster in the Bupivacaine group; total duration of motor block and sensory block was shorter in Ropivacaine group; time taken for mobilization was significantly lesser in Ropivacaine group; side effects like nausea/vomiting were also less in Ropivacaine group. *Conclusion:* It can be concluded that Ropivacaine 0.5% in 5% glucose is a good alternate to Bupivacaine heavy in short duration lower abdominal surgeries with shorter sensory and motor block duration and lesser incidence of adverse effects.

Keyword: Hyperbaric Ropivacaine; Spinal Anesthesia; Bupivacaine; Lower abdominal surgery.

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Introduction

Spinal Anaesthesia/Subarachnoid block is a commonly used technique in various types of surgeries. This technique was first performed by August Von Bier in 1898 [1]. Gradually ithas become one amongst the commonest procedures performed in the field of anesthesiology. It has successfully been used in lower abdominal and lower limb surgeries. Various aspects of Sub arachnoid block

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have been studied and experimented, especially in the aspect of basic physiology, clinical application and drug pharmacology. Spinal anesthesia causes profound nerve block in the lower part of body unless the drug blocks the cephalad segments by spreading through cerebrospinal fluid (CSF). This is associated with exaggerated fall in blood pressure and prolonged effect of spinal anaesthesia.

Since more than thirty years the most commonly used drug for spinal anesthesia in clinical practice is Bupivacaine but it is has many systemic adverse effects like- cardiovascular toxicity, central nervous system toxicity and muscular weakness. So there was a large scope and need ofcontinuous search for newer and safer local anesthetic agents in recent years [2]. That search has led to the introduction of newer drugs like levobupivacaine (s enantiomer of Bupivacaine) and Ropivacaine. Both of them have lower systemic toxicity.

Ropivacaine, s-enantiomer of a newer amidehas been evaluated in adults and older children in many studies [3]. In previous studies it has been found that Ropivacaine causes reduced cardiovascular and neurological toxicity [4,5]. Ropivacaine is less lipophilic and that's why unable to penetrate thick myelinated neurons, which supply muscles. This is the reason that it has differential effect on motor neurons. It selectively inhibits Aδ and C fibers (which transmit pain) than motor Aβ fibers [6]. It is extensively metabolized in liver by cytochrome P450 and very less amount of it getsexcreted out unchanged [7]. Recently, it has been used in adults for spinal anesthesiaand various studies have been reported regarding its clinical efficacy and safety. Ropivacaine has now been established in clinical use as sensory block for many purposes like-local infiltration, peripheral nerve block, and lumber epidural block and is a long acting local anesthetic which gives surgical anesthesia of good quality [8]. Ropivacaine is well known local anaesthetic drug which is tolerated very well regardless of the route through which it is administered. In previous studies Ropivacaineand Bupivacaine both were used by intrathecal route. It was found that duration of action of Ropivacainewas found to be short and thus making it a possible alternative for short day care surgeries. It has shown to be little less potent than Bupivacaine [9].

Europian union in February 2004 approved Ropivacaine for its use in spinal anesthesia. The issue regarding baricity of drug remained less addressed. Some studies have shown that adding glucose into the drug make it hyperbaric and a more predictable spread helps to decrease the side effects like episodes of hypertension, bradycardia and respiratory difficulties [10]. In the current study hyperbaric solution of Ropivacaine was compared with hyperbaric Bupivacaine for its clinical efficacy and side effects while giving subarachnoid block in lower abdominal surgeries.

Materials and Methods

After institutional ethical committee clearance, 80 patients posted for lower abdominal surgeries were registered in the study. All the registered patients were between age group of 20 to 60 years, belonging to ASA grade I, II and either sex. Patients of ASA grade III and above, having coagulopathy, shock, sepsis, anatomic deformities of spine, local skin infections on site of injection, with increased intra cranial pressure, patients on potent antiplatelet drugs and known allergy to the drugs used in the study; were excluded.

All the enrolled patients undergone thorough pre anesthetic checkup. All the routine investigations were done as per need and informed written consent was taken.

The patients were randomly distributed into two groups of 40 patients each with the help of envelope method. The spinal anaesthesia during the surgery was given by one anesthetist and data was recorded by another anesthetist (blind to the grouping and treatment of patients).

Group 1 (Ropivacaine group): Received 3 ml of 0.5% hyperbaric Ropivacaine in glucose 5% intrathecally.

Here 0.5% Ropivacaine in 5% glucose was prepared by mixing 2 ml 0.75% Ropivacaine in 1 ml of 15% glucose solution.

Group 2 (Bupivacaine group): Received 3 ml of 0.5% hyperbaric Bupivacaine (available commercially) Intrathecally.

Procedure- After taking into operation theatre, all the patients were given spinal anesthesia with 25 G needle after attaching monitors. Every patient was given 10 ml/kg ringer lactate for fluid preloading. Recording of vitals such as Systolic Blood Pressure (SBP), Diastolic blood pressure (DBP), Pulse Rate (PR), Respiratory Rate (RR) and SPO_2 was done at 3 minutes interval in the initial 15 minutes followed by 5 minutes interval upto next 15 minutes and thereafter at 10 minutes interval till end of surgical procedure. Time 0 was considered when intratheal drug was injected.

Sensory block characteristics werecompared for time of onset of sensory effect at T10 level (when

pin prick sensation was lost), time required to attain maximum cephalad spread and time required for sensory regression to L1.

Motor block characteristics were compared using modified Bromage scale regarding time taken to attain grade 3 motor block and total duration of grade 1 motor block.

As per Bromage scale grade 0 was given for no paralysis, grade 1 for Inability to lift outstretched leg, grade 2 for Inability to flex the knees and grade 3 for complete paralysis of lower limbs. If any incidence of hypotension (fall in BP > 20%) noted, Ephedrine 6 mg intravenous was given. Atropine 0.3 mg intravenous was given when heart rate decreased upto less than 50 per minute.

In the postoperative period, time of patient's mobilization and micturition were recorded. The time for analgesia and first requirement of analgesic drug was also noted. 50 mg tramadol was given when visual analogue scale was found > 3. The incidence of following adverse effects- Nausea/ vomiting and pruritus was noted upto 24 hours in this study.

Statistical Analysis- The data collected was entered in Microsoft excel version 2016 after examining the errors and codes. Statistical parameters like mean and standard deviation were used to express quantitative data whereas qualitative data was shown in terms of percentages and proportions. To compare the means, independent t-test was applied and to compare categorical data chi-square test was used. The p-value < 0.05 was considered as significant statistically. Graphs were formed using Excel software while Kaplan-Meier survival analysis curve was drawn using SPSS software version 23. Survival curve was drawn using Log rank test to compare two groups.

Observation and results

No significant difference was found regarding demographic profile and duration of surgery in between the groups (Table 1).

While observing the sensory block characteristics, mean sensory onset time at T 10 and time taken for achieving highest sensory level both were lesser in group 2 than in group 1 (p value=0.00). Regression time of sensory block at the level of L1 was found longer in group 2 in comparison to group 1 and difference was found significant (p value=0.00).

On comparing motor block characteristics, the onset of motor block (Bromage grade 3) was earlier in group 2 than that in group 1 (p value=0.00). The total motor block duration (Bromage grade 1) was found longer in group 2 than in group 1 (p value =0.00).

Mean time taken for mobilization as well as micturition of the patients were significantly lesser in group 1 than in group 2 (p value=0.00) (Table 1, Fig. 1).

Table 1: Comparison of demographic parameters in group 1 and group 2

Parameter	Mean (S.D.) of Group 1	Mean (S.D.) of Group 2	p-value
Age	38.43 (15.03)	36.80 (14.73)	0.63
Weight	62.42 (7.82)	62.23 (6.54)	0.90
Height	155.58 (6.00)	153.70 (5.63)	0.15
Duration of surgery	42.00 (13.21)	50.13 (14.43)	0.01

Table 2: Comparision of perioperative and post-operative measures in Group 1 and 2

Parameter Time (minutes)	Mean (S.D.) Group 1	Mean (S.D.) Group 2	p-value
Time to start of sensory block at T10	5.30	2.48	0.00
Time to highest sensory level	20.07 (1.84)	15.00 (1.19)	0.00
Regression to L1	67.87 (7.67)	110.37 (6.92)	0.00
Onset of motor block (Grade 3)	14.97 (1.54)	10.20 (1.24)	0.00
Duration of motor block (Grade 1)	92.75 (12.45)	230.00 (9.54)	0.00
Time to achieve complete analgesia	88.87 (6.84)	136.75 (11.79)	0.00
Time for rescue analgesia	108.12 (7.22)	155.00 (12.56)	0.00
Time taken to mobilize	231.37 (15.93)	327.87 (14.50)	0.00
Time taken for micturarition	250.12 (15.42)	341.50 (15.15)	0.00

A Kaplan Mierer plot was drawn to show the time of first rescue analgesia. It was 108.12 and 155.00 in group 1 and 2 respectively. The difference was statistically significant (p=0.00). (Figure 5).

The hemodynamic parameters (Pulse rate, Systolic Pressure, Diastolic Pressure) were comparable in both the study groups with p value >0.05. (Tables 3,4,5), (Figs. 2,3,4).

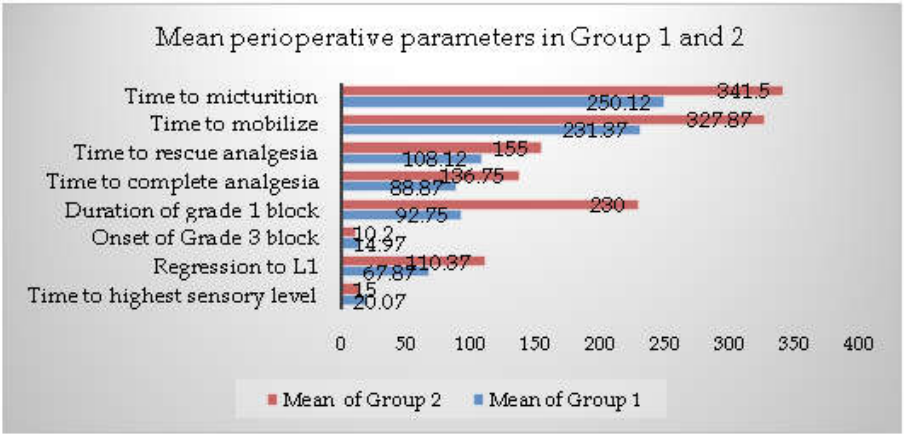

Fig. 1: Comparison of Perioperative measures in group 1 and 2

Table 3: Comparision of mean pulse rate at different time intervals during intraoperative period

Time (minutes)	Mean (S.D.) Pulse rate Group 1	Mean (S.D.) Pulse rate Group 2	p-value
0	85.70 (16.08)	85.95 (15.66)	0.94
3	83.70 (15.25)	81.90 (14.75)	0.59
6	80.30 (14.99)	78.25 (14.32)	0.53
9	79.00 (14.63)	77.80 (13.28)	0.70
12	78.67 (14.08)	77.40 (12.89)	0.67
15	77.90 (12.95)	77.30 (12.72)	0.83
20	77.25 (12.56)	77.05 (13.39)	0.94
25	77.10 (12.24)	77.15 (13.20)	0.98
30	77.13 (12.09)	76.70 (13.16)	0.88
40	77.20 (12.16)	76.25 (12.93)	0.73
50	76.90 (12.25)	75.75 (12.33)	0.67
60	76.85 (12.03)	75.65 (12.34)	0.66
70	77.15 (12.58)	76.10 (12.40)	0.70
80	77.00 (12.69)	76.15 (12.29)	0.76
90	76.68 (12.40)	75.80 (12.17)	0.75

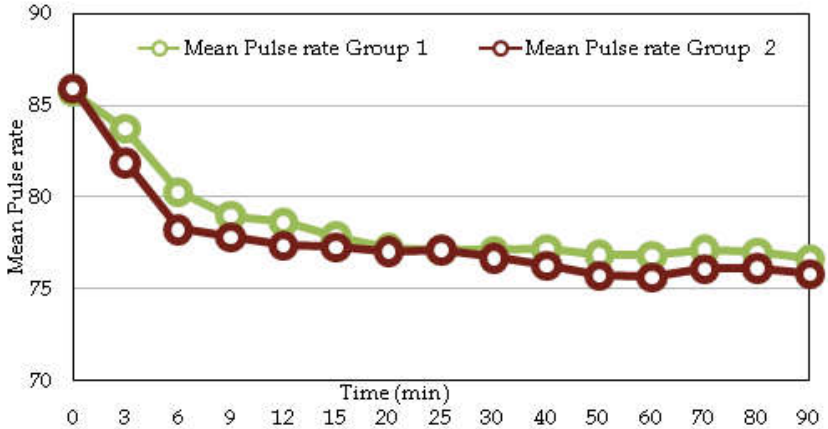

Fig. 2: Comparison of Mean pulse rate of two groups

Adverse effects- Two patients in group 1 experienced nausea/vomiting as compared to 13(32%) patients in group 2, which was statistically significant (p=0.00). No patient in group 1 and only one patient in group 2 showed incidence of pruritus, this difference was found statistically insignificant (p value= 0.50). (Table 6).

Table 4: Comparision of mean (S.D.) systolic blood pressure during intraoperative period

Time (minute)	Mean (S.D.) SBP Group 1	Mean (S.D.)SBP Group 2	p-value
0	122.75 (10.09)	119.45 (17.72)	0.30
3	118.40 (9.45)	117.20 (9.84)	0.58
6	114.45 (9.20)	110.60 (8.96)	0.06
9	112.10 (8.94)	109.80 (9.28)	0.26
12	111.55 (8.15)	110.10 (7.95)	0.42
15	111.15 (7.70)	110.05 (7.15)	0.51
20	111.85 (7.25)	110.05 (6.63)	0.25
25	111.80 (7.59)	110.58 (6.36)	0.43
30	111.10 (7.58)	110.88 (6.19)	0.88
40	111.25 (7.99)	110.80 (5.90)	0.77
50	111.20 (7.52)	110.50 (6.60)	0.66
60	110.83 (6.81)	110.45 (6.50)	0.80
70	111.00 (7.22)	110.98 (6.56)	0.98
80	110.85 (7.62)	111.45 (5.87)	0.74
90	110.68 (6.78)	110.60 (5.17)	0.95

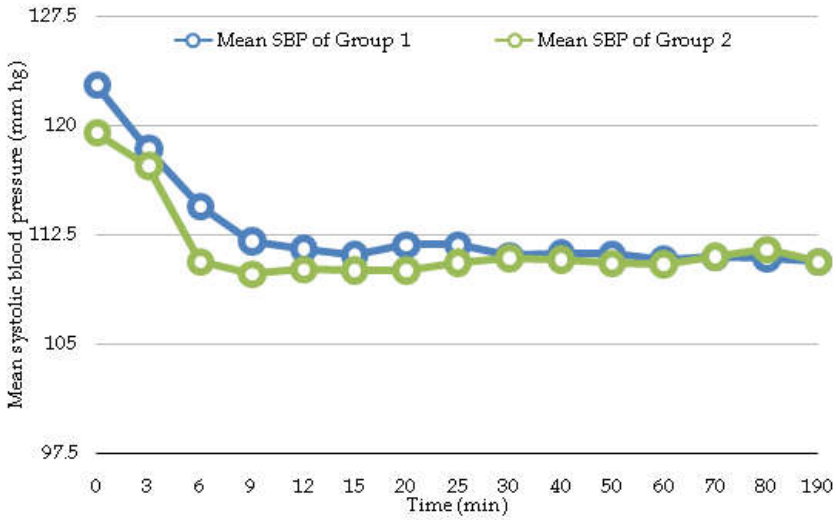

Fig. 3: Comparison of mean Systolic Blood Pressure (SBP) of two groups

Table 5: Comparision of mean (S.D.) diastolic blood pressure during intraoperative period

Time (minute)	Mean (S.D.) DBP of Group 1	Mean (S.D.) DBP of Group 2	p-value
0	76.75 (8.84)	78.70 (9.06)	0.33
3	73.75 (8.55)	72.95 (8.85)	0.68
6	70.45 (9.43)	69.35 (8.28)	0.58
9	68.90 (8.32)	69.50 (7.98)	0.74
12	69.25 (8.42)	69.15 (8.22)	0.96
15	69.48 (7.87)	69.20 (7.90)	0.88
20	69.35 (7.88)	69.40 (8.21)	0.98
30	69.15 (7.74)	69.50 (7.73)	0.84
40	69.30 (8.18)	69.15 (7.90)	0.93
50	69.10 (7.94)	69.10 (7.83)	1
60	69.28 (8.35)	69.00 (7.91)	0.88
70	69.40 (7.80)	69.45 (7.74)	0.97
80	68.75 (8.00)	69.95 (7.99)	0.50
90	68.95 (7.96)	70.00 (8.03)	0.56

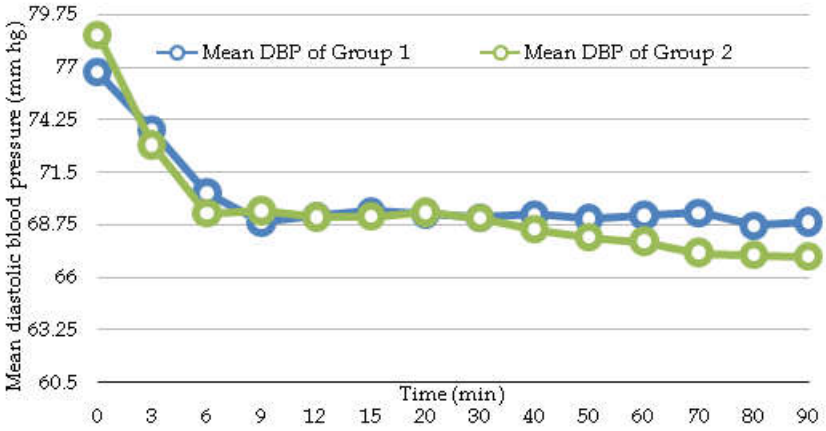

Fig. 4: Comparison of mean Diastolic Blood Pressure (DBP) of two groups

Table 6: Comparison of adverse effects of used drugs in group 1 and group 2

Adverse effect	Group 1 (no of patients)	Group 2 (no of patients)	p value
Nausea/Vomiting	02	13	0.00
Pruritus	00	01	0.50

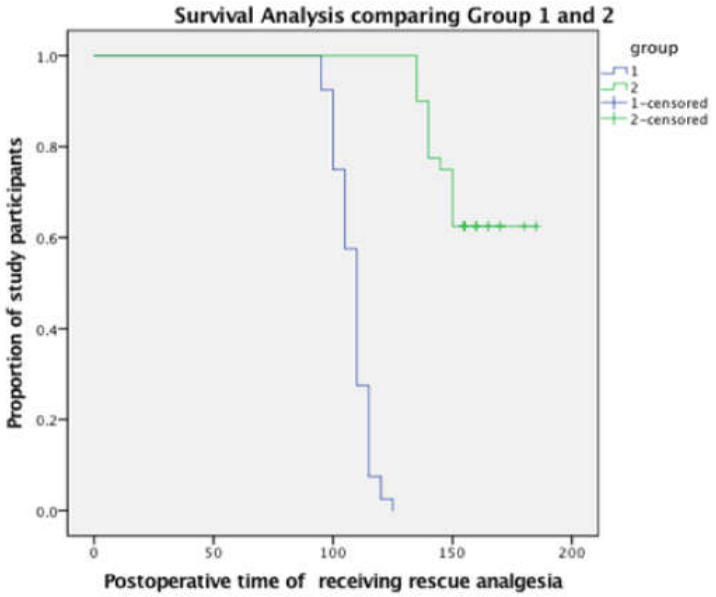

Fig. 5: Kaplin–meirer plot showing postoperative time of receiving rescue analgesia

Discussion

Role of Ropivacaine is well established when used in local infiltarion and epidural anesthesia, yet its role in spinal anaesthesia is continuously under scrutiny. In the present study hyperbaric solution was prepared by adding 5% glucose into Ropivacaine. Various studies have shown that addition of dextrose or glucose in local anaesthetic makes it heavy in comparison to cerebrospinal fluid [11]. Thus it helps local anesthetic to not spread in the cephalad spinal segments and reduces the side effects of high spinal block such as hypotension and nausea/vomiting.

The present study has shown that Ropivacaine group shows faster regression of sensory block. Thus it can be said that Ropivacaine can be a reliable option for short surgeries when given via intrathecal route. This fact was already been established in a previous study by Whiteside et al where they also concluded that the time for recovery with Ropivacaine was found less [12].

In Bupivacaine group the onset of motor blockgrade 3 was found earlier while the duration

of motor block grade 1 as well as the time taken for the mobilization was found longer. On the other hand in Ropivacaine group; onset of motor block grade 3 was late but duration of motor block grade 1 was shorter. The most interesting fact is that the time for mobilization and micturition was significantly shorter in Ropivacaine group. Thus it can be inferred that for day care short procedures Ropivacaine can be a good choice.

The hemodynamic parameters of two groups like pulse rate, mean systolic pressure and mean diastolic blood pressure were found comparable. This fact coresponds a previous study done by J.F. Luck who reported similar hemodynamic profile in Ropivacaine group where hyperbaric solutions of racemic Bupivacaine, Ropivacaine and Levobupivacaine were compared in spinal anaesthesia for caeserean section [13].

No analgesic drug was given as premedication in any of the groups. So it can be presumed that the drug used in spinal anaestheia were the sole reason for producing sensory analgesia in each group. It was seen that Bupivacaine produces analgesia for a longer time than Ropivacaine. This explains the early requirement of rescue analgesic drug in Ropivacaine group. This can also be understood by the early sensory regression in Ropivacaine group, which can be responsible for early onset of pain in postoperative period.

Ropivacaine group shows lower incidence of nausea, vomiting and pruritus. This can also be explained by shorter duration of sensoryas well as motor block by Ropivacaine. However the incidence of adverse effects was very small, so larger trials are needed to further verify the fact.

Conclusion

This study verifies that hyperbaric solution of both drugs Bupivacaine and Ropivacaine produce anaesthesia of good quality in which lower abdominal procedures of short duration can be performed. Ropivacaine is especially suitable for short day care procedures as time of mobilization, micturition is shorter and incidence of adverse effects is less. However larger sample size studies are required to establish the facts.

References

1. Geoffrey B. Rushman, N.J.H. Davies, Richard Stuart Atkinson. A Short History of Anaesthesia- the first 150 years. Butterworth-Heinemann. 1996.p.145.
2. De Beer DA, Thomas ML. Caudal additives in children—solutions or problems? Br J. Anaesth. 2003;90:487-98.
3. Markham *et al.* Ropivacaine. A review of its pharmacology and therapeutic use in regional anaesthesia. Drugs. 1996 Sep;52(3):429-49.
4. Habre W, Bergesio R, Johnson C, *et al.* Pharmacokinetics of ropivacaine following caudal analgesia in children. Pediatr Anesth. 2000;10:143-7.
5. McClure JH. Ropivacaine: An excellent historical, pharmacological and clinical review article. Br J. Anaesth. 1996;76:300-09.
6. Hansen TG. Ropivacaine: A pharmacological review. Expert Rev Neurother, 2004;4:781-91.
7. Ekstrom G, Gunnarsson VB. Ropivacaine: a new amide-type local anesthetic agent is metabolized by cytochromes P450 lA and 3A in human liver microsomes. Drug Metab Dispos. 1996;24:955-61.
8. Gautier *et al.* Intrathecal ropivacaine for ambulatory: a comparison between intrathecal bupivacaine and intrathecal ropivacaine for knee arthroscopy. Anesthesiology. 1999;91:1239-45.
9. Simpson D. Curran MP. Oldfield V. Keating GM. Ropivacaine: A review of its use in regional anaesthesia and acute pain management. Drugs. 2005;65:2675-717.
10. Kalpana R Kulkarni, Sunetra Deshpande and Konark Kondilya. A comparative evaluation of hyperbaric ropivacaine versus hyperbaric bupivacaine or elective surgery under spinal anaesthesia. Journal of Anaesthesiology and Clinical Pharmacology: 2014;30:238-42.
11. Bannister J, McClure JH, Wildsmith JA. Effect of glucose concentration on the intrathecal spread of 0.5% bupivacaine. Br J. Anaesth. 1990;64:232-4.
12. Whiteside JB, Burke D, Wildsmith JA. Spinal anaesthesia with ropivacaine 5 mg ml (-1) in glucose 10 mg ml (-1) or 50 mg ml (-1). Br J. Anaesth. 2001;86:241-4.
13. J.F. Luck, P.D.W. Fettes and J.A.W. Wildsmith. Spinal anaesthesia for elective surgery: a comparison of hyperbaric solutions of racemic bupivacaine, levobupivacaine, and ropivacaine. Br J. Anaesth. 2008;101:705-10.

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Effectiveness of Preoperative Audiovisual Information in Reducing Patient Anxiety about Spinal Anaesthesia: A Randomized Controlled Study

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Abstract

Aims: A high incidence of anxiety about anesthetic procedure is seen in patients undergoing surgical procedures, which can be related to their unawareness about anaesthesia and anaesthetist's role in perioperative care. we aimed at assessing the effectiveness of a simple informative audiovisual clip as preoperative educational tool in reducing the anxiety in patients undergoing surgical procedures under spinal anaesthesia. *Methods:* A prospective randomized study involving 200 patients undergoing surgery under spinal anaesthesia was conducted. 2 groups with 100 patients in each group were formed and named as group AV (those who were shown audiovisual clip) and group NV (patients in this group were not shown the audiovisual clip). Anxiety scores were assessed using the spielberger state - trait anxiety inventory at both preoperative visit and just before the surgery. Hydrodynamic parameters like Heart rate and mean arterial pressures were recorded. Appropriate statistical tests were applied for analysis of the obtained data. *Results:* Baseline anxiety scores and hemodynamic parameters were comparable in both the groups. Compared to AV group the patients in NV group showed statistically significant rise in anxiety scores when measured before the spinal anaesthesia ($p < 0.001$). Hemodynamic parameters were stable in AV group when compared to NV group ($p < 0.001$). Patients in AV group showed statistically significant decrease in anxiety scores from baseline values, when measured just before the spinal anaesthesia. *Conclusion:* Preoperative education in the form of informative audiovisual clip is effective in reducing patient anxiety about spinal anaesthesia.

Keywords: Anxiety; Audiovisual clip; Spinal anaesthesia; Spielberger state - trait anxiety inventory.

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Introduction

Significant number of patients (incidence of 60%-80% reported by many observers [1,2]) undergoing surgical procedures experience anxiety. Anxiety by increasing the levels of corticosteroids and stimulating sympathetic nervous system can lead to many undesirable effects like intraoperative hemodynamic disturbances, increased requirements of analgesics, prolongation of

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hospital stay and overall dissatisfaction about their perioperative course [3].

Because of short period of contact with the patients not much of information can be given to them and many a times patients will not understand whatever is explained to them due to many constraints.

Many methods of communication have been used to convey the relevant information to the patients about the perioperative care. one page information handout by Fitzgerald and elder 4, explaining about anaesthesia and common worries about the surgery and anaesthesia was a successful trial with significant reduction (40%) of preoperative anxiety. Others have studied the beneficial effects of video based information on reducing the anxiety scores [5,6]. We assumed that a audiovisual clip depicting the usual course of perioperative care from the time of patient's admission till discharge, including the preoperative visit, preoperative perperation, spinal anaesthesia procedure, intraoperative and postoperative care will be better understood and remembered by the patients.

We intended to develop a simple informative audiovisual clip of about 3 minutes, in locally spoken Kannada language and study the impact of the same in reducing the anxiety scores and hemodynamic stability. A well known psychological tool Spielberger State Trait Anxiety Inventory (STAI) was used to assess the baseline anxiety scores and scores before giving spinal anaesthesia.

Methods

After obtaining institutional ethical committee approval, we conducted this prospective randomized controlled study involving 200 patients divided into two groups of 100 each, who were posted for elective surgery under spinal anaesthesia. ASA I and II class Patients aged 18-60 years of either sex and those who could read Kannada or English language and able to complete the questionnaires were included in the study. Patients who were not willing to participate in the study, patients with significant Co-morbidity and those who underwent surgery under spinal anaesthesia were excluded from the study. Selected patients were enrolled for the study during pre anaesthetic visit a day before the surgery and a written informed consent for participation was taken. By using computerized table they were divided into two groups, group NV (Non Video) and group AV (Audio Visual) of 100 each. Group allocation was kept confidential by maintaining a sealed opaque covers and both patients and investigator were blinded till baseline anxiety scores were recorded. During preanaesthetic check up baseline vitals like Heart rate (HR) and mean arterial pressures (MAP) were recorded. Patients were given 2 questionnaires (STAI -T and STAI -S) containing 20 questions each in local Kannada language and they were explained about filling it. principal investigator assessed the baseline anxiety scores from the completed questionnaires. Then they were taken to a room where their group identity was revealed by another investigator after opening the allotment cover. Group NV patients were explained about the perioperative events, spinal anaesthesia procedure, it's effects, side effects and possible complications verbally and were asked to clarify the doubts if any.

Patients of AV group were taken to audiovisual room and were shown a audiovisual clip in Kannada language explaining the perioperative events, spinal anaesthesia procedure, it's effects, side effects and possible complications and the events were elobarated verbally also. Again patients were asked to clarify doubts if any and patients of both groups were ensured that qualified anaesthesiologist will take care of them during intraoperative and postoperative period.

On the day of surgery, STAI-S was repeated before taking the patients inside the operation theatre Main investigator conducted this assessment in preoperative waiting room, patients of both groups were given STAI -S questionnaire and were asked to fill the form after reading questions carefully. After completion of questionnaire, NBM status of patients confirmed and patients were taken inside the operation theatre.

Standard monitoring devices like electrocardiography, pulse oxymetry, and NIBP were applied and pre SAB (Sub Arachnid Block) vitals like Heart rate and mean arterial pressures were recorded. Intravenous fluids started after securing intravenous cannula of appropriate size. Patients were seated in sitting position, parts painted, draped and spinal anaesthesia was given at appropriate level using appropriate sized spinal needles and appropriate dose of 0.5% of bupivacaine. This spinal anaesthesia procedure was conducted by another anaesthetist not knowing the patient's group identity. Intraoperative monitoring done and after completion of surgery, patients were shifted to appropriate postoperative area for monitoring.

Specially developed audiovisual clip shown to patients of AV group consisted of all important

perioperative events in easily understandable manner. It begins with patient's admission and consists of preoperative visit to Anaesthetist, recording of vitals, entry into the operation theatre, application of monitors, securing intravenous lines, painting of back, draping under aseptic precautions, palpation of landmark, administration of local anaesthesia, lumbar puncture and injection of spinal drug. After assessing the adequate sensory and motor block positioning for surgery done. It also included the model postoperative care and discharge of patients to home. All these events were elobarated in local Kannada language.

For sample size estimation we referred to a similar study by Jlala *et al.* [3] who reported a prevalence of anxiety by STAI -S in low anxiety group (STAI <37) to be 58% among preoperative video group and 38% in patients of non video group. With type I error at 5% level of significance and 80% power of study, sample size of 98 in each group was obtained and to round off it was made to 100 patients in each group. Data was expressed in standard units like Mean ± standard deviation (SD) and percentage. Quantitative data was compared using student's t -test, when values were normally distributed. Mann-Whitney U test was used when values were nonnormally distributed. For categorical values, Chi-Square test was used. p value less than 0.05 was considered statistically significant.

Results

All the 200 participants enrolled for the study participated in the study completely and submitted the questionnaires back. Both the groups were comparable with respect to age, sex, ASA physical status classification and technical procedures undertaken inside the operation theatre (Table 1).

Basal anxiety scores of both the groups measured using A -Trait and A- State at enrollment for the study during pre anaesthetic visit were comparable.

Compared to group NV, patients of AV group showed statistically significant reduction in the anxiety scores at Pre -SAB assessment (Table 1 and Fig. 1).

Our secondary aim of the study was to assess the variation in hemodynamic parameters and baseline heart rate (HR) and mean arterial pressures (MAP) were comparable in both the groups. Patients of group AV showed 3.6% increase in mean heart rate from basal levels to pre spinal anaesthesia level. Mean heart rate was 85.20 ± 9.12 at preanaesthetic check up and raised to 88.12 ± 6.1 when measured just before the spinal anaesthesia procedure. However group NV patients showed statistically significant ($p < 0.05$) increase in mean heart rate from 86.80 ± 8.20 at pre anaesthetic visit to 104.82 ± 10.20 when measured during pre spinal anaesthesia procedure (Table 1 and Fig. 3). Increase in mean arterial pressures (MAP) from basal levels to pre spinal anaesthesia level was also statistically significant ($p < 0.05$) in NV group compared to AV group. Baseline mean arterial pressure was 94.16 ± 6.21 in NV group which increased to 116.71 ± 8.92 at pre spinal anaesthesia level, amounting to an increase by 22% from baseline values. Change in the mean arterial pressure in AV group was not statistically significant, which increased from

Table 1:

Parameter	Group NV	Group AV
Age (Years mean ± SD)	36.17 ± 10.92	37.08 ± 10.54
Gender (Male:Female)	54:46	49:51
ASA status (1/2)	70/30	68/32
STAI-T (mean ± SD)	54.12 ± 10.21	53.16 ± 10.56
Baseline STAI-S (mean ± SD)	55.30 ± 9.26	56.24 ± 9.27
STAI-S pre SAB (mean ± SD)	61.82 ± 10.12	52.12 ± 9.40
Baseline HR (mean ± SD)	86.80 ± 8.20	85.20 ± 9.12
HR pre SAB (mean ± SD)	104.82 ± 10.20	88.12 ± 6.4
Baseline MAP (mean ± SD	94.16 ± 6.21	101.76 ± 8.21
MAP pre SAB (mean ± SD)	116.71 ± 8.92	102.17 ± 9.24

Table 2:

Degree of Anxiety	Baseline		Pre SAB %	
	Group NV	Group AV	Group NV	Group AV
Low anxiety (STAI-S: 20-37)	5	13	2	10
Moderate anxiety (STAI-S:38-44)	12	16	5	28
High anxiety (STAI-S : 45-80)	83	81	93	62

101.76 ± 8.21 at baseline level to 102.17 ± 9.24 at pre spinal anaesthesia level, a mere increase of only 2% (Table 1, Fig. 2) suggesting a stable hemodynamic status.

STAI scores are usually divided into three categories (Table 1) as high anxiety (45-80), moderate anxiety (38-44) and no or low anxiety (20-37) based on the computed scores from the questionnaire containing 20 questions with answers expressed in 1-4 points for each question. When the prevalence of different degrees of anxiety was looked into, baseline anxiety scores in each of the no or low, moderate and high anxiety scores, both the groups were comparable with no statistically significant difference. High anxiety was prevalent in 83% of the patients in NV group compared to 81% among AV group. When the same high anxiety prevalence was calculated at pre spinal anaesthesia procedure level it was 93% in NV group compared to 62% in AV group, with a significant statistical difference (Table 2).

Females showed high prevalence (Table 3) of anxiety both at basal levels and pre spinal anaesthesia procedure level compared to males (Table 3). STAI-T and STAI-S were significantly less in males compared to females ($p < 0.05$). At pre spinal anaesthesia level also females had statistically significant increase in STAI-S scores compared to males ($p < 0.05$).

Table 3:

Anxiety score	Male	Female	p value
STAI-T	42.26 ± 9.02	55.18 ± 9.08	<0.001
STAI-S			
Baseline	43.86 ± 8.0	59.26 ± 7.6	<0.001
Pre- SAB	45.82 ± 7.0	61.34 ± 8.26	<0.001

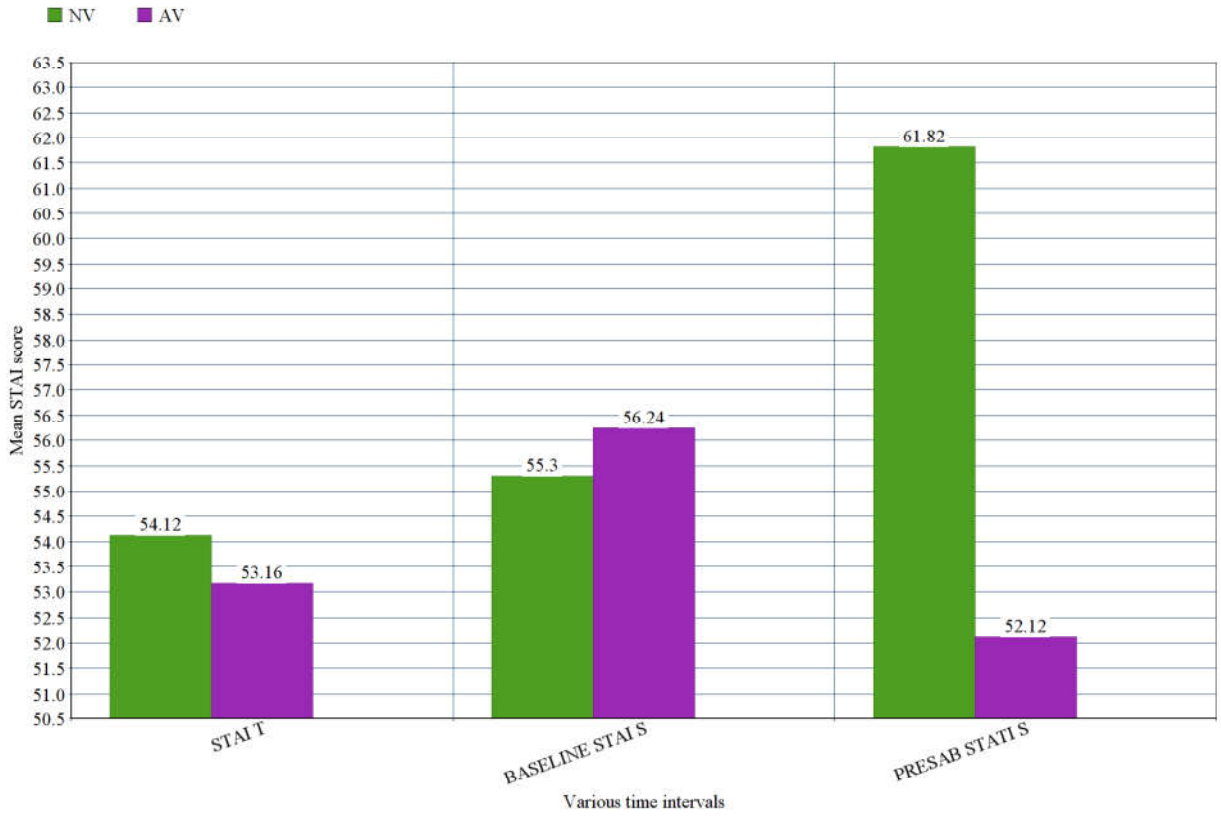

Fig. 1:

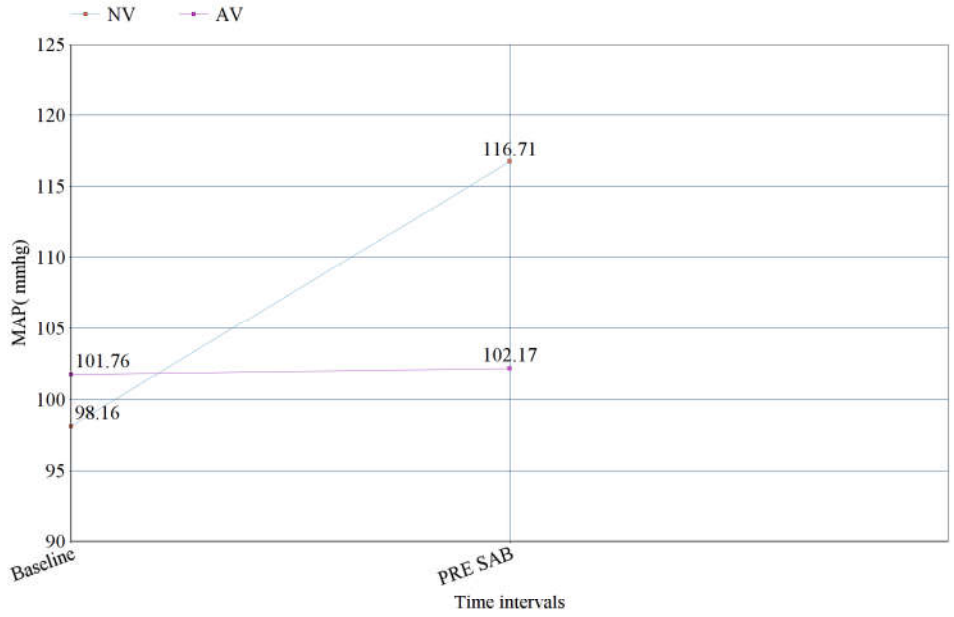

Fig. 2:

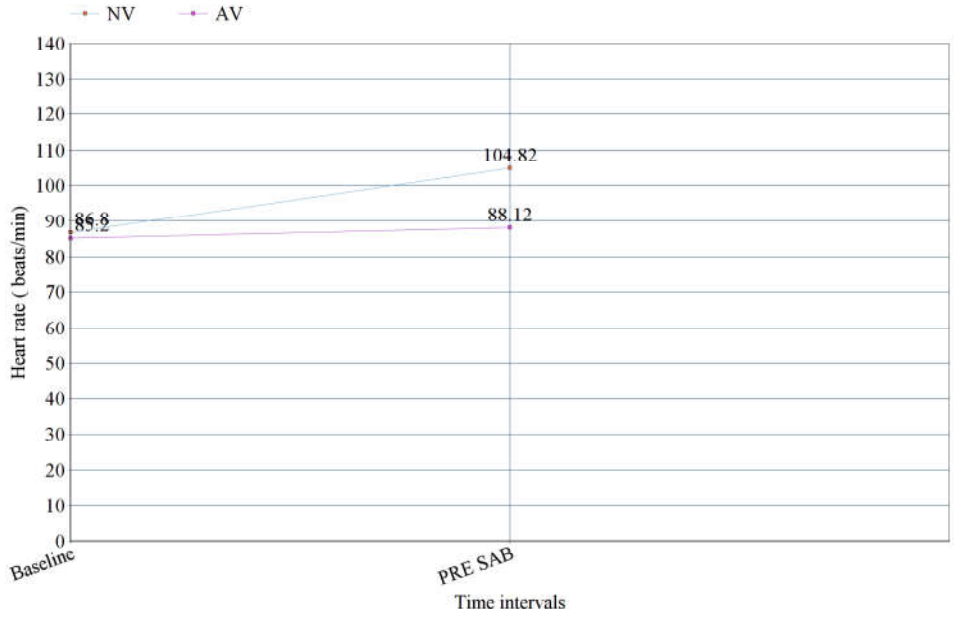

Fig. 3:

Discussion

Our study demonstrated that preoperative educational tool like audiovisual clip is effective in reducing patient anxiety. Reduction in the anxiety scores at the pre spinal anaesthesia level compared to basal values was statistically significant in those who saw the audiovisual clip and there was a similar statistically significant increase in the anxiety scores in those who didn't see it. This useful effect of the audiovisual clip can be related to It's specific effect or to the more quantity of preoperative educational information about the perioperative events. This is in accordance with the study done by Jlala HA *et al.*, who studied the effect of multimedia information on perioperative anxiety in patients undergoing procedures under regional anaesthesia [3], where they noticed reduction in the anxiety scores at pre anaesthesia procedure level and it was observed to be effective in the post operative period also. Similarly many international researchers have

studied the beneficial effects of such pre operative educational tools [4-8]. Due to limitations like illiteracy and complex structure of STAI in evaluation of perioperative anxiety, many Indian researchers have used visual analogue scores for the same. Not many studies have been done in our Indian setting and moreover we wanted to study the local population many of whom are not able to read the brochure materials and cannot search for it in the internet. Our present study revealed that female population had more anxiety scores both at basal and pre spinal anaesthesia level indicating the higher prevalence of anxiety in that group and also highlights the need for education focussing more on them through the possible educational portals. And when compared to other studies done outside the india [3], Indian studies revealed higher prevalence of anxiety overall. Above observations of higher prevalence of anxiety in females and among overall population points at importance of focusing more on health related education.

There was also a better hemodynamic stability following the use of audiovisual clip, which can be attributed to the reduction in the anxiety which in turn reduces the activation of hypothalamo pitutary axis and consequently decreased adrenocorticotrophin release and less cortisol levels. Finally there is reduced activation of sympathetic nervous system and evidently stable hemodynamic parameters.

We concluded from the present study that preoperative educational information in the form of audiovisual clip, is an effective way of reducing perioperative anxiety. We also concluded that routine use of such educational system can reduce patient discomfort about hospital stay and it can increase patient satisfaction.

Limitations of our study included, not focusing on the completely illiterate population which forms major section of population in our setting. Also we could not differentiate the anxiety related to surgery from the anxiety related to anaesthesia. Future scope of this study includes extending the follow up till sufficient time to evaluate the effects of such preoperative educational tool in reducing the incidence of postoperative stress disorder and also effect on the long term psychological behavior.

Conclusion

We concluded from the present study that preoperative educational information in the form of audiovisual clip, is an effective way of reducing perioperative anxiety. We also concluded that routine use of such educational system can reduce patient discomfort about hospital stay and it can increase patient satisfaction.

Conflicts of interest: nil

References

1. Norris W, Baird WL. Pre-operative anxiety: A study of the incidence and aetiology. Br J Anaesth 1967;39:503-9.
2. Shevde K, Panagopoulos G. A survey of 800 patients' knowledge, attitudes, and concerns regarding anesthesia. Anesth Analg. 1991;73:190-8.
3. Jlala HA, French JL, Foxall GL, Hardman JG, Bedforth NM. Effect of preoperative multimedia information on perioperative anxiety in patients undergoing procedures under regional anaesthesia. Br J Anaesth. 2010;104:369-74.
4. Doering S, Katzlberger F, Rumpold G, Roessler S, Hofstoetter B, Schatz DS, *et al.* Videotape preparation of patients before hip replacement surgery reduces stress. Psychosom Med 2000;62:365-73.
5. Crowe J, Henderson J. Pre-arthroplasty rehabilitation is effective in reducing hospital stay. Can J Occup Ther 2003;70:88-96.
6. Lee A, Gin T. Educating patients about anaesthesia: Effect of various modes on patients' knowledge, anxiety and satisfaction. Curr Opin Anaesthesiol 2005;18:205-8.
7. Ruffinengo C, Versino E, Renga G. Effectiveness of an informative video on reducing anxiety levels in patients undergoing elective coronarography: An RCT. Eur J Cardiovasc Nurs 2009;8:57-61.
8. Cassady JF Jr, Wysocki TT, Miller KM, Cancel DD, Izenberg N. Use of a preanesthetic video for facilitation of parental education and anxiolysis before pediatric ambulatory surgery. Anesth Analg 1999;88:246-50.
9. Graeff FG, Zangrossi H Jr. The hypothalamic-pituitary-adrenal axis in anxiety and panic. Psychol Neurosci 2010;3:3-8.

Original Research Article

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Proseal Laryngeal Mask Airway: An Alternative to Endotracheal Intubation in Adult Patients for Surgical Procedures Under General Anaesthesia

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Abstract

Introduction: An endotracheal tube always considered to be the gold standard to maintain an airway because of its inherent ability to provide positive pressure ventilation [1,2]. Haemodynamic responses, situations of failed intubation, unable to ventilate and unable to intubate are also a serious concern. With the advent of newer supraglottic airway devices, these drawbacks of tracheal tube are avoided. The Proseal laryngeal mask is a new laryngeal mask device with a cuff modified to improve the seal around glottis and a drainage tube to provide for aspiration of gastric contents. The aim of our study was to compare efficacy and safety of Proseal Laryngeal Mask Airway with portex cuffed endotracheal tube in patients undergoing surgeries under general anaesthesia. *Aim and Objectives:* To compare efficacy and safety of Proseal Laryngeal Mask Airway with Portex cuffed endotracheal intubation in sixty adult patients undergoing surgeries under general anaesthesia. *Results:* Both groups were comparable with respect to their demographic characteristics. Time taken for insertion in group P and group E was similar. The study participants where Proseal LMA was used had a statistically significant lower rates of HR, SBP, DBP and MAP, at 1, 3, 5, 10 mins and after removal of device than participants in whom endotracheal tube was used. Side effects were lower in group P than group E. *Conclusion:* Proseal LMA is suitable and safe alternative to endotracheal tube for airway management.

Keywords: Proseal Laryngeal Mask; Laryngoscopy; Intubation; Endotracheal tube.

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Introduction

An endotracheal tube always considered to be the gold standard to maintain an airway because of its inherent ability to provide positive pressure ventilation [1,2].

The major cause of sympatho-adrenal response to tracheal intubation is due to the stimulation of supraglottic region by tissue irritation induced by direct laryngoscopy.

Haemodynamic responses, situations of failed intubation, unable to ventilate and unable to

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intubate are also a serious concern. This precludes the global utility of the tracheal tube and asks for better alternatives. With the advent of newer supraglottic airway devices, these drawbacks of tracheal tube are avoided. Maintenance of a patent airway remains an important concern of an anaesthesiologist [3].

The first supraglottic airway device The Laryngeal Mask Airway was designed in 1981 by Dr. Archie Brain. Though it was highly satisfactory device in securing airway, its lacunae with positive pressure ventilation, especially in patients with obesity and decreased pulmonary compliance prompted him further to find a better airway device. This led him to design and develop the Proseal LMA. The proseal LMA was introduced by Dr. Archie Brain in 2000 [4].

The Proseal laryngeal mask is a new laryngeal mask device with a cuff modified to improve seal around glottis and a drainage tube to provide for aspiration of regurgitated gastric contents and prevent gastric insufflation. These features are designed to improve the safety of the mask and broaden its scope, especially when used with positive pressure ventilation. Proseal LMA is less invasive device and considered to cause less stress response [2,5,6].

The aim of our study was to compare efficacy and safety of Proseal Laryngeal Mask Airway with portex cuffed endotracheal tube in patients undergoing surgeries under general anaesthesia.

Material and Methods

Type of Study: Prospective randomized comparative study.

Sample size: 60.

Proseal Laryngeal Mask Airway (Group P) – 30.

Endotracheal tube (Group E) – 30.

Method of Randomization: After approval from hospital research and ethics committee, a prospective, randomized, comparative study was conducted on adult patients undergoing surgeries under general anaesthesia. Randomization was done using a computer generated random number table. Sample size was calculated using Winpepi software with confidance interval of 95% and power of study 80%. Minimum sample size calculated was 12, 6 in each group. For detailed study purpose, we took sample size 60, 30 in each group.

The study was conducted on 60 adult patients cases randomly divided into two groups of 30 each.

Group P: Proseal laryngeal mask airway was used.

Group E: Endotracheal tube was used.

Pre Operative Evaluation

All patients were thoroughly evaluated pre-operatively. All the necessary and relevant laboratory and other investigations were carried out. In the pre-operative room, the patient's pulse, blood pressure and heart rate was taken, with the patient lying comfortably in supine position.

Anaesthesia Procedure

During pre-anaesthetic assessment, a detailed history and examination of each patient was carried out to optimize them prior to surgery. All the patients were kept fasting for 8 hours. In the operating room, all monitors were attached to patients, pulse oximeter, ECG and non-invasive blood pressure cuff. A wide bore 20G intravenous line established. Intra-operatively end tidal carbon dioxide ($ETCO_2$) was monitored.

The patients were pre-medicated with intravenous Glycopyrrolate 0.004 mg/kg, Ondansetron 0.1 mg/kg, Midazolam 0.02 mg/kg, Pentazocine 0.3 mg/kg. General anaesthesia was induced with Propofol 2 mg/kg and Vecuronium 0.1 mg/kg. After induction, appropriate size of PLMA was used in P group and appropriate size portex ETT was used in E group. Anaesthesia was maintained with isoflurane in 60% N_2O / 40% O_2 mixture. Controlled mechanical ventilation was applied to maintain end tidal CO_2 between 30-40 mm of Hg.

Correct placement of PLMA or ET tube was indicated by normal thoraco-abdominal movements, bilaterally equal audible breath sounds on auscultation and regular waveform capnograph. Along with this, specific tests for correct placement of PLMA are no audible leak from the drain tube with peak airway pressure less than 20 cm of H_2O, gel displacement test, insertion of nasogastric tube and aspiration of gastric contents. Gastric tube of number 12 or 14 was inserted through a drain tube. Two attempts were allowed before gastric tube insertion was considered a failure and repositioning of PLMA was done. Haemodynamic responses pulse rate, systolic blood pressure, diastolic blood pressure, mean arterial pressure were recorded prior to induction, 1 min, 3 min, 5 min and 10 min after endotracheal intubation or PLMA insertion, and after removal of ETT or PLMA. After procedure reversal was done by using Inj. Neostigmine

0.05 mg/kg and Inj. Glycopyrrolate 0.008 mg/kg. Postoperative observations were done.

Clinical Parameters Monitored

1. Monitoring were done for following parameters:
2. Time taken for insertion of PLMA or ETT.
3. Ease of insertion of PLMA or ETT.
4. Attempts taken for insertion of Ryle's tube.
5. Time taken for insertion of Ryle's tube.
6. Haemodynamic changes after laryngoscopy and intubation or after insertion of PLMA and removal of device:
   - Heart rate monitoring.
   - Blood pressure monitoring (S.B.P, D.B.P, Mean B.P)
   - Oxygen saturation
   - $EtCO_2$
7. Perioperative complications
   - Cough
   - Laryngospasm
   - Bronchospasm
   - Blood on device
   - Aspiration
   - Hoarseness/sore throat

Statistical Analysis

All cases were completed in 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 variate] with 95% level of significance. A p – value < 0.05 was considered statistically significant.

- Results were statistically analyzed,
- Quantitative data was analyzed by paired and unpaired t test.
- Qualitative data was analyzed by chi square test.

Results

Both groups were comparable with respect to their demographic characteristics. Time taken for insertion in group P and group E was similar.

The study participants where Proseal LMA was used had a statistically significant lower rates of heart rate, systolic blood pressure, diastolic blood pressure and mean arterial pressure, at 1, 3, 5, 10 mins than the participants in whom endotracheal tube was used. These rates for group P remained lower than group E after removal of airway device.

There was no significant difference in SpO_2 and $EtCO_2$ in both the groups at 1 min, 3 mins, 5 mins, 10 mins after insertion of device and after removal of device.

Side effects such as cough, sore throat and blood on device were seen in both groups. Group E had more patients with cough and sore throat than group P, difference was statistically significant. Group P had more patients with blood on device than group E, this difference was also statistically significant.

Table 1: Distribution of different procedures

Type of Surgery	No of Cases Group P	No of Cases Group E
Diagnostic Hysterolaparoscopy	5	6
MTP with Tubal ligation	5	5
Fibroadenoma Excision	8	9
Breast abcess Incision and drainage	1	2
CRIF with K wire radius fracture	3	
Contracture release of right little finger	1	1
Dilatation and curettage with polypectomy	1	1
Diagnostic laparoscopy	3	2
Laparoscopic Tubal Ligation	3	3
Excision of lipoma over arm		1
Total	30	30

Table 2: Groups

Group P (n=30)	Proseal LMA
Group E (n=30)	Endotracheal tube

Discussion

Airway management is a fundamental aspect of anaesthetic practice and of emergency and critical care medicine. Traditionally, laryngoscopy and endotracheal intubation has been the mainstay in safeguarding the airway in patients. It is rapid, safe and non-surgical technique that achieves all the goals of airway management. Intubation has its own advantages such as prevention of aspiration and delivery of anaesthetic gases, leak free ventilation during mechanical ventilation and remains the gold standard procedure for airway management. Despite of advantages of endotracheal intubation it has its own complications [7]. Laryngoscopy and endotracheal intubation are noxious stimuli capable of producing a huge spectrum of stress responses such as tachycardia, hypertension, bronchospasm, raised intracranial pressure and intraocular pressure [8].

The haemodynamic changes brought about by laryngoscopy and intubation was first described by Reid and Brace [9]. The haemodynamic response is initiated within seconds of direct laryngoscopy and further increases with the passage of the endotracheal tube. The response is initiated within 5 s of laryngoscopy, peaks in 1–2 min and returns to normal levels by 5 min [10]. These changes are usually short lived and well tolerated by normal patients. In patients with cardiovascular disease, it can incite harmful effects such as myocardial ischaemia, ventricular dysrhythmias, ventricular failure and pulmonary oedema. It can also lead to cerebrovascular accidents in cerebrovascular disease patients [11]. This precludes global utility of the tracheal tube and asks for better alternative. With advent of newer supra-glottic airway devices these drawbacks of tracheal tube are avoided.

The Proseal Laryngeal Mask Airway is a new laryngeal mask device with a cuff modified to improve seal around glottis and a drainage tube to provide a bypass channel for regurgitated gastric contents, prevent gastric insufflation and allow the passage of a gastric tube. The features are designed to improve the safety of the mask and broaden its scope, especially when used with positive pressure ventilation [12].

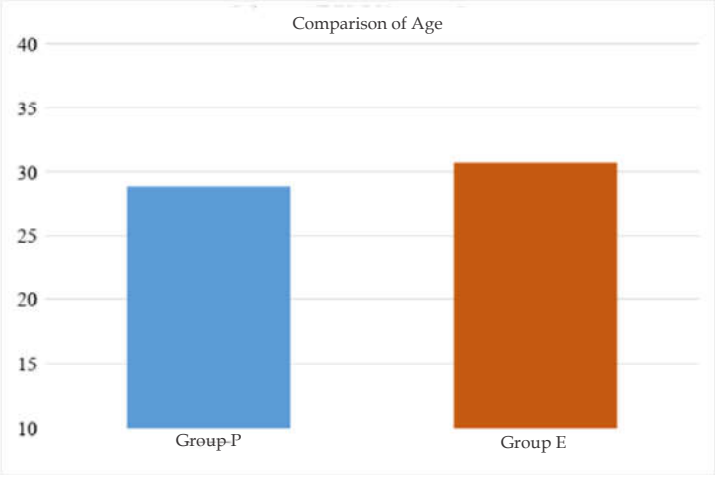
In this study we aimed to compare efficacy and safety of Proseal Laryngeal Mask Airway with Portex cuffed endotracheal intubation in adult patients undergoing surgeries under general anaesthesia.

Table 3: Gender Distribution

	Group P		Group E	
	No of Cases	**Percentage**	**No of Cases**	**Percentage**
Male	8	26.6%	5	16.6%
Female	22	73.3%	25	83.4%
Total	30	100%	30	100%

Table 4: Comparison of Age between two groups

Parameter	Group P (Mean ± SD)	Group E (Mean ± SD)	p-value
Mean Age (years)	28.8 ± 5.07	31.6 ± 6.26	0.08



Graph 1: Comparison of Age between two groups

Patient Characteristics across the groups

Both groups were similar in terms of age, gender, weight, ASA grading as shown in Table 3,4,5 and 6. Average duration of surgery was similar in both the groups, as shown in Table 7.

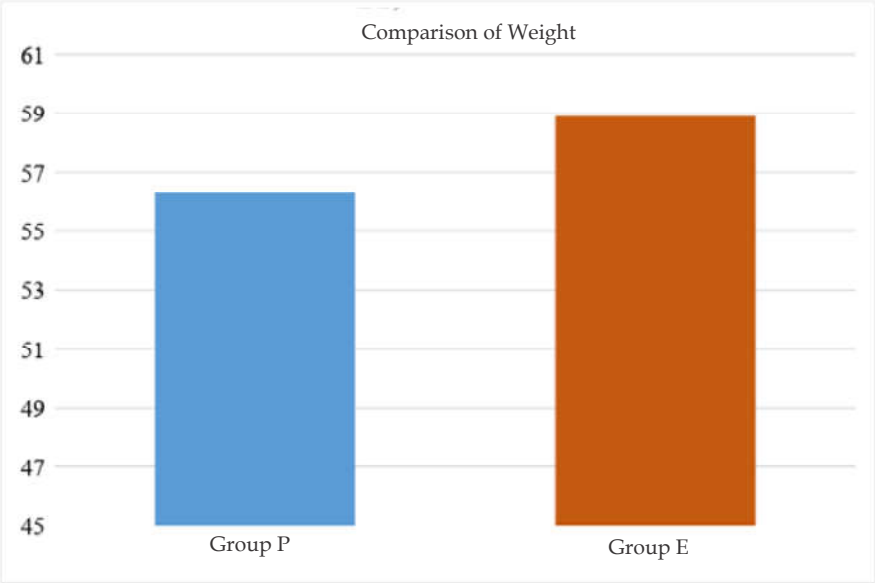
Insertion characteristics of device

Insertion rate was 100% for both groups. P group had 93.33% first attempt success at insertion and eventually 100% at the end of two attempts. In our study in Group P only 2 patients required second attempt for insertion. In Group E, all patients were intubated in first attempt as shown in Table 8.

In 2007, M Misra, B Ramamurthy conducted a study The Pro-seal LMAtm and tracheal tube: A comparison of events at insertion of the airway device. They found similar results as our study.

Table 5: Comparison of weight between two groups.

Parameter	Group P (Mean ± SD)	Group E (Mean ± SD)	p-value
Mean Weight (Kg)	56.3 ± 5.89	58.9 ± 6.20	0.1



Graph 2: Comparison of weight between two groups

Table 6: ASA Grade distribution

No of subjects	Group P	Group E
ASA Grade I	23	25
ASA Grade II	7	5

Table 7: Comparison of duration of surgery between two groups.

	Group P (Mean ± SD)	Group E (Mean ± SD)	p value
Duration of surgery (min)	42.3 ± 12.50	42.6 ± 10.56	0.9

Table 8: Insertion of Device

	Group P	Group E	p value
No. of attempts of insertion	I = 28 patients II = 2 patients	I = 30 patients	-
Time taken for insertion (seconds)	15.4 ± 2.87	15.9 ± 4.68	0.6
Time taken for RT insertion (seconds)	10.16 ± 1.89	12 ± 1.7	0.0001
No. of attempts taken for RT insertion (1/2/3/failed)	27/3/0	20/7/3/0	-

Group P had 88% first attempt success at insertion. This steadily rose to 98% at second attempt and eventually 100% at the end of three attempts [2].

Brimacombe J *et al.* have compared different techniques of PLMA insertion. Though the purpose of their study was different from ours, the observation in terms of first time success rate at insertion of PS-LMA by introducer tool technique and the number of attempts for successful airway attainment coincide with our study [13].

Time taken for insertion of device in Group P was 15.4 ± 2.87 seconds and in group E was 15.9 ± 4.68 seconds as shown in table 8. There were no statistically significant differences between two groups. (p-value > 0.05).

Sharma B, Sahai C *et al.* conducted a study Proseal Laryngeal Mask Airway: A study of 100 consecutive cases of Laparoscopic surgery. They found that mean time taken for the placement of the device was 13.51 seconds and range (5-33) seconds. Results were comparable to our study [14].

Shroff P, Kamath S conducted a study between the Proseal LMA and Endotracheal intubation for laparoscopic surgery and reported mean time for insertion of PLMA and ETT were 15 seconds and ETT 26 seconds respectively. Time taken for insertion of PLMA was comparable, but time taken for ETT insertion in our study was different [5].

Insertion characteristics of Ryle's tube

Mean time taken for insertion of Ryle's tube was 10 seconds in group P while it was 12 seconds group E. Similarly, the success rate of Ryle's tube in the first attempt was higher (90%) via Proseal than via nasal route in intubated patients (66.67%) with endotracheal intubation.

Namazi IJ, Garia N, Kumar RB *et al.* compared Proseal laryngeal mask airway and endotracheal tube in patients undergoing laproscopic surgeries under general anaesthesia. They reported the mean insertion time taken to insert NGT through PLMA was significantly less (9.4 seconds) than via nose (11.3 seconds) in intubated patients. Similarly success rate of NGT in the first attempt was higher via Proseal than via nasal route in intubated patients with endotracheal intubation [15].

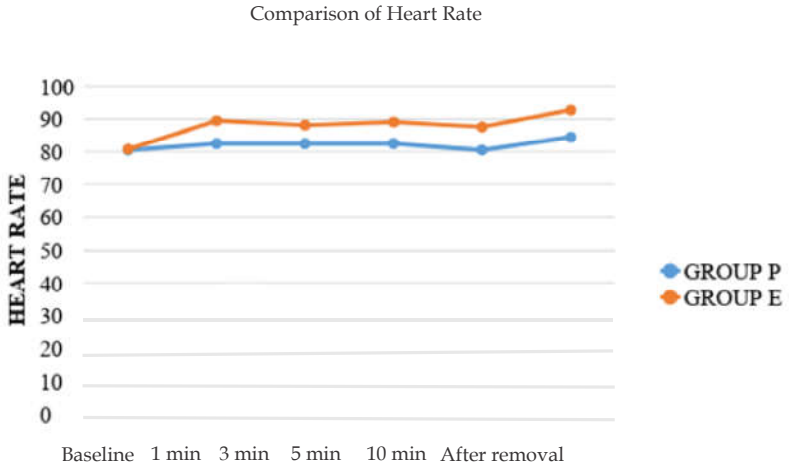
Comparison of Vital Parameters

Comparison of heart rate between two groups

As shown in Table 9 and Graph 3 The mean pulse rate in group P increased from baseline value 80.5 ± 6.13/min to 82.5 ± 5.51/min over five minutes after insertion. At ten minutes after insertion it returned to baseline value and again increased to 84.5 ± 5.51/ min after removal.

Table 9: Comparison of heart rate between two groups

Heart Rate	Group P Mean ± Sd	Group E Mean ± Sd	p Value	Significance
Baseline	80.5 ± 6.13	80.8 ± 6.13	>0.05	Not Significant
1 Min After Insertion	82.5 ± 5.51	89.5 ± 10.83	<0.05	Significant
3 Min After Insertion	82.5 ± 5.51	88.1 ± 12.46	<0.05	Significant
5 Min After Insertion	82.5 ± 5.51	89.0 ± 10.19	<0.05	Significant
10 Min After Insertion	80.5 ± 5.51	87.5 ± 12.02	<0.05	Significant
After Removal	84.5 ± 5.51	92.8 ± 6.13	<0.05	Significant



Graph 3: Comparison of Heart Rate between two groups

In Group E, mean pulse rate increased from baseline value 80.8 ± 6.13/min to 89.0 ± 10.19/min over five minutes after insertion. At ten minutes there was decrease in pulse rate, but it did not reach to baseline value. Pulse rate again increased to 92.8 ± 6.13/min after removal.

There was significant difference between two groups at 1 min, 3 mins, 5 mins and 10 mins and also after removal of device. Values were relatively lower in group P than group E. The difference between two groups was found to be statistically significant (p value <0.05).

Namazi IJ, Garia N, Kumar RB *et al.* compared Proseal Laryngeal Mask Airway and Endotracheal tube in patients undergoing laproscopic surgeries under general anaesthesia. They reported statistically significant ($p < 0.05$) increase in heart rate and mean blood pressure was observed which persisted till 5 minutes after intubation and during the time of extubation in the group E [15].

Mehta K, Sharma S *et al.* compared Proseal LMA with Endotracheal Intubation in Laparoscopic Tubal Ligation. They evaluated hemodynamic responses were lower for placement than ETT. Mean pulse rate increased from baseline value of 91.06 ± 10.22/min to 96.86 ± 9.13/min and 90.26 ± 10.74/min to 108.53 ± 12.04 after the placement of PLMA and ETT intubation respectively. The mean pulse rate was not changed after removal of PLMA in group [16].

These studies suggested that the increase in heart rate was considerably higher with endotracheal intubation as compared to proseal laryngeal mask airway insertion.

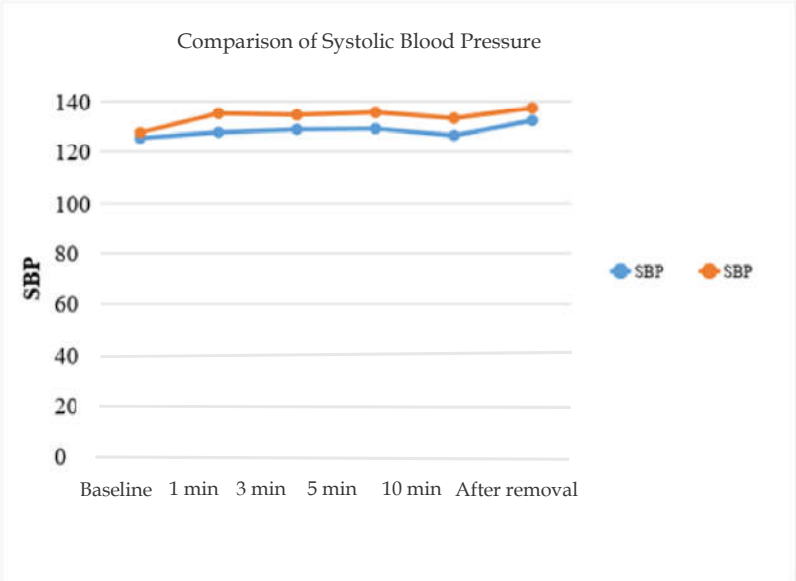
Comparison of Systolic Blood Pressure

As shown in table 10 and graph 4, in group P the systolic blood pressure increased from baseline value of before insertion 125.6 ± 6.08 mm of Hg to 129.4 ± 4.69 mm of Hg over 5 mins after insertion. At 10 mins there was again fall in systolic blood pressure to 126.6 ± 5.73 mm of Hg. And it increased to 132.6 ± 5.15 mm of Hg after removal of device.

In group E the systolic blood pressure increased from baseline value of 127.8 ± 6.67 mm of Hg to 135.8 ± 10.33 mm of Hg over 5 mins after insertion. At 10 mins there was fall in systolic blood pressure

Table 10: Comparison of systolic blood pressure between two groups

Systolic Blood Pressure	Group P Mean ± Sd	Group E Mean ± Sd	p Value	Significance
Baseline	125.6 ± 6.08	127.8 ± 6.67	>0.05	Not Significant
1 Min After Insertion	127.9 ± 5.84	135.46 ± 11.38	<0.05	Significant
3 Min After Insertion	129.1 ± 5.47	134.8 ± 9.04	<0.05	Significant
5 Min After Insertion	129.4 ± 4.69	135.8 ± 10.33	<0.05	Significant
10 Min After Insertion	126.6 ± 5.73	133.5 ± 11.39	<0.05	Significant
After Removal	132.6 ± 5.15	137.4 ± 8.27	<0.05	Significant



Graph 4: Comparison of systolic blood pressure between two groups

to 133.5 ± 11.39 mm of Hg. and it again increased to 137.4 ± 8.27 mm of Hg after extubation.

There was significant difference in systolic blood pressure values after insertion of device at 1 min, 3 mins, 5 mins, 10 mins and after removal of device. Values were relatively lower in group P and difference was found to be statistically significant (p-value <0.05).

Sharma B, Sahai C *et al.*, conducted a study of 100 consecutive cases of laparoscopic surgery. Their results were Pre-induction SBP 125.14 ± 18.89 mm of Hg reached upto 124.56 ± 24.50 mm of Hg at 1 min and 127.11 ± 23.37 mm of Hg at 5 mins after insertion of PLMA (p-value 0.5). They concluded that there were minimum haemodynamic responses to insertion of Proseal Laryngeal Mask Airway [14].

Misra M, Ramamurthy B. compared events at insertion of The Proseal LMA and tracheal tube, they concluded the hemodynamic changes observed were minimal with PLMA while with tracheal tube, significant changes were observed [2].

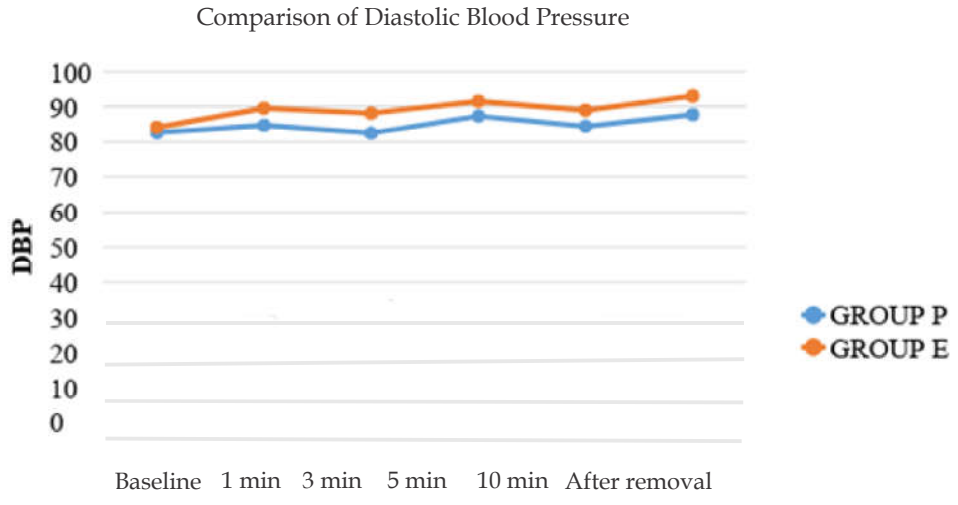
Comparison of Diastolic Blood Pressure

As shown in table 11 and graph 5, the baseline diastolic blood pressure in group P and Group E was 82.6 ± 5.75 mm of Hg and 84.1 ± 6.23 mm of Hg. There was no statistically significant difference. After 1 min of insertion the diastolic BP 84.7 ± 5.64 mm of Hg in group P and 89.5 ± 9.93 mm of Hg in group E. Difference was statistically significant (p-value < 0.05). Similarly there was statistically significant difference in mean diastolic blood pressure between two groups 3 mins, 5 mins and 10 mins after insertion of device. After removal mean diastolic blood pressure in Group P was 87.7 ± 7.53 mm of Hg and in group E 92.9 ± 6.51 mm of Hg. Difference was statistically significant.

Lim Y, Goel S, Brimacombe JR compared PLMA with endotracheal intubation in gynaecological laparoscopy. They concluded haemodynamic responses to placement and removal were lower for PLMA than the TT [17].

Table 11: Comparison of diastolic blood pressure between two groups

Diastolic Blood Pressure	Group P Mean ± Sd	Group E Mean ± Sd	p Value	Significance
Baseline	82.6 ± 5.75	84.1 ± 6.23	>0.05	Not Significant
1 Min After Insertion	84.7 ± 5.64	89.5 ± 9.93	<0.05	Significant
3 Min After Insertion	86.3 ± 5.48	90.1 ± 6.23	<0.05	Significant
5 Min After Insertion	87.3 ± 5.26	91.4 ± 8.20	<0.05	Significant
10 Min After Insertion	84.4 ± 6.02	88.9 ± 9.57	<0.05	Significant
After Removal	87.7 ± 7.53	92.9 ± 6.51	<0.05	Significant



Graph 5: Comparison of Diastolic Blood Pressure between two groups

Comparison of Mean Arterial Pressure

As shown in table 12 and graph 6, the baseline MAP in group P and group E was 82.9 ± 3.86 mm of Hg and 84.5 ± 4.04 mm of Hg. There was statistically significant difference at 1 min, 3 mins, 5 mins and 10 mins after insertion of device. After removal MAP was 87.9 ± 4.97 mm of Hg in group P and 92.4 ± 4.47 mm of Hg in group E. Difference was statistically significant.

Saraswat N, Kumar A *et al.* compared Proseal LMA and Endotracheal tube in patients undergoing laparoscopic surgeries under general anaesthesia. They concluded statistically significant increase in heart rate and mean blood pressure was observed 10 seconds after intubation and persisted till 3 mins after intubation and also during extubation in the ETT group. However statistically significant increase in PLMA group was seen only 10 seconds after insertion [18].

Mehta K, Sharma S *et al.* compared Proseal LMA with Endotracheal Intubation in Laparoscopic Tubal Ligation. They evaluated hemodynamic responses were lower for placement of PLMA than ETT. MAP increased from a baseline value of before insertion 91.02 ± 7.78 to 94.77 ± 8.49 and 90.94 ± 5.67 to 105.72 ± 10.19 after placement of PLMA and ETT and 89.55 ± 6.23 to 90.86 ± 5.86 and 94.08 ± 6.22 to 103.73 ± 6.16 after removal of PLMA and ETT. The increase in MAP was statistically significant in both groups after insertion 5, 10 mins and after removal [16].

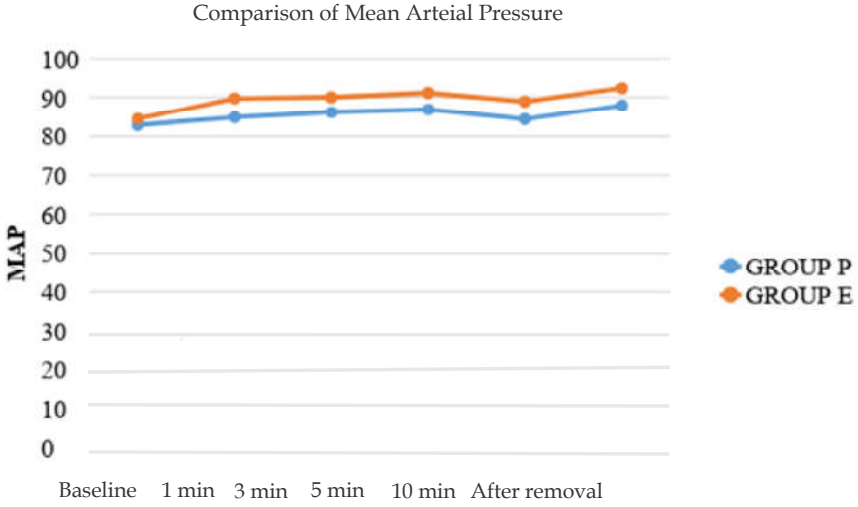
Comparison of End Tidal Carbon Dioxide

As shown in table 13 and graph 7, baseline EtCO2 in group P was 33.3 ± 1.03 and that in group E was 32.2 ± 1.33, there was no statistically significant difference between two groups (p-value > 0.05).

There was no significant difference in $EtCO_2$

Table 12: Comparison of Mean Arterial Pressures between Two Groups

Mean Arterial Pressure	Group P Mean ± Sd	Group E Mean ± Sd	p Value	Significance
Baseline	82.9 ± 3.86	84.5 ± 4.04	>0.05	Not Significant
1 Min After Insertion	84.9 ± 3.86	89.7 ± 6.76	<0.05	Significant
3 Min After Insertion	86.2 ± 3.78	90.0 ± 4.13	<0.05	Significant
5 Min After Insertion	86.9 ± 3.54	91.1 ± 5.69	<0.05	Significant
10 Min After Insertion	84.4 ± 3.96	88.9 ± 6.17	<0.05	Significant
After Removal	87.9 ± 4.97	92.4 ± 4.47	<0.05	Significant



Graph 6: Comparison of Mean Arterial Pressures between Two Groups

Table 13: Comparison of $EtCO_2$ between two groups

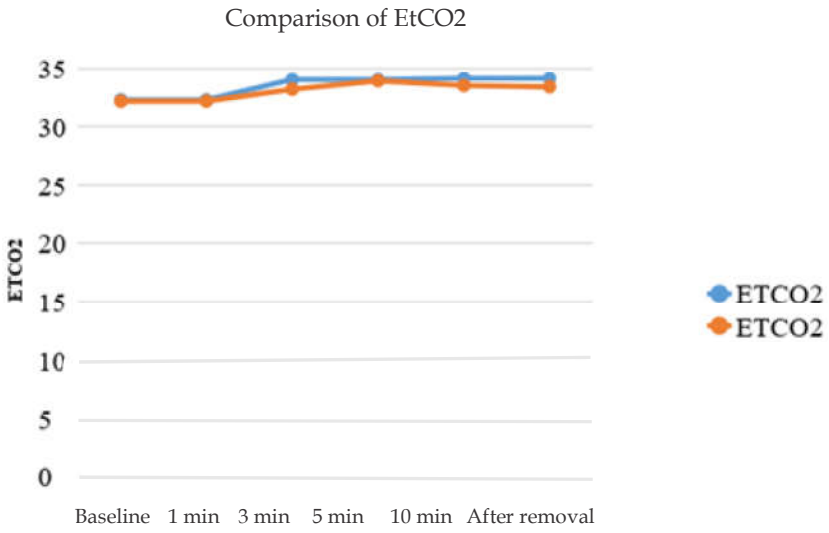
End Tidal Carbondioxide	Group P Mean ± Sd	Group E Mean ± Sd	p Value	Significance
Baseline	33.3 ± 1.03	32.2 ± 1.33	>0.05	Not Significant
1 Min After Insertion	32.3 ± 1.03	32.2 ± 1.60	>0.05	Not Significant
3 Min After Insertion	34 ± 1.23	33.2 ± 2.26	>0.05	Not Significant
5 Min After Insertion	34 ± 1.23	33.9 ± 1.47	>0.05	Not Significant
10 Min After Insertion	34.1 ± 1.25	33.5 ± 1.30	>0.05	Not Significant
After Removal	34.1 ± 1.25	33.4 ± 1.50	>0.05	Not Significant

in both the groups at 1 min, 3 mins, 5 mins and 10 mins after insertion of device and after removal of device.

Comparison of SpO_2

As shown in table 14 and graph 8, Baseline SpO_2 was 99.7 ± 0.7 in group P and group E. There was no statistically significant difference in SpO2 at 1min, 3mins, 5 mins and 10 mins after insertion of device and removal of device.

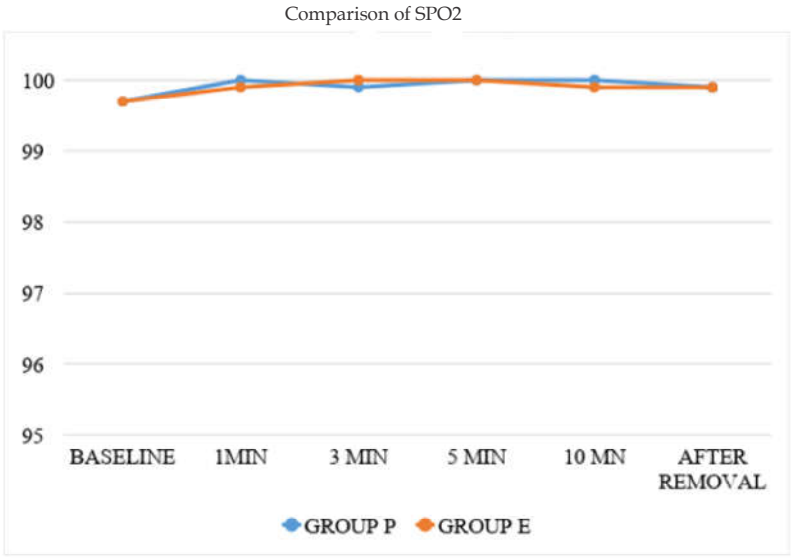
Lalwani J, Dubey KP *et al.* reported there was no significant difference in mean SpO_2 and $EtCO_2$ level recorded at different time intervals between PLMA and ETT groups (p-value >0.05) [19].



Graph 7: Comparison of $EtCO_2$ between two groups

Table 14: Comparison of SpO_2 between two groups

SpO_2	Group P Mean ± Sd	Group E Mean ± Sd	p Value	Significance
Baseline	99.7 ± 0.7	99.7 ± 0.7	>0.05	Not Significant
1 Min After Insertion	100 ± 0	99.9 ± 0.53	>0.05	Not Significant
3 Min After Insertion	99.9 ± 0.53	100 ± 0	>0.05	Not Significant
5 Min After Insertion	100 ± 0	100 ± 0	>0.05	Not Significant
10 Min After Insertion	100 ± 0	99.9 ± 0.53	>0.05	Not Significant
After Removal	99.9 ± 0.53	99.9 ± 0.53	>0.05	Not Significant



Graph 8: Comparison of SpO_2 between two groups

Perioperative complications

As shown in table 15, after extubation there was significant incidence of cough as compared to after removal of PLMA. In group P, only 6% of patients reported cough and in group E 30% of patients reported cough. Difference between two groups was statistically significant (p-value < 0.05).

As shown in table 15, Group E had more patients with sore throat than group P, this difference was statistically significant (p-value < 0.05).

Maltby JR, Beriault MT *et al.* reported that the incidence of cough was higher after endotracheal extubation [20].

Sinha *et al.* also reported that the incidence of cough was higher after endotracheal extubation [21].

Higgins PP, Mezei G *et al.* concluded that patients with tracheal tube had the greatest incidence of sore throat (45.4%) followed by patients with LMA (17.5%) [22].

As shown in table 15, blood on the posterior surface of PLMA was observed in three (10%) patients in group P but in group E only in two (6.66%) cases blood on ET tube was observed after extubation. This difference was statistically significant (p-value < 0.05).

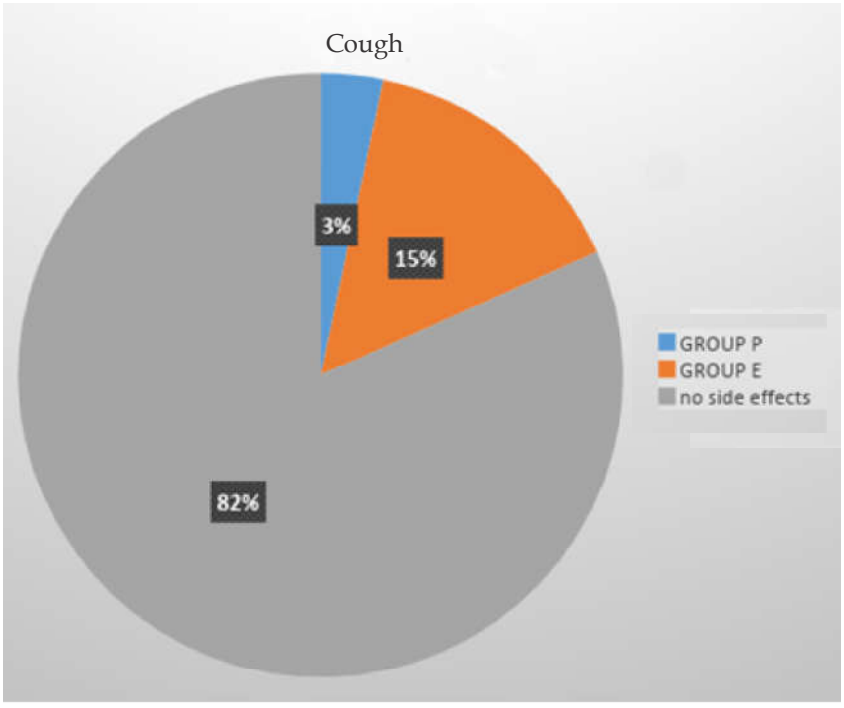
Lim Y, Goel S *et al.* reported 7% incidence of blood staining on PLMA and 6% in ET tube [17].

There was no incidence of aspiration in either group of patients during induction of anaesthesia, intraoperative period or after removal of the respective airway device. Kelly F, Sale S, Lardner D, Cox R *et al.* also reported the similar findings [23,24].

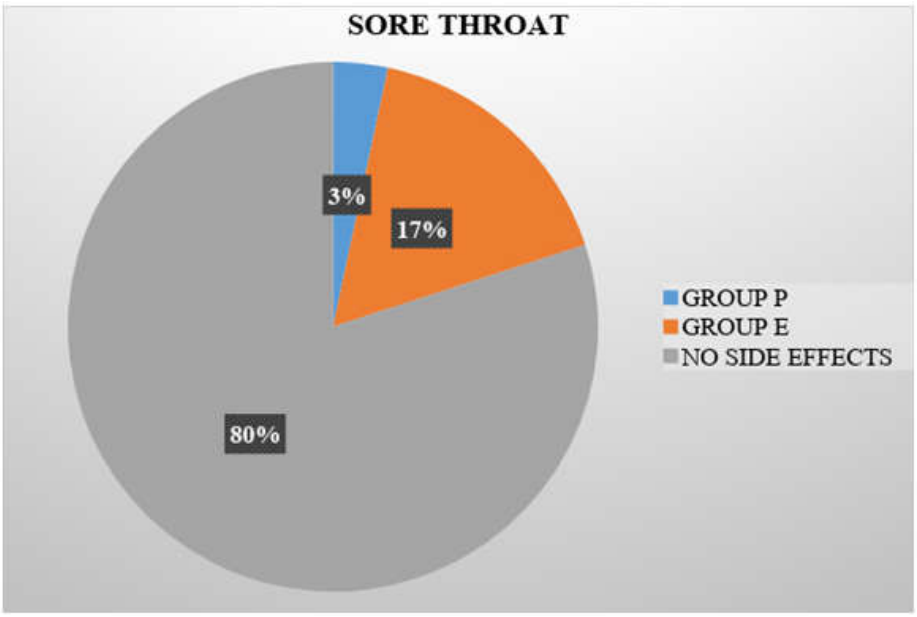
There was no incidence of laryngospasm or bronchospasm in either group of patients perioperatively.

Table 15: Incidence of perioperative complications in both groups

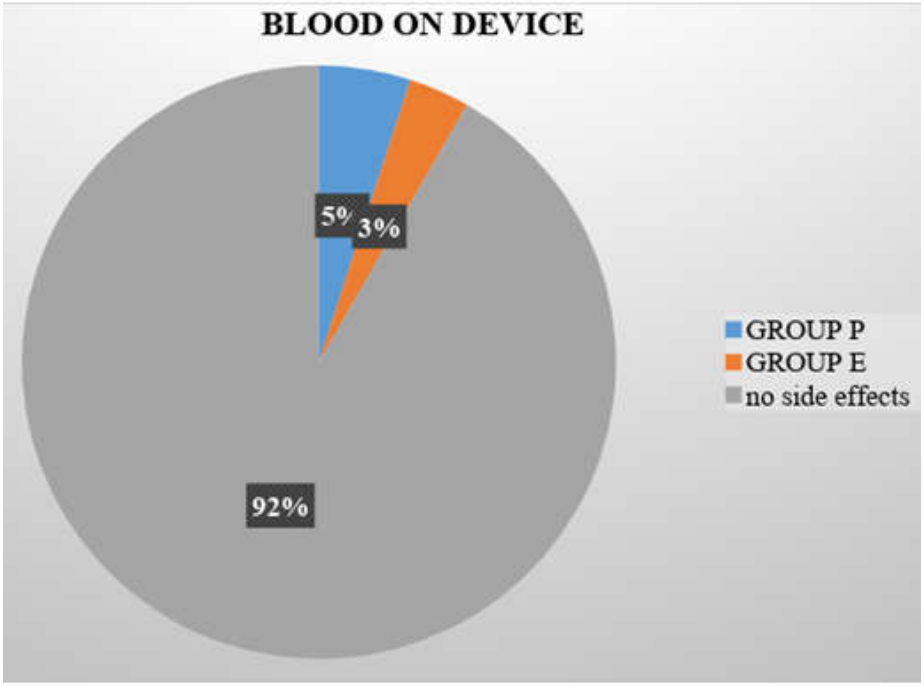
Complications	Group P		Group E		p Value
	Number	%	Number	%	
Cough	2	6.66	9	30	<0.05
Laryngospasm	0	0	0	0	
Bronchospasm	0	0	0	0	
Blood on device	3	10	2	6.66	<0.05
Aspiration	0	0	0	0	
Sore Throat	2	6.66	10	33.33	<0.05



Graph 9: Comparison of Cough Between two Groups



Graph 10: Comparison of Sore Throat Between two Groups:



Graph 11: Comparison of Blood on Device Between two Groups:

Conclusion

Based on our observations, results and discussion, we conclude that in the patients undergoing elective surgeries, Proseal LMA is suitable and safe alternative to endotracheal tube for airway management with respect to ease of insertion, haemodynamic parameters and reduced perioperative complications.

References

1. Dave NM, Iyer HR, Dudhedia V, Makwana J. An evaluation of the Proseal LMA in paediatric laparascopy. J anaesthesia clin pharmacol. 2009;25:7-3.
2. Misra MN, Ramamurthy B. The Proseal LMA and the tracheal tube: a comparison of events at insertion of the airway device. Internet Journal of Anaesthesiology. 2008;16:2.

3. Mathew OP. Maintenance of upper airway patency. The Journal of paediatrics. 1985 Jun 1;106(6):863-9.
4. Sharma B, Sood J, Kumara VP. Uses of LMA in present day anaesthesia. J Anaes Clin Pharmacol. 2007;23:5-15.
5. Shroff P, Kamath S. Randomized comparative study between the Proseal LMA and Endotracheal intubation for laparascopic surgery. Internet Journal of Anaesthesiology. 2005;11:1.
6. Patel MG, Swadia VN, Bansal G. Prospective randomized comparative study of use of PLMA and ET tube for airway management in children under general anaesthesia. Indian Journal of Anaesthesia. 2010;54(2):109-115.
7. Bon Sebastian, Anand T. Talikoti, Dinesh Krishnamurthy. Attenuation of haemodynamic responses to laryngoscopy and endotracheal intubation with intravenous dexmedetomidine: A comparison between two doses. Indian Journal of Anaesthesia. 2017;61(1):48-54.
8. Bon Sebastian, Anand T. Talikoti, Dinesh Krishnamurthy. Attenuation of haemodynamic responses to laryngoscopy and endotracheal intubation with intravenous dexmedetomidine: A comparison between two doses. Indian Journal of Anaesthesia. 2017;61(1):48-54.
9. Shribman AJ, Smith G, Achola KJ. Cardiovascular and catecholamine responses to laryngoscopy with and without tracheal intubation. British Journal of Anaesthesia. 1987;59:295-9.
10. Reid LC, Brace DE. Irritation of respiratory tract and its reflex effect on heart surgery. Surg Gynaecol obste. 1940;70:157-62.
11. Henderson J. In: Airway Management in the adult. Miller's Anaesthesia 7th ed. Miller RD, editor Philadelphia: Churchill Livingstone; 2010.pp 1573-610.
12. Prys-Roberts C, Greene LT, Meloche R, Foex P. Studies of anaesthesia in relation to hypertension. II. Haemodynamic consequences of induction and endotracheal intubation. British Journal of Anaesthesia. 1971;43:531-47.
13. Evans NR, Gardner SV, James MF, King JA, Roux P, Bennett P et al. The Proseal Laryngeal Mask: Results of a descriptive trial with experience of 300 cases. British Journal of Anaesthesia. 2002;88(4):534-9.
14. Brimacombe J, Keller C, Judd DV. Gum elastic bougie-guided insertion of the Proseal laryngeal mask airway is superior to the digital and introducer tool techniques. Anesthesiology. 2006;100:25-9.
15. Sharma B, Sahai C, Bhattacharya A, Kumra VP, Sood J. Proseal Laryngeal Mask Airway: A Study of 100 consecutive cases of laparoscopic surgery. Indian Journal of Anaesthesia. 2003;47(6):467-72.
16. Namazi IJ, Garia N, Kumar RB *et al.* The Comparison of Proseal Laryngeal Mask Airway and Endotracheal tube in patients undergoing laproscopic surgeries under general anaesthesia. Journal of Evidence Based Medicine and Healthcare. 2015;2(47):8347-8350.
17. Mehta K, Sharma S *et al.* A comparison of Proseal LMA with Endotracheal Intubation in Laparoscopic Tubal Ligation. International Journal Of Scientific Research. 2013;2(4):295-97.
18. Lim Y, Goel S, Brimacombe JR. The Proseal Laryngeal Mask Airway is an effective alternative to laryngoscope guided tracheal intubation for gynaecological laparoscopy. Anaesthesia Intensive care. 2007;35(1):52-6.
19. Saraswat N, Kumar A, Mishra A, Gupta A, Saurabh G, Srivastava V. Comparison of Proseal LMA and Endotracheal tube in patients undergoing laparoscopic surgeries under general anaesthesia. Indian Journal of Anaesthesia. 2011;55(2):129-34.
20. Lalwani J, Dubey KP, Sahu BS, Shah PJ. Proseal LMA: An alternative to endotracheal intubation in paediatric patients for short duration surgical procedures. Indian Journal of Anaesthesia. 2010;54(6):541-5.
21. Maltby JR, Beriault MT, Watson NC, Liepert DJ et al. LMA – Classic and LMA – Proseal are effective alternatives to Endotracheal intubation for gynecologic laparoscopy. Canadian Journal of Anaesthesia. 2003;50(1):71-7.
22. Sinha A, Sharma B, Sood J. Proseal as an alternative to endotracheal intubation in pediatric laparoscopy. Paediatr Anaesth. 2007;17:327-32.
23. Higgins PP, Chung F, Mezei G. Postoperative sore throat after ambulatory surgery. British Journal of Anaesthesia. 2002;88:582-4.
24. Kelly F, Sale S, Bayley G, Cook T, Stoddart P, White M. A cohort evaluation of the pediatric Proseal laryngeal mask airway in 100 children. Pediatr Anaesth. 2008;18:947-51.
25. Lardner D, Cox R, Ewen A, Dickinson D. Comparison of laryngeal mask airway (LMA)-ProsealTM and the LMA- ClassicTM in ventilated children receiving neuromuscular blockade. Can J Anesth. 2008;55:29-35.

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Evaluation of the Anaesthetic Management of Juvenile Nasopharyngeal Angiofibroma in a Tertiary Cancer Care Hospital: A Five Year, Prospective Observational Study

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Abstract

Background: Juvenile nasopharyngeal angiofibroma (JNA) is a rare, benign, vascular tumor in young males with potential life threatening complications. Advances in pre operative imaging, pre operative embolisation, and hypotensive anesthesia have made JNAs amenable to surgical resection with minimal complication. We present anesthetic management of JNAs that have been operated in our institute over the recent years. *Method:* After ethical committee approval, details of patients undergoing surgery for JNA were noted with regard to demographics, preoperative optimization and evaluation, intraoperative management and complications, and postoperative course. Twenty patients were evaluated and included in our study. *Results:* The age of JNA patients ranged from 9-17years. All our patients had undergone preoperative embolisation of the feeding artery. Standard anesthesia induction technique was used in all the patients. Controlled hypotension was achieved with the help of a combination of inhalational anesthetics and vasodilators. Average duration of surgery was 126.7 ± 55 minutes, and mean blood loss was 822 ± 291 ml. Seven patients were extubated in the operating room. The other 13 patients were remained intubated for 24 hours due to extensive surgery with a risk of postoperative hemorrhage, and were monitored in the postoperative intensive care unit. *Conclusion:* JNAs remain a challenge for anesthesiologists because of excessive intraoperative hemorrhage. Invasive monitoring, along with hypotensive anesthesia decreases bleeding and provides a clear field of vision for operating surgeon.

Keywords: JNA; Anesthesia management; Surgery; JNA bleeding; Hypotensive anesthesia.

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Introduction

Juvenile nasopharyngeal angiofibroma (JNA) is a benign tumor of the young male. The occurrence of JNA is about 0.5% [1-6], among all tumors of the head and neck region [7-10]. The occurrence of JNA in South Asian continent appears to be more than in the West [11]. JNA originates chiefly from the nasal cavity over the posterolateral wall just at the superior aspect of the sphenopalatine foramen. Tumor is locally aggressive, as it grows, erosion of the adjacent bone takes place, allowing extension

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into the ethamoid, sphenoid, and maxillary sinuses. From there the tumor may invade into the anterior, middle cranial fossa [8]. Staging of tumor is most commonly done according to system put forward by Radkowski et al. [12], [Table 1]. The etiopathogenesis of JNA is concealed. It might originate from the paraganglionic cells present at the end of maxillary artery, or it may be as per the "angiogenic and histogenetic theory", [8,13]. It is diagnosed based on history, clinical features, evaluation by endoscopy, and imaging modalities such as computed tomography, angiography, and magnetic resonance imaging. Handling of the tumor can lead to profuse bleeding, which is why preoperative biopsy is inadvisable. The most effective treatment modality of JNA Surgical excision [5]. Many surgical approaches are described, which ranges from transpalatal resection to open excision with midface degloving, lateral rhinotomy, and endoscopic resection. Minimally invasive approaches are now the treatment of choice if appropriate size and place tumor, but at centers with limited resources it is not used. The extent and site of tumor along with surgeon's preference will be deciding the type of surgery [8]. Inappropriate exposure can lead to incomplete removal of JNA, leading to recurrence or a massive intraoperative bleeding. Prior to surgery a preoperative angiography along with embolization of the feeding vessels is performed, generally it is done 24 to 72 hours prior to the operation to decrease risk of perioperative bleeding [2,14,15,16].

Our present study was undertaken with the primary aim to include JNA affected patients who are treated with different surgical modalities and to study the perioperative blood loss and its replacement involving different JNA stages, preoperative embolization, and different surgeries. Our secondary aim of the study was to analyze anesthetic management in these patients regarding anesthesia techniques, perioperative monitoring, and fluid replacement.

Methods

After obtaining Institutional Ethics Committee approval, this prospective observational study was conducted to include patients with JNA posted for tumor excision from a single tertiary care institute from the Indian subcontinent performed over a period of 5 years. Study duration was from February 2014 to March 2019. Data regarding patient demographics, symptoms, staging of tumor, pre operative investigations, pre operative embolisation, anaesthetic management, surgical technique, intra operative blood loss, intraoperative blood transfusion, post operative complications, number of days of hospital stay were noted. Inclusion criteria were all JNA patients who are undergoing surgical treatment with consent for inclusion in the study from the patient and parents or guardian. The patients who refuse to give consent were excluded from the study. Statistical analysis: Descriptive quantitative data are presented in form of mean ± standard deviation or quantal data and range of values are expressed in percentage.

Results

A total of 20 patients were included in the study. All the patients were male, with an average weight of 39 ± 9.3 kg and age between 9 and 17 years (Table 2).The presenting symptoms of these patients were nasal bleeding in 10 of them, followed by obstructive symptom of nose in 7 patients and local swelling over the nasal area in 3 patients. Other symptoms noted were change in voice, snoring, and anosmia.

Preoperative laboratory investigation included complete blood count and coagulation profile. Pre anesthetic airway examination revealed swelling in nasal area in 3 patients predicting difficult mask ventilation and 5 patient had anticipated difficult intubation with a Mallampati grade 3 in 4 patients and grade 4 in 1 patient. At the time of surgery, adequate blood was kept standby, 2 units (U) of packed red blood cells (PRBCs) were kept ready for the patient belonging to stage IIA or below, and 4U were arranged for patients of stage IIB and above.

In the operating room, standard monitoring consisted of noninvasive blood pressure, electrocardiogram, pulse oximetry, urinary output measurement and capnography. For patients with stage IIB and above invasive blood pressure and central venous pressure were monitored.

Three different consultant anesthesiologists were involved in the study period. Two large bore cannule were inserted in all patients. Induction of anaesthesia was carried out with propofol in 10 patients (50%) and thiopentone in remaining 10 patients (50%). Patients were preoxygenated for 3minutes rapid sequence intubation (RSI) was done in 3 patients as they had some continuous nasal bleeding. There was no difficult mask ventilation an any patient and none had difficult intubation on direct laryngoscopy. All patients received 2 μg/kg fentanyl.

Intraoperatively, as blood loss preventive strategy, all were positioned in 30 degree reverse trendelenburg position and hypotensive anesthesia was used to minimize surgical site bleeding by using inhalation anaesthetic isoflurane (1% to 3%) all along with the use of hypotensive drugs: esmolol (five patients), nitroglycerine (14 patients) and lignocaine (one patient).

Intraoperative core temperature was maintained using forced air warming devices in all patients. For postoperative analgesia, all the patients received drug IV paracetamol.

Mean intraoperative blood loss in patients with JNA was 822 ± 291 mL, intraoperative transfusion mentioned in Table 2.

Gelofusin was transfused in 4 patients each, and 15 ml/kg fresh frozen plasma was transfused in 4 patients. Three different Head and neck oncology surgeons were involved in the study period. Surgeries performed are as follows: transmaxillary excision (7/20; 35%), lateral rhinotomy (6/20; 30%), sub labial approach (4/20; 20%), and transpalatal excision (3/20; 15%).

At the end of surgery, 13 patients (65%) were kept electively intubated after reversal of neuromuscular blockade with neostigmine and glycopyrrolate and were kept on T-piece. None of them required elective ventilation. All patients were monitored overnight in the ICU and the trachea was extubated the following day after confirming no active nasal bleeding. None of the patient required reintubation or surgical reexploration.

The average duration of surgery was 127 minutes. The average length of stay postoperatively was 5 days.

Table 1: Radkowski Classification of Juvenile Angiofibroma

Stage	Details
IA	Limited to nose and nasopharyngeal area
IB	Extension into one or more sinuses
IIA	Minimal extension into pterygopalatine fossa
IIB	Occupation of pterygopalatine fossa without orbital erosion
IIC	Infratemporal fossa extension without cheek or pterygoid plate involvement
IIIA	Erosion of skull base(middle cranial fossa or pterygoids)
IIIB	Erosion of skull base with intracranial extension with or without cavernous sinus involvement

Source: Radkowski D, McGill T, Healy GB, Ohlms L, Jones DT. Angiofibroma: changes in staging and treatment. Arch Otolaryngol Head Neck Surg. 1996;122(2):122-129.

Table 2: Intraoperative details of the patients

Sl. No	Age in Years	Stage	Weight(Kg)	Surgical Approach	Duration in mins	Blood Loss in ml	Intra Operative Transfusion (Units)	Preop Embolisation
1	9	1B	40	LR	60	200	0	Y
2	10.8	1B	30	LR	70	400	0	Y
3	11	1B	35	LR	75	700	2	Y
4	13	1B	50	LR	90	600	2	Y
5	14.2	1B	42	LR	120	750	2	Y
6	17	1B	59	LR	120	800	2	Y
7	10	2A	36	SL	240	900	2	Y
8	9.8	2A	28	SL	120	1000	3	Y
9	14	2A	26	SL	90	750	3	Y
10	12	2A	30	SL	180	1400	4	Y
11	13.5	2A	33	TM	120	900	3	Y
12	15.6	2B	56	TM	120	650	0	Y
13	16.1	2B	50	TM	240	1450	3	Y
14	14.3	2B	38	TM	240	700	2	Y
15	10	2B	48	TM	120	800	2	Y
16	13	2B	35	TM	120	900	2	Y
17	12.5	2B	40	TM	90	750	1	Y
18	14.3	1B	31	TP	100	800	1	Y
19	12.2	1B	43	TP	110	800	2	Y
20	14.6	1B	33	TP	110	1200	3	Y

Abbreviations: Sl No-serial number; kg-kilogram; mins-minutes; ml-milliliter; Y-yes; LR - Lateral Rhinotomy; SL- Sub labial approach; TM- Trans maxillary; TP – Transpalatal.

Table 3: Comparison of various surgical approaches

Surgical procedure	Mean duration	Blood loss
Transpalatal	106 ± 5.7	933 ± 230
Sublabial	157 ± 66.5	1012 ± 278
Lateral rhinotomy	89 ± 25.77	575 ± 231
Transmaxillary	150 ± 62.44	878 ± 269

Discussion

In the present study, average blood loss in JNA surgeries is 822 ± 291 mL. Preoperative embolization was performed in all JNA patients. Postoperative period, 35% of patients are kept electively intubated in view of massive blood loss or extensive surgical procedure, with tracheal extubation done next day. In contrast to the previous studies regarding analysis of anesthetic management of patients with JNA published over a decade ago and involving 10 patients [17], our study involved a much larger group of 20 patients and is the first prospective observational study on JNA patients. The previous study included JNA cases with only lateral rhinotomy whereas the present study included different types of surgical procedure undertaken for JNA [17]. The previous study reported an average blood loss of 3,200 mL, much more than 822 mL reported in the present study. There is no mention regarding blood loss according to the JNA stage in the previous study in contrast to our study. We speculate that the recorded lesser blood loss in our study could be due to: our study including various types of surgeries other than lateral rhinotomy like transmaxillary approach, sublabial approach, transpalatal approach and had much shorter mean surgical time (127 min versus 6 hours) and all our head and neck surgeons had expertise of more than 10 years' experience in surgical excision of JNA. All patients were remined intubated in the previous study compared with only 65% in the present study. This is due to increased blood loss and longer duration of surgery in the previous study. Two IV cannulas were inserted in all patients in the previous study and in our study this suggests the notoriety of the association of JNA with blooding. Preoperative angiography was performed 48 hours before the surgery in all the patients in our study it helps in delineating the vascular supply and enables in embolization of feeder vessels of external and internal carotid arteries there by reduces intraoperative bleeding. To minimize intraoperative bleeding and to provide a good surgical field, the anesthesiologist needs to use hypotensive anesthesia in these patients. Various drugs have been described in the literature for inducing intraoperative hypotensive anesthesia [18,19]. In our institute we maintained hypotensive anaesthesia with isoflurane and hypotensive agents like nitroglycerine, esmolol. Face distortion due to local swelling may lead to difficult mask ventilation, but we didn't have any patient in our study. In active epistaxis due to JNA, a rapid-sequence induction is preferred as these patients are considered "full stomach" [20]. Though, all our patients were electively operated 3 patients were actively bleeding, rapid-sequence intubation was carried out in these patients. Long duration of surgery along with blood transfusions decreases the core body temperature, which can prolong recovery time. Hypothermia should be avoided using warm fluids, forced airwarming devices. One of the limitation of the study. is that it was carried out at a single center, hence the results may not be applied to other center. The uniformity of the results may be affected as multiple surgeons and anaesthesiologist were involved in the study.

Conclusion

We conclude that with advanced preoperative imaging, preoperative emboilisation, surgical technique and hypotensive anesthesia along with vigilant intraoperative management, JNA can be managed with minimal complication. Lower stages of JNA, minimally invasive surgery along with intraoperative blood conservative strategy, JNA can be extubated on table. Massive blood loss and blood transfusion further delays recovery.

References

1. Danesi G, Panizza B, Mazzoni A, Calabrese V. Anterior approaches in juvenile nasopharyngeal angiofibromas with intracranial extension. Otolaryngol Head Neck Surg. 2000;122(2):277-83.
2. Khalifa MA, Ragab SM. Endoscopic assisted antral window approach for type III nasopharyngeal angiofibroma with infratemporal fossa extension. Int J Pediatr Otorhinolaryngol. 2008;72(12):1855-60.

3. Singh A, Gunny R, Dunaway D, Hertley B. Juvenile nasopharyngeal angiofibroma involving the cavernous sinus: does surgery have a role? Int J Pediatr Otorhinolaryngol. 2008;3:128-131.
4. Yiotakis I, Eleftheriadou A, Davilis D, *et al*. Juvenile nasopharyngeal angiofibroma stages I and II: a comparative study of surgical approaches. Int J Pediatr Otorhinolaryngol. 2008;72(6):793-800.
5. Shamim AA, Ghias K, Khan MJ. Juvenile nasopharyngeal angiofibroma: experience at a tertiary care centre in Pakistan. J Pak Med Assoc. 2013;63(1):134-38.
6. Coutinho-Camillo CM, Brentani MM, Nagai MA. Genetic alterations in juvenile nasopharyngeal angiofibromas. Head Neck. 2008;30(3):390-400.
7. Fonseca AS, Vinhaes E, Boaventura V, *et al*. Surgical treatment of nonembolized patients with nasoangiofibroma. Braz J Otorhinolaryngol. 2008;74(4):583-87.
8. Ahmad R, Ishlah W, Azilah N, Rahman JA. Surgical management of juvenile nasopharyngeal angiofibroma without angiographic embolization. Asian J Surg. 2008;31(4):174-78.
9. Tang IP, Shashinder S, Gopala Krishnan G, Narayanan AN. Juvenile nasopharyngeal angiofibroma in a tertiary centre: ten-year experience. Singapore Med J. 2009;50(3):261-64.
10. Bales C, Kotapka M, Loevner LA, et al. Craniofacial resection of advanced juvenile nasopharyngeal angiofibroma. Arch Otolaryngol Head Neck Surg. 2002;128(9):1071-78.
11. Ahmed Z, Mutiullah S, Rahim D, Marfani MS. Juvenile nasopharyngeal angiofibroma: stage and surgical approach. J Liaquat Uni Med Health Sci. 2009;8(1):37-40.
12. Radkowski D, McGill T, Healy GB, Ohlms L, Jones DT. Angiofibroma: changes in staging and treatment. Arch Otolaryngol Head Neck Surg. 1996;122(2):122-29.
13. Hosseini SM, Borghei P, Borghei SH, Ashtiani MT, Shirkhoda A. Angiofibroma: an outcome review of conventional surgical approaches. Eur Arch Otorhinolaryngol. 2005;262(10):807-12.
14. Nicolai P, Berlucchi M, Tomenzoli D, *et al*. Endoscopic surgery for juvenile angiofibroma: when and how. Laryngoscope. 2003;113 (5):775-82.
15. Panda NK, Gupta G, Sharma S, Gupta A. Nasopharyngeal angiofibroma— changing trends in the management. Indian J Otolaryngol Head Neck Surg. 2000;64(3):233-239.
16. Hodges JM, McDevitt AS, El-Sayed Ali AI, Sebelik ME. Juvenile nasopharyngeal angiofibroma: current treatment modalities and future considerations. Indian J Otolaryngol Head Neck Surg. 2010;62(3):236-47.
17. Moulin G, Chagnaud C, Gras R, et al. Juvenile nasopharyngeal angiofibroma: comparison of blood loss during removal in embolized group versus nonembolized group. Cardiovasc Intervent Radiol. 1995;18(3):158-61.
18. Ballah D, Rabinowitz D, Vossough A, et al. Preoperative angiography and external carotid artery embolization of juvenile nasopharyngeal angiofibromas in a tertiary referral paediatric centre. Clin Radiol. 2013;68(11):1097-1106.
19. Kopec´ T, Borucki Ł, Szyfter W. Fully endoscopic resection of juvenile nasopharyngeal angiofibroma— own experience and clinical outcomes. Int J Pediatr Otorhinolaryngol. 2014;78(7):1015-58.
20. Ezri T, Roth Y, Geva D, Konichezky S, Marshak G, Halperin D. Anesthetic management of juvenile nasopharyngeal angiofibroma resection. J Cardiothorac Vasc Anesth. 2003;17(5):622-24.

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Comparison of I-gel Supraglottic Airway with LMA Classic in Children Undergoing Elective Surgeries

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Abstract

Background: A new SADs called I-gel has several advantages such as easy insertion, stability after insertion and minimal risk of tissue compression. Incidence of postoperative complication was not differ among I- gel and c-LMA. Very few reports that have evaluated the paediatric I-gel, especially in small children. *Methodology:* Total 90 ASA grade I-II patients of 1-12 years age group (45 patients in Group I: I – gel, 45 patients in group L: c-LMA classic) who undergone elective urology surgery from civil hospital, Ahmedabad were included in the study. A supraglottic device was inserted after required depth of anaesthesia achieved. The ease of insertion, insertion time, attempt of insertion and sealing pressure were noted. Vital parameter during surgery and complication in post anaesthesia care unit were recorded. *Result:* Success rate for first attempt in I-gel group was significantly higher (85.0%) as compared to cLMA (80.0%). The insertion time was shorter with I-gel (14.64 + 16.7 sec) than with c-LMA (20.11 + 28.5 sec). Airway leak pressure of I-gel is higher (26 + 2.63 mmHg) than c-LMA (22 + 2.3 mmHg). On removal, blood stain was present in one patient in I-gel group and 3 patient in c-LMA group. There was no significant change in hemodynamic parameters before and after insertion in both the group. *Conclusion:* I-gel is superior than c-LMA in terms of significantly easier and more rapid insertion with high leak pressure. The hemodynamic changes after insertion and the postoperative complication are not significantly differ between c-LMA and I-gel patients.

Keywords: I-gel; LMA Classic; Leak pressure; Insertion time.

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Introduction

Paediatric patient is associated with higher rates of complication of laryngoscopy and intubation. Oxygenation and ventilation without endotracheal intubation are facilitated by supraglottic airway devices [1]. Supraglottic airway devices (SADs) have been increasingly used in recent years in suitable cases. Insertion into hypopharynx is easy to form a seal around the larynx and useful for difficult and failed intubation. Drainage of gastric fluid and visualization the larynx without cervical

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spine neck extension is possible with SADs. These devices have minimal cardiovascular responses than the tracheal tube [2].

A new SADs called I-gel (Intersurgical, Wokingham, UK) was developed by Dr. Mohammad Aslam Nasir and it has soft gel-like thermoplastic elastomer, a non inflatable cuff and a channel for gastric suction catheter placement. The soft non inflatable cuff creates a perfect fit with accurately mirrors the perilaryngeal frame work [2]. It has several advantages such as easy insertion, stability after insertion and minimal risk of tissue compression [3,4].

Recent studies showed that I- gel is better device as compared to LMA Classic (c-LMA) for easier insertion and maintenance of anaesthesia [5,6]. It provided a higher leak pressure [7,8] a shorter insertion time [9] and improved glottis view compared with c-LMA in children [9]. There were no differences in the incidence of postoperative airway complication, hoarse cry or sore throat [10]. Very few reports that have evaluated the paediatric I-gel, especially in small children. Hence, we decided to compare clinical performance of both devices in paediatric patient undergoing elective surgery.

Aims & Objective

a) To compare the clinical performance of both the devices regarding number of attempts, ease of insertion, sealing quality and time to successful device placement. b) to compare hemodynamic effects and complication of both devices.

Methodology

This observational comparative study was conducted in anesthesia department of institute of kidney disease and research center, civil hospital, Ahmedabad after institutional ethics committee approval. Total 90 ASA grade I-II patients of 1-12 years age group who undergone elective urology surgery were included in the study. Patients with upper respiratory tract infection, significant cardiovascular, pulmonary, renal or hepatic diseases, oropharyngeal pathology were excluded. Patients were randomly divided into two groups of 45 each by sealed envelope technique - Group I: I – gel, group L: c -LMA classic.

All patients underwent thorough preoperative assessment. Patient's history and demographic data were noted. Airway assessment including mouth opening, neck movements, teeth, mallampatti grading and systemic examination and pre operative investigations were carried out. All patients were kept nil per orally. On arrival in the operation theatre, vital parameters were noted and routine monitoring ECG, NIBP and SpO_2 were applied.

All patients were given 0.5 mg/kg of midazolam syrup, injection glycopyrrolate 0.004 mg/kg and fentanyl 2 μg/kg intravenously prior to induction of anaesthesia. Patients were induced with 6% sevoflurane in oxygen. After required depth of anaesthesia achieved, the supraglottic device was inserted in "sniffing" position by an experienced anaesthesiologist as per standard procedure recommended by manufacturer. There was a subjective scale of 1-3 (1= Very easy, 2= Easy, 3= Difficult) for ease of insertion assessment. Ventilation was considered inadequate, if there was no square shaped capnography wave and or inadequate chest movement and second attempt was done. Failure was considered when there was not successful insertion in three attempts. This patient was then excluded from the study and tracheal intubation was planned. Insertion time was calculated from placement from grasping of the device to observing a first square wave capnograph trace. The sealing pressure was measured by an aneroid manometer (Mallinckrodi Medical) placed at the proximal end of the supraglottic device via a connector (maximal allowable was 40 cm H_2O). The air leak was detected by auscultation of anterior neck for all patients.

Heart rate, diastolic, systolic and mean blood pressure, end tidal carbon dioxide tension and oxygen saturation were recorded after induction at one, five minutes after airway device placement, every 5 minutes till half an hour and then after every 10 minutes up to 1 hours, at 90 minutes and 120 minutes. After shifting to post anaesthesia care unit, parents were assessed about hoarse cry, sore throat or any other discomfort. Normal insertion time for the I- gel and c-LMA was 9.25 ± 1.08 seconds and 12.95 ± 1.08 seconds respectively.

Statistically analysis: Continuous variables are expressed as mean ± standard deviation (SD). The comparison of between the groups was performed by Z test. Qualitative data was compared using Fischer's exact test. A value of p less than 0.05 is considered significant.

Results

The present study was conducted among 90 peadiatrict patients belonging to ASA physical

Table 1: Demographic and surgical profile of study participants *.

Variables	Group I (n= 45)	Group L (n= 45)	p value
Age (year)	5.3 ± 3.4	8.2 ± 5.0	0.01
Weight (kg)	16.1 ± 5.4	15.3 ± 5.1	0.74
Duration of surgery (min.)	35.6 ± 21.7	52.8 ± 19.0	0.37
Duration of anaesthesia (min.)	38.5 ± 21.9	55.1 ± 18.9	0.33

*p value was calculated by Z test

Table 2: Airway insertion and maintenance characteristics of study participants

Variable	Group I (n=45)	Group L (n=45)	p value
Insertion success			
Success rate	45 (96.3%) out of 47	45 (97.5%) out of 46	0.005*
First attempt	40 (85.0%)	36 (80.0%)	
Second attempt	5 (11.3%)	8 (17.7%)	
Third attempt	0 (0.0%)	1 (2.0%)	
Ease of insertion			
Very easy	0 (0.0%)	0 (0.0%)	1.0*
Easy	45 (100%)	44 (98%)	
Difficult	0 (0.0%)	1 (2%)	
Insertion time (sec)	14.6 ± 16.7	20.1 ± 28.5	0.001#
Peak inspiratory pressure (mmHg)	12.5 ± 1.5	12.8 ± 1.6	0.80#
Leak pressure (mmHg)	26.0 ± 2.6	22.0 ± 2.3	0.01#

*p value was calculated by fisher test. #p value was calculated by Z test

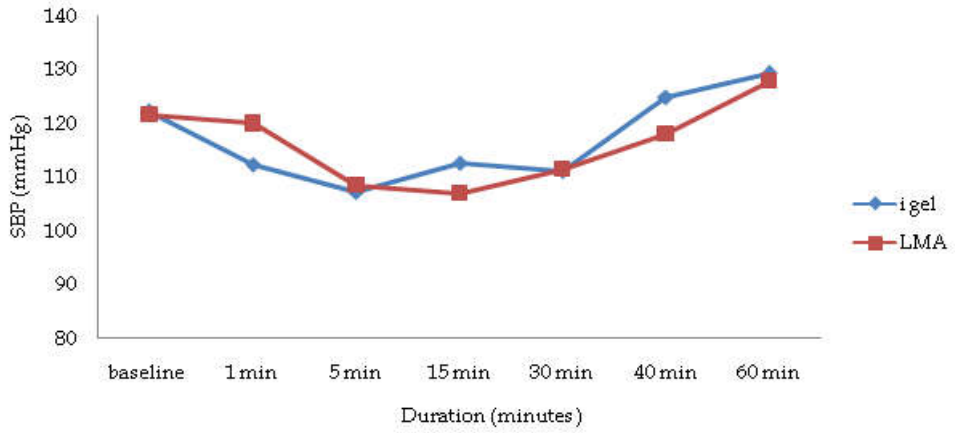

Fig. 1: Intra-operative systolic blood pressure (mmHg) at different time intervals in 2 groups

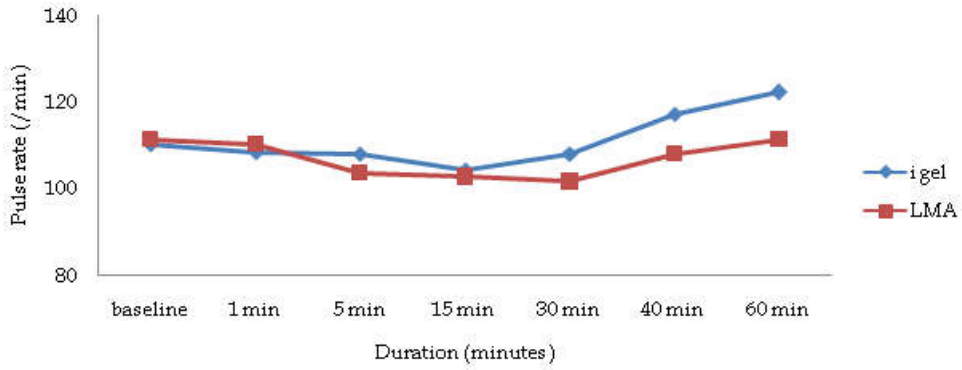

Fig. 2: Intraoperative mean pulse rate (/min) at different time intervals in 2 groups

status I and II. Significant difference was not observed in two groups of patients respect to weight, duration of surgery and duration of anesthesia (Table 1, p>0.05). However, patients in group L (8.19 ± 5.03 year) were elder as compared to patients in group I (5.35 ± 3.47 year, p = 0.01). Distribution of urological surgeries and used device size were similar between two groups.

Table 2 shows that overall success rate was similar with I-gel and c-LMA. However, the insertion success rate at first attempt was significantly high with I-gel as compared to c-LMA. Significant difference was not found between I-gel and c-LMA with regard to peak inspiratory pressure and ease of insertion. Insertion time for I-gel device was 14.6 ± 16.7 seconds which was significantly shorter than c-LMA device (20.1 ± 28.5, p = 0.001). Airway leak pressure for I-gel group (26.0 ± 2.6 mmHg) was also significantly higher than the c-LMA group (26.0 ± 2.6 mmHg).

During insertion, one patient of group I (2.2%) had laryngospasm as compared to none in group L. During maintenance, child movement was observed only in one patient with c-LMA (2.2%). Coughing and blood stain on removal were reported higher with c-LMA as compared to I-gel. (2.2% in group I v/s 4.4% in group L for cough and 2.2% in group I v/s 6.6% in group L for blood stain on removal) but statistically not significant. None of the patients had hypoxia, laryngeal stridor, bronchospasm, regurgitation aspiration, loss of airway, wheeze and loss of tooth.

Mean SBP and pulse rate was comparable in both groups. After induction, there was fall in SBP and returned to baseline after 1 hour. There was no statistically significant difference in change in SBP in both groups (Fig. 1). In both groups, rise in pulse rate during induction and insertion was observed; thereafter heart rate decreased, which was statistically not significant (Fig. 2).

Discussion

The I-gel is a single use supraglottic airway device, available in CE marked paediatric sizes and officially launched for use in January 2010. Result of our study showed that the overall insertion success rate was similar with both the devices. However, success rate for first attempt in I-gel group was significantly higher (85.0%) as compared to c-LMA (80.0%). R Goyal *et al.* [11] found that insertion of I gel was successful on first attempt (95.0%) which was high as compared to laryngeal mask airway (90.0%). This is in consonance with various studies [12,13].

In the present study, we observed that the insertion time was shorter with I-gel (14.64 ± 16.7 sec) than with c-LMA (20.11 ± 28.5 sec). Lee *et al.* [9] also found the shorter insertion time with I-gel as compared with the c-LMA. A report by RM Bringer *et al.* [14] has revealed that the median insertion time for the I-gel in paediatric patients was 14 sec. Ease of insertion of I-gel can be partially explained by less flexible stem and there is no need for cuff inflation. The insertion of c-LMA is difficult due to a large cuff which can impede digital intra oral position and propulsion in the pharynx. The lack of back plate which cause cuff more likely to fold over at the bases of mouth.

In our study, It was found that airway leak pressure of I-gel is higher (26 ± 2.63 mmHg) than c-LMA (22 ± 2.3 mmHg). Similar results were found by Lee et al. [9]. Theiler *et al.* [15] compared I gel with aura Once and found that average leak pressure was higher with I-gel (22 mmHg v/s 19 mmHg) but difference was not considered clinically significant. We found that laryngospasm in one child during I- gel insertion, one child moved in cLMA group during maintenance in L group and during removal coughing occurred in one child in I-gel group and 2 patient in c-LMA group. The study of R.M. Beringer *et al.* [14] showed similar complication rate in both groups (13, 11%). However, anaesthetic technique is known to affect complication rates.

On removal, blood stain was present in one patient in I-gel group and 3 patient in c-LMA group. R.M. Beringer *et al.* [14] found that blood on 3% of I-gel following removal which was less compared with 3-6% for Clma [16]. Singh *et al.* [17] reported that the incidence of lip, tongue and dental trauma was 16.7% in the L group and 3.3% (1/30) patients in I group. The I-gel-filled cuff is less traumatic to the airway as compared with more traditional air-filled cuffs, as non inflatable cuff inserts less pressure on the perilaryngeal tissue. Postoperative vomiting was significantly higher in L group; it might be due to gastric insufflations.

We did not observed significant changes in hemodynamic parameters like systolic blood pressure and heart rate before and after insertion in both the group. This finding was supported by the finding of Shin *et al.* [18].

Conclusion

I-gel is comparable to the c-LMA with regards to securing airway in children undergoing elective surgery. I-gel is better than c-LMA in terms of significantly easier and more rapid insertion with

high leak pressure. The hemodynamic changes after insertion and the postoperative complication are not significantly different between c-LMA and I-gel patients.

Limitation

Only children with normal airway anatomical structure were included. The anaesthetist were more experience in inserting the LMA Classic than the I-gel and this may lead to bias.

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References

1. White MC, Cook TM, Stoddart PA. A critique of elective pediatric supraglottic airway devices. Pediatric Anesthesia. 2009 Jul;19:55-65.
2. Ramesh S, Jayanthi R. Supraglottic airway devices in children. Indian journal of anaesthesia. 2011 Sep;55(5):476.
3. Bopp C, Carrenard G, Chauvin C, Schwaab C, Diemunsch P. The I-gel in paediatric surgery: Initial series. Inamerican Society of anesthesiologists (aSa) annual Meeting 2009 Oct.pp.17-21.
4. Beylacq L, Bordes M, Semjen F, Cros AM. The I-gel®, a single use supraglottic airway device with a non-inflatable cuff and an esophageal vent: an observational study in children. Acta Anaesthesiologica Scandinavica. 2009 Mar;53(3):376-9.
5. Katz SH, Falk JL. Misplaced endotracheal tubes by paramedics in an urban emergency medical services system. Annals of emergency medicine. 2001 Jan 1;37(1):32-7.
6. Holm Knudsen RJ, Rasmussen LS. Paediatric airway management: basic aspects. Acta Anaesthesiologica Scandinavica. 2009 Jan;53(1):1-9.
7. Saran S, Mishra SK, Badhe AS, Vasudevan A, Elakkumanan LB, Mishra G. Comparison of i-gel supraglottic airway and LMA-ProSeal™ in pediatric patients under controlled ventilation. Journal of anaesthesiology, clinical pharmacology. 2014 Apr;30(2):195.
8. Kim H, Lee JY, Lee SY, Park SY, Lee SC, Chung CJ. A comparison of i-gel™ and LMA Supreme™ in anesthetized and paralyzed children. Korean journal of anesthesiology. 2014 Nov;67(5):317.
9. Lee JR, Kim MS, Kim JT, et al. A randomised trial comparing the I-gel(TM) with the LMA(TM) in children. Anesthesia 2012; 67: 606–11.
10. Das B, Mitra S, Jamil SN, Varshney RK. Comparison of three supraglottic devices in anesthetised paralyzed children undergoing elective surgery. Saudi journal of anaesthesia. 2012 Jul;6(3):224.
11. Goyal R, Shukla RN, Kumar G. Comparison of size 2 i-gel supraglottic airway with LMA ProSeal™ and LMA Classic™ in spontaneously breathing children undergoing elective surgery. Pediatric Anesthesia. 2012 Apr;22(4):355-9.
12. Karippacheril JG, Varghese E. Crossover comparison of airway sealing pressures of 1.5 and 2 size LMA ProSeal™ and LMA Classic™ in children, measured with the manometric stability test. Pediatric Anesthesia. 2011 Jun;21(6):668-72.
13. Shimbori H, Ono K, Miwa T, Morimura N, Noguchi M, Hiroki K. Comparison of the LMA-ProSeal™ and LMA-Classic™ in children. British journal of anaesthesia. 2004 Aug 6;93(4):528-31.
14. Beringer RM, Kelly F, Cook TM, Nolan J, Hardy R, Simpson T, White MC. A cohort evaluation of the paediatric i-gel™ airway during anaesthesia in 120 children. Anaesthesia. 2011 Dec;66(12):1121-6.
15. Theiler LG, Kleine-Brueggeney M, Luepold B, Stucki F, Seiler S, Urwyler N, Greif R. Performance of the pediatric-sized i-gel compared with the Ambu AuraOnce laryngeal mask in anesthetized and ventilated children. Anesthesiology: The Journal of the American Society of Anesthesiologists. 2011 Jul 1;115(1):102-10.
16. Goldmann K, Jakob C. Size 2 ProSeal™ laryngeal mask airway: a randomized, crossover investigation with the standard laryngeal mask airway in paediatric patients. British journal of anaesthesia. 2004 Dec 10;94(3):385-9.
17. Singh I, Gupta M, Tandon M. Comparison of clinical performance of I-Gel™ with LMA-Proseal™ in elective surgeries. Indian journal of anaesthesia. 2009 Jun;53(3):302.
18. Shin WJ, Cheong YS, Yang HS, Nishiyama T. The supraglottic airway I-gel in comparison with ProSeal laryngeal mask airway and classic laryngeal mask airway in anaesthetized patients. European Journal of Anaesthesiology (EJA). 2010 Jul 1;27(7):598-601.

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Thyromental Height as a Predictor of Difficult Laryngoscopy

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Abstract

Introduction: Intubation and maintenance of the airway is one of the most important steps in anaesthesia practice and a fundamental responsibility of the anaesthesiologist. Airway assessment is an integral part of pre-anaesthetic evaluation to recognize a potentially difficult airway. A range of bedside screening tests are available to predict a difficult airway but with doubtful accuracy. Hence, identifying a single reliable predictor of difficult intubation is valuable. Hence, the present study aims to evaluate the usefulness of thyromental height test alone as a single predictor of difficult laryngoscopy in our population. *Methods:* After ethical clearance and taking informed consent, we conducted a randomized prospective observational study on 315 adult patients posted for elective surgical procedures under general anaesthesia with endotracheal intubation. Airway was assessed and Thyromental Height (TMH) was measured on the day before surgery. Intra – operatively laryngoscopy was performed and Cormack- Lehane'sgrading noted. The preoperative assessment data and laryngoscopy findings were used together to evaluate the accuracy of TMHT in predicting difficult laryngoscopy. *Results:* Mean TMH observed in our study was 52.80 mm. TMHT at cut off of 50 mm had high sensitivity of 82.3% and high negative predictive value of 96.7%, but with low specificity of 63.7% (P value 0.000). When the cut off revised to 48 mm, sensitivity and specificity had best compromise, sensitivity of test decreased to 64.7% and specificity increased to 79.7% (p value 0.002). *Conclusion:* The present study demonstrates the practicality of TMHT. It confirms the good sensitivity of TMHT for predicting difficult intubation, but validation will require further studies in more diverse patient population.

Keywords: Thyromental height; Cormack-Lehane grading; Difficult laryngoscopy.

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Introduction

Endotracheal intubation is one of the gold standard techniques for maintaining a definitive airway in the practice of clinical anaesthesia. Failure in maintaining the airway is an important cause of mortality and morbidity in anaesthesia [1]. The American society of anaesthesiologists closed claims database analysis has revealed that as many as 1/3rd of the anaesthesia related deaths are due to an inability to maintain a patent airway [2]. Difficult intubation is associated with serious

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complications and is the second most frequent proclaimed damaging event leading to anaesthesia malpractice claims [3].

Most airway catastrophes occur when difficult airway in not anticipated and accurate prediction of difficult airway can guide the preparation for its appropriate management [4]. Airway assessment is an integral part of preanaesthetic evaluation in order to recognise potential difficulty that may be encountered in managing a given airway. A range of screening tests are available to predict a difficult airway but with doubtful accuracy. The performance of these tests varies considerably between studies. These tests are not very sensitive or specific when they are used alone and many tests have to be employed in combination to predict a difficult airway with greater accuracy. Thus multi-factorial indices outperform a single test to predict difficult airway. These multi-factorial indices are cumbersome to apply in daily clinical practice. Hence, identifying a single predictor of difficult intubation can be valuable. Thus there is a need for a single test with high sensitivity, specificity and positive predictive value for identifying difficult airway.

A study done in a population in Iran has found that thyrometal height test (TMHT) alone can accurately predict difficult laryngoscopy [5]. The present study aims to evaluate the usefulness of TMHT as single predictor of difficult laryngoscopy in Indian population. The objective was to correlate TMHT to Cormack-Lehane laryngoscopy grading for prediction of difficult laryngoscopy.

Materials and Methods

This prospective observational study was conducted in adults of either gender aged 18-70 years after obtaining Ethical Committee approval and prior informed consent in subjects scheduled to undergo surgery under general anaesthesia with endotracheal intubation. Subjects with obvious airway malformations, need for rapid sequence intubation or awake intubation, cervical spine abnormalities and those with head and neck radiotherapy were excluded from the study. During the preanaesthetic evaluation a routine airway assessment was done along with the Thyromental height test. The thyromental height was measured as the distance between the anterior border of the thyroid cartilage and a tangential line drawn from the anterior border of the mentum with the patient lying supine with his/her mouth closed with the help of a depth gauge (Fig. 1).

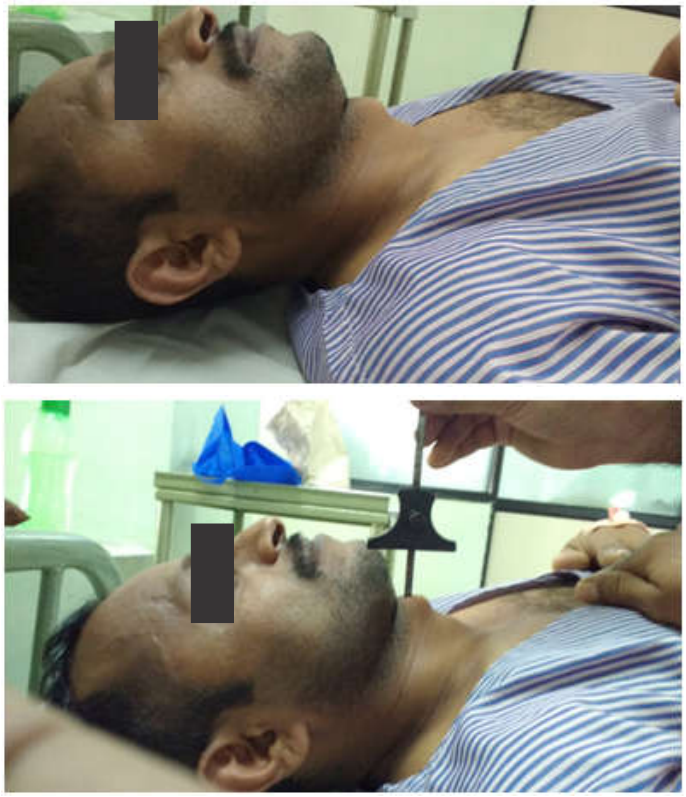

Fig. 1: Thyromental height test (TMHT); Patient lying supine with mouth closed thyromental height is measured using a depth gauge.

A standard anaesthesia protocol was followed in all subjects. After instituting minimal mandatory monitoring, general anaesthesia was induced with fentanyl 2 mcg/kg and propofol 2 mg/kg. Muscle relaxation was facilitated with atracurium 0.5 mg/kg. Subjects were mask ventilated for 3 min with 100% oxygen following injection atracurium and laryngoscopy was performed with Macintosh direct laryngoscope blade size 3 in all subjects. The direct laryngoscopic view of the larynx was graded by Cormack-Lehane (CL) grading system from grade 1 to grade 4 (Grade 1: full visualisation of glottis; Grade 2: partial visualisation of glottis, only posterior commissure is seen; Grade 3: visualisation of only epiglottis; Grade 4: no laryngeal structures are visible). All attempts at laryngoscopy were performed by the same anaesthesiologist in all study subjects. Cormack-Lehane grade 1 & 2 was classified as easy laryngoscopy and grade 3 & 4 was classified as difficult laryngoscopy.

A study to evaluate the thyromental height in predicting difficult laryngoscopy has shown the sensitivity to be 82.6% [5]. Expecting similar results with precision of ± 1%, power of study at 80% and an alpha error 5% the required sample size was estimated to be 315 subjects. The data collected from the study population were analysed with statistical software SPSS version 18.0. To test the efficacy between the different cut-off points for the thyromental height, various indicators such as sensitivity, specificity, accuracy, positive predictive value, and negative predictive value were calculated. Mcnemars test was used to compare the efficacy of TMHT to CL grading.

Results

Table 1: Demographic variables

Variable	n=315
Age (years)*	43.37 ± 14.54
Gender (male/female)†	159/156
Height (cm)*	162.6 ± 7.9
Weight (kg)*	65.3 ± 7.3
BMI (kg/m2)*	24.72 ± 2.74

* Data presented as Mean ± SD; † number

Table 2: Distribution of easy and difficult laryngoscopy in study population

Laryngoscopy		Number of subjects	Total
Easy (%)	CL grade 1	131 (41.6)	281 (89.2)
	CL grade 2	150 (47.6)	
Difficult (%)	CL grade 3	34 (10.8)	34 (10.8)
	CL grade 4	0 (0)	

Table 3: Efficacy of TMHT at cut-off of 48 mm

TMHT (n)	Difficult laryngoscopy [CL grade 1 & 2; n (%)]	Easy laryngoscopy [Cl grade 3 & 4; n (%)]
< 48mm (79)	22 (27.8) [TP]	57 (72.1) [FP]
> 48mm (236)	12 (5) [FN]	224 (94.9) [TN]

Table 4: Efficacy of TMHT at cut-off of 50 mm

TMHT (n)	Difficult laryngoscopy [CL grade 1 & 2; n (%)]	Easy laryngosocpy [CL grade 3 & 4; n (%)]
< 50mm (130)	28 (21.5) [TP]	102 (78.4) [FP]
> 50mm (185)	6 (3.2) [FN]	179 (96.7) [TN]

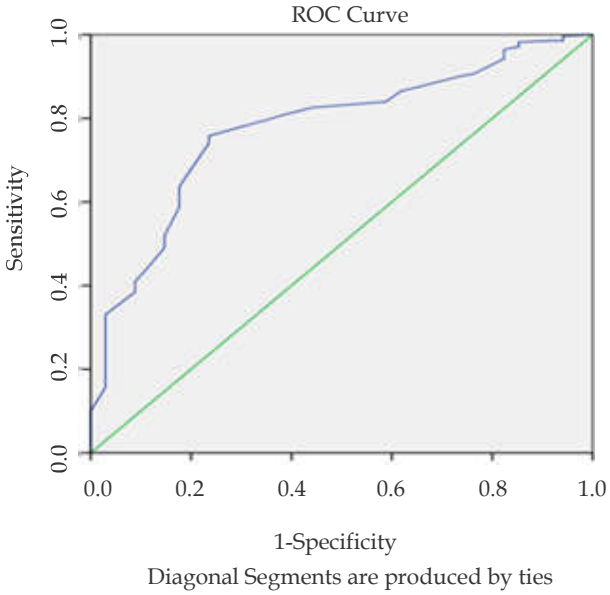

Fig. 2: ROC curve of TMHT at cut-off of 50 mm

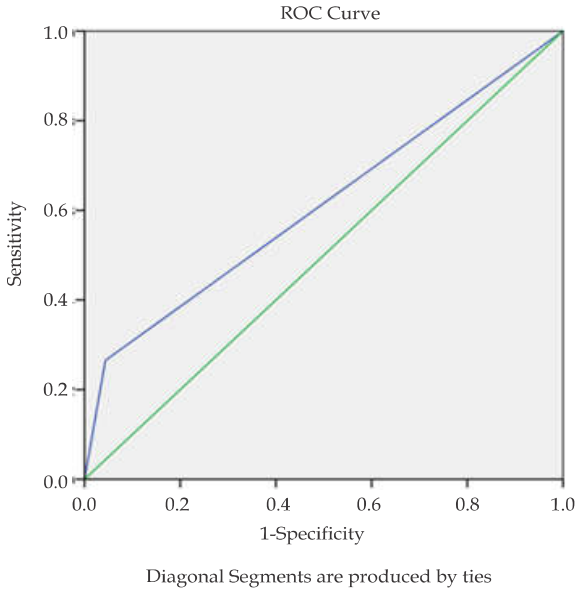

Fig. 3: ROC curve at TMHT at cut-off of 48mm

Table 5: Comparative efficacy of TMHT at 50 mm and 48 mm cut-off

Parameter	TMHT 50 mm cut-off	TMHT 48 mm cut-off
True positive (n)	28	22
False positive (n)	102	57
True negative (n)	179	224
False negative (n)	6	12
Sensitivity (%)	82.3	64.7
Specificity (%)	63.7	79.7
Positive predictive value (%)	21.5	27.8
Negative predictive value (%)	96.7	94.9
Accuracy (%)	65.7	78.09
P value	0.000	0.002

The demographic parameters of the study subjects have been shown in table 1. The laryngoscopic grading as noted during direct laryngosocpy in the study population has been shown in table 2. Of the 315 study subjects 281 had easy laryngoscopy and 34 had difficult laryngoscopy, thus resulting in an incidence of 10.8% of difficult laryngosocpy.

Receiver operating characteristic (ROC) curve analysis for prediction of difficult laryngoscopy was done with TMHT test at cut-off values of 50 mm and 48 mm. In the ROC curve analysis, on the x-axis we plot 1-specificity and on y-axis we plot sensitivity. At a cut-off value the area under curve (AUC) was 0.778 i.e., 77.8%. At a cut-off value of 50 mm sensitivity was 82.3% and specificity was 63.7%. At a cut-off value of 48 mm the AUC was 0.611 i.e., 61.1%. At a cut-off value of 48 mm the sensitivity was 64.7% and specificity was 79.7%, which were closer to each other.

TMHT at cut off of 50 mm, for prediction of difficult laryngoscopy, has high sensitivity of 82.3% and low specificity of 63.7%, low positive predictive value of 21.5%, high negative predictive value of 96.7% and accuracy of 65.7% with p value <0.000. TMHT at 48 mm cut off, had low sensitivity of 64.7%, but high specificity of 79.7% and high negative predictive value of 94.9% and accuracy of 78.09% with p value < 0.002. On comparision of efficacy and predictive value of TMHT for prediction of difficult airway, in our population, it had high specificity of 79.7% and high negative predictive value and better accuracy at cut off of 48 mm.

Discussion

Unanticipated difficult airway is a major concern for anaesthesiologists. Difficult or failed tracheal intubation is well recognized as a major cause of morbidity and mortality in anaesthetic practice as per ASA closed claim audit [2]. Unanticipated difficult intubation is a risk to the patient's life and a challenge to the skill of the anaesthesiologist. Many anatomical characteristics and pathological conditions (like Pierre Robin syndrome, Ludwig's angina) have been suggested to be useful in anticipating difficult intubation by altering or distorting the regional anatomy of the airway. In the absence of pathological conditions, radiographic methods are time consuming and cannot be used routinely for prediction of the difficult intubation.

The need to predict potentially difficult tracheal intubation with an accurate marker, even before laryngoscopy, has received more importance but with limited success. Predicting difficult airway pre- operatively aids not only in managing the intubation time better, but also decreases airway management related morbidity. It is seen that weight, head and neck movement, jaw movement, receding mandible, buck teeth, modified Mallampati classification, thyromental distance, sternomental distance, mouth opening and Wilson risk score are commonly used, but are not foolproof to predict a difficult intubation [6].

Hence, there is a need for a test, which is (a) quick and easy to perform; (b) is highly sensitive (so that majority of difficult cases can be identified); and (c) highly specific (so that false-positive rate will be low when the test is used routinely) d) and have minimal false positive and false negative values [7]. There is still no available single standard method that meets the criteria or a consensus regarding the reliability of the ideally preferred tests [8,9]. Recently, thyromental height test (TMHT) has been proposed as one of the highly sensitive and specific bedside tests to predict difficult airway.

Etezadi *et al.* [5] suggested that TMHT is a promising single anatomical measurement technique with high sensitivity, specificity, PPV and NPV. In our study, the prediction of difficult laryngoscopy was done by measuring thyromental height and correlating it to Cormack Lehane's grading at intubation. Cormack- Lehane grade III and IV are considered as difficult intubation and CL gradeI and II as easy intubation. Out of 315 cases studied, we found 134 patients had CL- gradeI, 150patients had CL- II, 34 patients had CL- III, and none have CL- IV.

Etezadi *et al.* [5] suggested that TMHT has high sensitivity of 82.6%, high specificity of 99.31%, PPV of 90.47% and NPV of 98.63% and accuracy of 98.08% at a cut-off value of 50 mm. In our study, range of TMH measured was 32-73mm. The mean

of TMHT was 52.80 mm. In our study, we have taken the TMHT cut-off value of 50 mm as taken by Etezadi et al. At 50 mm cut off, 130 cases were found <50 mm and 185 cases were >50 mm TMH. Inour study at cut off of 50 mm TMH, true positives, false positives, true negatives, false negativesdetected by the test are 28, 102, 179 and 6 respectively. Sensitivity of 82.3%, specificity of 63.7%, positive predictive value of 21.5% negative predictive value of 96.7%, and accuracy of 78.09% were obtained with TMHT at a cut off of 50 mm.

In our study, specificity and accuracy of the test are not the same as Etezadi *et al.* [5] study, but we found that TMHT has both high sensitivity of 82.3% and high NPV of 96.7% at 50 mm cut off.

A similar study was done by Nilesh *et al.*[10] In their study of thyromental height test for prediction of difficult laryngoscopy in patients undergoing coronary bypass graft surgery, it showed sensitivity of 75%, specificity of 97%, PPV of 73%, NPV of 97% and accuracy of 95% at cut off of 50 mm. In our study TMHT at cut off of 50 mm showed sensitivity of 82.3%, specificity of 63.7%, positive predictive value of 21.5% and negative predictive value of 96.7%, and accuracy of 78.09%. Our study showed good sensitivity of 82.3%, and good NPV of 96.7%, but specificity, PPV and accuracy are lower than Nilesh *et al.* [10] study at cut off of 50 mm. Nilesh *et al.* [10] revised TMHT and found best compromise between sensitivity and specificity of test at cut-off 52.17 mm. At this cut off, it showed an increased sensitivity to 81.25% and specificity to 92.3%. In our study, we found best compromise between sensitivity and specificity of TMHT at cut off of 48 mm, and it showed a sensitivity of 64.7% and specificity of 79.7% which are lower than Nilesh *et al.* [10] study at cut off 52.17.

One more study was done by Selvi *et al.* [11] in Turkey. In their study on evaluation of the reliability of pre-operative descriptive airway assessment in difficult laryngoscopy in prediction of the Cormack-Lehane score compared the predictive values of different airway assessments tests (Modified Mallampati Test (MMT), Upper Lip Bite Test (ULBT), and Thyromental distance measurement test (TMD) including thyromental height measurement test. In their study, TMHT has both high sensitivity (91.89%) and high NPV (98.63)%, however specificity and PPV values significantly decreased (52.2%, 14.7%, respectively) at the 50 mm cut off point.

They have revised the cut off value to 43.5 mm, where they found best compromise between sensitivity (64.86%) and specificity (78.02%). But at 43.5 mm cut-off of TMHT they detected lower sensitivity and better specificity. In our study TMHT at cut off of 50 mm showed sensitivity of 82.3%, specificity of 63.7%, and positive predictive value of 21.5% and negative predictive value of 96.7%. Compared to Selvi et al. study, in our study, TMHT at cut off of 50 mm has lower sensitivity, comparable NPV and better specificity and positive predictive value. But in our study, best compromise between sensitivity (64.7%) and specificity (79.7%) was found at 48 mm. TMHT at cut off of 48 mm in our study showed lower sensitivity and better specificity when compared to 50 mm.

So, when we revised the TMH cut-off to 48 mm we detected 79 patients, <48 mm TMH and 236 patients >48 mm TMH. True positives, true negatives, false positives, false negatives detected by TMHT at 48 mm cut off are 22, 57, 224, and 12 respectively. Specificity of the test increased to 79.7% and accuracy was improved to 78.09% at 48 mm cut off in our study population. On comparison of efficacy of TMHT at 50 mm and 48 mm, specificity and accuracy are better at 48 mm but sensitivity is better at 50mm cut off of TMH.

Contrary to Etezadi *et al.* [5] and Selvi *et al.* [11] and Nilesh *et al.* [10] results, we couldn't verify the same efficiency of TMHT at either 50 mm or 48 mm. Efficacy of TMHT to predict difficult laryngoscopy also depends on patient's race and anatomical variations of airway. It must be mentioned that anatomical differences and measurement errors may affect the results.

According to our study in clinical practice, a TMH value smaller than 50 mm can be used as an early warning system, alerting the clinician to the probability of difficult intubation due to high sensitivity of 82.3% and this will identify most patients in whom intubation will be difficult in reality. It can be predicted that the patients with TMH value greater than 50 mm will have easy intubation since NPV value is 96.7%.

The present study demonstrates the practicality of TMHT in predicting difficult intubation which has a good sensitivity and negative predictive value, but validation will require further studies in more diverse patient population with regard to race, age, sex, which may result in more revealing results.

References

1. Aitkenhead A. Injuries associated with anaesthesia. A global perspective. British Journal of Anaesthesia. 2005;95(1):95-109.

2. Caplan RA, Posner KL, Ward RJ, Cheney FW. Adverse respiratory events in anaesthesia: A closed claims analysis. Anaesthesiology. 1990;72:828-33.
3. Miller CG. Management of the difficult intubation in closed malpractice claims l: ASA newsletter 2000; 64(6)13-16 and 19.
4. Biebuyck J, Benumof J. Management of the Difficult Adult Airway with Special emphasis on Awake Tracheal Intubation. Anesthesiology. 1991; 75(6):1087-1110.
5. Etezadi F, Ahangari A, Shokri H, Najafi A, Khajavi M, Daghigh M et al. Thyromental Height: a new clinical test for prediction of difficult laryngoscopy. Anesthesia & Analgesia. 2013;117(6):1347-1351.
6. Wilson ME, Speigelhalter D, Robertson JA, Lesser P. Predicting difficult intubation. Br J Anaesth. 1988; 61:211-6.
7. Aktas S, Atalay YO, Tugrul M. Predictive value of bedside tests for difficult intubations. Eur Rev Med PharmacolSci. 2015;19:1595-9.
8. Randell T. Prediction of difficult intubation. ActaAnaesthesiolScand. 1996;40:1016-23.
9. Yildiz TS, Korkmaz F, Solak M, Toker K, Erciyes N, Bayrak F, et al. Prediction of difficult tracheal intubation in Turkish patients:a multi-center methodological study. Eur J Anaesthesiol. 2007; 24:1034-40.
10. Jain N, Das S, Kanchi M. Thyromental height test for prediction of difficult laryngoscopy in patients undergoing coronary artery bypass graft surgical procedure. Ann Card Anaesth. 2017;20:207-11.
11. Selvi O, Kahraman T, Senturk O, Tulgar S, Serifsoy E, Ozer Z. Evaluation of the reliability of preoperative descriptive airway assessment tests in prediction of the Cormack-Lehane score: A prospective randomized clinical study. Journal of Clinical Anesthesia. 2017;36:21–26.

Original Research Article

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Comparison of the Analgesic Effect of Tramadol Suppository with a Combination of Tramadol and Diclofenac Suppository after Lower Abdominal Surgeries

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Abstract

Background and aim of the study: The rationale behind this study was to reduce the side effects of standard dose of tramadol by reducing the dose of tramadol and to achieve same analgesic effect by combining with diclofenac. So this study compares the analgesic efficacy and side effect profile of rectal tramadol 100 mg with combination of rectal tramadol 50 mg and rectal diclofenac 50 mg in patients undergoing lower abdominal surgeries. *Materials and Methods:* Two hours after the establishment of spinal anaesthesia, patient were administered either tramadol 100 mg rectally in Group T (n=50) or combination of tramadol 50 mg rectally and diclofenac 50 mg rectally in Group TD (n=50). Using 0-10 numeric rating scale (NRS), pain at the surgical site at rest during postoperative period was measured. Any side effects like nausea, vomiting, pruritus, dizziness, headache, drowsiness, gastritis, Sweating etc. for 24 h was noted. *Results:* The mean duration of effective postoperative analgesia was 314.5 ± 7 minutes and 318.9 ± 5 minutes in group T and TD respectively. The difference between the groups with respect to duration of effective postoperative analgesia was not statistically significant. Group T had a statistically higher incidence of nausea and vomiting than group TD. *Conclusion:* The combination of low dose tramadol and diclofenac may be a better alternative to standard dose tramadol as it provides same quality and duration of analgesia with fewer side effects.

Keywords: Tramadol; Diclofenac; Postoperative analgesia; Nausea and vomiting.

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Introduction

Postoperative pain relief is a universal concern because pain relief is a fundamental human right. Unrelieved acute pain results in potentially life-threatening adverse physiological effects, development of chronic pain syndromes and may cause psychological disturbances. Systemically administered analgesics include NSAIDS and opiates which are administered either parenterally or rectally in the postoperative period [1].

Tramadol is a centrally acting opioid analgesic, which acts on μ opioid receptors, and is classified as a phase II analgesic according to the WHO

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pain score [2] but its analgesic effect is because of mixed opioid and non-opioid activities [3,4]. Analgesic Action of Tramadol has multiple mechanism like inhibition of the opioid receptor, inhibition of noradrenaline (norepinephrine) and serotonin (5-hydroxytryptamine; 5-HT) reuptake. One of the most frequent side effects of tramadol is nausea and vomiting [5]. Other adverse effects are generally similar to those of opioids, although they are usually less severe, and can include respiratory depression, dysphoria and constipation [5].

Diclofenac is one of the most commonly used Non-Steroidal Anti-Inflammatory Drugs (NSAIDs) and is classified as a phase II analgesic according to the WHO pain score. This acts by potent cyclo-oxygenase inhibition, reduction of arachidonic acid release, and enhancement of arachidonic acid uptake. Its common adverse effects are gastric irritation, dyspepsia, peptic ulcer or bleeding, nephrotoxicity, asthma, and anaphylactic reactions [6]. However, after intravenous and oral administration of tramadol, peak concentrations are reached rapidly and this has been associated with higher incidence of nausea and vomiting. This limits the use of tramadol as a postoperative analgesic [7]. Rectal administration of tramadol may be an alternative in this situation as the incidence of nausea and vomiting is relatively less than intravenous tramadol [8]. Rectal administration of tramadol is convenient to use, and is an established route of administration of the drug for postoperative pain in adults [2,9]. But the incidence of nausea and vomiting associated with rectal tramadol (100 mg) is relatively more when compared to rectal diclofenac (100 mg) [10].

The present study has been carried with hypothesis that the reduction of dose of tramadol and diclofenac to half of standalone dose of the both drugs will lead to reduction in incidence of side effects of both the drugs with same analgesic efficacy in patients undergoing lower abdominal surgeries.

Materials and Methods

This was a prospective, randomised, double-blind, parallel-group controlled trial. After Institutional Ethic Committee approval and informed consent, 100 ASA 1 or 2 patients aged between 18-60 years, undergoing elective lower abdominal surgeries under spinal anaesthesia were prospectively included in the study. The exclusion criteria were ASA status more than 2; major co-existing medical illness such as severe asthma, uncontrolled hypertension or diabetes; peptic ulcer disease or gastrointestinal bleeding; already on long-term analgesics and known hypersensitivity to any of the study medications.

After inclusion, patients were randomized by using computerised generated random table numbers and allotment was done using coded sealed opaque envelopes and informed written consent was obtained. Participants were enrolled by one of the authors, and the group assignment was done by another.

All the patients were pre-medicated with oral alprazolam 0.5 mg and oral ranitidine 150 mg on the previous night of surgery. Patients was kept nil orally for at least 8 hours.

On arrival to the operating room, intravenous line was secured with 18G intravenous cannula in all patients and was preloaded with lactated ringer's solution at 15 ml/kg. Patients were connected to all standard monitors such as pulse oximetry, ECG, Non-invasive Blood pressure monitors. Baseline values of parameters like heart rate, blood pressure, and SPO_2 were recorded.

All patients received Inj. Ranitidine 50 mg intravenously. Under aseptic precaution, all patients underwent lumbar puncture in left lateral position at L3-4 inter laminar space using 25G Quincke's spinal needle and received standard spinal anaesthesia with 3.5 ml of bupivacaine (heavy) 0.5% to achieve block level up to T4. Two hours after the establishment of spinal anaesthesia, patient were administered with either tramadol 100 mg rectally in Group T (n=50) or combination of diclofenac 50 mg rectally and tramadol 50 mg rectally in Group TD (n=50).

Vital parameters like heart rate, blood pressure, SPO_2 were monitored during intraoperative and postoperative period.

Using 0-10 numeric rating scale (NRS), pain at the surgical site at rest during postoperative period was measured at intervals of 0, 1, 2, 3, 4, 8, 12, 16, 20 and 24 h. Time 0 begins when study drug was administered. Effective pain control was defined as NRS score ≤ 3. The duration for which NRS score was ≤3 after insertion of suppository was considered as duration of effective postoperative analgesia. When NRS score was more than 3, supplementary rescue analgesic intravenous morphine was administered initially 0.1 mg/kg. If pain relief was not adequate, patients were administered with subsequent doses of intravenous morphine 0.02mg/kg to maximum dose of 0.2 mg/kg.

Any side effects like nausea, vomiting, pruritus, dizziness, drowsiness, gastritis were noted for

24 h. Side effects were treated with intravenous Ondansetron 4 mg (Nausea and Vomiting), intravenous promethazine 25 mg (pruritus), and intravenous pantoprazole 40 mg (Gastritis). Patients who had dizziness and drowsiness were monitored till above side effects subside.

Severity of nausea and vomiting was assessed using 0-10 numeric rating scale (NRS) where scale "0" (labelled "no nausea") and "10" (labelled "unbearable vomiting"), patients with score of 1-3, 4-7, 8-10 were considered as equivalent adjectival scale mild, moderate and severe respectively.

Statistical analysis

As our pilot study was with no previous information being available regarding expected means or standard deviations, a pre-study power calculation was not possible. The number of participants was based on a feasible convenience sample and was therefore arbitrarily decided. The study was analysed with null hypothesis that the postoperative analgesia in both the groups will be adequate. The primary outcome of the study was to compare the analgesic efficacy between the two groups. The secondary outcome of the study was to compare the side effect profile between the groups in patients undergoing lower abdominal surgeries. Pearson's chi-squared test was used to determine the normality of distribution of data. Statistical testing of ordinal data (age and sex of the patient, weight and height of the patients, Type and duration of surgery) was done using fisher's exact test. The remaining variables were analysed for statistical significance using two tailed unpaired 't' test. The results are presented as mean ± standard deviation (SD), number (n) of cases. A p value of < 0.05 was considered statistically significant.

Results

The two groups were more or less homogenous with regard to age and sex distribution, weight and height of patients, type and duration of surgery. There was no significant difference between the two groups with regard to cardiorespiratory parameter in the intraoperative and postoperative period. The mean duration of effective postoperative analgesia was 314.5 ± 7 minutes and 318.9 ± 5 minutes in group T and TD respectively. The difference between the groups with respect to duration of effective postoperative analgesia was not statistically significant. The incidence of nausea was comparatively high in group T (n= 15) than in group TD (n=3). The incidence of vomiting was comparatively high in group T (n=9) than in group TD (n=0). So the difference in incidence of nausea and vomiting was statistically significant between group T and group TD. There was no statistically significant difference between the two groups regarding the incidence of other side-effects.

Table 1: Demographic profile of patients, duration of surgery

Variables	Group T (n= 50) (Mean ± SD)	Group TD (n= 50) (Mean ± SD)	'p' value
Age (years)	48.4 ± 2.45	50.1 ± 3.04	0.238
Sex (Male:Female)	9:51	10:50	0.342
Height (cm)	155.3 ± 3.05	156.6 ± 2.48	0.432
Weight (Kg)	53.7 ± 3.25	55.6 ± 3.65	0.602
Type of Surgery			
• Vaginal Hysterectomy	51	50	
• Inguinal Hernioplasty	9	10	0.456
Duration of Surgery (minutes)	95 ± 82	92 ± 10	0.125

Table 2: Number of patients with NRS < 3 after insertion of suppository

Time (after insertion of suppository) (minutes)	60	120	180	240	270	300	315	330	345
Group T (n)	50	50	50	50	50	50	49	10	0
Group TD (n)	50	50	50	50	50	50	50	15	0
'p' value	0.999	0.999	0.999	0.999	0.999	0.999	0.876	0.234	

Table 3: Total rescue analgesic consumption (Intravenous morphine in mg) in 24 hours (Mean ± SD)

Group T	Group TD	'p' value
9.54 ± 0.34	9.13 ± 0.43	0.675

Table 4: Postoperative characteristics

Characteristics	Group T	Group TD	p value
Duration of effective postoperative analgesia (Minutes) (Mean ± SD)	314.5±7	318.9±5	0.435
Side-effect Profile			
• Nausea and Vomiting (n)	15	3	0.0013
Mild (NRS 1-3)	2	2	
Moderate (NRS 4-7)	6	1	
Severe (NRS 8-10)	7	0	
• Drowsiness (n)	1	0	0.436
• Gastritis (n)	0	1	0.437
• Dizziness (n)	1	0	0.442
• Headache (n)	2	0	0.586
• Sweating (n)	1	0	0.441

Discussion

Postoperative pain relief is one of the most important aspects of postoperative care of the surgical patients. Postoperative pain is associated with grave physiological and psychological trauma, resulting in altered cardiorespiratory parameters, restless and delirium. Most of the times, pain relief is inadequate in anticipation of side-effects associated with the analgesics. The lower abdominal surgeries like vaginal hysterectomy, inguinal hernioplasty etc. are associated with moderately severe postoperative pain which can be treated effectively with tramadol (Phase 2 analgesic in WHO ladder). But administration of tramadol either intravenously or rectally in postoperative period is associated with side-effects such as nausea or vomiting, headache, sedation, delirium, sweating. Among these, nausea and vomiting are minor but most common and troublesome side-effect associated with tramadol which makes its less suitable for use as a postoperative analgesic [11]. Various routes of tramadol administration have been tried to reduce the incidence and severity of postoperative nausea and vomiting but with limited success.

Our study shows that low dose combination of tramadol and diclofenac will provide similar quality and duration of analgesia as the standard dose of tramadol alone with significantly less incidence of nausea and vomiting when compared to the standard dose of tramadol alone.

The review of literatures in Medline to best our ability did not show any similar studies to compare our study results.

In our study, both groups were demographical comparable. Patients in group T had NRS score less than 3 for 314.5 ± 7 h whereas patients in group TD had NRS score less than 3 for 318.9 ± 5 h. So the analgesic efficacies of both groups were comparable with regards to duration and quality of analgesia. So pain relief provided by combination of tramadol 50 mg and diclofenac 50 mg was similar to the tramadol 100 mg alone.

The incidence and severity of nausea and vomiting was clinically and statistically high in group T patients when compared to group TD. Incidence of headache was also high in group T than group TD. Incidence and severity of other side effects were comparable between two study groups. This significant difference between the two groups with regards to incidence of nausea and vomiting is explained by the fact that it is the peak concentration of tramadol achieved which determines the incidence and severity of the nausea and vomiting [7,12].

We also observed that the incidence of gastritis which is a common side effect associated with standard dose diclofenacas observed by various studies [13,14,15] was also significantly less in our low dose tramadol and diclofenac combination group.

The limitation of our study is that patients who were undergoing vaginal hysterectomy and inguinal hernioplasty were included. So the results cannot be generalized to other gynaecologic and general lower abdominal surgeries.

Conclusion

The combination of low dose tramadol and diclofenac may be a better alternative to standard dose tramadol as it provides same quality and duration of analgesia with fewer side effect.

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References

1. Mitra S, Khandelwal P, Sehgal A. Diclofenac–tramadol vs. diclofenac–acetaminophen combinations for pain relief after caesarean section. ActaAnaesthesiol Scand. 2012;56:706-11.
2. Zwaveling J, Bubbers S, Van Meurs AH, Schoemaker RC, Van Heel IR, Vermeij P. Pharmacokinetics of rectal tramadol in postoperative paediatric patients. Br J Anaesth. 2004;93:224–7.
3. Eggars KA, Power I. Tramadol. Br J Anaesth. 1995; 74:247–9.
4. Lee CR, McTavish D, Sorkin EM. Tramadol: A preliminary review of its pharmacodynamic and pharmacokinetic properties and therapeutic potential in acute and chronic pain states. Drugs. 1993;46:313–40.
5. Dayer P, Desmeules J, Collart L. Pharmacology of tramadol. Drugs. 1997;53:18-24.
6. Lethola J, Sipponen P.A gastroscopic and histological double-blind study of the effects of diclofenac sodium and naproxen on the human gastric mucosa. Scandinavian J rheumatology 1977;6:97-102.
7. Petrone D, Kamin M, Olson W. Slowing the titration rate of tramadol HCl reduces the incidence of discontinuation due to nausea and or vomiting: a double-blind randomized trial. J Clin Pharm Ther 1999;24:115–23.
8. Gadani HN, Chaudhary VP. Comparative study of the analgesic efficacy of rectaltramadol versus intravenous tramadol for adult tonsillectomy. Anesthesia: Essays and Researches. 2010;4:102-5.
9. Lintz W, Barth H, Osterloh G, Schmidt-Bothelt E. Pharmacokinetics of tramadol and bioavailability of enteral tramadol formulations. 3rd Communication: suppositories. Arzneimittelforschung. 1998;48: 889–99.
10. Vyankatesh JS, Ramesh VD, Ganesh K, Vikram S, Jamadar NP.Comparative study of analgesic efficacy of rectal suppository of tramadol versus diclofenac in suppressing postoperative pain after caesarean section. International J Healthcare & Biomedical Research. 2013;1:52-7.
11. Pluim MA, Wegener JT, Rupreht J, Vulto AG. Tramadol suppositories are less suitable for post-operative pain relief than rectal acetaminophen/ codeine. Eur J Anaesthesiol. 1999 Jul;16:473-8.
12. McEvoy GK, Miller J, Litvak K *et al.* editors. AHFS Drug Information. United States of America: American Society of Health-System Pharmacists; 2003. ISBN 1-58528-039-9.
13. Colbert S, McCory C, O'Hanlon D, Scully M, Tanner A, Doyle M. A prospective study comparing intravenous tenoxicam with rectal diclofenac for pain relief in day case surgery. Eur J Anaesthesiol 1998;15:544-8.
14. Mahdavi A, Telkabadi Z, Aleyasin A *et al.* Comparison of Morphine Suppository and Diclofenac Suppository for Pain Management After Elective Caesarean Section. *ActaMedicaIranica*, 2016:54;709-12.
15. Bakhsha F, Niaki AS, Jafari SY *et al.* The Effects Of Diclofenac Suppository And Intravenous Acetaminophen And Their Combination On The Severity of Postoperative Pain In Patients Undergoing Spinal Anaesthesia During Cesarean Section. Journal of Clinical and Diagnostic Research. 2016;10:9-12.

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A Comparison Study Quality of Anaesthesia for Lower Limb Orthopaedic Surgery: Bupivacaine with Adjuvant Clonidine versus Bupivacaine with Adjuvant Midazolam

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Abstract

Background: Spinal anesthesia is the most commonly used anesthesia for orthopedic surgery. Despite of using long acting local anesthetic like Bupivacaine, the duration of anesthesia is short. Therefore, various drug combinations like Clonidine, Ketamine, Opioids etc. have been tried to prolong duration of analgesia. *Methodology:* This study was conducted among 60 participants GMERS Hospital, Valsad. Patients were randomly allocated to 2 groups. Thirty subjects were in each group who received either 0.5% heavy Bupivacaine 3 ml (15 mg) + Clonidine 0.3 ml (45 µg) (Group A) or 0.5% heavy Bupivacaine 3 ml (15 mg) + Midazolam 0.2 ml (1 mg) + 0.9% normal saline 0.1 ml (Group B). Time required for sensory block, motor blockade, level of sedation and post operatively pain measurement was assessed. *Result:* The present study showed that significant decrease in mean arterial pressure and heart rate at 30, 45 and 60 min in patients with adjuvant clonidine as compared to midazolam. Mean time for sensory onset, sensory regression to S2 from highest sensory level, two segment sensory regression, total duration of motor blockade and onset of grade-3 motor blockade in patient with adjuvant Clonidine was significantly higher as compared to adjuvant Midazolam. Post operatively there was no significant difference in mean postoperative systolic blood pressure, diastolic blood pressure, pulse rate, saturation and respiratory rate. Sedation score was also higher in patients with adjuvant Clonidine group. Most common reported adverse events with Clonidine was hypotension and bradycardia. *Conclusion:* Adjuvant Clonidine 45 µg intrathecal hyperbaric Bupivacaine (0.5%) significantly prolongs duration of motor and sensory block. It provides adequate hemodynamic stability, prolongs postoperative analgesia without any significant side effects.

Keywords: Bupivacaine; Clonidine; Motor blockade; Analgesia

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Introduction

Spinal anesthesia is the most commonly used anesthesia for orthopedic surgery. Despite of using long acting local anesthetic like Bupivacaine, the duration of anesthesia is short [1]. Therefore, various drug combinations like Clonidine, Midazolam, opioids etc. have been used to prolong duration of analgesia. Clonidine as the Alpha 2-adrenergic agonist increases the effects of local anesthetics [2]. Intrathecal Clonidine is being assesed as an alternative to opioids to increase the analgesic effect of local anesthesia [3] Midazolam a short acting benzodiazepine acts on benzodiazepine-GABA

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receptor potentiates the analgesic effect of local anesthetic agent induced neuroaxial blockade [4]. Intrathecal or epidural Midazolam produces modulation of spinal nociceptive processing without neurotoxicity, sedation or respiratory depression [5].

This study was conducted to evaluate analgesic effect, hemodynamic stability and side effects of intrathecally administered Clonidine or Midazolam as an adjuvant to Bupivacaine heavy (0.5%) for orthopedic surgery.

Methodology

This randomized comparative study was carried out on 60 participants during Jan 2017 to December 2017 in GMERS hospital, Valsad after getting permission from the Institutional Ethical Committee. Subjects of 20 to 65 years age group and who fit in American Society of Anaesthesiologist Grade I and II operated for Lower limb orthopedic surgery were enrolled in the study. Subjects with regional anaesthesia's contraindication and known drug allergy were excluded. After obtaining written informed consent, patients were randomly allocated to 2 groups. Thirty subjects were in each group who received either 0.5% heavy Bupivacaine 3 ml (15 mg) + Clonidine 0.3 ml (45 µg) (Group A) or 0.5% heavy Bupivacaine 3 ml (15 mg) + Midazolam 0.2 ml (1 mg) + 0.9% normal saline 0.1 ml (Group B). All the drugs were introduced intrathecally. Randomization was done by computer method.

Under all aseptic precautions, subarachnoid block was done at L2-L3 or L3-L4 space with 23G Quincke's spinal needle in a sitting position. Time required for sensory block to reach level T10 as T0, time to reach highest sensory level as T1 and time for sensory regression to S2 as T3 were noted. Motor blockade was evaluated with modified Bromage score. Time for complete motor blockade was observed every minute till first 20 minutes. Level of sedetion was assessed using Chernik sedation score at 60 minutes intra-operatively. Post operatively pain measurement was done by Ten Point visual analogue scale (VAS). Time to achieve highest sensory level was recorded. Patient's blood pressure, pulse rate, oxygen saturation and respiratory rate were recorded at 1, 5, 10, 20, 30, 45, 60 minutes after giving spinal anesthesia. Hypotension was defined as a decrease of systolic blood pressure more than 20% of baseline value. Bradycardia was defined as a decrease in pulse rate to less than 60 per min. All patients were observed for next 24 hours. Results were statistically analyzed using SPSS software. All the results are expressed as the number, mean ± standard deviation (SD), percentages. The comparison of between the groups was performed by T test. A value of p less than 0.05 is considered significant.

Results

The present study was carried out among 60 participants belonging to ASA physical Status I and II, operated for lower limb orthopedic surgery. There was no significant difference in two groups of patients respect to gender, age, BMI and duration of surgery (Table 1, p>0.05).

Table 1: Demographic profile of study participants.

Demographic parameter	Group A (30)	Group B (30)	p value*
Age	44.0 + 1.6	45.0 + 1.4	>0.05
Weight	58.3 + 8.4	58.7 + 9.9	>0.05
Height	163.1 + 7.4	163.7 + 7.1	>0.05
BMI	23.3 + 3.6	21.6 + 3.3	>0.05
Male: Female	15:15	18:12	>0.05
ASA Grade I/II	25:5	21:9	>0.05
Duration of surgery	120 + 11.2	121.2 + 13.4	>0.05

*p value was calculated by T test

Table 2 describes the characteristics of spinal anesthesia in two groups. In Group A, mean time for sensory onset (8.0 ± 0.7), two segment sensory regression (148.0 ± 4.9), sensory regression to S2 from highest sensory level (276.8 ± 4.7), mean time for onset of grade-3 motor blockade (9.0 ± 0.7) and total duration of motor blockade (298.0 ± 9.6) was significantly higher as compared to Group B.

Table 2: Comparison of mean duration of surgery, 2 segments regression, onset of sensory block and motor blockade in Groups.

Variable	Group A	Group B	p value
Sensory onset	8.0 ± 0.7	4.7 ± 1.1	<0.05
Highest sensory level	12.1 ± 0.9	9.6 ± 1.1	<0.05
Two segment sensory regression from highest sensory level	148.0 ± 4.9	134.7 ± 3.9	<0.05
Sensory regression to S2 from highest sensory level	276.8 + 4.7	188.6 + 7.1	<0.05
Onset of grade-3 motor blockade	9.0 + 0.7	7.3 + 0.7	<0.05
Total duration of motor blockade	298.0 +9.6	216.2 + 10.1	<0.05

*p value was calculated by t test.

The intraoperative pulse rate was significantly lower in Group A at 30, 45 and 60 min time point as compared to Group B (p <0.05). Fall in mean arterial pressure in Group A at 30, 45 and 60 min was also higher as compared to Group B and it was statistically significant (p <0.05).

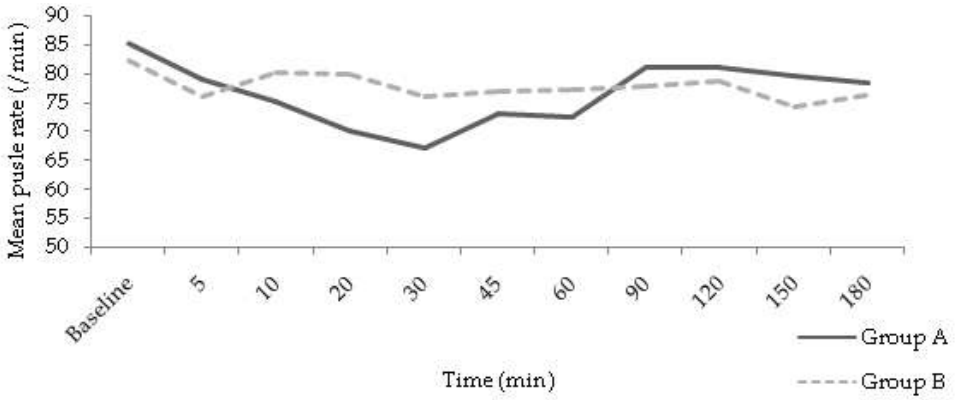

Fig. 1: Intraoperative mean pulse rate (/min) at different time intervals in 2 groups

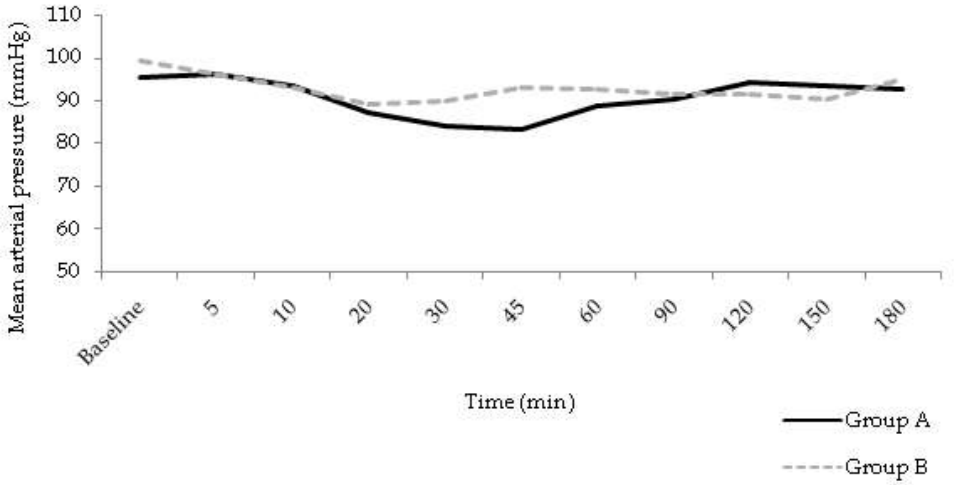

Fig. 2: Intra-operative mean arterial pressure (mmHg) at different time intervals in 2 groups

Post operatively there was no significant difference in mean postoperative systolic blood pressure, diastolic blood pressure, pulse rate, saturation and respiratory rate. Duration of post operative analgesia in group A (326.4 ± 4.3) was significantly higher as compared to Group B (252.8 ± 7.6). Only 4 patients developed sedation score 1 in group B. In Group A, sedation score 1 and 2 was observed in 22 and 8 patients respectively and it was significantly higher than Group A.

Adverse effects like hypotension and bradycardia were more common in Group A as compared to Group B (Hypotension: Group A- 30% v/s Group B-13.3%, Bradycardia: Group A- 26.6% v/s Group B-3.3%). Six subjects in Group A (20%) had dryness of mouth as compared to none in Group B. There was no significant difference in incidence of nausea, vomiting and shivering among these groups. Respiratory depression and urinary retention were not seen in any groups.

Discussion

Effective control of postoperative pain is an important challenge in perioperative care. Despite of use of a long acting local anaesthetic like bupivacaine, the duration of spinal anesthesia is short and higher doses of analgesics are required in the postoperative period. The present study showed that significant decrease in mean arterial pressure and pulse rate at 30, 45 and 60 min in patients in clonidine as compared to midazolam. Dobrydnjov noticed that significant bradycardia with 30 ug clonidine as compared to 15 ug clonidine [6]. One study with 75 ug clonidine reported significant decrease in MAP [7].

Mean time for sensory onset, sensory regression to S2 from highest sensory level, two segment sensory regression, total duration of motor blockade and onset of grade-3 motor blockade in patient with adjuvant Clonidine was significantly higher as compared to adjuvant Midazolam.

Mean time of total duration of motor blockade in group A was significantly higher than Group B. D. Kock observed that adjuvant Clonidine (45 ug) to spinal anesthesia significantly increases duration of sensory and motor Block. It provides adequate hemodynamic stability and prolong postoperative analgesia without significant side effects [8].

Neelakshi reported that postoperative analgesia duration was highest with Clonidine (426.7 + 151.8 mins) compared to Fentanyl group (284.6 + 30.1 mins), Midazolam group (270.5 + 36.2 mins) and control group (146.8 + 26.6 mins). Addition of Clonidine, Fentanyl and Midazolam to Bupivacaine heavy (0.5%) significantly improved the onset and duration of sensory and motor block, increased the duration of analgesia. Their result is comparable with our study [9]. Post operatively there was no significant difference in mean postoperative systolic blood pressure, diastolic blood pressure, pulse rate, saturation and respiratory rate. Similar to our study, Hema saxena reported that duration of post operative analgesia in patients with adjuvant Clonidine and MIdazolam was higher than control group [10]. Sedation score was also higher in patients with adjuvant Clonidine. Most common reported adverse events with Clonidine was hypotension and bradycardia.

Conclusion

Adjuvant Clonidine 45 µg intrathecal hyperbaric Bupivacaine (0.5%) significantly prolongs duration of motor and sensory block. It provides adequate hemodynamic stability, increases postoperative analgesia without any significant side effects.

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References

1. Raval DL, Chaudhary M. A clinical comparative study between dexmedetomidine v/s clonidine with bupivacaine intrathecally in major orthopaedic lower limb surgery. Journal of Research in Medical and Dental Science. 2014 Jan 1;2(1):77-83.
2. Eisenach JC, De Kock M, Klimscha W. α2-Adrenergic Agonists for Regional AnesthesiaA Clinical Review of Clonidine (1984-1995). Anesthesiology: The Journal of the American Society of Anesthesiologists. 1996 Sep 1;85(3):655-74.
3. Neves JF, Monteiro GA, Almeida JR, Sant'anna RS, Saldanha RM, Moraes JM, Nogueira ES, Coutinho FL, Neves MM, Araujo FP, Nobrega PB. Postoperative analgesia for caesarean section: Does the addition of clonidine to subarachnoid morphine improve the quality of analgesia? Revista Brasileira de Anestesiologia. 2006;56(4):370-76.
4. G. Edward Morgan, Maged S. Mikhail, Michael J. Murray. Clinical Anaesthesiology 4th ed. McGraw Hill publication; Pain management 359-12, Spinal anaesthesia 289-23.
5. Naguib M, El Gammal M, Elhattab YS, Seraj M. Midazolam for caudal analgesia in children: comparison with caudal bupivacaine. Canadian Journal of Anaesthesia. 1995 Sep 1;42(9):758-64.
6. Dobrydnjov I, Axelsson K, Samarütel J, Holmström B. Postoperative pain relief following intrathecal bupivacaine combined with intrathecal or oral clonidine. Acta anaesthesiologica scandinavica. 2002 Aug;46(7):806-14.
7. Strebel S, Gurzeler JA, Schneider MC, Aeschbach A, Kindler CH. Small-dose intrathecal clonidine and isobaric bupivacaine for orthopedic surgery: a dose-response study. Anesthesia & Analgesia. 2004 Oct 1;99(4):1231-8.
8. De Kock M, Gautier P, Fanard L, Hody JL, Lavand'homme P. Intrathecal Ropivacaine and Clonidine for Ambulatory Knee ArthroscopyA Dose–Response Study. Anesthesiology: The Journal of the American Society of Anesthesiologists. 2001 Apr 1;94(4):574-8.
9. Bhure A, Kalita N, Ingley P, Gadkari CP. Comparative study of intrathecal hyperbaric Bupivacaine with Clonidine, Fentanyl and Midazolam for quality of anaesthesia and duration of post operative pain relief in patients undergoing elective caesarean section. People's J Sci Res. 2012;5(1):19-23.
10. Saxena H, Singh S, Ghildiyal S. Low dose intrathecal clonidine with bupivacaine improves onset and duration of block with haemodynamic stability. Internet J Anesthesiol. 2010;23(11):9137.

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Comparison of Intravenous Dexmedetomidine Alone and in Combination with Midazolam as Premedication in Patients Receiving Spinal Anaesthesia

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Abstract

Study Objective: To compare intravenous dexmedetomidine in combination with midazolam and dexmedetomidineas premedication in patients receiving spinal anaesthesia. *Design:* Prospective randomized controlled double blind study. *Methodology:* 60 patients belonging to ASA physical status I and II scheduled for surgery under spinal anaesthesia were randomly selected for the study and were randomly divided into two groups of 30 each. Group DM patients received intravenous dexmedetomidine 1 µg/kg in combination with midazolam 0.025 mg/kg (bolus) and group D patients received intravenous dexmedetomidine1 µg/kg (bolus) as premedication before receiving 3 ml (15 mg) of intrathecal hyperbaric bupivacaine (spinal anaesthesia). Hemodynamic changes, to note down the level of sedation, additional analgesic requirements preoperatively, and complication if any were studied. *Results:* Ramsay sedation score was statistically significant in the dexmedetomidine in combination with midazolam group (DM) for 20 minutes in comparison with Dexmedetomidine (D) group, and there after the sedation scores were similar in both the groups (sedation score of 2-3) without any respiratory depression. The time request for analgesia, hemodynamic parameters and side effects were similar in either of the groups. *Conclusion:* Intravenous bolus of dexmedetomidine (D) is sufficient to provide adequate sedation with good hemodynamic stability and without respiratory depression in patients who receive spinalanesthesia.

Keywords: Intravenous; Dexmedetomidine; Midazolam; Hyperbaric bupivacaine; Intrathecal; Ramsay sedation score; and Spinalanesthesia.

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Introduction

Spinal anesthesia may be defined as the interruption of conduction of nerve impluses by injecting an anesthestic into subarachnoid space that reduces sensitivity to pain without loss of conscious. Procedures below the level T10 can be performed under spinal anesthesia. Spinal anesthesia(subarachnoid block) has least failure rates, easy to administer and cost effective. It also has the advantage of being free from the risk of intubation and pulmonary aspiration. However, the patient's anxiety presents as disadvantage of spinal anesthesia [1,2,3], which is more common

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among younger patients, women, and people with negative experience of anesthesia or fear of death [1,2,3]. Anxiolytics will be benifical for the patients [1,2].

High catecholamine levels increase arterial blood pressure, heart rate, and oxygen consumption [2]. Various agents such as phenothiazine, benzodiazepines, barbiturates, opioids are anxiolytics and provide sedation. Commonly used drug is midazolam which is a benzodiazepine, as it is a water soluble agent, its onset time is much faster then other benzodiazepines, and it has a relatively short elimination half-life (2-4 h) [1]. Its sedative effect is shown in many studies [4]. Dexmedetomidine is a selective, specific, and highly potent apla-2 adrenoreceptor agonist (1620:1 α_2 to α_1) is also used for permedication [5,10,11] due to its sedative and analgesic effect. The analgesic effect is due to the activation of the alpha2- adrenergic receptors [3,5]. Dexmedetomidine decreases the stress response; in turn reduce the heart rate and blood pressure by decreasing the catecholamine secretion. It doesn't cause respiratory depression in comparison with benzodiazepines and opioids [4,5,6]. Various studies have shown the sedative and analgesic effect of dexmedetomidine on acute postoperative pain after major surgical procedures [2,3,5,7]. Midazolam is the most popular anxiolytic and hypnotic agent used in surgical and non-surgical settings. Therefore, midazolam is preferred drug. However, intravenous midazolam should be used in tittered doses to achieve and maintain the desired sedative level as well as to minimize side effects due to over-dosage [1,12].

In view of these facts, this study was planned to analyze the effects of intravenous dexmedetomidine in combination with midazolam (DM) and intravenous dexmedetomidine (D), on duration of sedation and the intraoperative hemodynamic profile when given intravenously in patients receiving intrathecal bupivacaine (spinal anaesthesia).

Aims and Objectives

To analyze the difference between intravenous dexmedetomidine 1 µg/kg in combination with midazolam 0.025 mg/kg and intravenous dexmedetomidine 1 µg/kg when given as premedication in patients receiving intrathecal hyperbaric bupivacaine 3 ml (15 mg).

1. To compare level of sedation.
2. Assess the hemodynamic stability.
3. Additional analgesic requirements post operatively.
4. Complications if any.

Materials and Methods

This study was conducted on patients undergoing elective surgery under spinal anaesthesia for a period of 18 months. Written inform content was obtained after explaining the patients the procedure.

Inclusion Criteria

1. Patients under ASA grade 1 & 2.
2. Patients undergoing elective surgeries.
3. Patients giving valid consent.
4. Patients aged between 18 yrs to 55 yrs.

Exclusion Criteria

1. Patient refusal.
2. Patients with ASA grade 3 & 4.
3. Patients posted emergency surgery.
4. Patients on any opioids or any sedative medication in the week prior to the surgery.
5. Patient with history of alcohol or drug abuse.
6. Patients who are allergic to any of the test drugs.
7. Contraindication to spinal anesthesia (example; coagulation profile derangement, infection at local site, preexisting neurological defects.

Study Design

Pre anesthetic evaluation was done the day prior to surgery. Nil per oral guidelines were followed prior to the day of surgery and patient had received proton pump inhibitor as premedication, no anxiolytics were given. With the consent of the patients, the study was conducted. 60 patients (of either sex) were randomly divided into two groups, DM group and D group.

According to ASA standard monitoring. Patients peripheral oxygen saturation, blood pressure (systolic, diastolic, mean arterial pressure), electrocardiogram were monitored including Ramsay sedation scoring, and basal values were noted. The study drugs were premixed to a total volume of 10 ml in a 10 ml syringe and were administered intravenously over a 10 minutes period as a single dose (bolus). 5 minutes after receiving

the premedication, the patient was placed in lateral position and dural puncture was performed at L3-L4 interspace using standard mid line approach with a 23G Quincke needle. Hyperbaric bupivacaine 0.5% 3 ml (15 mg) was injected intrathecally. All the parameter of sedation and anxiety and the vital signs in this study was done by the same observer to minimize inter observer variation.

Parameters Evaluated

1. Level of Sedation was assessed using Ramsay Sedation Score

1. Patient anxious and agitated.
2. Patient cooperative, oriented and tranquil.
3. Patient responds to commands.
4. Patient has a brisk response to a light glabellar tap or loud auditory stimulus.
5. Patient asleep, sluggish response to light glabellar tap or loud auditory stimulus.
6. Patient does not respond to painful stimulus.

The score were revaluated during the surgery and post operatively up to 120 minutes.

2. Hemodynamic Assessment

Systolic, diastolic, mean arterial blood pressure, heart rate, oxygen saturation, end tidal carbon dioxide concentration were recorded before premedication, 2 minutes after end of premedication, immediately before and after dural puncture and every 15 minutes for 120 minutes after spinal anesthesia.

Hypotension was considered when mean arterial pressure decreases to less than 20% from baseline. They were treated with intravenous sympathomimetic drug (Ephedrine).

Bradycardia (heart rate less than 60 beats/min or 20% the base line) was treated with intravenous atropine in boluses of 0.6 mg.

3. Severity of pain by visual analogue scale postoperatively

The intensity of pain was assessed using a 10-cm visual analog scale (VAS; 0: no pain and 10: worst imaginable pain). The number that correlates with the position on the VAS the patient pointed to, was noted. The time for the first request for postoperative analgesia and the number of patients who required supplemental analgesia was also recorded. All patients were observed during the postoperative period for 2 hours and later 6th hourly to know the duration, quality and intensity of pain.

4. Complications

Complications in relation to respiratory or cardiovascular problem, nausea vomiting and headache were noted down.

Statistical Methodology

The statistical analysis was done using SPSS (Statistical Package for Social Sciences) Version 17.0 statistical Analysis Software. The values were represented in Number (%), Mean, and Standard Deviation. Level of significance: "p" is level of significance.

Results

With an objective to analyze the sedative effects of intravenous dexmedetomidine 1 µg/kg in combination with midazolam 0.025 mg/kg and

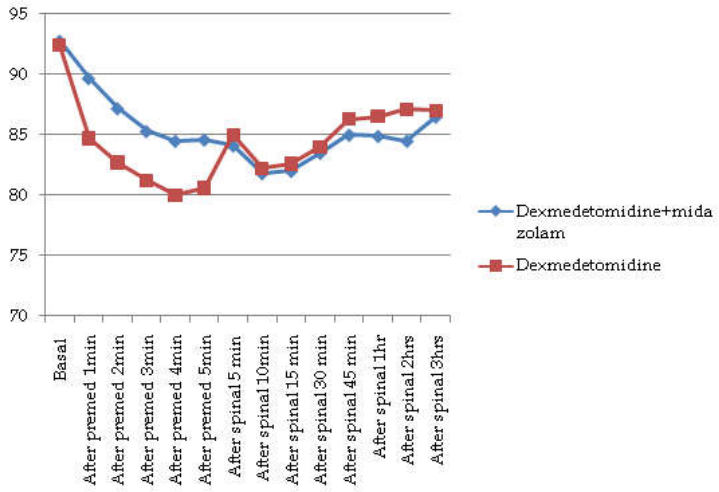

Chart 1:

dexmedetomidine 1 µg/kg as premedication in patients receiving spinal anesthesia. A total of 60 patients were enrolled in this study and were randomly distributed into two equal groups, comprising of 30 patients each. Group DM comprised of 30 patients who were given dexmedetomidine in combination with midazolam, while Group D comprised of 30 patients who were given intravenous dexmedetomidine as premedication.

Haemodynamically in both the groups patients were stable through out the procedure, nil statistical signifiance.

There is no statistical difference in the mean SpO_2 recording among two groups of patients except in the 30th min (p value 0.023) and in the 45th min (p value 0.014) of the DM group.

Group DM showed higher Ramsay Sedation Score than Group D, which is statistically significant at 10th, 15th and 30th minute (p 0.016, p 0.031, p 0.007 respectively). Ramsay Sedation Score in group DM than group D was not statistically significant at 5, 45, 60, 120 and 180 minutes.

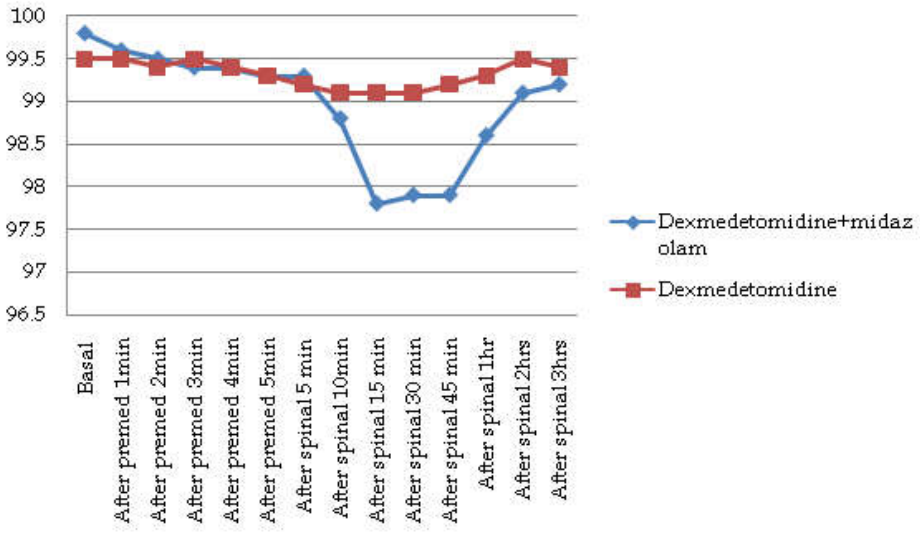

Chart 2: line graph showing SpO_2

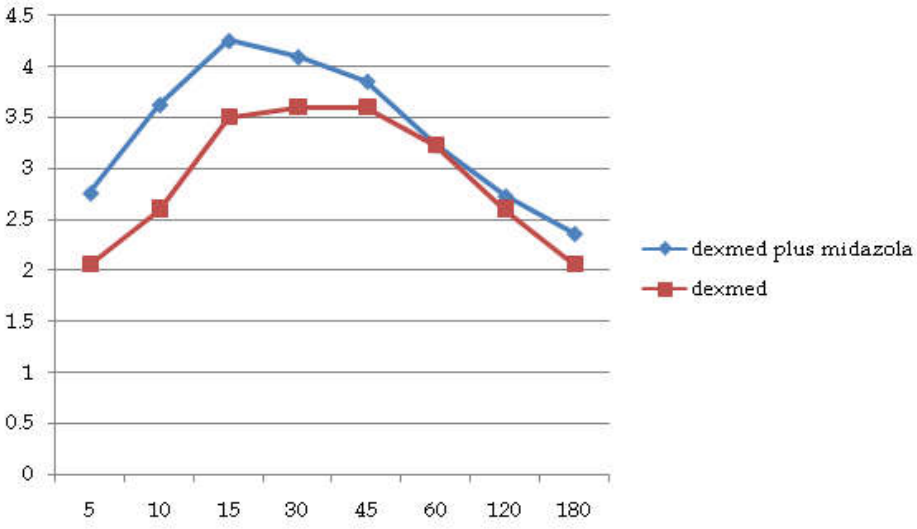

Chart 3: Line graph showing level of sedation.

Discussion

Procedures below the level of T10 may be performed under spinal anesthesia (subarachnoid block). Spinal anaesthesia is the most preferred anesthesia because of its least failure rates, easy to administer and cost effective. It also has the advantage of being free from the risk of intubation and pulmonary aspiration.

Patient undergoing spinal anesthesia will be anxious, more common among younger patients, women, and people with negative experience of anesthesia or fear of death [1,2,3]. High catecholamine levels increase arterial blood pressure, heart rate, and oxygen consumption [2,16]. Anxiolytic will be benifical for the patient [1,2,3]. Various agents such as phenothiazines, benzodiazepines, barbiturates, opioids are anxiolytics and provide sedation. Commonly used drug is midazolam with rapid onset and short acting. Its sedative effect is shown in many studies [4].

The present study was planned with an objective to analyze the sedative effects of intravenous dexmedetomidine 1 µg/kg (iv bolus) in combination with midazolam 0.025 mg/kg (iv bolus) and dexmedetomidine 1 µg/kg (iv bolus) as premedication in patients receiving intrathecal hyperbaric bupivacaine. Both the groups did not have statistically significant differences in their demographic data.

Variable	DM group	D group	p value
Age	36.8 ± 15.5	36.5 ± 14.0	0.615
Height	167.13 ± 11.00	165.87 ± 11.00	0.423
Weight	59.7 ± 15	59.1 ± 15.80	0.268
BMI	21.29 ± 3	21.34 ± 2.5	0.405
ASA I/II	22/08	22/08	0.432

Gertler *et al.* [5], Bloor BC *et al.* [8], Dyck JB *et al.* [9], Hall JE *et al.* [11], in their studies have shown that after administration of a intravenous bolus of 1 µg/kg dexmedetomidine, initially resulted in a transient increase of the blood pressure and a reflex decrease in heart rate, especially in younger, healthy patients. Dexmedetomidine does not appear to have a direct effect on heart [7]. A biphasic cardiovascular response is noted after the administration of dexmedetomidine [4,7,8,10]. The initial reaction can be explained by the peripheral α_{2B} –adrenoceptor stimulation of vascular smooth muscle and can be attenuated by slow infusion over 10 or more minutes. Another possible explanation for subsequent heart rate decrease is the stimulation of the presynaptic α2-adrenoceptor, leading to a decreased norepinephrine release [9]. In the present study group there was nil statistical significance changes in the heart rate. (DM group patients had a basal mean heart rate of 83.9 ± 6.5 & after premedication 74.4 ± 7.6. D group patients had a basal heart rate of 84.5 ± 6.5, after premedication 70.3 ± 5.9).

Linag *et al.* [17] study 8 of 63 patients had respiratory depression which appears to be a CNS mediated effect [1]. Hall JE *et al.* [11], Bhana *et al.* [16], Venn *et al.* [17], al in their study they have shown that dexmedetomidine does not cause any respiratory depression. There was a nil statistical significane fall in the SpO_2 in either of the group except at 30th min (p value 0.023) and 45th min (p value 0.014) in DM group as compared to D group, probably due to the synergistic action. Respiratory rate were similar in the groups. With nil statistical significance.

In the present study, Ramsay sedation score was statistically significant in the DM group at the 10th min (p value 0.016), 15th min (p value 0.031), and 30th min (p value 0.007) probably due the synergistic effect. Eren *et al.* [19], in their study have shown that rapid and short acting midazolam [1] showed initial high Ramsay sedation score. Midazolam in doses of 1mg to 2.5mg iv the onset of action is 30 to 60 seconds, with a peak effect in 3 to 5 mins and duration of sedation 15 to 80 minutes [1].

Non of the patients required rescue analgesia. Postoperative request for first analgesia in either of the groups was almost the same.The incidences of side effects in both the groups were statistically insignificant. Three patients had nausea and vomiting (PONV). One patient of each in either group had headache. Two patients in either group had bradycardia similar to Eren et al study.

Conclusion

In conclusion, intravenous bolus supplementation of dexmedetomidine during subarachnoid block produces satisfactory arousal sedation with good hemodynamic stability and without causing respiratory depression. Addition of intravenous midazolam to dexmedetomidine may be beneficial for patients who are highly anxious and who require deeper sedation.

References

1. Stoelting RK, Hiller SMB Pharmacology & Physiology in Anesthetic practice. 4th ed.

Indianapolis, Indiana. 2006;140-147.

2. Barash PG, Cullen BF, Stoelting RK. Hand book of Clinical Anesthesia. Philadelphia, Pennsylvania: JB Lippincott; Preoperative medication; 1991.p. 22–31.
3. Erkola O, Korttila K, Aho M *et al*. A Comparison of intramuscular dexmedetomidine and midazolam premedication for elective abdominal hysterectomy. AnesthAnalg. 1994;79:646–53.
4. White PF, Negus JB. Sedative infusions during local and regional anesthesia: a comparison of midazolam and propofol. J ClinAnesth. 1991;3(1):32-39.
5. Gertler R, Brown HC, Mitchell DH *et al.* Dexmedetomidine: a novel sedative analgesic agent, Baylor University Medical Center proceeding. Jan 2001;14:13-21.
6. Hsu YW, Cortinez LI, Robertson KM, Keifer JC, *et al.* Dexmedetomidine pharmacodynamics: part I: crossover comparison of the respiratory effects of dexmedetomidine and remifentanil in healthy volunteers. Anesthesiology. 2004;101:1066–76.
7. Kanazi GE, Aouad MT, Jabbour-Khoury SI, et al. Effect of low-dose dexmedetomidine or clonidine on the characteristics of bupivacaine spinal block. ActaAnaesthesiol Scand. 2006 Feb;50(2):222-7.
8. Bloor BC, Ward DS, Belleville JP, et al. Effects of intravenous dexmedetomidine in humans. II. Hemodynamic changes. Anesthesiology. 1992; 77:1134–42.
9. Dyck JB, Maze M, Haack C, *et al.* The pharmacokinetics and hemodynamic effects of intravenous and intramuscular dexmedetomidine hydrochloride in adult human volunteers. Anesthesiology. 1993;78:813–20.
10. Xu H, Aibiki M, Seki K, *et al.* Effects of dexmedetomidine, an alpha 2-adrenoceptor agonist, on renal sympathetic nerve activity, blood pressure, heart rate and central venous pressure in urethane-anesthetized rabbits. J AutonNerv Syst. 1998;71:48–54.
11. Hall JE, Uhrich TD, Barney JA, *et al.* Sedative, amnesic and analgesic properties of small dose Dexmedetomidine infusions. Anesth Analg 2000; 90:699–705.
12. McCutcheon CA, Orme RM, Scott DA, *et al.* Comparison of dexmedetomidine versus conventional therapy for sedation and hemodynamic control during carotid endarterectomy performed under regional anaesthesia. AnesthAnalg. 2006; 102:668–75.
13. Patki A, Shelgaonkar VC. A comparison of equisedative infusions of propofol and midazolam for conscious sedation during spinal anesthesia - a prospective randomized study. J Anaesthesiol Clin Pharmacol. 2011;27:47–53.
14. Kamibayashi T, Maze M. Clinical uses of alpha 2-adrenergic agonists. Anesthesiology. 2000;93:1345–49.
15. Bergese SD, Patrick Bender S, McSweeney TD, *et al.* A comparative study of Dexmedetomidine and midazolam alone for sedation during elective awake fiberoptic intubation. Journal of Clinical Anesthesia. 2010 Feb;22(1):35-40.
16. Bhana KNL, McClellan GJ, McClellan KJ. Dexmedetomidine. Drugs. 2000;59:263–8.
17. Venn RM, Grounds RM. Comparison between dexmedetomidine and propofol for sedation in the intensive care unit: patient and clinician perceptions. Br J Anaesth. 2001;87:684–90.
18. Liang Y, Gu M, Wang S, *et al.* Comparison of Dexmedetomidine and Midazolam for Sedation in Gynecologic Surgery Under Epidural Anesthesia. 2011;1:12-18.
19. Eren G, Gukurova Z, Demir G, *et al*. Comparison of Dexmedetomidine and three different doses of midazolam in preoperative sedation. Journal of Anaesthesiology Clinical Pharmacology. 2011 Jul-Sep;27(3):367-72.

Original Research Article

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A Comparative Study between Bupivacaine and Clonidine Combination versus Bupivacaine (Plain) for Brachial Plexus blocks using Supraclavicular Approach

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Abstract

Background: Brachial plexus block achieves ideal operating conditions by producing complete muscle relaxation, maintaining stable intra-operative hemodynamics and associated sympathetic block. Usage of adjuvant drugs along with local anesthetic, to lower the dose of each agent and enhance analgesic efficacy and thereby reducing the incidence of adverse events is a routine practice in regional anesthesia. *Aim:* To assess the anesthetic and analgesic effect of adding clonidine with bupivacaine as a regional anesthetic agent for brachial plexus block during upper limb surgeries. *Methodology:* A prospective longitudinal study was conducted for a period of one year from the anesthesiology department of Vinayaka Missions Medical College Hospital Salem. A total of 60 patients were included for the study and it was divided into two groups. Group A patients received 25 ml of 0.5% bupivacaine and group B patients received 25 ml of 0.5% bupivacaine along with 0.2 ml (30 mcg) clonidine. Onsite time and the duration of sensory and motor block was recorded along with the duration of analgesia and the maximum number of doses of analgesics required were also noted. Vitals were recorded at intervals of 5 min for first 30 min, then after every 10 min till end of surgery, and then hourly after surgery. *Results:* The onset of sensory and motor block was found to be much quicker and prolonged for a longer duration among the patients who received bupivacaine along with clonidine and the difference in time duration was found to be statistically significant. Similarly, the post-operative analgesia effect was found to be longer (487.9 mins)among the group received bupivacaine with clonidine with a less number of additional requirement of analgesia dose (1.1 dose) whereas the analgesia effect among the group received bupivacaine alone was 303.6 mins with mean additional dose of analgesia of 2.4 and the difference was found to be statistically significant. Vital parameters were normal and were almost similar among both the groups. *Conclusion:* Thus, our study had demonstrated that addition of clonidine as an adjuvant drug along with bupivacaine as a regional anesthetic agent in supraclavicular brachial plexus block had significatly prolonged the duration of analgesia and improved the quality of anesthesia.

Keywords: Brachial plexus block, Bupivacaine, Clonidine, Analgesia.

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Introduction

Today, usage of regional anesthesia has become more common in the field of anesthesiology. Particularly for upper limb surgeries using brachial plexus block as a regional anesthesia has become a routine practice. Brachial plexus block achieves ideal operating conditions by producing complete muscle relaxation, maintaining stable intra-operative hemodynamics and associated sympathetic block [1]. In this approach the plexus is blocked at the site where it is most compactly arranged at the level of nerve trunks and so the the onset of action is rapid with a very high success rate for extending the duration of block [2,3].

Usage of adjuvant drugs along with local anesthetic, to lower the dose of each agent and enhance analgesic efficacy and thereby reducing the incidence of adverse events is a routine practice in regional anesthesia [4]. Drugs like morphine, pethidine, fentanyl, clonidine, dexamethasone, midazolam are commonly used along with local anaesthetic for this purpose [5]. However their use is limited because of side effects, like deep sedation respiratory depression and psychomotor effects. Drugs with minimal side effects are always looked for. Clonidine is a selective α2 adrenergic agonist with some α1 adrenergic property [6]. Clonidine possibly enhances or amplifies the sodium channel blockade action of local anaesthetics by opening up the potassium channels resulting in membrane hyperpolarization, a state in which the cell is unresponsive to excitatory input [7-9]. Because of this property clonidine has the effect in reducing the onset time, improving the efficacy of the block during surgery and extending postoperative analgesia and it is often related to the dose ranging between 0.1 and 0.5 μg/kg. Bupivacaine is the routine anesthetic drug used for regional anesthesia and in this study we assess the effectiveness of bupivacaine after adding clonidine as an adjuvant.

Aim

To assess the anesthetic and analgesic effect of adding clonidine with bupivacaine as a regional anesthetic agent for brachial plexus block during upper limb surgeries.

Methodology

A prospective longitudinal study was conducted for a period of one year from the anesthesiology department of Vinayaka Missions Medical College Hospital Salem. The study was started after getting the clearance from the institutional ethical committee and the informed consent was obtained from all the study subjects. Patients who have been posted for the upper limb surgeries and in the age group of 15 to 60 years and their systolic BP less than 140 mm hg and diastolic BP less than 90 mm hg were included for the study. Patients belonging to ASA class III and IV, history related to adverse events with clonidine, patients with medical complications like severe anemia, severe hypovolemia, shock and septicemia were excluded from the study. Patients with abnormal bleeding and clotting time along with patients on anticoagulant therapy were also excluded from the study. Patients were then randomly divided into two groups of 30 in each group, Group A patients received 25 ml of 0.5% bupivacaine and group B patients received 25 ml of 0.5% bupivacaine along with 0.2 ml (30 mcg) clonidine. On arrival in the operation room, baseline heart rate, blood pressure and oxygen saturation were recorded and monitored throughout the procedure. An intravenous line was secured in the unaffected limb and Ringer's lactate was started. Before the procedure, visual analogue scale (VAS) on 0-10 was explained to the patient for the assessment of pain where 0 denotes no pain and 10 denotes worst pain. All the patients received brachial plexus block through the supraclavicular approach. The goal of this block was to bring the tip of the needle in the proximity of the lower trunk, which was manifested by a twitch of the fingers in either flexion or extension. Sensory block (four nerve territories) was assessed by pin prick test using a 3-point scale and the motor blockade was determined by thumb abduction (radial nerve), thumb adduction (ulnar nerve), thumb opposition (median nerve), and flexion of elbow (musculocutaneous nerve) according to the modified Bromage scale on a 3-point scale. Onset time for the motor and sensory block was also recorded and then onwards both sensory and motor blocks were assessed at 15, 30, 45, 60, 90, and 120 min; and then hourly (even after surgery) after the completion of injection, until they had resolved. Vitals were recorded at intervals of 5 min for first 30 min, then after every 10 min till end of surgery, and then hourly after surgery. Sedation score was recorded according to modified Ramsay Sedation Scale. Adverse effects like hypotension, bradycardia, nausea, vomiting following the anesthetic drug were documented and the need for any other additional medications was also recorded. Diclofenac sodium was used as

the rescue analgesia for the patients who had the complaint of pain with VAS score of more than 3 and the time between the complete sensory block and the first analgesic request was recorded as duration of post operative analgesia (DOPOA).

All the data were eneterd and analysed using SPSS version 21. Mean and standard deviation was derived for all the parametric variables and student T test and chi-square test was used to assess the statistical inference between the two groups considering $p < 0.05$ as statistically significant.

Results

The demographic variable between the two groups was shown in table 1. It is seen from the table that the mean age was almost similar among both the groups and the proportion of males were more than females in both the groups and majority of the patients had ASA grading as grade I among both the groups and also the body weight between the two groups did not show statistical significant difference (Table 1). The onset of sensory block and motor block was found to be much early in the group which received bupivacaine with clonidine (5.1 mins and 8.4 mins) than that of the group received bupivacaine alone (11.2 mins and 19.9 mins) and similarly the duration of both sensory and motor block was prolonged among group B (bupivacaine plus clonidine) when compared to group A (bupivacaine alone) and this difference was found to be statistically significant (Table 2). The post-operative analgesia effect was found to be longer (487.9 mins) among the group received bupivacaine with clonidine with a less number of additional requirement of analgesia dose (1.1 dose) whereas the analgesia effect among the group received bupivacaine alone was 303.6 mins with mean additional dose of analgesia of 2.4 and the difference was found to be statistically significant (Table 3).

Table 1: Distribution of the demographic variables between the two groups

Demographic variable		Group A (n=30) (bupivacaine alone)	Group B (n=30) (bupivacaine plus clonidine)	p value
Age	Mean ± SD	33.7 ± 13.4	32.9 ± 15.2	0.728 *
Gender	Male	24	22	0.646 **
	Female	6	8	
Weight	Mean ± SD	69.6 ± 14.8	71.7 ± 16.1	0.814 *
ASA grade	Grade I	27	28	0.866 **
	Grade II	3	2	

*- p value derived by student T test
**- p value derived by Chi-square test

Table 2: Onset and duration of sensory and motor blockade among the two groups

Variable	Group A (n=30) (bupivacaine alone) (mean ± SD)	Group B (n=30) (bupivacaine plus clonidine) (m ean ± SD)	p value
Onset of sensory block (in mins)	11.2 ± 3.8	5.1 ± 2.8	<.001
Onset of motor block (in mins)	19.9 ± 5.4	8.4 ± 3.9	<.001
Duration of sensory block (in mins)	258.6 ± 79.9	432.5 ± 81.3	<.001
Duration of motor block (in mins)	289.8 ± 80.9	491.4 ± 78.2	<.001

p value derived by student T test

Table 3: Post-operative analgesia effect between the two groups

Variable	Group A (n=30) (bupivacaine alone) (mean ± SD)	Group B (n=30) (bupivacaine plus clonidine) (mean ± SD)	p value
Duration of post-operative analgesia (in mins)	303.6 ± 86.7	487.9 ± 92.3	<.001
Mean number of dosage of regional analgesia required in 24 hrs of Post – operative period	2.4 ± 1.1	1.1 ± 0.7	<.001

p value derived by student T test

Table 4: Heart rate measured between the two groups measured during intra and post-operative period

Heart rate	Group A (n=30) (bupivacaine alone) (mean ± SD)	Group B (n=30) (bupivacaine plus clonidine) (mean ± SD)	p value
0 min	76 ± 5.5	74 ± 4.8	0.817
5 mins	78 ± 6.8	79 ± 5.9	0.799
15 mins	82 ± 7.1	80 ± 6.5	0.651
30mins	80 ± 5.8	88 ± 7.4	0.0214
60 mins	78 ± 6.3	86 ± 6.8	0.0341
2 hrs	81 ± 8.1	80 ± 5.9	0.645
6 hrs	79 ± 7.9	81 ± 6.3	0.591
12 hrs	80 ± 6.6	78 ± 7.9	0.816
24 hrs	78 ± 5.9	77± 8.2	0.889

Table 5: Systolic blood pressure measured between the two groups measured during intra and post-operative period

Systolic BP	Group A (n=30) (bupivacaine alone) (mean ± SD)	Group B (n=30) (bupivacaine plus clonidine) (mean ± SD)	p value
0 min	128 ± 14.6	126 ± 16.2	0.714
5 mins	130 ± 16.2	124 ± 15.8	0.582
15 mins	126 ± 12.8	120 ± 14.5	0.359
30mins	126 ± 13.5	118 ± 13.9	0.0314
60 mins	124 ± 12.8	114 ± 12.1	0.0137
2 hrs	124 ± 11.9	120 ± 12.6	0.616
6 hrs	120 ± 10.8	118 ± 11.4	0.738
12 hrs	124 ± 11.2	122 ± 12.2	0.815
24 hrs	126 ± 10.6	124 ± 11.4	0.882

Table 6: Diastolic blood pressure measured between the two groups measured during intra and post-operative period

Diastolic BP	Group A (n=30) (bupivacaine alone) (mean ± SD)	Group B (n=30) (bupivacaine plus clonidine) (mean ± SD)	p value
0 min	82 ± 6.8	80 ± 6.1	0.818
5 mins	80 ± 5.9	78 ± 5.6	0.742
15 mins	78 ± 6.1	78 ± 7.1	1.000
30mins	77 ± 6.2	74 ± 6.4	0.0761
60 mins	78 ± 5.9	72 ± 5.8	0.0612
2 hrs	76 ± 6.4	74 ± 6.2	0.834
6 hrs	80 ± 5.8	78 ± 5.9	0.782
12 hrs	82 ± 6.4	82 ± 6.1	1.000
24 hrs	84 ± 5.4	85 ± 4.7	0.914

Table 7: SpO_2 measured between the two groups measured during intra and post-operative period

SPO2	Group A (n=30) (bupivacaine alone) (mean ± SD)	Group B (n=30) (bupivacaine plus clonidine) (mean ± SD)	p value
0 min	**98 ± 1.2**	99 ± 1.1	0.899
5 mins	98 ± 1.1	98 ± 0.9	1.000
15 mins	98 ± 0.8	96 ± 1.2	0.789
30mins	99 ± 1.4	98 ± 0.8	0.894
60 mins	96 ± 1.2	98 ± 1.1	0.815
2 hrs	98 ± 1.1	99 ± 1.2	0.808
6 hrs	99 ± 0.6	98 ± 0.8	0.899
12 hrs	98 ± 0.8	98 ± 1.1	1.000
24 hrs	99 ± 0.6	99 ± 0.8	1.000

Heart rate was measured at regular intervals for the first 24 hours and the heart rate did not show a statistical significant difference between the two groups except at the 30th and 60th minute reading in which the patients who received bupivacaine with clonidine showed a higher heart rate than the group which received bupivacaine alone (Table 4) and similarly during that period the systolic and diastolic BP of the bupivacaine with clonidine group showed a significantly lower BP than that of the patients receiving bupivacaine alone whereas all the other blood pressure readings taken between the two groups upto 24 hrs did not show a statistical significant difference (Table 5 and 6). Oxygen saturation measured over a period of 24 hrs between the two groups showed almost no difference the saturation was ranging between 97–99% throughout the entire period among the two groups (Table 7).

Discussion

Supraclavicular block often offers dense anesthesia of brachial plexus which helps in carrying out surgical procedures in the upper limb. This approach provides the best efficacy in providing a complete arm block just from a single injection. Bupivacaine, being a long acting amide is the preferred local anaesthetic drug commonly used for regional anesthesia. Along with a regional anesthetic drug using an adjunct like opioids, epinephrine, α2 adreno receptor agonist had become a routine practice among anesthetist to further improve the efficacy of the anesthetic agent and analgesia effect produced by the regional anesthesia. Clonidine is a α2 adrenoceptor agonist commonly used as as adjunct with the regional anesthesia. In the present study we compared the anesthetic and the analgesia effect between the two groups in which one group of patients received only bupivacaine as the regional anesthesia and for the other group along with bupivacaine, clonidine was given as adjunct and the anesthetic and analgesic effect was observed between the two groups. Anesthetic effect was assessed by the onset and duration of the motor and sensory block and the analgesic effect was assessed by the duration of analgesia and the number of additional analgesic drugs used for pain relief. Vital parameters like heart rate, blood pressure and SpO_2 were measured at regular intervals over a period of 24 hrs among both the groups to assess for any significant difference in the vitals after using an adjunct drug in regional anesthesia. In the present study the mean duration of onset of sensory and motor block among the group which received clonidine as an adjunct along with bupivacaine was 5.1 and 8.4 mins respectively and similarly the duration of sensory and motor block was 432.5 mins and 491.4 mins and the analgesic effect was seen for 487.9 mins with an additional number of analgesic dose of only 1.1, whereas among the group which received only bupivacaine drug without the adjunct the mean time of onset of sensory and motor block was 11.2 and 19.9 mins and the mean duration of sensory and motor block was 258.6 and 289.8 mins respectively and the post-operative analgesic effect was for 303.6 mins with a mean dose of anesthetic agent of 2.4. In our study we found a statistically significant benefit among the group which received clonidine as an adjunct drug than the group which received only bupivacaine. All the vital parameters measured between the two groups showed almost similar results and no adverse events was seen among the subjects in both the groups.

Chakraborty, *et al.,* Iohom, *et al.* and a meta-analysis study by Popping, *et al.* had shown that the onset of sensory block was much early among the group which received clonidine as a adjunct drug when compared with a placebo group [10-12]. Similarly onset of motor block was also found to be early in the studies done by Chakraborty, *et al.* and Iohom, *et al.,* whereas Popping *et al.* study showed no significant difference in the onset of motor block between the group received clonidine and the placebo [10-12].

The results of the study done by Iskandar, et al. and Cucchiaro, *et al.* was almost supporting our results mentioning that the duration of sensory block was more among the clonidine group compared to the placebo, whereas a study by Duma et al. did found a significant increase in the duration of sensory block in the clonidine group [13-15]. The results of our study related to the duration of motor block was almost in par with the studies done by Erlacher, *et al.* and Popping et al. quoting the duration of motor block was higher among the patients who received clonidine compared to placebo [12,16]. The prolonged analgesic effect in the clonidine group with lesser number of analgesic doses which was shown in our study was also proven by the studies done by Murphy *et al.* and Eledjam, *et al.* [17,18]. In the present study all the hemodynamic parameters were within the normal range among both the groups and it was substantiated by the study done by Culebras, *et al.* and Prashant Sirohiya *et al.*, where they found no bradycardia or hypotension among the group received clonidine [19,20].

Conclusion

Thus, our study had demonstrated that addition of clonidine as an adjuvant drug along with bupivacaine as a regional anesthetic agent in supraclavicular brachial plexus block had significatly prolonged the duration of analgesia and improved the quality of anesthesia in terms of onset and duration of sensory and motor block with hemodynamic stability and lack of side effects, thus making clonidine an attractive choice as an adjuvant to bupivacaine for supraclavicular brachial plexus block.

References

1. Khanduri KC. Regional anaesthesia techniques for orthopaedic surgery. MJAFI. 2008;64:108-10.
2. Kohli S, Kaur M, Sahoo S, Vajifdar H, Kohli P. Brachial plexus block: comparison of two different doses of clonidine added to bupivacaine. J Anaesthesiol Clin Pharmacol. 2013;29(4):491-95.
3. Soni CM, Parikh H. Comparison of the motor and sensory block by Ropivacaine and bupivacaine in combination with lignocaine in supraclavicular block. Nat J Med Res. 2013;3(4):353-57.
4. Gautham HR, Prakash CS. Effect of plain and alkalinized lignocaine on supraclavicular block. Int J Sci Study. 2014;2(7):44-49.
5. Merlin D Larson. History of anaesthetic practice. In: Miller RD. Anaesthesia, 6th ed. Elsevier, Churchill Livingstone, Philadelphia. 2005;23.
6. Groban L. Central nervous system and cardiac effects from long-acting amide local anaesthetic toxicity in the intact animal model. Reg Anesth Pain Med. 2003;28:3.
7. Weinberg GL. Current concepts in resuscitation of patients with local anaesthetic cardiac toxicity. RegAnesth Pain Med. 2002;27:568.
8. Gaumann D, Forster A, Griessen M, Habre W, Poinsot O, Della Santa D. Comparison between clonidine and epinephrine admixture to lidocaine in brachial plexus block. Anesth Analg. 1992;75:69-74.
9. Singelyn FJ, Gouverneur JM, Robert A. A minimum dose of clonidine added to mepivacaine prolongs the duration of anesthesia and analgesia after axillary brachial plexus block. Anesth Analg. 1996;83:1046-50.
10. Chakraborty S, Chakrabarti J, Mandal MC, Hazra A, Das S. Effect of clonidine as adjuvant in bupivacaine-induced supraclavicular brachial plexus block: A randomized controlled trial. Ind J Pharmacol. 2010; 42(2):74-77.
11. Iohom G, Machmachi A, Diarra DP, Khatouf M, Boileau S, Dap F, Boini S, Mertes PM, Bouaziz H. The effects of clonidine added to mepivacaine for paronychia surgery under axillary brachial plexus block. Anesth Analg. 2005;100(4):1179-83.
12. Pöpping DM, Elia N, Marret E, Wenk M, Tramèr MR. Clonidine as an adjuvant to local anaesthetics for peripheral nerve and plexus blocks: a meta-analysis of randomized trials. Anesthesiology. 2009; 111(2):406-15.
13. Iskandar H, Benard A, Ruel-Raymond J, Cochard G, Manaud B. The analgesic effect of interscalene block using clonidine as an analgesic for shoulder arthroscopy. Anesth Analg. 2003;96(1):260-2.
14. Cucchiaro G, Ganesh A. The effects of clonidine on postoperative analgesia after peripheral nerve blockade in children. Anesth Analg., 2007;104(3): 532-7.
15. Duma A, Urbanek B, Sitzwohl C, Kreiger A, Zimpfer M, Kapral S. Clonidine as an adjuvant to local anaesthetic axillary brachial plexus block: a randomized, controlled study. Br J Anaesth. 2005; 94(1):112-6.
16. Erlacher W, Schuschnig C, Koinig H, Marhofer P, Melischek M, Mayer N, Kapral S. Clonidine as adjuvant for mepivacaine, ropivacaine and bupivacaine in axillary, perivascular brachial plexus block. Can J Anaesth. 2001;48(6):522-5.
17. Murphy DB, McCartney CJ, Chan VW. Novel analgesic adjuncts for brachial plexus block: a systematic review. Anesth Analg., 2000;90(5): 1122-8.
18. Eledjam JJ, Deschodt J, Viel EJ, Lubrano JF, Charavel P, d'Athis F, du Cailar J. Brachial plexus block with bupivacaine: effects of added alpha-adrenergic agonists: comparison between clonidine and epinephrine. Can J Anaesth. 1991;38(7):870-5.
19. Culebras X, Van Gessel E, Hoffmeyer P, Gamulin Z. Clonidine combined with a long acting local anaesthetic does not prolong postoperative analgesia after brachial plexus block but does induce haemodynamic changes. Anesth Analg., 2001;92(1):199-204.
20. Prashant Sirohiya, Kiwi Mantan, H. Rehman, Meera Kumari, Vishal Devra, Raghvendra Singh. Effect of bupivacaine and bupivacaine-clonidine combination in supraclavicular brachial plexus block – A comparative study. IAIM. 2016;3(5): 29-37.

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Midazolam Pre-Treatment before Etomidate Anaesthesia

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Abstract

Introduction: Etomidate a GABA receptor stimulating hypnotic agent is short-acting, has minimal residual sedation and a favourable haemodynamic profile and is thus a common choice for short term procedures especially in the haemodynamically compromised patients. But it has undesirable side effects of pain on injection and myoclonus. The problem of pain on injection has been solved by a new lipid formulation for etomidate. Myoclonus is seen in up to 50 to 80% of patients during induction of anaesthesia with etomidate if no supplemental agents are used. A number of drugs have been investigated for the suppression of etomidate-induced myoclonus. Ideally a pre-treatment drug for preventing myoclonic movements should be short acting, not have significant effects on respiration and haemodynamics and not prolong recovery from anaesthesia. Etomidate has a less inhibitory effect on the pharyngo-laryngeal reflex, hence blunting the responses to laryngoscopy and endotracheal intubation is also necessary. *Materials and Methods:* This study was conducted to study the effect of pre-treatment with midazolam on etomidate induced myoclonus.We studied 30 patients who were given Midazolam pre-treatment before administration of Etomidate. *Results:* 23.33% (7/30) patients developed myoclonus and none of them had severe myoclonus. Vital were not significantly affected. *Conclusion:* Midazolam is a good pre-treatment option before etomidate as it reduces incidence and severity of etomidate induced myoclonus without significant adverse effects.

Keywords: Cardio-stable, Etomidate, Midazolam, Myoclonus, Pain, Pre-treatment.

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Introduction

There are many anaesthetic agents for induction of anaesthesia like sodium thiopentone, propofol, ketamine, methohexital. The present financial pressure to reduce anaesthesia turnover time has created a demand for an induction agent with a rapid onset and minimal residual sedation thereby minimising the timerequired for emergence and time spent in the recovery room.

Etomidate a short acting GABA receptor stimulating hypnotic agent has manypositive characteristics like rapid onset/offset, minimal residual sedation and favourable haemodynamic profile, that is why it is common choice for short term procedures especially in the haemodynamically compromised patients [1]. It has been a preferred agent for cardiac surgeries [2,3]. Two undesirable

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side effects of etomidate are pain on injection and myoclonus. Although the problem of pain on injection has been solved by a new lipid formulation for etomidate, the problem of etomidate - induced myoclonus, especially for short term procedures has yet to be solved. Myoclonus is seen inup to 50 to 80% of patients during induction of anaesthesia with etomidate if nosupplemental agents are used [4].

Myoclonus is defined as an involuntary, short contraction of some musclefibres, of a whole muscle, or of different muscles of one group, leading to ashort observable movement of the corresponding body part usually not longerthan 100 ms [5].

The mechanism of etomidate-induced myoclonus appears to be disinhibition subcortical structures that normally suppress extra pyramidal motor activity. The fact that etomidate induced myoclonic activity may be associated with seizure activity on the EEG suggests caution in the use of this drug for the induction of anaesthesia in patients with a history of seizures.

A number of drugs have been investigated for the suppression of etomidate-induced myoclonus like benzodiazepines in the form of midazolam, flunitrazepam, diazepam, opioids in the form of fentanyl, sufentanil, remifentanil, magnesium sulfate, rocuronium, lignocaine, dexmedetomidine, rocuronium, thiopental, droperidol [6–8]. The effects of benzodiazepines on the different GABA receptors may explain the mechanism by which these drugs reduce the incidence of myoclonic movements. Ideally a pre-treatment drug for preventing myoclonic movements should beshort acting, not have significant effects on respiration and haemodynamics and not prolong recovery from anaesthesia. Moreover, etomidate being cardio-stablehas a less inhibitory effect on the pharyngo laryngeal reflex, hence blunting the responses to laryngoscopy and endotracheal intubation is also necessary especially in cardiac patients. One should keep in mind all these problems while selecting a pre-treatment drug to make etomidate an ideal induction agent. Thus. this study was conducted to study the effect of pre-treatment with midazolam on etomidate induced myoclonus.

The objective of the study was to study the effect of midazolam pre-treatment on induction with etomidate. The parameters studied were haemodynamic response to laryngoscopy and intubation during anaesthetic induction with etomidate, incidence and severity of etomidate induced myoclonus after pre-treatment, incidence and severity of pain on etomidate injection and postoperative complications like nausea vomiting, thrombophlebitis after etomidate anaesthesia if any.

Material and Methods

A prospective, observational study was conducted on 30 ASA Class 1 and 2 adult patients of either sex undergoing elective surgical procedures under general anaesthesia necessitating endotracheal intubation. After thorough pre anaesthetic check up patients with following problems were excluded from the study:

- Patients with anticipated difficult intubation assessed by using Mallampati grading.
- Patients of known case of epilepsy or with past history of episodes of convulsion.
- Raised intracranial and/or raised intraocular pressure.
- History of allergy to lipid emulsion.
- Open globe injury.

The patients receive pre-treatment with midazolam 0.015 mg/kg iv. All the patients were give nalprazolam 0.25 mg per oral night before surgery. On the day of surgery premedication was given with inj. Glycopyrrolate 0.2 mg intramuscular 30 minutes before surgery. In the operation theatre monitors were attached and baseline vital parameters inthe form of pulse, systolic blood pressure, diastolic blood pressure, mean blood pressure and SpO_2 were recorded. Then pre-treatment drug inj. midazolam 0.015 mg/kg was injected. Ninety seconds after giving study drug patients were induced with injetomidate 0.3 mg/kg intravenously and Rocuronium 0.9 mg/kg intravenously. After giving 2-3 ml of Etomidate patients were assessed for pain on injection. Onset time of appearing myoclonic movements after completion of etomidate injection and total duration of myoclonus was also noted. Vital parameters in the form of pulse, systolic blood pressure, diastolic blood pressure, mean blood pressure and SpO_2 were recorded before pre-treatment (baseline), after pre-treatment, after induction and 1,3 and 5 minutes after intubation. Anaesthesia was maintainted with conventional methods. Postoperatively patients were assessed for side effects like nausea, vomiting, thrombophlebitis for 24 hours.

Results

All the patients studied were adults. The mean

age was 32 ± 8.23 years, the mean weight was 50 ± 7.18 kg and there were 11 male patients and 19 female patients.

The mean pulse rate at baseline was 87 ± 16.36. Mean pulse rate after giving pre-treatment, after giving etomidate and 1, 3, 5 minutes after intubation was documented. It was noted that after pre-treatment there was no change inmean pulse rate but it increased significantly after etomidate ($p < 0.05$). Pulse rate increased significantly at 1, 3, 5 minutes after intubation.

The mean systolic blood pressure before pre-treatment was 116 ± 8.46 mmHg Mean systolic blood pressure after pre-treatment, after etomidate and 1, 3, 5 minutes after intubation was documented. Mean systolic blood pressure after pre-treatment and after etomidate was not significantly different from baseline while there was increase in mean systolic blood pressure after intubation and the difference was statistically significant ($p<0.05$) at 1 and 3 minutes whereas it was not significantly different at 5 minutes.

SpO_2 did not fall before pre-treatment, after pre-treatment, after giving etomidate, and 1 minute, 3 minute and 5 minutes after intubation.

Myoclonus developed in 7 patients (23.33%). Mean time of onset of myoclonus was 13 ± 8.96 seconds. Mean duration of myoclonus was 21 ± 17.96 seconds. 3 patients had grade 1 and 4 patients had grade 2 myoclonus. No patient developed complications like nausea, vomiting, thrombophlebitis for 24 hours in the postoperative period.

Discussion

Etomidate is an anaesthetic induction agent in the clinical practice which is characterized by rapid onset, very few side effects on cardiovascular and respiratory functions as well as minimum histamine release.

For short term procedures requiring general anaesthesia, rapid clearance of the anaesthetic is desirable. Etomidate, because of its minimal respiratory side effects and favourable haemodynamic profile, is a common choice for shortterm procedures, especially in the haemodynamically compromised patients. Two undesirable side effects of etomidate are pain on injection and myoclonus. Although the problem of pain on injection has been solved by a new lipid formulation for etomidate as previous studies say, the problem of etomidate induced myoclonus, has yet to be solved.

This study was conducted in 30 adult ASA- class I and II patients of either sex undergoing elective surgery under general anaesthesia necessitating endotracheal intubation.

After thorough preanaesthesia check-up any patient with any contraindication to use etomidate were excluded from the study like history of allergy to lipid emulsion, history of epilepsy or any episode of focal or generalised convulsion, patients with increased intracranial and/or intraocular pressure, open globeinjury. Patients with anticipated difficult airway assessed by Mallampatti's grading were also excluded from the study.

In this study haemodynamic response to laryngoscopy and intubation in was studied. Difficult intubation can affect the duration of laryngoscopy and duration of the laryngoscopy is the major determining factor for haemodynamic response.

All patients were given tablet Alprazolam 0.25 mg night before surgery Premedication was given with inj. Glycopyrrolate 0.2mg intramuscular 30 minutes before surgery.

The study was to observe the effect of midazolam on etomidate induced myoclonus. Any other benzodiazepine or opioid if used in premedication might affect the result of study so only glycopyrrolate was usedas premedication.

Myoclonus is defined as an involuntary short contraction of some muscle fibresor a whole muscle, or different muscles of one group, leading to a short observable movement of the corresponding body part not longer than 100 ms.

Aissaoui Y *et al.* investigated the influence of pre-treatment with a low dose of etomidate on etomidate induced myoclonus, 87% patients in control group developed myoclonic movements [9].

Choi JM *et al.* compared the effect ofpre-treatment with low dose of rocuronium (0.06 mg/kg) on the occurrence of etomidate-induced myoclonus with control group and found that 63% patientsin control group had myoclonus [10].

Mizrak A *et al.* found the incidence of etomidate induced myoclonus was 64% in control group [11].

It was observed in various studies that incidence of myoclonus is 50-80% inetomidate anaesthesia when no pre-treatment agent has been given. Keeping in mind such a high incidence of myoclonus (50-80%) control group was not taken in our study.

Schwarzkopf KR *et al.* studied effect of pre-treatment with etomidate 0.05 mg/kg IV and midazolam 0.015 mg/kg IV onetomidate induced

myoclonic muscle movements which was compared with placebo in a randomized double-blind study [12].

Huter Lars *et al.* studied the effect of 0.015 mg/kg IV Midazolam on Etomidate induced myoclonus, which was administered 90 seconds before induction of anaesthesia with etomidate 0.3 mg/kg iv [4].

Ideally, a pre-treatment drug for preventing myoclonic movements should beshort acting, not have significant effects on respiration and haemodynamics, andnot prolong recovery from anaesthesia especially in short term procedures.

Therefore, a low dose of midazolam 0.015 mg/kg IV was selected in our study for evaluation.

Etomidate is attractive for short term anaesthesia because it allows early recovery and relative cardiovascular stability. Hence, for short lasting procedures, any co-medication given for anaesthetic or sedative purpose or toreduce myoclonus should not interfere with this favourable pharmacodynamic profile.

Although opioids have been shown to reduce myoclonus, administration of opioid like high doses of fentanyl may be undesirable for short-term procedures because of potential respiratory depression. High doses of fentanyl are also associated with apnea.

After proper preoxygenation baseline pulse, systolic, diastolic blood pressure were taken. Then pre-treatment drug was injected. After giving pre-treatment drug pulse, blood pressure, and SpO_2 were recorded. After ninety seconds of giving pre-treatment drug, patients were induced with inj. etomidate 0.3 mg/kg IV and vital parameters were recorded.

Pain on injection is one of the all bothersome side effects of etomidate [13]. Pain on injection was graded as [7]:

- Grade 1 - Mild (pain reported only in response to questioning and without any behavioral sign).
- Grade 2 - Moderate pain (pain reported in response to questioning and accompanied by behavioural sign or pain reported spontaneously without questioning).
- Grade 3 - Severe pain (strong vocal response or response accompanied byfacial grimacing, arm withdrawal).

Y. Nyman *et al.* found a significantly lower incidence of injection pain in the Etomidate-Lipurogroup as compared with the Propofol-Lidocaine group (5.0% Vs 47.5%, $p<0.05$) [14].

Pain on injection has been a problem with etomidate induction like other anaesthetic agents like propofol. Pain on injection is specially not acceptable in children.

Like propofol and other general anaesthetics, etomidate at high concentration activates transient receptor potential type A-1 channels, a mechanism that mayunderlie pain during injection. Transient receptor potential type A-1 channels are involved in inflammation and pain sensation. But in our study, a new lipid formulation of etomidate was used. In this new lipid formulation, etomidate is dissolved in a fat emulsion of medium and long chain triglycerides. Therefore, with Etomidate-Lipuro side effect of pain oninjection has almost gone making it a suitable induction agent for anaesthesia.

After complete injection of etomidate, inj Rocuronium 0.9 mg/kg IV was given to facilitate endotracheal intubation and isoflurane (0.8%) or halothane (0.5%)was started.

Succinylcholine is the most commonly used agent to facilitate endotracheal intubation. It is associated with fasciculations. Succinylcholine induced fasciculations could have been difficult to differentiate from etomidate induced myoclonus so succinylcholine was avoided and rocuronium was the agent used for endotracheal intubation.

After etomidate injection patients were observed for myoclonus. Myoclonus was graded as [4]:

- Grade 0 - No myoclonus.
- Grade 1 - Mild myoclonus (only mild fasciculation involving face and/ordistal upper and /or lower extremities).
- Grade 2 - Moderate myoclonus (marked movements of the face and /orlimbs).
- Grade 3 - Severe myoclonus (involving limbs and trunk).

Schwarzkopf KR *et al.* found a significantly low incidence (20%) of etomidate induced myoclonus in midazolam group (0.015 mg/kg IV) given as pre-treatment compared to placebo group (90%) [12].

Lars Huter *et al.* found that incidence of etomidate induced myoclonus in midazolam pretreated group (0.015 mg/kg IV) was 10% compared to 50% incidence in control group [4].

The incidence of myoclonus in midazolam pretreated group in present study was similar to above mentioned study.

Do *et al.* studied the effect of injectionrate on etomidate-induced myoclonus. In the fast injection group 28% (7/25) of the patients showed myoclonus of a severe grade. In contrast, only 4% (125) of the patients showed severe myoclonus in slow injection group [15].

The neurologic mechanism of myoclonus is a disinhibition phenomenon of subcortical structure. That is etomidate depresses cortical activity before it depresses subcortical activity, thus depresses the neural circuits prior to excitatory circuits and not caused by an epileptic focus.

Benzodiazepines prevent myoclonus by inhibiting subcortical neuronal activity. The different effects of benzodiazepines on the different GAB Areceptors also explain the mechanism by which these drugs reduce the incidence of myoclonic movements.

Time of onset of appearing myoclonic movements after etomidate injection wasalso recorded in present study. Mean time of onset of myoclonus was 13 ± 8.96 seconds.

Much literature is not available about the effect of pre-treatment on the onset and duration of etomidate induced myoclonus. Only one study noted that pre-treatment with remifentanil reduces the duration of myoclonus. Larger studies are required to further evaluatethe effect of midazolam on characteristics of etomidate induced myoclonus.

Conclusion

Midazolam is a good pre-treatment option before induction with etomidate. Midazolam pre-treatment resulted in reduced incidence and severity of etomidate induced myoclonus. It did not result in any significant adverse effect of the vital parameters and did not result in any nausea, vomiting and thrombophlebitis in the post-operative period.

References

1. Forman SA. Clinical and Molecular Pharmacology of Etomidate. Anesthesiol J Am Soc Anesthesiol. 2011;114:695–707.
2. De Jong A, Jaber S. Etomidate for anesthesia induction: friends or foe in major cardiac surgery? Crit Care [Internet]. 2014 [cited 2019 May 5];18. Available from: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4331132/.
3. Wagner CE, Bick JS, Johnson D, Ahmad R, Han X, Ehrenfeld JM, et al. Etomidate Use and Postoperative Outcomes among Cardiac Surgery Patients. Anesthesiol J Am Soc Anesthesiol. 2014;120:579–89.
4. Hüter L, Schreiber T, Gugel M, Schwarzkopf K. Low-dose intravenous midazolam reduces etomidate-induced myoclonus: a prospective, randomized study in patients undergoing elective cardioversion. AnesthAnalg. 2007;105:1298–302.
5. Doenicke AW, Roizen MF, Kugler J, Kroll H, Foss J, Ostwald P. Reducing myoclonus after etomidate. Anesthesiology. 1999;90:113–9.
6. Zhou C, Zhu Y, Liu Z, Ruan L. Effect of pretreatment with midazolam on etomidate-induced myoclonus: A meta-analysis. J Int Med Res. 2017;45:399–406.
7. Guler A, Satilmis T, Akinci SB, Celebioglu B, Kanbak M. Magnesium sulfatepretreatment reduces myoclonus after etomidate. AnesthAnalg. 2005;101:705–9.
8. Gultop F, Akkaya T, Bedirli N, Gumus H. Lidocaine pretreatment reduces the frequency and severity of myoclonus induced by etomidate. J Anesth. 2010;24:300–2.
9. Aissaoui Y, Belyamani L, El Wali A, Idrissi Hajjouji SM, Atmani M, DrissiKamili N. Prevention of myoclonus after etomidate using a priming dose. Ann Fr Anesth Reanim. 2006;25:1041–5.
10. Choi JM, Choi IC, Jeong YB, Kim TH, Hahm KD. Pretreatment of rocuronium reduces the frequency and severity of etomidate-induced myoclonus. J Clin Anesth. 2008;20:601-4.
11. Mizrak A, Koruk S, Bilgi M, Kocamer B, Erkutlu I, Ganidagli S, *et al.* Pretreatment with dexmedetomidine or thiopental decreases myoclonus after etomidate: a randomized, double-blind controlled trial. J Surg Res. 2010;159:e11-16.
12. Schwarzkopf KRG, Hueter L, Simon M, Fritz HG. Midazolam pretreatment reduces etomidate-induced myoclonic movements. Anaesth Intensive Care. 2003;31:18–20.
13. Helmers JH, Adam AA, Giezen J. Pain and myoclonus during induction with etomidate. A double-blind, controlled evaluation of the influence of droperidol and fentanyl. Acta Anaesthesiol Belg. 1981;32:141–7.
14. Nyman Y, Von Hofsten K, Palm C, Eksborg S, Lönnqvist PA. Etomidate-Lipuro is associated with considerably less injection pain in children compared with propofol with added lidocaine. Br J Anaesth. 2006;97:536–9.
15. Do SH, Han SH, Park SH, Kim JH, Hwang JY, Son IS, *et al.* The effect of injection rate on etomidate-induced myoclonus. Korean J Anesthesiol. 2008;55:305–7.

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A Comparative Study of 0.2% Ropivacaine vs 0.25% Bupivacaine in Transverse Abdominus Plane Block for Post Operative Analgesia in Patients Undergoing Abdominal Surgery

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Abstract

Introduction: Several modalities have been used to alleviate pain after laparoscopic abdominal surgeries – like nonsteroidal anti-inflammatory drugs (NSAIDs), opioids (both intravenous and patient controlled analgesia, infiltration of local anaesthetic, thoracic epidural block and multimodal analgesia. Apart from providing post operative pain relief, regional anaesthetic techniques improve patient recovery by preventing the neuroendocrine responses to surgery and reducing the postoperative opioid requirements. *Aim:* To compare the efficacy of 0.2% ropivacaine and 0.25% bupivacaine when used in USG guided Transversus abdominus plane block for post operative analgesia in abdominal surgeries. *Material and Methods:* 50 patients scheduled for elective lower abdominal surgeries. The patients were randomly divided into two groups of 25 each- Group B receiving 0.25% bupivacaine, group R receiving 0.2% ropivacaine. Conducted in Department of Anesthesiology, Great Eastern Medical School & Hospital, Srikakulam. *Result:* Results showed no significant differences between the study groups in terms of age, weight and gender distributions. VAS showed significant difference between the study groups at 6 hrs and 12 hrs. The mean postoperative VAS in group B (0.25% bupivacaine) was maximum at the end of 6 hrs (4.08) whereas the mean postoperative VAS in group R (0.2% ropivacaine) was maximum at the end 12 hrs (4.0). *Conclusions:* Ropivacaine can be used as a safe alternative to Bupivacaine, routinely for TAP block for patients undergoing abdominal surgeries.

Keywords: Laparoscopic abdominal surgeries; Nonsteroidal anti-inflammatory drugs.

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Introduction

Postoperative analgesia can be achieved by the use of oral or parenteral analgesics, peripheral nerve blocks, neuraxial blocks with local anaesthetics, intrathecal opioids, adjunctive techniques such as transcutaneous electrical nerve stimulation and physical therapy. Pain experienced by patients after abdominal surgery is mainly derived from the anterior abdominal wall incision. Therefore provision of postoperative analgesia after abdominal surgery dominantly from skin incision sites, creation of pneumoperitoneum and trauma created by surgery by blocking the sensory nerve

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supply to the anterior abdominal wall appears to be a promising approach. Although laparoscopic surgeries result in less pain than open surgeries, still the pain arises pre itself.

Several modalities have been used to alleviate pain after laparoscopic abdominal surgeries – like nonsteroidal anti-inflammatory drugs (NSAIDs) (including parecoxib/valdecoxib, ketoprofen, paracetamol, opioids (both intravenous and patient controlled analgesia, infiltration of local anaesthetic (both before and after creation of pneumoperitoneum, thoracic epidural block and multimodal analgesia (using opioid, NSAID and infiltration of local anaesthetic) [1]. Apart from providing post operative pain relief, regional anaesthetic techniques improve patient recovery by preventing the neuroendocrine responses to surgery and reducing the postoperative opioid requirements. Transversus abdominis plane (TAP) block is a regional analgesic technique that blocks abdominal neural afferents by introducing local anaesthetic into the neurofascial plane between the internal oblique and the transversus abdominus muscles thereby reducing the postoperative pain of abdominal surgeries. Based on anatomic studies, previously, the lumbar triangle of Petit was used as an access point to this neurofascial plane [2]. A loss of resistance technique was used to locate the transversus abdominis plane. Correct localization of the plane was found to be difficult and imprecise in blind technique, especially in elderly and obese patients. To overcome this, ultrasound guidance is being increasingly used to locate the Transversus abdominis plane. Ultrasound based studies have shown their superiority and accuracy over the blind abdominal wall injections.

Ultrasound guided nerve blocks have several advantages as direct visualization of neural structures and related structures like blood vessels and tendons, Guidance of the needle under real-time visualization., Avoidance of complications like intravascular and intraneuronal injection, Monitoring the spread of local anaesthetic and allowing repositioning of the needle after an initial injection to facilitate delivery of local anaesthetic to areas that may not be completely blocked with a single dose. Can be used in patients with poor twitch response to nerve stimulation.

Various local anaesthetic agents have been used to provide effective and adequate postoperative analgesia. The new long-acting amino-amide local anaesthetic, ropivacaine, an S- enantiomer of bupivacaine has higher anaesthetic potency with long duration of action and less toxicity profile as compared to Bupivacaine. It is 2-3 times less lipid soluble and has a smaller volume of distribution, greater clearance, and shorter elimination half-life than Bupivacaine in humans. The two drugs have a similar pKa and plasma protein-binding.

Ultrasound guided TAP block using 0.75% ropivacaine has been used for post operative analgesia in patients undergoing total abdominal hysterectomies, caesarean sections and laparoscopic cholecystectomy. The search of literature revealed no data comparing the efficacy of 0.2% Ropivacaine and 0.25% bupivacaine in ultrasound guided TAP block for post operative analgesia in abdominal surgeries. Therefore the present study is aimed at comparative evaluation and relative efficacy of 0.2% ropivacaine and 0.25% bupivacaine in ultrasound guided TAP block for post operative analgesia in abdominal surgeries.

Material and Methods

A prospective, randomized, double blinded, comparative study done in 1 and half year (August 2015 to February 2017) in Department of Anesthesiology, Great Eastern Medical School & Hospital, Srikakulam. Patient of either sex between 18-60 years of age, ASA grade I and II. Total number of subjects in study are 50 (randomly divided into two groups of 25 each).

The present study was conducted after obtaining approval of the hospital ethics committee, a written informed consent was obtained from 50 patients scheduled for elective lower abdominal surgeries. The patients were randomly divided into two groups of 25 each- Group B receiving 0.25% bupivacaine, group R receiving 0.2% ropivacaine.

Inclusion criteria

1. ASA physical status I or II
2. Aged between18 to 60 yrs
3. Body weight 50-75kgs (BMI >18.5 and <25)
4. Patients undergoing elective abdominal surgeries under general anesthesia
5. Patients giving valid consent

Exclusion criteria

1. Patients with history of sensitivity to local anesthetics
2. Patients with abnormal liver function infection at injection site
3. Patients with clotting abnormalities

4. Patients who were not unable to interpret VAS before surgery.
5. Pregnant women.

Preoperative Assessment and Premedication

The principal investigator evaluated patients preoperatively, discussed the methodology and took the written informed consent on the day prior to surgery. They were explained about linear visual analog scale for pain (0 – no pain, 10 – worst imaginable pain) in their own vernacular language. All patients received adequate fasting orders preoperatively according to the surgery planned.

Randomisation and blinding

Randomisation was done by simple random method. 50 slips labelled B (25) indicating 0.25% Bupivacaine or R (25) indicating 0.2% Ropivacaine were kept folded in an opaque box by an anaesthesiologist not involved in the study. Patient picked up a slip from the box and handed over the slip to that anaesthesiologist. The anaesthesiologist not involved in the study unfolded the slip and allotted the patient into group 1 (B) or group 2 (R) based on the slip picked up by that patient. Study drug was prepared by the anaesthesiologist not involved in the study based on the slip picked up by that particular patient and handed over to the primary investigator conducting this study.

Intraoperative Management

Procedure on day of surgery

The patient was shifted to the operating room and an intravenous access was established. Pulse rate (PR), non invasive blood pressure (NIBP), continuous electrocardiogram (ECG), respiratory rate (RR), end tidal carbon dioxide and arterial oxygen saturation (SpO_2) were monitored using multichannel monitors. Baseline readings were noted and monitored every 5 minute intervals for first 30 minutes of surgery and then every 15 minutes till the end of surgery.

Induction of anaesthesia

All patients received a standardized general anaesthetic technique. They were administered injection inj. Glycopyrrolate 10 mcg/kg intravenously iv and inj. Fentanyl 2 mcg/kg iv. They were preoxygenated with 100% oxygen for 3 mins. Intravenous induction was achieved with Propofol 2-2.5 mg/kg. After confirming the ability to ventilate the lungs, intravenous Vecuronium 0.1 mg/kg was used for neuromuscular blockade. Patients ventilation was assisted with 2% Sevoflurane in 100% oxygen for 3 minutes, followed by laryngoscopy and orotracheal intubation was performed using either 7 or 7.5 mm internal diameter polyvinyl chloride cuffed orotracheal tube in women and either 8 or 8.5 mm internal diameter polyvinyl chloride cuffed orotracheal tube in men. Maintainance of anesthesia was done with sevoflurane1-1.2 MAC, 66% N_2O, 33% O_2. Inj Fentanyl 1 mcg/kg as needed to maintain intraoperative analgesia was given. Injection Paracetamol 1 gm IV was given at the time of skin closure.

At the end of surgery

Hemodynamic parameters of the patient were noted and TAP block was administered

Group R (n=25): Patients in this group received 20 ml 0.2% Ropivacaine in TAP block on each side.

Group B (n=25): Patients in this group received 20 ml of 0.25% Bupivacaine in TAP block on each side.

Post block hemodynamic parameters of the patient were noted.

After giving TAP block

Oral suction was performed and reversal of neuromuscular blockade was done with Neostigmine 0.05 mg/kg and Glycopyrrolate 0.01 mg/kg after confirming the return of neuromuscular function. Then patient was extubated and shited to postoperative recovery ward. All patients received injection Diclofenac 75 mg IV in the ward and this was continued 12th hourly in the ward.

Results

The following observations, including patients preoperative hemodynamic parameters, the postoperative hemodynamic parameters, the pain scores using visual analogue score were recorded in a preformed proforma.

Table 1: Demographic Data

Characteristics	Group B	Group B	p value
Age in years (Mean ± SD)	49.28 ± 6.37	47.32 ± 8.01	0.3
Weight in kg (Mean ± SD)	60.7 ± 8.0	67.2 ± 10.6	0.06
Gender (Male/Female)	11/14	13/12	0.5

The patients had mean age (mean + SD) of 49.28 ± 6.37 and 47.32 ± 8.01 years in Group B and Group

R respectively. The mean age of the patients in both the groups was comparable and the difference was statistically not significant (p>0.05).

The mean body weight of patients (mean + SD) in group B and R was 60.7 ± 8.0 and 67.2 ± 10.6 kgs respectively. The body weight of patients in both the groups was comparable and statistically non significant (p > 0.05).

The male: female ratio in group B was 11: 14 as compared to 13:12 in group R. The sex ratio of two groups were comparable to each other and statistically non significant (p>0.05).

The two groups were comparable with respect to age, weight, gender (Table 1).

Table 2: Type of surgery comparison between two groups

Type of surgery	Group B		Group R	
	No	%	No	%
Total laproscopic hysterectomy (TLH)	09	36	08	32
Laproscopic anterior resection (LAR)	08	32	09	36
Lap hemicolectomy (LHC)	06	24	07	28
Laproscopic bilateral inguinal hernioplasty (LIH)	02	8	01	

We conducted the study in 4 types of lower abdominal surgeries i.e. total laproscopic abdominal hysterectomy, laprocopic anterior resection, laproscopic hemicolectomy and laproscopic bilateral hernioplasty (Table 2)

Hemodynamic Parameters

Table 3: Pre block variation of hemodynamic parameters

Hemodynamic parameters	Group B		Group R		p value
	Mean	SD	Mean	SD	
Heart Rate	78.24	9.25	73.84	6.88	0.45
Mean Arterial Pressure	77.56	11.03	75.52	7.17	0.44

The preblock hemodynamic parameters were comparable in both groups B and R. The p value is not significant among the groups. The post block heart at 6 hrs, 12 hrs and 24 hrs among B group and R group were significant whereas at 30 min, 1 hr and 3 hrs they were not significant (Table 3).

Table 4: Variation of post block mean arterial pressure among the groups

MAP	Group B		Group R		p value
	Mean	SD	Mean	SD	
30 min	77.56	9.50	73.28	7.42	0.08
1 hour	78.4	8.70	76.56	9.56	0.48
3 hours	78.77	9.23	78.2	8.87	0.25
6 hours	82.4	9.60	79.52	8.46	0.27
12 hours	79.48	8.38	80.84	8.97	0.58
24 hours	76.36	6.56	76.24	6.04	0.95

The above table 4 shows that mean arterial pressures at 30 min, 1 hr, 3 hrs, 6 hrs, 12 hrs and 24 hrs were not significant among B and R groups.

Table 5: VAS score among groups

VAS after extubation	Group B		Group R		p value
	Mean	SD	Mean	SD	
30 min	1.12	1.48	1.0	1.11	0.33
1 hour	1.8	1.38	1.6	1.22	0.21
3 hours	2.48	0.96	2.28	1.1	0.24
6 hours	4.08	1.49	2.7	0.79	<0.001
12 hours	3.36	0.66	4.0	2.5	0.03
24 hours	3.92	1.49	3.92	0.91	0.50

VAS was not significant at 30 min, 1 hr, 3 hrs and 24 hrs but statistically significant at 6 hrs and 12 hrs (Table 5).

Table 6: Comparison of duration of analgesia

	Group B		Group R		„p" value
	Mean	SD	Mean	SD	
Time to first rescue analgesic requirement	401.73	297.85	747.5	394.7	<0.00001

The mean duration of analgesia (mean + SD)

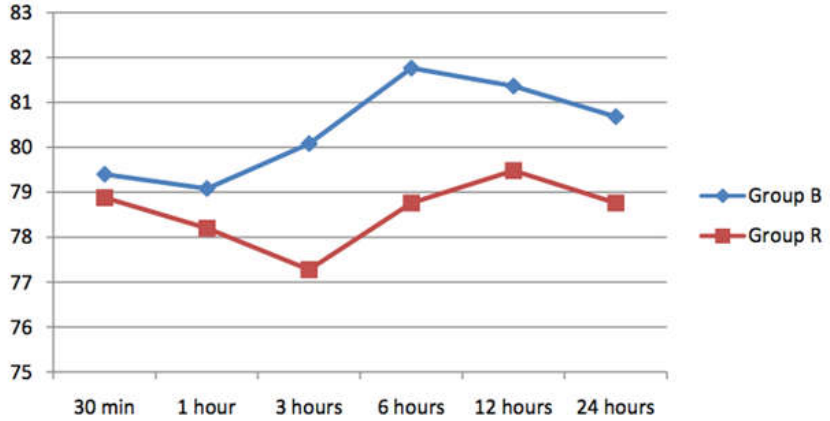

Fig. 1: Variation of post block heart rate among the groups

were 410.73 + 297.85 mins in group B and 747.5 + 394.7 mins in group R. The difference was statistically highly significant in group R compared to group B (p value <0.001) (Table 6).

Table 7: Patients who received rescue analgesia at the corresponding time interval

	Group B	Group R
<30 min	1	1
30 min-1 hr	2	1
1 hr-3 hrs	2	1
3 hrs-6 hrs	3	2
6 hrs-12 hrs	14	2
12 hrs-24 hrs	1	

The above table 7 shows that 2, 3, 3, 4, 9, and 2 patients received rescue analgesia at 30 min, 1 hr, 3 hrs, 6 hrs, 12 hrs and 24 hrs respectively in B group whereas 1, 1, 2, 2, 2 and 12 people received rescue analgesia at 30 min, 1 hr, 3 hrs, 6 hrs, 12 hrs and 24 hrs respectively in R group. 2 patients in B group and 5 patients in R group did not receive any rescue analgesia in 24 hrs.

Discussion

Pain after laparoscopic abdominal surgeries is due to many causes, some of which include - abdominal wall distension and incision at the trocar site. Several modalities have been used to alleviate pain after surgery. Ultrasound guided transversus abdominis plane block has become an integral part of multimodal analgesia after abdominal surgeries. Various drugs such as ropivacaine, bupivacaine, and levobupivacaine have been used in ultrasound guided TAP block [2]. In posterior approach of TAP block, a local anaesthetic is injected in the neurofascial plane between internal oblique and the transversus abdominis muscles, in order to block the nerves of the abdominal wall – namely the T7-T12 intercostal nerves, ilioinguinal nerve, iliohypogastric nerve and the lateral cutaneous branches of dorsal rami of the L1-L3 spinal nerves.

Performance of TAP block has become an integral part of the multimodal regimen for providing postoperative analgesia in number of surgeries. In addition to providing real time visualization of the neural structures, use of ultrasound helps in delineating trajectory of needle and navigating it away from other anatomical structures. Thus it avoids intravascular and intraneuronal injection [3].

The present study showed that when administered via ultrasound-guided TAP block with ropivacaine (0.2%) provided more effective pain relief in the immediate post-operative period as compared to bupivacaine (0.25%). The findings are in synchrony with the previous studies, which found ropivacaine to be more effective than bupivacaine.

Gaurav Kuthiala and Geeta Chaudhary [4] stated that a strict correlation exists between the lipid solubility of the local anaesthetic and its potency and toxicity. According to minimum local anaesthetic concentration (MLAC) studies, which are based on effective analgesia in 50% of patients) ropivacaine has similar potency to bupivacaine at higher doses. (eg, doses required for peripheral nerve blocks for surgical anaesthesia), ropivacaine is less potent than bupivacaine and levobupivacaine at lower doses, such as those used for epidural or intrathecal analgesia.

However, Olivier *et al.* [5] and Ahmed *et al.* [6] concluded that postoperative analgesic efficacy is comparable at all concentrations i.e. 0.2%, 0.5% and 0.75% of ropivacaine. Therefore, we presumed that even low concentrations of ropivacaine i.e. 0.2% ropivacaine would be equipotent or superior to 0.25% bupivacaine in transverse abdominus plane block in patients undergoing abdominal surgeries and conducted the above study.

Demographic Data

The difference in the mean age (mean + SD) 49.28 ± 6.37 and 47.32 ± 8.01 years, body weight 60.7 ± 8.0 and 67.2 ± 10.6 kgs and sex ratio 11: 14 and 13:12 of the patients in B group and R group were statistically non significant (p>0.05). Thus showing that baseline characterstics were comparable among the groups (Table 1).

Type of surgery

In our study, we chose patients undergoing four types of lower abdominal surgeries which included total laproscopic hysterectomy (TLH), laproscopic anterior resection (LAR), laproscopic hemicolectomy (LHC) and laproscopic bilateral inguinal hernia (LIH). In B group 9 underwent TLH (36%), 8 underwent LAR (32%), 6 underwent LHC (24%) and 2 underwent LIH (8%) whereas in R group 8 underwent TLH (32%), 9 underwent LAR (36%), 7 underwent LHC (28%) and 1 underwent LIH (4%) (Table 2).

Mark J Young *et al.* [7] described TAP block as an effective component of multimodal postoperative analgesia for a wide variety of abdominal procedures including large bowel resection, open/

laparoscopic appendectomy, cesarean section, total abdominal hysterectomy, laparoscopic cholecystectomy, open prostatectomy, renal transplant surgery, abdominoplasty with/without flank liposuction, and iliac crest bone graft.

Hemodynamic Variations

In our study, preoperative hemodynamics (mean + SD) - pulse rate (per min) (group B 78.24 + 9.24 vs group R 73.84 + 6.88) and mean arterial pressure (group B 77.56 + 11.03 vs group R 75.52 + 7.17) were comparable between the groups and statistically non significant. ($p>0.05$) (Table 3).

The mean heart rate per min at 30 min, 1 hour, 3 hours, 6 hours, 12 hours, and 24 hours in the postoperative period were compared between 0.25% bupivacaine and 0.2% ropivacaine. The results of both the studies were comparable at 30 min, 1 hr and 3 hrs but statistically significant difference was seen at 6 hrs (group B 81.76 ± 8.35 vs group R 78.76 ± 4.94), 12 hrs (group B 81.36 ± 10.14 vs group R 79.48 ± 4.36) and 24 hrs (group B 80.68 ± 11.87 vs group R 78.76 ± 4.03).

The relative rise in pulse rate in Group B could possibly be explained because of the shorter duration and reduced efficacy of analgesia in the bupivacaine group as compared to the ropivacaine group.

The mean arterial pressure in mm of Hg (mean + SD) at 30 mins, 1 hour, 3 hours, 6 hours, 12 hours, and 24 hours in postoperative period was also compared between 0.25% Bupivacaine and 0.2% Ropivacainegroups. The mean arterial pressure in both the groups were comparable and showed no significant difference.

This is similar to findings by Dr. Dipikapatel *et al.* [8] who compared 0.25% bupivacaine and 0.5% ropivacaine for TAP block in lower abdominal surgeries.They found that at 6, 12 and 18 hours, there was a significantly low pulse rate and low blood pressure in Group R compared to Group B ($p < 0.05$). This difference was attributed to a relative rise in pulse and systolic blood pressure in Group B because a longer duration of analgesia was maintained in Group R.

Neha faluda *et al.* [9] who also compared 0.25% bupivacaine and 0.5% ropivacaine, found that the difference between the mean pulse rate and mean systolic and diastolic blood pressure were statistically non-significant between group B and group R at all periods of time in the first 24 hrs.

VAS pain score

In our study, the mean postoperative VAS in group B (0.25% Bupivacaine) was maximum at the end of 6 hrs whereas the mean postoperative VAS in group R (0.2% Ropivacaine) was maximum at the end of 12 hrs. VAS score were not only lower in patients receiving 0.2% Ropivacaine but also statistically significant at 6 hrs (group B 4.08 ± 1.49 vs group R 2.7 ± 0.79).

At 12 hrs (group B 3.36 ± 0.66 vs group R 4 ± 2.5) the Ropivacaine group had significantly more pain when compared to the Bupivacaine group. This was because group B had already received rescue analgesia while group R had not. This suggests that Ropivacaine provides longer duration of analgesia when compared to 0.25% Bupivacaine.

Neha Sharma *et al.* [10] conducted a study in 60 adult patients undergoing elective abdominal surgery under general anaesthesia. They compared 0.25% Bupivacaine with 0.5% Ropivacaine in TAP block. The mean pain scores at 0 min, 30 min and 4 h were similar in both the groups and inter group comparison was not statistically significant. However, comparison of pain score at 8h and 12h post operatively showed significant difference in both the groups with Bupivacaine having significantly higher VAS scores both at rest and on coughing.

Sharadha Sinha *et al.* [11] conducted a study on sixty adults undergoing elective.

laparoscopic cholecystectomy who were randomised to receive ultrasound-guided TAP block at the end of the surgical procedure with either 0.25% bupivacaine (Group I, $n = 30$) or 0.375% ropivacaine (Group II, $n = 30$). The pain scores were significantly lower at 10 min, 30 min and 1 h post-operatively in Group II as compared to Group I.

Dipikapatel *et al.* [12] found that there was statistically significant difference in VAS score at 6 hours ($p<0.05$) and 12 hours ($p<0.01$) after performing the block. They found that VAS scores were higher in the Bupivacaine group as compared to the Ropivacaine group.

Duration of analgesia

The mean time to first request for rescue analgesia in patients receiving 0.25% Bupivacaine was 410.73 ± 297.85 mins and 747.5 ± 394.7 mins in patients receiving 0.2% Ropivacaine. It indicates that mean duration of analgesia with 0.2% ropivacaine (approximately 12.5 hrs) was significantly higher than 0.25% bupivacaine (approximately 6 hrs). This

finding is similar to that of other studies (Table 6).

Dipika Patel *et al.* [12] who compared 0.25% bupivacaine with 0.5% ropivacaine found that the mean duration of analgesia was 7.38 ± 2.35 hours in bupivacaine group and 9.98 ± 2.38 hours in ropivacainegroup. The difference was statistically highly significant in ropivacaine group compared to bupivacaine group ($p<0.01$). Neha Fauladi *et al.* [9] found that the mean duration of analgesia in their study was longer in Ropivacaine group (12.61 ± 5.13 hour) as compared to Bupivacaine group (9.92 ± 4.81) by 2.69 ± 0.52 hours, which was statistically significant.

Venkateshmurthy *et al.* [13] compared 0.5% bupivacaine with 0.75% ropivacaine, not exceeding 2.5 mg/kg body weight in unilateral TAP block in 60 patients following inguinal hernia repair. In their study TAP block was used as a sole anaesthetic agent. In group B the duration of analgesia was 573.00 ± 45.72 mins, in group R it was 675.54 ± 30.31 mins. (p value of < 0.001). All studies therefore showed ropivacaine to have better analgesic potency as well as longer duration of analgesia following TAP block.

These may be explained by intrinsic vasoconstrictor effect of ropivacaine. Hui-Jin Sung *et al.* [14] stated that aminoamide local anesthetics induce vasoconstriction at low doses and vasodilation at high doses. Depending on the vascularity of the injection site vasoconstriction induced by local anesthetic and addition of epinephrine may contribute to decreased absorption of local anesthetics into systemic circulation. This leads to prolonged nerve exposure to local anesthetics and reduced plasma levels, in addition to the potency of intrinsic vasoconstriction being partially associated with duration of anesthesia produced by the local anesthetic. They concluded that the octanol/ buffer partition coefficient of local anesthetics is the primary factor in determining the potency of local anesthetic-induced vasoconstriction. They determined the order of potency of vasoconstriction induced by local anesthetics in isolated endothelium-denuded aorta to be levobupivacaine > ropivacaine >lidocaine > mepivacaine.

However, Rathman *et al.* [15] showed that bupivacaine inhibits thromboxane A2 induced vasoconstriction. This is not seen with Ropivacaine which might explain the shorter duration of action of Bupivacaine as compared to Ropivacaine.

Since the above two studies have been conducted in rats, still a lot of research needs to be conducted using different concentrations of Bupivacaine and Ropivacaine before extrapolating this data to humans.

Timing of request for rescue dose

In 0.25% bupivacaine group, majority of patients (14 out of 25) received first dose of rescue analgesic between 6 hrs to 12 hrs. In 0.2% ropivacaine group, majority of patients (13 out of 25) received first dose of rescue analgesic between 12 hrs to 24 hrs. These results suggest that 0.2% ropivacaine provided longer duration of analgesia in majority of patients when compared to 0.25% bupivacaine. This also explains the mean duration of analgesia in 0.25% bupivacaine as 410.73 + 297.85 mins and in 0.2% ropivacaine as 747.5 + 394.7 mins. In our study out of 50 patients, 2 patients from 0.25% bupivacaine group and 5 patients from 0.2% ropivacaine group did not request for rescue analgesia in first 24 hrs.

El Dawlatley *et al.* [16] studied the analgesia of USG guided TAP block following laproscopic cholecystectomy and reported reduced rescue analgesic requirement.

Madhumani N. Rupasinghe *et al.* [17] retrospectively reviewed the 24 hrs total PCA morphine requirement with or without TAP block following ceasarean section to achieve a desired (VAS) visual analog pain score of 3 or less in patients. They observed over 30% reduction in morphine usage for those who received the TAP block.

Gildasio S. De Oliveira [5] compared postoperative opioid requirement in patients undergoing laproscopic surgery who received TAP blocks with either 0.25% ropivacaine, 0.5% Ropivacaineor saline. There was significant reduction in opioid consumption in the Ropivacaine groups as compared to saline group. However the opioid requirement was comparable between the 0.25% Ropivacaine and 0.5% Ropivacaine.

Complications

In our study, none of the patients from either group encountered complications like intra abdominal organ injury, local anaesthetic toxicity or transient femoral palsy as we did not cross the toxic dose of both the drugs and used ultrasound for visualisation of drug deposition in the right plane.

Lancaster and Chadwick reported a case of liver laceration after USG-guided TAP block, which was likely as a result of failure to adequately visualize the needle during the procedure. Another important concern is the local anaesthetic toxicity, particularly when B/L blocks were performed. TAP block has been shown to cause systemic toxicity if local anaesthetic spills over into the adjacent muscles or/ and if toxic dose of local anaesthetic has been used.

Transient femoral nerve palsy after TAP block is the result of local anaesthetic incorrectly injected between the transversus abdominis muscle and the transversalis fascia and accumulating around the femoral nerve. It is characterized by quadriceps femoris paresis, hypoesthesia over the anterior aspect of the thigh and absent patellar reflex. While it is not a major cause of postoperative morbidity, it may cause patient discomfort and anxiety as well as unexpected injuries due to falls. It is a self-limiting complication, but patients require overnight admittance for observation, thus increasing length of stay and hospital costs. Performing the TAP block under ultrasound guidance and injecting the least volume of local anaesthetic required are effective ways to reduce its occurrence [18].

Conclusion

VAS showed significant difference between the study groups at 6 hrs and 12 hrs. The mean postoperative VAS in group B (0.25% bupivacaine) was maximum at the end of 6hrs (4.08) whereas the mean postoperative VAS in group R (0.2% ropivacaine) was maximum at the end 12 hrs (4.0). Mean duration of analgesia was 410 minutes with SD of + 297.85 mins (approximately 7 hrs) in Bupivacaine group and 747.5 minutes with SD of +394.7 mins (approximately 12.5 hrs) in Ropivacaine group which was found to be statistically significant. In 0.25% bupivacaine group, majority of patients (14 out of 25) received rescue analgesia after 6 hrs. In 0.2% ropivacaine group, majority of patients (13 out of 25) received rescue analgesia after 12 hrs. 2 patients in bupivacaine group and 5 patients in ropivacaine group did not receive any rescue analgesia in 24 hrs. Hemodynamic parameters like heart rate showed no significant difference at 30 min, 1 hr, 3 hrs and 6 hrs whereas showed a significant difference at 12 hrs and 24 hrs. The mean arterial pressure did not show any significant difference at any time interval. During the study, no patients had complications related to procedure or side effects due to the study drugs. 0.2% Ropivacaine when compared with 0.25% Bupivacaine, provides a longer duration of analgesia and potent analgesic efficacy in ultrasound guided TAP block. Thus, it is concluded that Ropivacaine can be used as a safe alternative to Bupivacaine, routinely for TAP block for patients undergoing abdominal surgeries.

References

1. Michaloliakou C, Chung F, Sharma S. Preoperative multimodal analgesia facilitates recovery after ambulatory laparoscopic cholecystectomy. Vol. 82, Anesthesia and analgesia. 1996.p.44–51.
2. Niraj G, Searle A, Mathews M, Misra V, Baban M, Kiani S, *et al.* Analgesic efficacy of ultrasound-guided transversus abdominis plane block in patients undergoing open appendicectomy. Br J Anaesth. 2009;103(4):601–5.
3. Jain PN, Ranganathan P. Ultrasound in anaesthesia. Indian J Anaesth. 2007;51(3):176– 83.
4. Kuthiala G, Chaudhary G. Ropivacaine: A review of its pharmacology and clinical use. Indian J Anaesth. 2011;55(2):104–10.
5. De Oliveira GS, Fitzgerald PC, Marcus RJ, Ahmad S, McCarthy RJ. A dose-ranging study of the effect of transversus abdominis block on postoperative quality of recovery and analgesia after outpatient laparoscopy. Anesth Analg. 2011;113(5):1218–25.
6. El Abdein Mohamed AZ. Assessment of the analgesic potency of ropivacaine 0.2% versus ropivacaine 0.5% in transversus abdominis plane block after cesarean delivery. Egypt J Anaesth [Internet]. 2016;32(3):385–90.
7. Young MJ, Gorlin AW, Modest VE, Quraishi SA. Clinical implications of the transversus abdominis plane block in adults. Anesthesiol Res Pract. 2012;2012.
8. Patel D, Patel B, Patel H, Shah D, Vachhrajani P. Transversus Abdominis Plane Block for Post Operative Analgesia in Lower Abdominal Surgery - A Comparison of Bupivacaine and Ropivacain. 2016;5(12):446–50.
9. Fuladi N, Deshmukh S, Bhure A. Comparative Study of Bupivacaine 0.25% Versus Ropivacaine 0.5% in Transversus Abdominis Plane Block for Postoperative Analgesia in Lower Abdominal Surgeries: a Randomised Controlled Trial. J Evol Med Dent Sci [Internet]. 2014;3(17): 4569–76.
10. Sharma N, Mehta N, Sharma S. An evaluation of (0.25%) Bupivacaine Vs (0.5%) Ropivacaine for postoperative analgesia using ultrasound guidedtransversus abdominis plane block for abdominal surgeries: A comparative study. Indian J ClinAnaesth. 2016;3(4):635–9.
11. Sinha S, Palta S, Saroa R, Prasad A. Comparison of ultrasound???guided transverses abdominis plane block with bupivacaine and ropivacaine as adjuncts for postoperative analgesia in laparoscopic cholecystectomies. Indian Journal of Anaesthesia. 2016.60:264–9.
12. Patel D, Patel B, Patel H, Shah D, Vachhrajani P. Transversus Abdominis Plane Block for Post Operative Analgesia in Lower Abdominal Surgery :A Comparison of Bupivacaine and Ropivacain. 2016;5(12):446–50.
13. Thimmarayappa VMK, Mj S, Nadkarni MD.

For their duration of anaesthesia/analgesia in Transversus Abdominis Plane block for unilateral inguinal hernia repair. pp.329–34.

14. Sung HJ, Ok SH, Sohn JY, Son YH, Kim JK, Lee SH, *et al.* Vasoconstriction potency induced by aminoamide local anesthetics correlates with lipid solubility. J Biomed Biotechnol. 2012;2012:170958. doi: 10.1155/2012/170958. Epub 2012 Jun 17.
15. Hahnenkamp K, Nollet J, Mper DS, Halene T, Rathman P, Mortier E, *et al.* Bupivacaine Inhibits Thromboxane A2-Induced Vasoconstriction in Rat Thoracic Aorta. AnesthAnalg [Internet]. 2004;99(1):97–102.
16. El-Dawlatly AA, Turkistani A, Kettner SC, Machata AM, Delvi MB, Thallaj A, *et al.* Ultrasound-guided transversus abdominis plane block: description of a new technique and comparison with conventional systemic analgesia during laparoscopic cholecystectomy. Br J Anaesth. 2009 Jun;102(6):763-7. doi: 10.1093/bja/aep067. Epub 2009 Apr 17.
17. Rupasinghe MN, Osborne SC, Aseem R. Requirement Post Cesarean Section with and without TAP Block- A Retrospective Chart review. 2013;1:1–2.
18. Christie LE, Picard J, Weinberg GL. Local anaesthetic systemic toxicity. BJA Educ [Internet]. 2015;15(3):136–42.

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Comparative Study of the Effect of Dexmedetomidine v/s Fentanyl on Intraoperative Hemodynamic Response in Robot Assisted Lower Abdominal Onco-Surgeries in Steep Trendlenburg Position

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Abstract

Introduction: Carbon dioxide insufflation for pneumoperitoneum causes increase plasma levels of catecholamines and vasopressin which leads to hemodynamic disturbances. These effects are exaggerated by the trendelenburg position and long duration of surgery in robot assisted surgeries. This study was designed to evaluate the effect of Dexmedetomidine and fentanyl on hemodynamics in robot assisted surgeries in trendlenberg position. *Methods:* After obtaining Ethical committee clearance and patients consent, randomised comparative study on 40 ASA I and II patients, who were randomly allocated to receive either dexmedetomedine or fentanyl intravenous infusion was done. Patients with ASA III & IV, on β blockers, HR<55 bpmin were excluded. Intraoperative Hemodynamics, recovery and emergence was assessed. Students 't' test was used. *Results:* The study included 40 patients undergoing robotic lower abdominal surgeries requiring steep trendlenberg positions. Dexmedetomedine group of patients showed better intra operative hemodynamics at various time intervals as compared to Fentanyl group of patients.

Keywords: Robot; Trendlenburg position; Dexmedetomedine.

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Introduction

Robotic assisted surgeries are becoming popular due to its several benefits like early recovery, less tissue damage, minimal incision and shorter hospital stay.Anaesthetic management has become complicated in these surgeries due to cardiopulmonary changes occurring during creation of pneumoperitoneum with CO_2 with patients in trendlenberg position and maintenance of immobility of patients throughout the surgery. Pneumoperitoneum is associated with sympathetically mediated adverse haemodynamic effect like elevation of arterial pressure, heart rate, decrease in cardiac output due to pneumoperitoneum and increase of systemic and pulmonary vascular resistances. Peritoneal insufflations also results in ventilatory and respiratory changes and can contribute to stress response. These effects are further exaggerated by the trendlenberg position.

Dexmedetomidine, an alpha 2 selective

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adrenoceptor agonists is known to maintain stable hemodynamics due to its effect on central sympatholytic system. Fentanyl being an opioid analgesic acts via opioid receptors to blunt hemodynamic responses. Opioids are known to cause acute hyperalgesia [1] in the immediate postoperative period and also ileum and urinary retention with prolonged sedation. Recent studies have shown that Dexmedetomedine has an opioid equivalent analgesic actions in laparoscopic surgeries [2,3].

The study was aimed to compare the effect of Dexmedetomedine Vs Fentanyl on hemodynamic response to tracheal intubation, following pneumoperitoneum and intraoperative period in patients undergoing robotic oncology surgeries in trendlenberg position.

Methods

After obtaining approval from hospital ethical committee and informed consent from all the patients, a prospective randomised controlled study was conducted on forty patients aged 18-60 years, with American Society Anaesthesiologists (ASA) status I and II who were undergoing elective robotic oncology surgeries requiring trendelenberg position.

Exclusion criteria were patient with acute and chronic renal failure, compromised cardiovascular function, severe deranged liver function, patients with ASA Grade III and IV, emergency cases, patients on β blocker and patients with HR <55/min.

The study drugs were then prepared as follows: 2 ml (200 µg) of study drug Dexmedetomidine was diluted in 48ml of normal saline to make 50 ml (concentration 4 µg/ml.). 4 ml (200 µg) of study drug fentanyl was diluted in 46 ml normal saline to make 50 ml (conc. 4 µg/ml).

Intra Venous access was secured with a 18 G cannula and infusion of Ringer's lactate was started.

The prepared drug Dexmedetomidine or fentanyl was given as follows:

Group-D (N=20): IV Dexmedetomidine 1 µg/kg/hr was given as loading dose over 10 minutes prior to induction and then continued intraoperatively with Dexmedetomidine of 0.5 µg/kg/hrIV infusion.

Group-F (N=20): IV fentanyl 1 µg/kg/hr was given as a loading dose over 10 minutes prior to induction and then continued intraoperatively with fentanyl of 0.5 µg/kg/hrIV infusion.

Hemodynamic parameters as ECG, HR, RR, SBP, DBP, MAP and SpO_2 were recorded at baseline.

The patient was pre-oxygenated with 100% oxygen for three minutes. Following this, Inj. Glycopyrrolate 0.2 mg IV (as and when required when HR<50/min), Inj. Ondansetron 4 mg I.V and IV Midazolam 1mg were given before induction.

Anaesthesia induced with IV Propofol 1 mg/kg and inhalation agent with vecuronium as a muscle relaxant. Intraoperatively anaesthesia maintained with Inhalational agents, Muscle relaxant infusion and Study drug infusion with Positive Pressure Ventilation.

Intraoperatively parameters like ECG, HR, SBP, DBP, MAP, SpO_2, and $EtCO_2$ were continuously recorded.

The above parameters were then recorded at predetermined time intervals as follows: prior to infusion of study drug, 10 minutes after the study drug, after Inj. of induction drug, after intubation, five minutes after intubation, after pneumoperitoneum, 15 minutes after pneumoperitoneum, 30 minutes after pneumoperitoneum, 45 minutes after pneumoperitoneum, 60 minutes after pneumoperitoneum, every 30 mins thereafter till the release of pneumoperitoneum and five minutes after release of pneumoperitoneum.

Adverse effects like bradycardia, tachycardia, hypotension, hypertension, nausea,vomiting, respiratory depression, if any, noted during operative procedure, were treated as follows:

Bradycardia - (HR<50/min): Inj. Glycopyrrolate 0.2 mg I.V

Tachycardia – (HR >30% above baseline value): Inj. Propofol 20 mg I.V in titrated dose

Hypotension – (SBP<60 mmHg) Inj. Ephedrine 6 mg I.V in titrated dose.

Hypertension – (SBP> 140 mmHg): Inj. Propofol 20 mg I.V in titrated dose and 0.25% bupivacaine 5ml of epidural top up and IV Fentanyl 25 microgram.

Infusion of drug (Dexmedetomidine or fentanyl) was stopped and isoflurane was discontinued 10 minutes before reversal. Residual paralysis was reversed with Inj.Neostigmine 0.05 mg/kg IV, and Inj. Glycopyrrolate 8 µg/kg IV. Patient was extubated once extubation criterias were fullfilled.

Parameters were again recorded at five minutes after extubation.

Results

Demographic profile including age, sex, weight,

ASA physical status, duration of anaesthesia and type of operation were comparable in both groups and not of much statistically significant.

The preoperative baseline haemodynamic parameters like mean HR, SBP, DBP, SpO_2 in Group D and in Group F were not significant between two groups.

At 10 mins after Loading Dose there was 18% fall in HR, 12.5% fall in SBP, 10.5% fall in DBP and 9.5% fall in MAP in Group D as compared to 2% fall in HR, 11.3% fall in SBP, 9.6% in DBP and 10.5% fall in MAP fall in Group F patients.

After intubation there was 21% fall in HR, 13.3% fall in SBP, 9.4% fall in DBP and 9.5% fall in MAP in Group D patients as compared to 2% fall in HR, 7.6% fall in SBP, 3.6% fall in DBP, 6.7% fall in MAP in Group F patients.

After insufflation there was 29.8% fall in HR, 20% fall in SBP, 17.5% fall in DBP and 17% fall in MAP in Group D patients as compared to 12.3% fall in HR, 7.6% fall in SBP, 3.5% increase in DBP and 2% fall in MAP in Group F patients.

Throughout intraoperative period of pneumoperitoneum Group D showed significant fall in HR, SBP, DBP, MAP from baseline and more stable values at all points of time intervals where as it remains similar to baseline values or at sometimes above baseline values in Group Fpatients (Graph 1,2,3).

At extubation there was 24.5% fall in HR, 13.98% fall in SBP, 10.5% fall in DBP and 10.5% fall in MAP in Group D patients as compared to 5.6% fall in HR, 4.6% fall in SBP, 0% variation in DBP and 2% increase in MAP in Group F patients.

Intraoperative hypertension was found in 3 patients (15%) in Group D and 6 patients (30%) in Group F patients and 3 (50%) patients in Group F needed treatment of Hypertension.

Intraoperative Bradycardia was found in 4 (20%) patients in Group D and 2 (50%) patients required intervention.

Intraoperative tachycardia was found in 5 (25%) patients in Group F. 8 patients (40%) of patients were sedated at the end of surgery but arousable to commands with no respiratory depression in group D patients and were shifted to ICU with ET tube in situ.

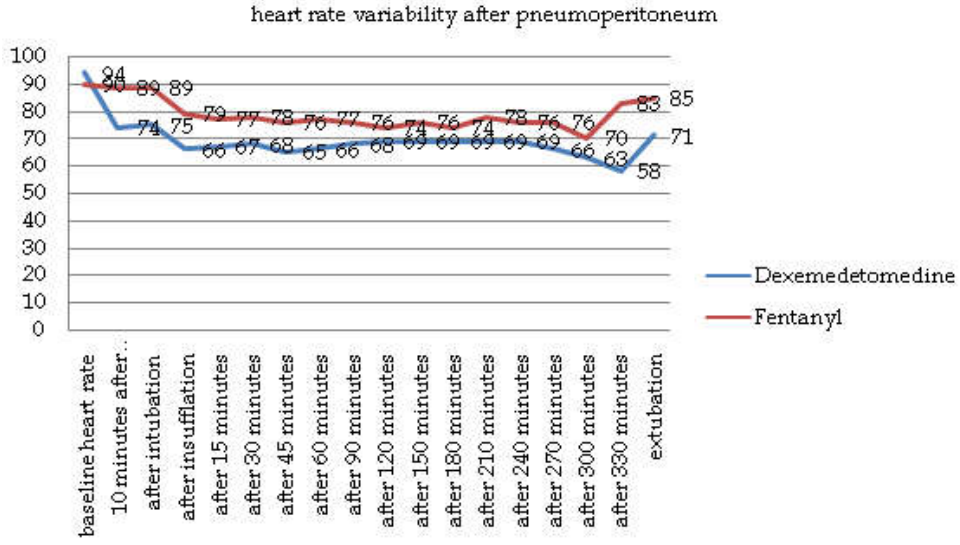
In fentanyl group of patients, 4 (20%) patients were sedated and responding to painful stimuli with no respiratory depression and were shifted to ICU with ET tube in situ. (Table 1).

Table 1:

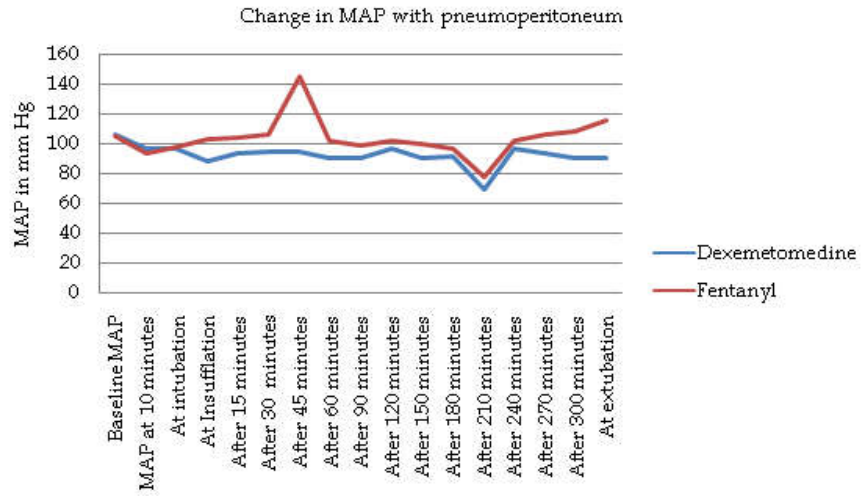
	Dexmedetomedine	Fentanyl
Intraoperative Bradycardia	4 (20%)	0
Treatment	2 (50%)	0
Intraoperative Tachycardia	0	5 (25%)
Treatment		0
Intraoperative Hypertension	3 (15%)	6 (30%)
Treatment	1 (5%)	4 (20%)
Sedation	8 (40%)	6 (30%)
Respiratory Depression	0	0
ECG Abnormality	0	0

Extubation response was smooth in Dexmedetomidine group of patients as compared to Fentanyl group of patients.

None of our patients in both groups have any respiratory depression. None developed any ECG abnormality.



Graph 1:



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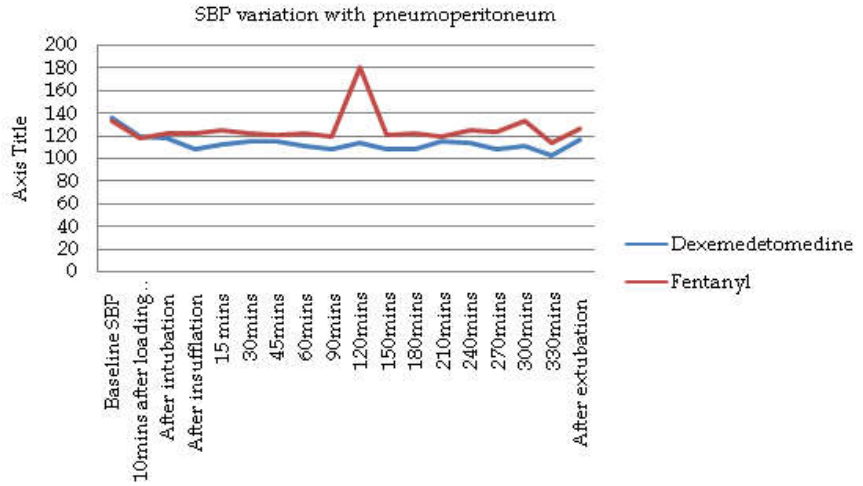

Graph 3:

Discussion

Pneumoperitoneum is known to increase systemic vascular resistance, mean arterial pressures, cardiac filling pressures and cardiac index. CO_2 insufflation results in hypercarbia due to peritoneal absorption of CO_2 which results in increase in HR, BP and increased risk of arrythmias due to sympathetic nervous system stimulation and also decreases myocardial contractility [4,5].

The hemodynamic changes are further exaggerated with the increasing degree of steep trendlenberg position [6].

The opioid free and opioid sparing analgesic techniques are known to reduce the side effects associated with opioids and hence helps in faster recovery, early ambulation, early oral intake [7]. Side effects like PONV, postoperative ileus seen in these kind of surgeries along with postoperative hyperalgesia are known to be aggravated with the use of opioids [1].

Alpha 2 agonists are shown to be effective as sole analgesic agents intraoperatively with better and stable hemodynamic control with sympatholytic, antinociceptive and sedative properties [8, 9]. A variety of pharmacological agents namely opioids, beta blockers, calcium channel blockers, combined alpha and beta blockers, lignocaine, and alpha-2 receptor agonists have been used to maintain stable hemodynamics in the perioperative period. Fentanyl being widely used intraoperatively for control of hemodynamics, is associated with side effects such as respiratory depression and increased incidence of postoperative nausea and vomiting (PONV). No studies have been done to study the effects of Dexmedetomidine and fentanyl on the hemodynamic profile in robotic surgeries requiring steep trendlenberg positions. Hence, this study was done to compare the efficacy of the two study drugs

on the hemodynamic changes intraoperatively in robotic surgeries.

Our study demonstrates that use of Dexmedetomidine for intraoperative infusion helps attenuates stress responses to different noxious stimuli during surgery and helps maintain haemodynamic stability perioperatively.

Our observation shows significantly less increase in HR in Dexmedetomidine group as in comparison with fentanyl group after intubation, after pneumoperitoneum, intraoperative period and after extubation which is in accordance with that of other studies. This is because Dexmedetomidine effectively blunts sympatho adrenal response to intubation and has good sympatholytic activity. Suparto *et al.*, [13] concluded that both Dexmedetomidine at 1 µg/Kg and fentanyl at 1 µg/Kg given intravenously as single bolus dose prior to anaesthesia induction produced lowering of blood pressures and cardiac rates, with significantly lower mean heart rates with Dexmedetomidine i.e., 21% decrease in Dexmedetomidine group vs 2% decrease in fentanyl group.

In our study, there is less fluctuation in SBP, DBP and MAP in Dexmedetomidine group in comparison to fentanyl after intubation, after pneumoperitoneum and after extubation. This implies that Dexmedetomidine had attenuated stress response perioperatively. Similar findings were observed by Patel CR *et al.* [15] and Jayshree P Vaswani *et al.* [10] and also Feld JM *et al.* [11] in which HR and BP decreased.

Intraoperatively throughout hemodynamics was more stable in Dexmedetomidine (0.5 µg/kg infusion) group of patients when compared to Fentanyl (0.5 µg/kg infusion) group of patients which is consistent with that of Sharif SM *et al.*, [16] who observed that both Dexmedetomidine (1 µg/kg) and fentanyl (2 µg/kg), when used as premedicant before induction attenuated the haemodynamic response to pneumoperitoneum during laparoscopic surgeries.

Hall JE *et al.*, [17] in their study concluded that small doses of Dexmedetomidine led to significant sedation which could be reversed by the help of verbal or physical stimuli and it resolved completely after two hour of termination of infusion. In our study, no stastically significant sedation was seen in any patient though eight patients had sedation score ≤ 3 in Group D.

Group D patients had less extubation response as compared to Group F patients which is similar to Goyal S *et al.* [18] study.

Limitation

We have done a small study of 40 patients and could not analyse the post op analgesic requirement and total amount of the study drug consumed, cost effectiveness of the study drugs and also requirement of inhalational agents in the two study groups.

Conclusion

To conclude Dexmedetomedine causes greater attenuation of hemodynamic response to tracheal intubation, following pneumoperitoneum and perioperatively with stable hemodynamics as compared to Fentanyl in surgeries requiring pneumoperitoneum in steep trendlenberg position. Dexmedetomedine patients had better sedation score and easy arousability.

Hence, intravenous premedication with Dexmedetomedine in dose of 1µg/kg as loading dose over 10 minutes prior to induction in robotic assisted surgeries requiring steep trendlenberg position followed by 0.5 µg/kg infusion till surgery is over, may be recommended for better haemodynamic stability during perioperative period.

References

1. Angst MS, Clark JD. Opioid-induced hyperalgesia: A qualitative systematic review. Anesthesiology 2006;104:570-87.
2. Tufanogullari B, White PF, Peixoto MP, Kianpour D, Lacour T, Griffin J, *et al.* Dexmedetomidine infusion during laparoscopic bariatric surgery: The effect on recovery outcome variables. AnesthAnalg. 2008;106:1741-8.
3. Jung HS, Joo JD, Jeon YS, Lee JA, Kim DW, In JH, *et al.* Comparison of an intraoperative infusion of dexmedetomidine or remifentanil on perioperative haemodynamics, hypnosis and sedation, and postoperative pain control. J Int Med Res 2011;39:1890-9.
4. Hirvonen EA, Nuutinen LS, Kauko M. Haemodynamic changes due to Trendelenburg positioning and pneumoperitoneum during laparoscopic hysterectomy. Acta Anaesthesiol Scand. 1995;39:949.
5. Cunningham AJ, Turner J, Rosenbaum S, Rafferty T. Transoesophageal echocardiographic assessment of haemodynamic function during laparoscopic cholecystectomy. Br J Anaesth. 1993;70:621.
6. Kadono Y, Yaegashi H, Machioka K, Ueno S, Miwa S, Maeda Y, Miyagi T, Mizokami A, Fujii Y, Tsubokawa T, Yamamoto K, Namiki M. Cardiovascular and

respiratory effectsof the degree of head-down angle during robot-assisted laparoscopic radical prostatectomy.Int J Med Robot. 2013 Mar;9(1):17-22. doi: 10.1002/rcs.1482. Epub 2013 Jan 25.

7. Cepeda MS, Farrar JT, Baumgarten M, Boston R, Carr DB, Strom BL. Side effects of opioids during short-term administration: Effect of age, gender, and race. ClinPharmacolTher. 2003;74:102-12.
8. Feld JM, Laurito CE, Beckerman M, Vincent J, Hoffman WE. Non-opioid analgesia improves pain relief and decreases sedation after gastric bypass surgery. Can J Anaesth. 2003;50:336-41.
9. Bhana N, Goa KL, McClellan KJ. Dexmedetomidine. Drugs. 2000;59:263–8.
10. Jayshree P Vaswani *et al.* Jayshree P Vaswani et al., Dexmedetomedine vs Fentanyl: Effect on the Haemodynamic Response in Laparoscopic Surgeries Journal of Clinical and Diagnostic Research. 2017 Sep;11(9):UC04-UC08.
11. Feld JM, Feld JM, Hoffman WE, Stechert MM, Hoffman IW, Ananda RC. Fentanyl or dexmedetomidine combined with desflurane for bariatric surgery. J Clin Anesth. 2006;18:24-8.
12. Lovina Neil *et al.* Effect of Dexmedetomidine Versus Fentanyl on Haemodynamic Response to Patients Undergoing Elective Laparoscopic Surgery: A Double Blinded Randomized Controlled Study Journal of Clinical and Diagnostic Research. 2017 Apr;11(4):UC01-UC04].
13. Suparto, Flores OC, Layusa CAA. A Randomized controlled trial on the effectiveness of dexmedetomidine versus fentanyl in attenuating the sympathetic response to direct laryngoscopy and endotracheal intubation.
14. Maj KedokiIndon. 2010; 60:126–32. [Who concluded that both Dexmedetomidine at 1 µg/Kg and fentanyl at 1 µg/Kg given intravenously as single bolus dose prior to anaesthesia induction produced lowering of blood pressures and cardiac rates, with significantly lower mean heart rates with Dexmedetomidine.]
15. Patel CR *et al.* Effect of intravenous infusion of Dexmedetomidine on perioperative haemodynamic changes and postoperative recovery: a study with entropy analysis. Indian J. Anaesth. 2012;56:542–46.
16. Shareef SM *et al.* A comparative study of the haemodynamic changes with Dexmedetomidine Vs Fentanyl during laparoscopic cholecystectomies under general anaesthesia. J of Dental and Medical Sciences. 2016;15:01-09.
17. Hall JE, Uhrich TD, Barney JA, Arain SR, Ebert TJ. Sedative, amnestic, and analgesic properties of small-dose dexmedetomidine infusions. Anaesth Analg. 2000;90:699–705.
18. Goyal S, Gupta KK, Mahajan V. A comparative evaluation of intravenous dexmedetomidine and fentanyl in breast cancer surgery: A prospective, randomized, and controlled trial. Anesth Essays Res. 2017;11:611-6.

Original Research Article

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Efficacy of Intrathecal Fentanyl with 0.5% Hyperbaric Bupivacaine in Intraoperative and Post Operative Analgesia in Cesarean Section: A Randomized Controlled Trial

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Abstract

Background: Caesarean delivery requires significant traction of peritoneum and intra-abdominal organs. Intra operative visceral pain is sometimes a problem during spinal anaesthesia. Increasing the dose of local anaesthestic is associated with less intra operative visceral pain. *Objective:* To evaluate the quality of intra operative analgesia and post-operative analgesia when fentanyl is added to intrathecal bupivacaine for caesarean section. *Methods:* Double blind, randomized controlled trial was conducted among 80 patients aged between 18-35 years from February 2007 to January 2008. 80 patients of the age group 18-35 years undergoing cesarean section, belonging to ASA Grade 1 were considered for this study. The patients were randomly divided into two groups of 40 patients each. Epi info 7 was used for analysis. *Results:* age and anthropometric characters (height and weight) were calculated in terms of mean and Standard deviation. As seen no significant difference was seen either in age, height or weight ($p>0.05$). For Mean BP at the time of arrival and during positioning for intrathecal injection: $p > 0.05$- not significant. After intrathecal injection: $p < 0.01$- highly significant. 1 min, 2 min, 3 min, 4 min, 5 min, 6 min, 7 min after intrathecal injection: $p > 0.05$ – not significant. *Conclusion:* Addition of fentanyl (12.5 µg) to 0.5% hyperbaric Bupivacaine (10 mg) provides early onset of sensory blockade, improvement in intraoperative analgesia and significant increase in the duration of postoperative analgesia.

Keywords: Analgesia; Fentanyl; Bupivacaine; Cesarean Section.

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Introduction

Caesarean delivery requires significant traction of peritoneum and intra-abdominal organs. Intra operative visceral pain is sometimes a problem during spinal anaesthesia. Increasing the dose of local anaesthestic is associated with less intra operative visceral pain, but higher sympathetic blockade. Neuraxial administration of opioids in conjunction with local anaesthetic improves the quality of intraoperative analgesia and prolongs the duration of post-operative analgesia [1]. The advantages of post-operative analgesia are better

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pulmonary function, early ambulation and low risk for deep vein thrombosis [2]. Fentanyl is a synthetic & lipophilic opioid it has rapid onset of action following intrathecal administration and it does not tend to migrate higher up to cause delayed respiration. Being a lipophilic opioid, it has rapid onset of action following intrathecal administration and it does not tend to migrate higher up to cause delayed respiratory depression. So, the rationale behind the study was to evaluate the effects of intrathecally administered Fentanyl (12.5 µg) on the onset and duration of sensory blockade of 0.5% hyperbaric bupivacaine (10 mg), quality of intra operative analgesia and post-operative analgesia.

Materials & Methods

Study Area- Tertiary care teaching– Major operation theatre, Department of Anaesthesiology, Pushpagiri Institute of Medical Sciences, Thiruvalla, Kerala.

Study type- Double blind, randomized control study.

Study population- 80 patients of the age group between 18 and 35 years who presented for cesarean section.

Study duration- February 2007 to January 2008.

Sampling technique- Purposive Sampling Technique.

Inclusion criteria- Patients admitted for cesarean section of age group between 18 and 35 years of ASA Grade I.

Exclusion criteria-

1. Age less than 18 years and more than 40 years.
2. Body weight more than 70 kg.
3. Co-existing system illness like hypertension, diabetes mellitus, bronchial asthma, cardiovascular disease.
4. Patients with fetal distress, fetal anomalies.
5. Patients with known drug allergies.

Methodology- 80 patients of the age group 18-35 years undergoing cesarean section, belonging to ASA Grade 1 were considered for this study. The patients were randomly divided into two groups of 40 patients each.

Group A- 40 patients of this group received 2 ml of 0.5% injection hyperbaric bupivacaine (10 mg) with 0.25 ml of normal saline.

Group B- 40 patients of this group received 2 ml of 0.5% injection hyperbaric bupivacaine (10 mg) with 0.25 ml (12.5 µg) fentanyl. All study agents are introduced intrathecally and total volume of agents administered were 2.25 ml. All patients were kept fasting for 8 hrs prior to surgery. They were premedicated with Tab Ranitidine 150 mg and Metoclopramide 10 mg in elective cases and injection Ranitidine 50 mg and injection Metoclopramide 10 mg respectively in emergency cases. In the operating room, all patients were preloaded with 15 ml/Kg Ringer lactate. Baseline heart rate, blood pressure, rate of respiration, fetal heart rate were recorded before spinal anesthesia.

Study tool- In order to compare the data and to draw conclusions; the mean and standard deviation of heart rate, BP, Respiratory rate, Mcgill Pain Score, Bromage scale and duration of analgesia were calculated.

Consent Type- Written Informed consent

Ethical Considerations- The study was approved by ethics committee of the medical faculty, Pushpagiri Institute of Medical Sciences, Thiruvalla.

Statistical Analysis- Data will be consolidated and entered a Microsoft Excel spreadsheet and then transferred to Epi info version (7.1.3.0. centre for disease control and prevention, Atlanta, Georgia, USA, 2013) software for analysis. student t- test was used.

Results

Table 1: Mean body characteristics in Group A and Group B

Parameters	Group	Mean	+ SD	t value	p value
Age (years)	Group A	26.55	2.44	0.741	> 0.05
	Group B	26.15	2.39		
Height (cm)	Group A	157.83	3.74	-1.534	> 0.05
	Group B	161.85	16.17		
Weight (kg)	Group A	64.23	3.04	0.767	> 0.05
	Group B	62.88	10.66		

As per table 1 age and anthropometric characters (height and weight) were calculated in terms of mean and Standard deviation. As seen no significant difference was seen either in age, height or weight ($p>0.05$).

Table 2: Mean systolic BP in Group A and Group B

SBP	Group	Mean	+ SD	t value	p value
At the Time of Arrival	Group A	118.60	9.98	-1.757	> 0.05
	Group B	122.63	10.50		
Positioning	Group A	118.03	10.25	-1.666	> 0.05
	Group B	121.93	10.69		
After Intrathecal Injection	Group A	111.08	9.11	-3.092	< 0.01
	Group B	117.73	10.10		
After Injection – 1 minute	Group A	107.48	14.67	-0.400	> 0.05
	Group B	108.68	12.04		
After Injection – 2 minute	Group A	101.93	10.95	-0.767	> 0.05
	Group B	104.13	14.45		
After Injection – 3 minute	Group A	100.80	12.30	-0.902	> 0.05
	Group B	103.18	11.22		
After Injection – 4 minute	Group A	104.03	11.79	0.394	> 0.05
	Group B	102.98	12.06		
After Injection – 5 minute	Group A	106.60	11.44	0.987	> 0.05
	Group B	104.33	9.03		
After Injection – 6 minute	Group A	108.23	8.54	1.575	> 0.05
	Group B	105.08	9.33		
After Injection – 7 minute	Group A	111.25	9.32	1.846	> 0.05
	Group B	107.68	7.94		
After Injection – 8 minute	Group A	113.05	7.17	2.127	< 0.05
	Group B	109.63	7.23		
After Injection – 9 minute	Group A	114.05	5.52	1.603	> 0.05
	Group B	111.55	8.17		
After Injection – 10 minute	Group A	115.90	8.85	5.875	< 0.001
	Group B	111.98	8.52		
After Injection – 20 minute	Group A	114.45	6.68	0.973	> 0.05
	Group B	112.93	7.32		
After Injection – 30 minute	Group A	115.93	6.01	0.662	> 0.05
	Group B	114.90	7.72		

In table 2 At the time of arrival and during positioning for intrathecal injection: $p > 0.05$- not significant. After intrathecal injection: $p < 0.01$- highly significant. 1 min, 2 min, 3 min, 4 min, 5 min, 6 min, 7 min after intrathecal injection: $p > 0.05$ – not significant. After 8 minutes of intrathecal injection: $p < 0.05$ – significant. After 9 minutes of intrathecal injection: $p > 0.05$ – not significant. After 10 minutes of intrathecal injection: $p < 0.001$- highly significant. After 20 and 30minutes of intrathecal injection: $p > 0.05$- significant.

As per Figure 1- at the arrival, positioning, and after intrathecal injection the mean diastolic BP was higher in group B and after that it was higher in group A which was found to be highly significant ($p<0.05$).

As per Figure 2 the mean values of heart rate was higher in group B patients and was significant except in time interval of 8 min, 9 min and 10 min were group A has higher mean heart rate then group B which was also significant. ($p<0.05$).

In Figure 3 mean respiratory values was calculated after injection which shows the rates in group A was not crossed rates of group B patient and they were found to be highly significant ($p<0.05$).

Discussion

The addition of opioid to local anaesthetics has become a well-accepted practice in the

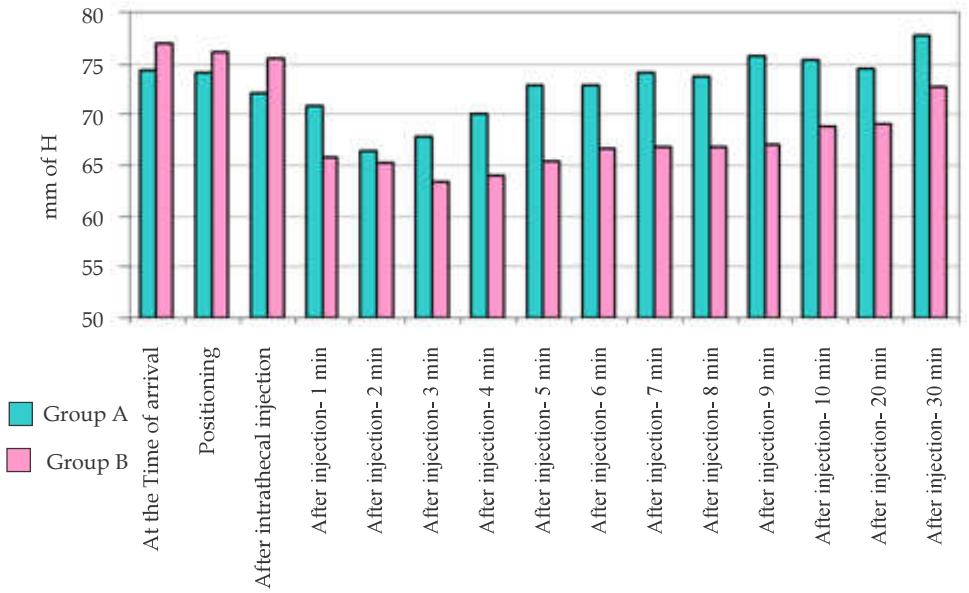

Fig. 1: Mean Values of Diastolic BP in both the groups

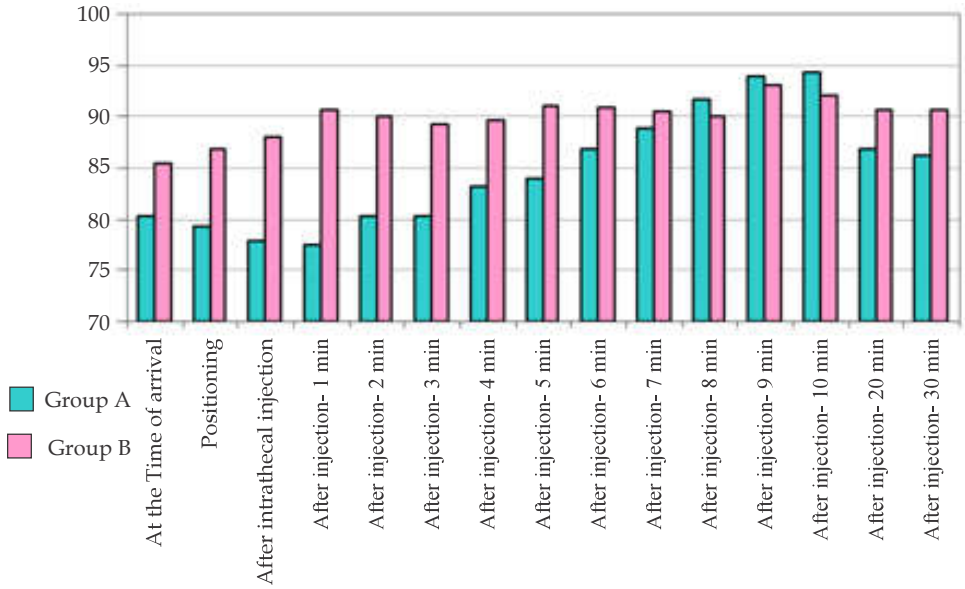

Fig. 2: Mean Values of Heart Rate in both groups

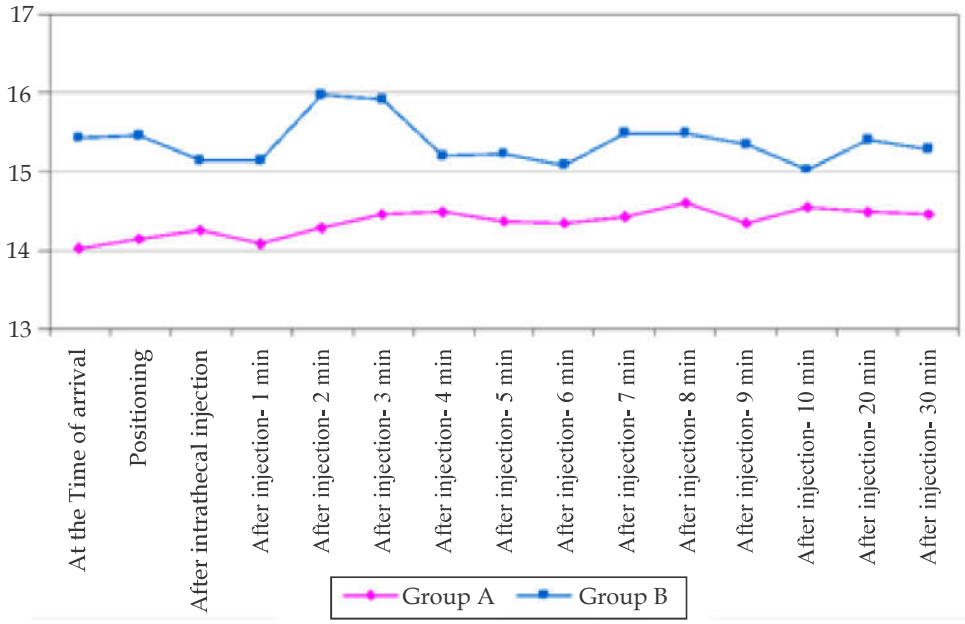

Fig. 3: Mean values of Respiratory Rate in both the groups

management of spinal anaesthesia for cesarean section. Use of morphine via subarachnoid route has limited use due to respiratory depression in the routine postoperative pain management. Fentanyl which is more lipid soluble than morphine has a rapid onset of action and it does not migrate higher up to cervical region. The evidence of side effects particularly respiratory depression is limited. Advantage of using intrathecal Fentanyl is its extremely rapid onset of action. Analgesia has been reported to occur within five to ten minutes. The present study was undertaken to evaluate the effects of intrathecally administered fentanyl (12.5 µg) on the onset and duration of sensory blockade of hyperbaric Bupivacaine, quality of intra operative analgesia, duration of post-operative analgesia and incidence of side effects. This dose of fentanyl was chosen because of studies by Ferrante *et al.* [5] showed that this was the optimal dose of intrathecal fentanyl with maximum clinical effect. This was a prospective randomized study conducted on two groups of 40 patients each.

Systolic blood pressure was recorded and fall in systolic blood pressure from baseline value was

recorded. Fall in blood pressure more than or equal to 30% from baseline was taken as hypotension. This study showed that Group B patients had incidence of fall in systolic blood pressure more than Group A. This study is consistent with the study by Cousins *et al.* [2] where it was found that there was no incidence of fall in heart rate in either groups. This is supported by the study by Ferrante *et al.* [5] where it was found that incidence of intraoperative hypotension is more with injection Bupivacaine - Fentanyl group [Bupivacaine 10 mg injection + Fentanyl 12.5 µg] than with injection Bupivacaine (10 mg). Similarly, there was no significant difference in number of patients experiencing fall in heart rate in both Group A and Group. 4 With respect to respiratory rate, no incidence of fall in rate of respiration in both Group A and Group B. The difference is found to be statistically not significant ($p > 0.05$) at all intervals of time. This study is consistent with studies by Cousins *et al.* [2] where it was found that there was no incidence of fall in rate of respiration in either groups.

The duration of effective analgesia was assessed using McGill scoring system. The duration of effective analgesia was taken as the interval between administration of spinal drug and time at which the patient complained of discomfort due to pain (McGill pain score). At that time rescue analgesic was given. The mean time for effective analgesia (minutes) in Group. A was 153.23 minutes. The mean time for effective analgesia (minutes) in Group B was 226.18 minutes.The difference in mean time for complete analgesia was found to be statistically significant ($p <0.001$). This study is consistent with studies with Cousins [2], Rexed *et al.* [3] and Melzack *et al.* [6] In studies by Cousins *et al.* [2] and Kelly *et al.* [8], Christopher *et al.* [9], Carles *et al.* [10] it was found that the mean time for effective analgesia (minutes) in injection Bupivacaine group was 150 ± 10.48 minutes and the mean time for effective analgesia (minutes) in injection Bupivacaine-Fentanyl group was 248 ± 11.76 minutes.

Conclusion

Addition of fentanyl (12.5 µg) to 0.5% hyperbaric Bupivacaine (10 mg) provides early onset of sensory blockade, improvement in intraoperative analgesia and significant increase in the duration of postoperative analgesia. Further studies with larger sample size is advised to determine the desired results.

Source of Funding- None

Conflict of Interest- None declared

References

1. IASP Sub-committee on Taxonomy. Pain Terms: A list with definition and notes on usage pain. 1979; 6:249.
2. Cousins MJ, Bridenbaugh PO. Neural Blockade in Clinical Anaesthesia and Management of Pain 3rd edn. Philadelphia: Lippincott –Raven. 1998.pp.472–5.
3. Rexed B. The Cyto Architectonic organization of the spinal cord in the cat. J Comp Neurolo. 1952;96:415.
4. Ready LB, Miller RD. Acute perioperative pain**.** 5th edn. Churchill Livingstone Inc. 2000.pp.23–25.
5. Ferrante FM. Acute post operative pain management. In: Longnecker DE, Tinker DH and Morgan GE (ed.) Principles and Practice of Anaesthesiology. Mosby Year Book Inc. 1998;2331–45.
6. Melzack R. The Mc Gill Pain Questionnaire. Major properties and scoring methods. Pain. 1975;1: 277–99.
7. Hammer M. Control of Post operative pain nausea and vomiting. In: Morgan GE and Hall GM (ed.) Short Practice of Anaesthesia. Chapman and Morgan. 1998.pp.853–58.
8. Kelly DJ, Ahmmad M, Brull SJ. Pre emptive analgesia. Recent advances and current trends. Can J Anaesthesia. 2001;48:1091–01.
9. Christopher L Wu. Acute Postoperative Pain In: Ronald D Miller (ed.). Anaesthesia. Churchill Livingstone Inc. 2005;2732–44.
10. Carles RB, Gary RS. Local Anaesthetics In: Ronald D Miller (ed.) Anaesthesia. Churchill Livingstone Inc. 1994.pp.297–10.

Original Research Article

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A comparative study of Inj. Bupivacaine 0.5% and Inj. Ropivacaine 0.5% for Supraclavicular Brachial Plexus Block

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Abstract

Context: Bupivacaine is a commonly used local anesthetic in peripheral nerve blocks. Ropivacaine is a newer local anesthetic and has better safety profile. The study was done to compare the two drugs. *Aims:* To compare the effects of Inj. Bupivacaine 0.5% and Inj. Ropivacaine 0.5% as local anesthetic for supraclavicular brachial plexus block in upper limb orthopedic surgeries. *Study design:* Randomized comparative study. *Methods:* The study was done at a medical college hospital. The patients included in the study were randomized into two groups (Bupivacaine and Ropivacaine) and were given 30 ml of respective drug under ultrasound guidance. The drugs were compared in terms of time taken for onset of action, duration of sensory and motor block, side effects. *Statistical analysis used:* Chi-square test and student's t-test. *Results:* The time taken for onset of sensory block was less with Bupivacaine (16.6 + 3.2 min) than with Ropivacaine (19.9 + 4.0 min) (p=0.0001). The onset of motor block was earlier with Bupivacaine (21.4 + 2.6 min) in contrast to Ropivacaine (25.9 + 2.4 min) (p=0.001). The duration of sensory blockade (Bupivacaine– 343.8 + 44.4 min; Ropivacaine– 317.9 + 29.1 min) and motor blockade (Bupivacaine– 387.4 + 36.0 min; Ropivacaine– 368.7 + 33.1 min) was longer with Bupivacaine (p=0.003; p=0.019 respectively). There were no adverse effects in both the groups. *Conclusion:* At equal volumes, Bupivacaine has advantage over Ropivacaine for supraclavicular brachial plexus block.

Keywords: Supraclavicular brachial plexus block; Ropivacaine; Bupivacaine.

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Introduction

Brachial plexus block is preferred over general anesthesia for upper limb surgeries. It achieves complete relaxation, sympathetic block while maintaining stable intra-operative hemodynamics. Hence it is considered to be ideal. The sympathetic block decreases post-operative pain, vasospasm and edema. At supraclavicular level, the middle and lower plexus are blocked. Thus, it is suitable for upper limb surgeries. Ultrasound guided peripheral nerve block provides a higher rate of block success.

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Local anesthetic drugs have been traditionally used to provide anesthesia and analgesia in peripheral nerve blocks. Now, with evolving surgical procedures that are more complex, they need extended duration of anesthesia due to prolonged procedures. Hence, there is a need for increasing the duration of the block.

Bupivacaine has both properties of high quality block and longer duration of action. Hence, it is the preferred local anesthetic for peripheral nerve blocks. Ropivacaine is a newer drug that seems to be equal or superior to Bupivacaine in terms of neuronal blocking potential [1]. It has been shown in various studies that safety profile of Ropivacaine is better than Bupivacaine. It has lower central nervous system and cardiac toxicity [2]. Thus, it can be used in higher concentration. However, the limitation with Ropivacaine is that it has less intense motor block compared to Bupivacaine [3]. So this study was done to compare the efficacies of Bupivacaine and Ropivacaine in supraclavicular brachial plexus block.

Materials and Methods

The study was carried out in a medical college hospital from October 2013 to June 2015. It was a prospective randomized comparative study. The objective was to compare the effects of Inj. Bupivacaine 0.5% and Inj. Ropivacaine 0.5% in supraclavicular brachial plexus block for upper limb orthopedic surgeries. The two drugs were studied and compared with respect to onset time of sensory and motor blockade; duration of sensory and motor block; adverse effects, if any. The sample size was calculated using statistical formula at 0.05 alpha error and 0.2 beta error. The study was done after clearance from institutional ethical committee.

All the patients between 18 to 60 years of age, weighing 50 to 80 kilograms, with ASA grade I and II, posted for elective upper limb surgeries were included in the study. Patients with known hypersensitivity to the drugs used in the study were excluded. Patients with coagulopathy/ on anticoagulant medications, those with neuromuscular disorders, those with severe hepatic/renal/respiratory/cardiac diseases were excluded from the study. All those patients who had infection at the site where the block is given and those refused to give consent were also excluded. A total of 78 patients were included in the study. They were randomized to two groups of 39 each – Group B and Group R. It was done using computer generated randomization table.

During the pre-operative visit, basic demographic characteristics; detailed history including previous medical illness and allergies; examination findings; relevant investigations done were recorded. Written informed consent was documented from all the patients. At the time of surgery, the supraclavicular area was aseptically prepared and draped after placing the patient in proper position. The best possible view of brachial plexus was obtained by placing the ultrasound probe over supraclavicular fossa in coronal oblique plane. The probe used in the study was a linear 38 mm, high frequency 10-15 MHz transducer of Sonosite M Turbo ultrasound machine. After visualizing the brachial plexus, the block was given using a 5 cm 22G insulated block needle by lateral to medial "in plane" approach. The needle was advanced towards the target nerves along the long axis of transducer, while the needle shaft and tip were visualized in real time. After negative aspiration for blood, 30 ml of local anesthetic drug was injected to cause hydro dissection of the planes around the plexus. Patients in group B received 30 ml of 0.5% (5 mg/ml) Bupivacaine and those in group R received 30 ml of 0.5% (5 mg/ml) Ropivacaine. The spread of local anesthetic was observed and the needle repositioned as needed to ensure distribution around all the nerve trunks and divisions within the plexus sheath.

The quality of sensory block was assessed using 23G hypodermic needle by pin prick method along the dermatomes C4–T2. It was assessed once in every minute for first 30 minutes, then every 30 minutes till patient recovered normal sensation. It was recorded according to Visual Analog Scale (VAS) i.e., 0– no pain; 2– annoying (mild pain); 4– uncomfortable (moderate pain); 6– dreadful (severe pain); 8– horrible (very severe pain); 10– agonizing (worst possible pain).

The quality of motor block was examined at same intervals and rated according to Modified Lovett's Scoring i.e., Grade 6 – normal; Grade 5 – slightly reduced muscular force; Grade 4 – pronounced reduction; Grade 3 – slightly impaired mobility; Grade 2 – pronounced mobility impairment; Grade 1 – almost complete paralysis; Grade 0 – complete paralysis.

The time taken for onset of motor block was defined as interval between completion of injection of study drug and development of Lovett's grade 1 motor block. The time taken for onset of sensory block was defined as time span from completion of injection of study drug till VAS score of zero on pin prick testing. The duration of motor blockade was

defined as the gap between onset of motor block and complete recovery of motor power. It was assessed objectively as time taken from Lovett's grade 1 to Lovett's grade 6. The duration of sensory block was defined as time from onset of sensory block (VAS score of zero) till patient feels pin prick (VAS score of two).

Patients were monitored for any adverse effects like nausea, vomiting, bradycardia, convulsions, restlessness, disorientation, drowsiness and other complications.

Statistical analysis was done using student's t - test for non parametric data and chi square test for categorical data. A two tailed p value less than 0.05 was considered statistically significant.

Results

The present study was done on 78 patients between 18-60 years of age, who underwent elective upper limb surgeries lasting more than 30 minutes. Patients were randomized to two groups of 39 each. Group B received 30 ml of 0.5% Bupivacaine. Group R received 30ml of 0.5% Ropivacaine for brachial plexus block by ultrasound guided supraclavicular approach. There was no statistically significant difference between the two study groups with respect to baseline characteristics like age, gender, weight and duration of surgery (Table 1). The types of surgeries performed were almost identical in both the groups.

The mean onset time of sensory and motor blockade was 16.6 ± 3.2 min and 21.4 ± 2.6 min respectively in Bupivacaine group when compared to 19.9 ± 4.0 min and 25.9 ± 2.4 min respectively in Ropivacaine group. Thus, we found that onset of both sensory and motor blockade was earlier with Bupivacaine than with Ropivacaine (p=0.001) (Table 2).

The mean duration of sensory and motor blockade in Bupivacaine group was 343.8 ± 44.4 min and 387.4 ± 36.0 min respectively in contrast to Ropivacaine group having mean duration of sensory blockade and motor blockade of 317.9 ± 29.1 min and 368.7 ± 33.1 min respectively. Thus, we found that duration of sensory and motor blockade was longer with Bupivacaine (p=0.001; p=0.019 respectively) (Table 2).

Table 1: Baseline characteristics of patients in Bupivacaine and Ropivacaine group

Baseline characteristics	Bupivacaine (n=39)	Ropivacaine (n=39)	Level of significance #
Gender			
Male	26 (52.0%)	24 (48.0%)	0.637
Female	13 (46.4%)	15 (53.6%)	
Age	36.2 + 10.6*	36.9 + 9.1*	0.758
Weight			
50-60 kg	8 (61.5%)	5 (38.5%)	
61-70 kg	15 (44.1%)	19 (55.9%)	0.55
71-80 kg	16 (51.6%)	15 (48.4%)	
Duration of surgery	126.4 + 33.0*	116.2 + 36.5*	0.196

*Mean + SD

#p value obtained for assessing significant difference between the two groups with respect to baseline characteristics (Chi square test was used for categorical data and student t – test for non parametric data).

Table 2: Outcome measures in Bupivacaine and Ropivacaine groups

Outcome measures	Bupivacaine (n=39) Mean + SD	Ropivacaine (n=39) Mean + SD	Level of significance #
Onset of sensory blockade	16.6 + 3.2	19.9 + 4.0	0.0001
Onset of motor blockade	21.4 + 2.6	25.9 + 2.4	0.0001
Duration of sensory blockade	343.8 + 44.4	317.9 + 29.1	0.003
Duration of motor blockade	387.4 + 36.0	368.7 + 33.1	0.019
Adverse effects			
Nil	37 (94.9%)	39 (100%)	0.152
Vomiting	2 (5.1%)	0 (0%)	

SD- Standard Deviation

#p value calculated for statistically significant difference between Bupivacaine and Ropivacaine groups with respect to outcome measures (Chi square test was done for categorical data and students t-test for non parametric data)

In our study, 2 patients in the Bupivacaine group had vomiting and none in Ropivacaine group. The variations in hemodynamic parameters like heart rate, systolic and diastolic blood pressure were similar in both the groups (p=0.05) and all of them were hemodynamically stable. This signifies that adverse effects were not significant with either drug during the study.

Discussion

The brachial plexus block is one of the commonly used peripheral nerve block technique. The supraclavicular approach provides a successful blockade as it causes homogenous spread of anesthetic agent throughout the plexus. There is dissimilarity among various local anesthetics with respect to their duration and onset of action. Ropivacaine is a recently added long acting local anesthetic. It is shown to be equally potent as Bupivacaine, with lesser side effects.

In our study, we observed that onset of sensory and motor block was earlier with Bupivacaine than with Ropivacaine. This was similar to the study conducted by Tripathi D *et al.* [4]. They showed that the peak effect of sensory and motor blockade was earlier with Bupivacaine in contrast to Ropivacaine (p=0.05). Similarly, in another study by Narendra Babu *et al.* [5], the time of onset of sensory and motor block was less for Bupivacaine when compared to Ropivacaine.

In our study the duration of both sensory and motor block was found to be longer for Bupivacaine. Similar results were reflected in a study by Narendra Babu *et al.* [5]. In another study by Mc Glade *et al.* [6], they observed that quality of anesthesia was similar with both Bupivacaine and Ropivacaine. They also noted that motor block lasted for extended duration with Bupivacaine.

In the study led by Mclellankj *et al.* [7], they found Ropivacaine to be equally efficacious as Bupivacaine. Though Ropivacaine had lesser potential for motor block, it was better tolerated. So, they concluded Ropivacaine as preferred choice in view of it's lesser central nervous system and cardiac toxicity.

In a study by Singelyn FJ [2], it was inferred that Ropivacaine was as efficient as Bupivacaine in terms of duration and quality of analgesia, anesthesia and motor block. It was concluded that Ropivacaine was superior to Bupivacaine with earlier onset of sensory and motor block. However, this remains debatable.

In the study led by Reader *et al.* [8], 0.75% Ropivacaine was compared with equal volume of 0.5% Bupivacaine. The onset and duration were found to be identical in both the groups. They concluded that a concentration of 0.75% was required for Ropivacaine to provide anesthesia akin to equal volume of 0.5% Bupivacaine.

In our study, there was not much distinction between the two groups in terms of hemodynamic parameters monitored during surgery. This was akin to the study led by Tripathi D *et al.* [4]. In their study hemodynamics remained stable in both Bupivacaine and Ropivacaine groups. Singelyn FJ [2] in his study, found Ropivacaine to be safer due to lower neurologic and cardiac toxicity. Similarly, in another study by Mclellankj *et al.* [7], Ropivacaine was better tolerated and preferred choice due to reduced cardiotoxic potential. Vaghadia *et al.* [9], in their study also got similar results. They concluded that Ropivacaine lesser toxicity even in case of inadvertent intravenous injection. In our study as the block was given under real time ultrasound guidance, the drug was properly deposited avoiding intravascular injections. Thus, systemic side effects were almost negligible with both groups. The limitation of our study is that results cannot be generalized to situations where the block is given without ultrasound guidance.

Conclusion

From our study, we deduce that at equal volumes and concentration, Bupivacaine has an edge over Ropivacaine for ultrasound guided supraclavicular brachial plexus block. Bupivacaine has earlier onset and extended duration of sensory and motor block. We also infer that ultrasound guided technique allows the drug to be properly deposited and avoids intravascular injection. Thus, it minimizes the adverse effects of both the drugs.

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Conflict of interest: Nil

Abbreviations

ASA - American Society of Anesthesiologists

Inj. - Injection

mg - milligram

mm - millimeter

cm – centimeter

ml – milliliter

MHz – Mega Hertz

G – Gauge

VAS – Visual Analog Scale

Min – minutes

References

1. Lew E, Vloka JD, and Hadzic A. Ropivacaine for peripheral nerve blocks: Are there advantages. Techniques of Regional Anaesthesia and Pain Management. 2001;5:56-59.
2. Singelyn FJ. Clinical application of Ropivacaine for upper extremity. Current topics in medicinal chemistry. 2001;1:219-25.
3. Feldman HS, Arthur GR, Covino BG. Comparative systemic toxicity of convulsant and supraconvulsant doses of intravenous Ropivacaine, Bupivacaine and Lidocaine in the conscious dog. Anesth Analg 1989;69:794-801.
4. Tripathi D, Shah K, Shah C, Shah S, Das E. Supraclavicular Brachial Plexus Block for Upper Limb Orthopedic Surgery: A Randomized, Double Blinded Comparison Between Ropivacaine and Bupivacaine. The Internet Journal of Anesthesiology 2012;30:1-10.
5. Narendra Babu MC, Sreeraghu GM, Sreeharsha S, Chandra D, Dhingra U. Journal of Evolution of Med and Dent Sci. 2014;3:10722-10732.
6. McGlade DP, Kalpokas MV, Mooney PH, Chamley D, Mark AH, Torda TA. A comparison of 0.5% Ropivacaine and 0.5% Bupivacaine for axillary brachial plexus. Anaesth intensive care. 1998; 26:515-520.
7. Mclellankj, Faulds D. Ropivacaine An update of its use in regional anesthesia. Drugs. 2000;60:1065-1093.
8. Reader JC, Drosdahl S, Klaastad O. Axillary brachial plexus block with Ropivacaine 7.5mg/ml. A comparative study with Bupivacaine 5mg/ml. Acta Anesthesiol Scand. 1999;43:794-798.
9. Vaghadia H, Chan V, Ganapathy S, Lui A, McKenna J, Zimmer K. A Multicentric trial of Ropivacaine 7.5mg/ml vs Bupivacaine 5mg/ml for supraclavicular brachial plexus anesthesia. Can J Anesth. 1999;46:946-51.

Original Research Article

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Can Bedside Assessment Tests Predict Difficult Intubation in Oral Cancer Surgery Patients: A Prospective Observational Study

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Abstract

Background: We evaluated usefulness of Mallampati test, Inter incisor distance, Thyromental distance and Sternomental distance in predicting difficult intubation in oral cancer surgery patients. *Methods:* Preoperatively, assessment of airway predictors was done in 111 patients undergoing oral cancer surgery. Difficult intubation was defined as Cormark and Lehane grading of grade 3 & 4. *Results:* Incidence of difficult intubation was found to be 18% patients. By using Receiver operating characteristic analysis, Inter incisor distance < 2.55 cm, Thyromental distance < 8.75 cm were found to be the cut off points of difficult intubation. Sensitivity and specificity for predicting difficult intubation by Interincisor distance was 60% and 78% respectively with a positive predictive value of 39% and with higher negative predictive value of 89%. AUC (area under curve) with 95% confident interval showed 0.69% for Inter incisor distance, 0.64% for Thyromental distance and 0.57% with Sternomental distance. *Conclusions:* Inter incisor distance and Mallampati grading was a better predictor compared to other parameters and Sternomental distance showed the least significance in predicting a difficult airway in oral cancer surgery patients.

Keywords: Oral cancer surgery; Difficult intubation; Bedside assessment test; Mallampatti grading; Inter incisor distance.

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Introduction

Oral cancer is among the top three types of cancers in India [1]. In India, 20 per 100000 population are affected by oral cancer which accounts for about 30% of all types of cancer [2]. Different methods have been done to predict difficult intubation for patients posted for various surgeries. Identifying patients who are at risk of difficult intubation helps anesthesiologist in planning management of airway. Multiple studies have been done to to assess the usefulness of bed side screening test in patients posted for general surgeries. But there has been a paucity in studies conducted for patients posted for oral cancer cases. These patients already present with underlying pathology in the oral-pharyngeal cavity which can increase the chance of difficult mask ventilation and intubation.

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The main objective of the study was to determine the incidence of difficult intubation in patients posted for elective oral cancer surgery. The second aim of the study was to assess the usefulness of bedside test to predict difficult intubation in these set of patients.

Methods

We prospectively analysed the data of 111 patients scheduled for oral cancer surgery for airway management during the perioperative period at our institution. After ethical committee approval, we prospectively studied the patients from September 2018-January 2019. Informed consent was obtained from all the patients before the surgery. Out of the 111 patients, 4 cases were electively planned for fibre optic intubation. All adult patients who were posted for benign or malignant disease were included in the study. Patients who were tracheostomised were excluded from the study. All cases were managed by an anaesthetic consultant or specialist registrars with at least 3 years of anaesthesia experience.

Preoperatively, data were collected on patients characteristics followed by airway examination. Bedside assessments which was includedwere– Modified Mallmapatti score (3, 4), Inter incisor distance (IID), Thyromental distance (TMD) and Sternomental distance (SMD). With patient in sitting position at the eye level of anesthesiologist, Mallampati grade was assessed with mouth opened as wide as possible with tongue protruding. IID was measured with mouth fully opened without use of any accessory muscles. In edentulous patients, inter gingival distance was used as inter incisor distance. TMD, SMD was measured along a straight line from the lower border of mandibular mentum to thyroid notch and sternal notch with head in extended position without using accessory muscle. After keeping patients nil per oral for 8 hours, patients were premedicated with glycopyrrolate and midazolam. Patients were pre oxygenated and induced with fentanyl (1-2 mcg/kg), propofol (2 mg /kg) and after check ventilation, succinylcholine (1.5-2 mg /kg) was given. Laryngoscopic view was graded according to Cormark and Lahenes (5) laryngoscopic grading. Mallampati grades were classified as lower grade (Grade 1 & 2) and higher grade (Grade 3, 4). Cormark and Lahene grading were also classified as Lower grade (Grade 1, 2) and Higher grade (grade 3, 4) respectively.

Results

In this study, data from 111 patients scheduled for oral cancer surgeries were analyzed.

Demographic profile and airway characteristics of the study population are presented in table 1 and table 2.

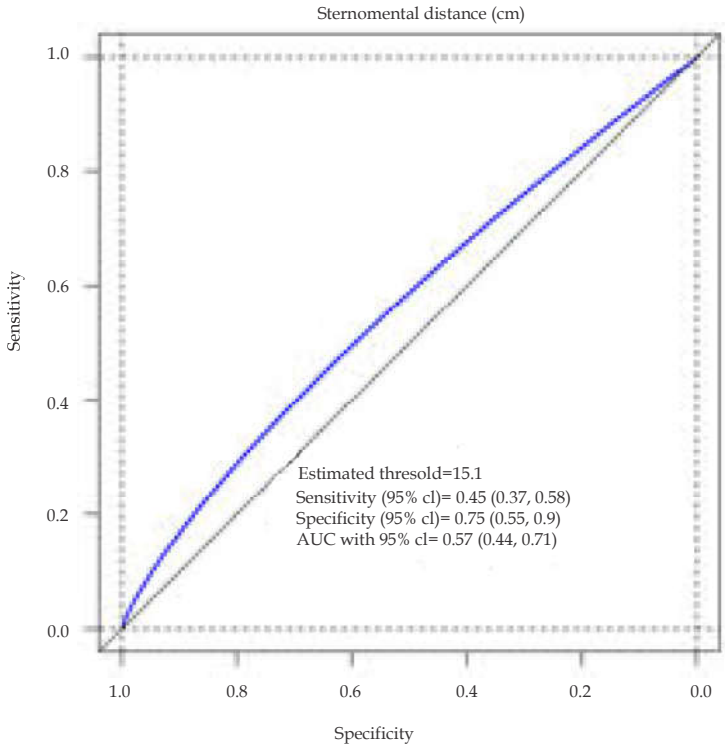
Table 1: All most equal number of males and females participated in this study. About 37 patients (33.33%) and 14 patients (12.61%) had Mallampati grade 3 & 4 respectively.

Table 1: Qualitative Variables (Frequency & Perecentage)

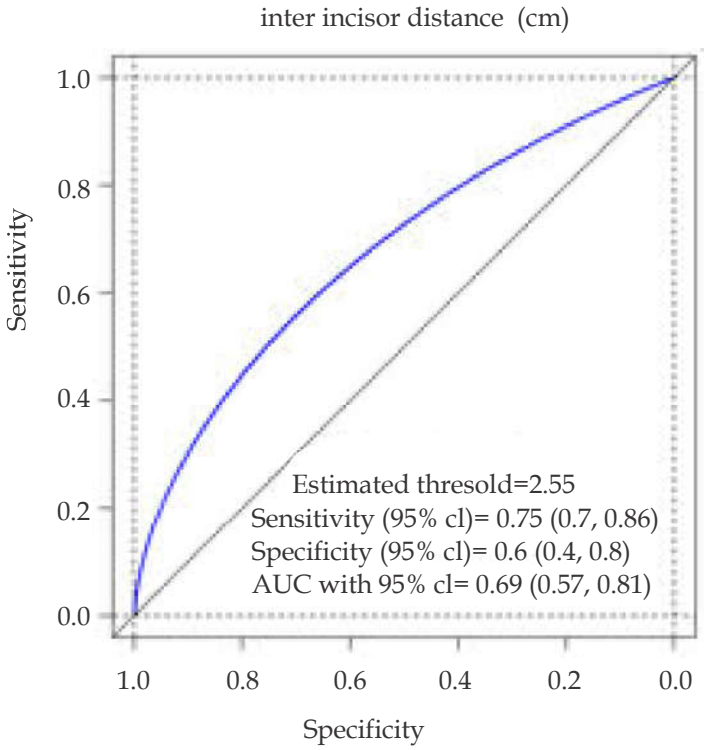
	Levels	Frequency	Percentage
Variables	female	58	52.25
sex	male	53	47.75
	1	1	0.9
Mallampati grade	2	59	53.15
	3	37	33.33
	4	14	12.61
	1	50	47.17
Cormark Lahene Grading of Laryngoscopy	2	36	33.96
	3	19	17.92
	4	1	0.94
	higher grade	51	45.95
Mallampatti grade	Lower grade	60	54.05
	higher grade	20	18.87
Cormark Lahene Grading	lower grade	86	81.13

Table 2: The mean age and weight of the patients were 53.21 ± 12.86, 54.05 ± 11.0 respectively. Mean inter incisor distance was 3.16 ± 1.75 cm. Mean Sterno'mental distance was 15.63 ± 2.32 cm. Mean Thyro mental distance was 8.67 ± 1.59 cm.

Table 3: Quantitative analysis in this table shows inter incisor distance of 2.62 ± 0.93 had higher grades of Cormark Lahene grading under direct laryngoscopy and 3.41 ± 1.83 had lower Grades of laryngoscopic findings which was found to be significant.



Graph 1:



Graph 2:

Tabel 4: Sensitivity and specificity for predicting difficult intubation by IID was 60% and 78% respectively with a positive predictive value of 39% and with higher negative predictive value of 89%.

Table 5: Sensitivity of predicting difficult intubation by Sternomental distance was 25% and specificity of 52%. The positive predictive value was found to be only 11% and higher negative predictive value of 75%.

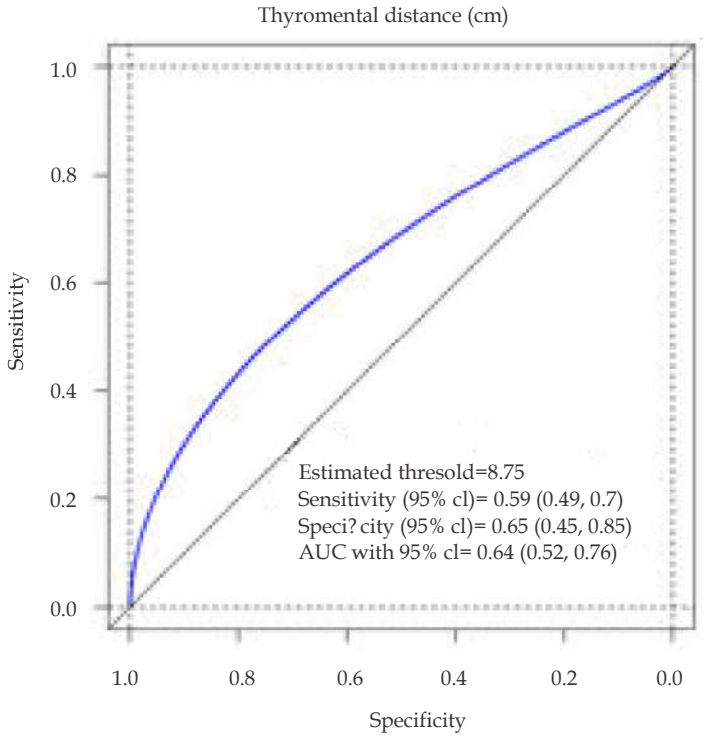
Table 2: Quantitative Variables

	N	Mean	Sd	Median	Iqr	Min	Max
Age	111	53.21	12.86	56	21	28	85
Weight	111	54.05	11.04	53	13.5	30	100
Inter Incisor Distance cm	111	3.16	1.75	3	1.9	-3	15.2
Sternomental distance cm	111	15.63	2.32	16	2.5	7	22
Thyromental Distance cm	111	8.67	1.59	9	1.5	4	16

Table 3: CL grade vs other predictors

Summary: Quantitative

Variable	Group	N	mean	SD	Test stat	P.value
Age	Higher Grade	20	51.5	12.81	t stat= 0.68	0.5
	Lower Grade	86	53.67	12.89		
Weight (kg)	Higher Grade	20	60.7	13.78	t stat=2.56	0.017
	Lower Grade	86	52.35	10.04		
Inter Incisor Distance (cm)	Higher Grade	20	2.62	0.93	T stat= -2.75	0.008
	Lower Grade	86	3.41	1.83		
Sternomental Distance	Higher Grade	20	16	1.69	t stat= 1.16	0.254
	Lower Grade	86	15.47	2.38		
Thyromental Distance	Higher Grade	20	8.12	1.13	t stat= -2.2	0.034
	Lower Grade	86	8.81	1.67		



Graph 3:

Table 6: Sensitivity of predicting higher Cormark Lahene grading with Thyromental distance was 65% and specificity of 59%. The positive predictive value was found to be only 27% and negative predictive value of 88%.

Table 7: Odds ratio was 5.289 and 5.323 of interinsicor distance and mallampati grade.

AUC (Area under curve) with 95% confident interval showed 0.69% for Inter incisor distance, 0.64% for Thyromental distance and 0.57% with Sternomental distance.

Table 4: Epi test: CL grading vs Inter Incisor Distance

Point estimates and 95 % CIs:	
Apparent prevalence	0.29 (0.21, 0.39)
True prevalence	0.19 (0.12, 0.28)
Sensitivity	0.60 (0.36, 0.81)
Specificity	0.78 (0.68, 0.86)
Positive predictive value	0.39 (0.22, 0.58)
Negative predictive value	0.89 (0.80, 0.95)
Positive likelihood ratio	2.72 (1.59, 4.63)
Negative likelihood ratio	0.51 (0.30, 0.89)

Table 5: Epi test: CL grading vs Sternomental distance

Point estimates and 95 % CIs:	
Apparent prevalence	0.43 (0.34, 0.53)
True prevalence	0.19 (0.12, 0.28)
Sensitivity	0.25 (0.09, 0.49)
Specificity	0.52 (0.41, 0.63)
Positive predictive value	0.11 (0.04, 0.24)
Negative predictive value	0.75 (0.62, 0.85)
Positive likelihood ratio	0.52 (0.24, 1.16)
Negative likeihood ratio	1.43 (1.04, 1.98)

Table 6: Epi test: CL grading vs Thyromental distance

Point estimates and 95 % CIs:	
Apparent prevalence	0.45 (0.36, 0.55)
True prevalence	0.19 (0.12, 0.28)
Sensitivity	0.65 (0.41, 0.85)
Specificity	0.59 (0.48, 0.70)
Positive predictive value	0.27 (0.15, 0.42)
Negative predictive value	0.88 (0.77, 0.95)
Positive likelihood ratio	1.60 (1.06, 2.41)
Negative likelihood ratio	0.59 (0.32, 1.10)

Table 7: Complete Contigency Table

Variables	**Levels**	**Lower Grade**	**Higher Grade**	**chi. square**	**p value**	**OR. CI**
Inter incisor distance	Above threshold	67 (89.3)	8 (10.7)	9.511	0.002	1
	Below threshold	19 (61.3)	12 (38.7)			5.289 (1.889, 14.808)
Sternomental distance	Above threshold	45 (75)	15 (25)	2.536	0.111	1
	Below threshold	41(89.1)	5 (10.9)			0.366 (0.122, 1.096)
Thyromental distance	Above threshold	51 (87.9)	7 (12.1)	2.949	0.086	1
	Below threshold	35 (72.9)	13 (27.1)			2.706 (0.981,7.464)
Mallampati grade	Lower grade	55 (91.7)	5 (8.3)	8.5	0.004	1
	Higher grade	31 (77.4)	15 (32.6)			5.323 (1.765, 16.049)

Discussion

Difficult intubation is one of the most feared complication faced by anesthesiologist while managing airway during general anesthesia. It can be due to variety of factors which include patient factors, clinical condition of the patient and the experience of the anesthesiologist managing the case. Clinical bedside assessments can be done prior to surgery, to predict a difficult airway. Multiple studies which have been done prior, to determine which bedside assessment test can be of a better predictor to anesthesiologist. But, there are only few studies in literature that assess the usefulness of these bedside test in oral cancer surgeries.

India has worlds highest number (nearly 20%) of Oral cancers with an estimate of 1% of population having oral premalignant lesions [6]. Approximately 95% of oral cancers occur in people older than 40 years, with an average age at diagnosis of approximately 60 years [7]. This study has been done to find usefulness of these clinical bedside tests as a predictor test in these set of patients. For a predictor test to be clinically useful, it should have very high sensitivity with minimal false negative results reducing the incidence of unexpected difficult intubation for an unprepared anesthesiologist.

In our study, percentage of difficult intubation was found to be 18% (20/106) which was higher compared to studies done on general population [8,9]. The increase in percentage of difficult intubation in our study might due to the different set of population being taken up, the factors being distortion of airway due to tumor, history of surgery, radiation, oral submucosal fibrosis etc. In our study, as the grade of Mallampati grade increased, higher the chance of difficult intubation was seen with significant p value < 0.05 and Odds ratio of 5.32 (CI of 1.765-16.049) which was significant compared to retrospective study done by Healy et (10) where the odds ratio was found to be 1.62.

By using Receiver operating characteristic analysis, inter incisor distance <2.55 cm, Thyromental distance <8.75 cm were found to be the cut off points of difficult intubation.Inter incisor distance < 4 cm is associated with difficult intubation [11]. The mean inter incisor distance in our study was 3.16 ± 1.75 cm which was less compared to study done by Wilson et al. [12] where mean was of 3.8 ± 0.7 cm in difficult intubation cases. This difference in Inter incisor distance could be due to painful conditions in oral cancer cases. The sensitivity and specificity of predicting difficult intubation was 60% and & 78% with positive predictive value of 39% and negative predictive value of 89% with odds ratio of 5.28. Sensitivity to predict difficult intubation by IID was better in comparison to study done by Cattano *et al.* [13]. It was found that sensitivity, specificity and negative predictive value was similar to study done by Khan *et al.* [8] with lesser positive predictive value.

Thyromental distance showed a sensitivity of 65% and specificity of 59% with PPV of 27% and a NPV of 88%. Sensitivity and PPV of our study was higher compared to study done by cattono *et al.* [13, 14,15] but lesser compared to study done by Patel [9] and Khan [8]. Sensitivity of predicting difficult intubation by Sternomental distance was 25% and specificity of 52% which was least among all. The positive predictive value was found to be only 11%. Sensitivity and specificity was less compared to other studies [8,9,15].

Conclusion

In conclusion, we found that Inter incisor distance and Mallampati grading was a better predictor compared to other parameters and Sternomental distance showed the least significance in predicting a difficult airway in oral cancer surgery patients. We recommend usage of combination of these test and other predictors in further studies as multiple factors contribute to difficult airway in oral cancer surgery.

References

1. Elango JK, Gangadharan P, Sumithra S, Kuriakose MA. Trends of head and neck cancers in urban and rural India. Asian Pac J Cancer Prev. 2006;9:529-532.
2. Sankaranarayanan R, Ramadas K, Thomas G. Effect of screening on oral cancer mortality in Kerala, India: a cluster- randomised controlled trial. The Lancet. 2005;365:1927–1933.
3. Samsoon GL, Young JR. Difficult tracheal intubation: a retrospective study. Anaesthesia. 1987;42:487–90.
4. Mallampati Sr, Gatt SP, Gurgino LD, Desai SP, WrakseB, Freiburger D. A clinical sign to predict difficult tracheal intubation : A prospective study. Can AnaesthSoc J. 1985;32:429-434.
5. Cormack RS, Lehane J. Difficult tracheal intubation in obstetrics. Anaesthesia. 1984;39:1105–11.
6. Chaturvedi P. Effective strategies for oral cancer control in India. J Cancer Res Ther. 2012;8:55-56.
7. Mashberg A, Samit AM. Early detection, diagnosis, and management of oral and oropharyngeal cancer. CA Cancer J Clin. 1989;39:67-88.

8. Khan ZH, Kashfi A, Ebrahimkhani E. A comparison of the upper lip bite test (a simple new technique) with modified Mallampati classification in predicting difficulty in endotra- cheal intubation: a prospective blinded study. Anesth Analg. 2003;96:595-597.
9. Patel B, Khandekar R, Diwan R, Shafi A. Validation of modified mallampati distance and sternomental distance to predict difficult endotracheal intubation in adults. Indian J Anaesth. 2014;58:171-75.
10. Healy D W *et al.* A comparison of the Mallampati evaluation in neutral or extended cervical spine positions: a retrospective observational study > 80,000 patients. Br J Anesth. 2016;116(5):690-98.
11. Benumof and Hagberg's Airway Management, 3 ed, 2013.
12. Wilson ME, Spiegelhalter D, Robertson JA, Lesser P. Predicting difficult intubation. Br J Anaesth. 1988;61:211–6.
13. Cattano *et al.* Prospective study of risk factors assessment of the difficult airway : an italian survey of 1956 patients. Anesthesia and analgesia. 2004; 99(6):1774-99.
14. Arne J *et al.* Preoperative assessment for difficult intubation in general and ENT surgery: predictive value of a clinical multi- variate risk index. Br J Anaesth. 1998;80:140-146.
15. Etezadi *et al.* Thyromental Height: A New Clinical Test for Prediction of Difficult Laryngoscopy. AnesthAnalg. 2013;117:1347-51.

Original Research Article

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A Comparative Study of Effect of Short-term Sedation of Post-operative Mechanically Ventilated Patients with Dexmedetomedine and Propofol

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Abstract

Background and Objectives: Post-operative mechanically ventilated patient in the intensive care unit (ICU) frequently need sedation and analgesia to facilitate care. Inadequate Sedation in patients admitted to the ICU after surgery leads to patient discomfort, ventilator asynchrony, accidental device removal, and increase metabolic demands during respiration. Careful drug selection for sedation by the ICU team is essential so that patients can be easily weaned from mechanical ventilation after stopping sedation to achieve lesser duration of mechanical ventilation and to decrease ICU stay. Dexmedetomidine, a short-acting alpha-2-agonist, has anxiolytic, anesthetic, hypnotic, and analgesic properties.Propofol is recommended for the short-term (<24 h) treatment of anxiety in post-operative mechanically ventilated patients. The objective of this study was to compare the efficacy and safety of dexmedetomidine versus propofol for post-operative mechanically ventilated patients in ICU before weaning from mechanical ventilation. *Methodology:* Thirty patients aged above 20 years after major abdominal or pelvic surgeries requiring at least 6 hrs artificial ventilation admitted to ICU were included as subjects and they were randomly divided into two groups of fifteen each. Group D received Dexmedetomidine, a loading dose of 2.5 µg/kg and a maintenance dose of 0.5 µg/kg/hr and Group P received Propofol, a loading dose of 1 mg/kg and a maintenance dose of 0.5 mg/kg/hr. Both the groups were compared for level of sedation using Ramsay sedation score, hemodynamic variables, safety profile and fentanyl requirement to achieve adequate analgesia. *Results:* Ramsay sedation score was within the desired level (2-4) in both Dexmedetomidine and Propofol groups ($p>0.05$). Patients who received Dexmedetomidine infusion had significantly decreased heart rates when compared to patients who received Propofol infusion ($p<0.00$). Total Fentanyl dose requirement was significant in Propofol group (66.3 ± 10.1 µg) when compared to Dexmedetomidine group. (31.0 ± 9.5 µg; $p=0.001$). *Conclusion:* Dexmedetomidine and Propofol are safe sedative drugs for post-operative mechanically ventilated patients.To compare with Propofol, Dexmetomidine induces less sedation level with the same duration of mechanical ventilation and has its own analgesic effect and shortens the length of patient's stay in ICU. Bradycardia was noted more frequently in Dexmedetomidine while arterial hypotension, general malaise and delirium in Propofol group.Fentanyl requirement was more with Propofol group.

Keywords: Dexmedetomidine; Propofol; Short-Term Sedation; Postoperative Sedation.

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Introduction

The Intensive Care Unit is an environment of high level stress and discomfort for patients. The use of adequate sedation and analgesia are important in order to modulate physiological response to stress and pain, hence reducing morbidity and mortality in the ICU [2]. Post-operative patients requiring mechanical ventilation in an intensive care unit are exposed to different noxious stimuli including postoperative pain, multiple venipuncture, invasive monitoring, and endotracheal intubation; therefore they are usually managed using a continuous-infusion of sedative [1]. The sedation of the patients reduces the stress response, provides anxiolysis, improves the tolerance of ventilator support and facilitates nursing care. whereas, inadequate sedative techniques may adversely affect such patients resulting in unstable hemodynamics and increased morbidity and mortality.

The ideal agent should satisfy the physician's desire for an effective, safe, titratable, cheap and rapidly acting drug that has both sedative and analgesic properties, and should also prevent anxieties and unpleasant memories for the patient [3]. The consequences of inadequate sedation and analgesia can be substantial, including self-removal of important intraluminal tubes and vascular catheters, aggressive behaviour by patients against care providers and poor patient–ventilator synchrony [4]. Oversedation can lead to prolonged duration of mechanical ventilation, longer ICU stay.

For decades, Gama aminobutyric acid receptor agonists like propofol and benzodiazepines such as midazolam have been most commonly administered sedative drugs for ICU patients Worldwide [5]. As pain is often the culprit in agitation, an opioid analgesic is recommended, in addition to the previously mentioned agents, to provide adequate analgesia [7]. Benzodiazepines are anxiolytic and amnestic agents, but they can also cause paradoxical agitation in the elderly. Propofol (2,6, di-isopropylphenol) is a short acting and rapidly metabolized intravenous anaesthetic agent and the rapid metabolism of the drug and virtual lack of cumulation would make it suitable for continuous infusion in the ICU. But it can cause dose dependent respiratory depression, hypotension and hyperlipidaemia.It lacks analgesic properties and prolonged use of high dose propofol causes prolonged infusion syndrome [6].

Now newer drugs are being used for sedation in critically ill patients which have benefits over the conventional drugs. Alpha 2 agonist dexmedetomidine has sedative and analgesic effects and has been proved for ICU sedation for up to 24 h [1], with a unique mechanism of action, providing sedation and anxiolysis via receptors within the locus ceruleus, a small nucleus present in the pons, analgesia via receptors in the spinal cord and attenuation of the stress response with no significant respiratory depression. In addition to sedation, dexmedetomidine provides analgesic effects, sympatholytic blunting of the stress response, preservation of neutrophil function and may establish a more natural sleep-like state [5]. It produces mild cognitive impairment allowing easy communication between the healthcare provider and the patient. It also has the advantages of reducing the costs of ICU stay and more natural liberation from mechanical ventilation [9,10].

The present randomized prospective study was undertaken in a manner to evaluate sedative and analgesic properties, safety profile, cardiovascular responses, ventilation and extubation characteristics with dexmedetomidine compared to propofol, in order to provide alternative or better sedation in post-operative mechanically ventilated patients.

Objectives of the Study

To evaluate

1) Onset, duration and level of sedation
2) Hemodynamic parameters (HR, BP, SpO_2)
3) Requirement of Fentanyl analgesia

Materials and Methods

A randomized prospective study was undertaken in the Intensive Care Unit of Bapuji Hospital attached to JJM Medical College, Davanagere during the academic year from July 2013 to July 2014.

A total of 30 patients aged above 20 years after major abdominal or pelvic surgeries requiring at least 6 hrs artificial ventilation admitted to Intensive care units of the above hospital were included as subjects. The permission from Institutional ethical review committee was obtained before the study was started. An informed bilingual written consent was obtained either from patient if they were conscious and co-operative or immediate Kith and Kins of the patients. The inclusion and exclusion criteria were as follows-

Inclusion Criteria

- Patients aged 20 years and above
- Post operative mechanically ventilated patients who require atleast 6 hrs artificial ventilation after major abdominal or pelvic surgery.

Exclusion Criteria

- Neurological procedures
- Known allergy to propofol or dexmedetomidine
- Known or suspected pregnancy
- Gross obesity (over 50% above ideal body weight)
- Severe hepatic or renal disease
- Spinal or epidural anaesthesia
- History of corticosteroid therapy within the last 3 months
- Uncontrolled diabetes

About 30 patients who satisfied the inclusion and exclusion criteria were allocated randomly in to two groups by using random numbers table.

Group D - Dexmedetomidine group received a loading dose- 2.5 µg/kg and a maintenance dose- 0.5 µg/kg/hr.

Group P - Propofol group received a loading dose- 1 mg/kg and a maintenance dose- 0.5 mg/kg/hr.

Anaesthetic technique prior to entry into the ICU was carried out with, 5 mg/kg thiopental sodium, 2-3 µg/kg fentanyl and vecuronium 0.05 mg/kg.

After admission to ICU, patients were randomized into either of one group, an IV line was secured and patients were connected to multipara mointor which records heart rate, non-invasive measurements of SBP, DBP, MAP, and continuous ECG monitoring and oxygen saturation. Patients were immediately artificially ventilated with synchronized intermittent mandatory ventilation (SIMV) with pressure support mode. Sedatives used before study enrollment was discontinued prior to the initiation of the study drug.

Each patient received study drug after randomization. Optional loading doses (upto 2.5 µg/kg dexmedetomidine or 1 mg/kg propofol) was administered at the investigator's discretion. The starting maintenance infusion dose of study drug was 0.5 µg/kg/hr for dexmedetomidine and 0.5 mg/kg/hr for propofol corresponding to the midpoint of the allowable infusion dose range.

Dosing of study dose was adjusted by managing clinical team based on sedation assessment performed with the Ramsay Sedation Score (RSS), a minimum of every 1 hour for first 6 hours, thereafter every 2 hours. Analgesia with fentanyl bolus doses (0.5-1 µg/kg) was administered as needed. No other sedatives or analgesics or muscle relaxants were allowed during the study period. Study drug infusion was stopped at the time of extubation in both the groups or after a maximum of 24 hours.

The following parameters were assessed

1. Onset of sedation in both groups
2. Level of sedation was assessed by Ramsay sedation score initially every 1 hr for 6 hours, there after every 2 hours till extubation or up to 24 hours
3. Hemodynamic parameters (HR, BP, SpO_2)
4. Pain assessment using visual analog score
5. Total fentanyl requirement and duration of ICU stay.

Statistical Methods

- Results are presented as Mean, Standard deviation and Number and percentages.
- Unpaired 't' test was used to compare the mean levels between 2 groups.
- Categorical data was analysed by chi square test.
- A p value of 0.05 or less was considered to be statistically significant.
- SPSS Ver 17 was used for analysis.
- Microsoft word and Excel have been used to generate graphs, tables etc.

Results

1. Age Distribution

Table 1: Age Distribution

Age (years)	dexmed	propofol
Mean Age ± SD	38.2 ±12.9	39.1 ± 13.7
T value	0.24	
P value	0.81, NS	

The mean age of patients of Dexmedetomidine group was 38.2 ± 12.9 years and that of Propofol group was 39.1 ± 13.7 years. There was no statistically significant difference in the age of patients between Dexmedetomidine and Propofol groups. Both groups were similar with respect to age distribution (p=0.81) (Table 1).

2. Sex Distribution

Table 2: Sex Distribution

Sex	Dexmed		Propofol	
	Number	%	Number	%
Male	7	46.6	8	53.3
Female	8	53.3	7	46.6
Total	15	100	15	100

About 46% of patients in Dexmedetomidine group and 53% of patients in Propofol group were males (Table 2).

3. Weight Distribution

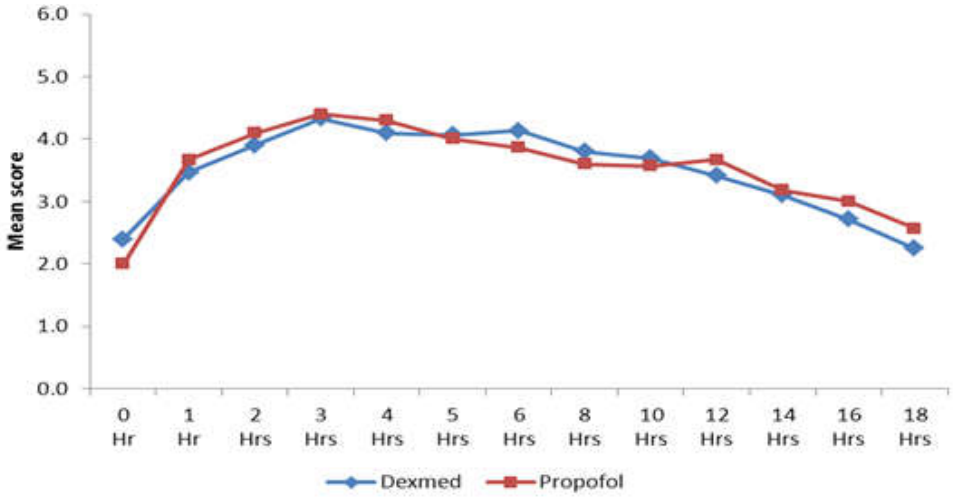
The mean weight of patients of Dexmedetomidine group was 60.93 ± 11.45 kg and that of Propofol group was 66.47 ± 10.98 kg.

4. Sedation Score Comparison

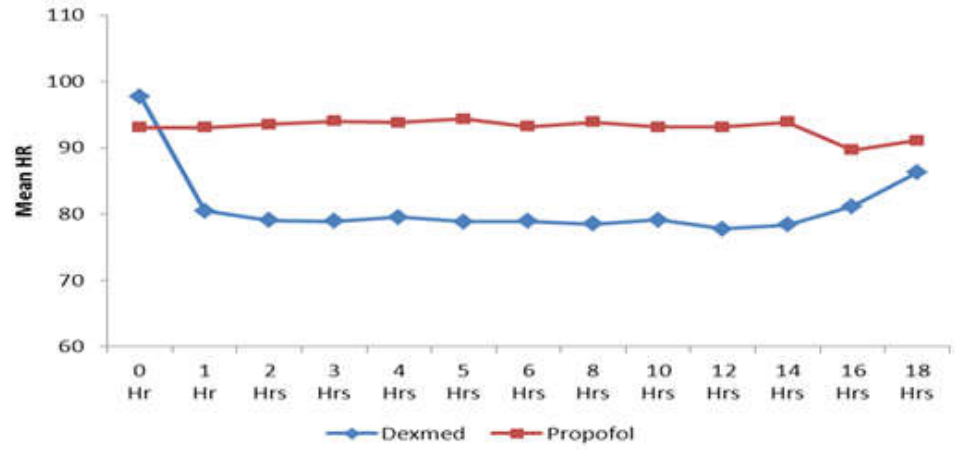
The mean Ramsay sedation scores in both groups at different intervals. The mean Ramsay sedation score ranged from 2.3 to 3.5 in Group D and 2.6 to 3.7 in Group P. The sedation scores were not statistically significant between Group D and Group P (Graph 1).

5. Heart Rate Comparison

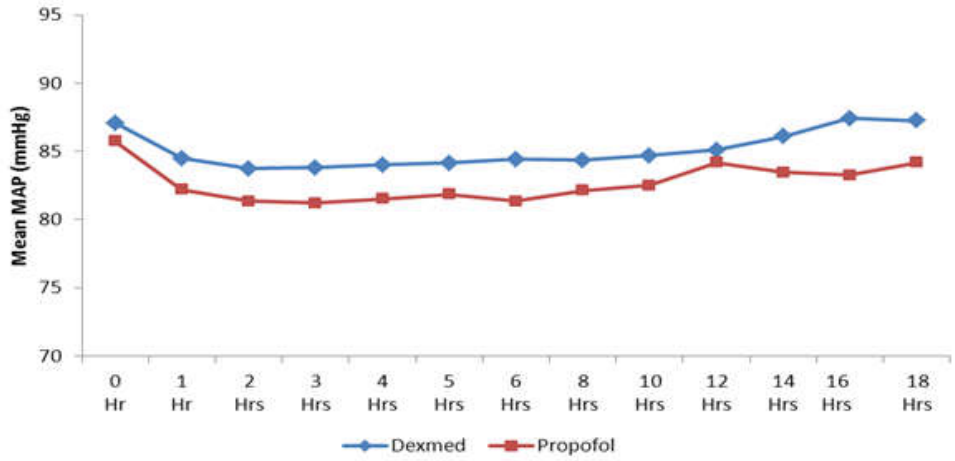
The basal heart rate were comparable in both the groups. Statistical evaluation between the groups showed a significant fall in heart rate in Group D after drug administration and the fall in heart rate was maintained throughout the study period. A fall of 17 beats per min was observed immediately after administration of Dexmedetomidine. The mean



Graph 1: Sedation Score Comparison



Graph 2: Heart Rate Comparison



Graph 3: Map Comparison

heart rate ranged between 77 – 97 bpm in Group D and 89 – 93 bpm in Group P. There was statistically highly significant fall in heart rate in Group D compared to Group P (p=0.00) (Graph 2).

6. SBP Comparison

The mean SBP were ranged from 113.0 to 117.7 mmHg in Group D, while that in Group P were ranged from 110.0 to 119.6 mmHg. There was no statistically significant difference in SBP between Group D and Group P.

7. DBP Comparison

The mean basal DBP were comparable in both groups (P=0.16). The mean DBP were ranged from 69.0 to 72.0 mmHg in Group D and that in Group P were ranged from 65.5 to 70.8 mmHg. There was no statistically significant difference in DBP among the two groups.

8. MAP Comparison

The basal MAP in group D was comparable to Group P (p=0.49). The mean MAP during study period were ranged from 83.7 to 87.4 mmHg in Group D whereas the mean MAP in Group P were ranged from 80.7 to 85.7 mmHg. There was no statistically significant differences in MAP among the two groups (Graph 3).

9. SpO_2 Comparison

The oxygen saturation level was ranged from 98.0 to 99.0% in Group D and that in Group P was ranged from 98.1 to 99.1%. There was no statistically significant difference in oxygen saturation between Group D and Group P.

10. VAS Score Comparison

The mean VAS in Group D were ranged from 2.2 to 3.1 after the infusion of Dexmedetomidine while that of mean VAS in Group P were ranged from 2.0 to 4.0 after the infusion of Propofol. There was no statistically significant difference in VAS between Group D and Group P.

11. Total Dose of Fentanyl Requirement

The mean dose of Fentanyl requirement to achieve adequate analgesia was 31.0 ± 9.5µg in Group D and that of mean Fentanyl requirement in Group P was 66.3 ± 10.1µg. Statistical evaluation between the groups showed a statistically highly significant reduction in the dose of Fentanyl requirement in Group D compared to group P (p=0.001).

12. Number of Days of ICU Stay

Table 3: Number of Days of ICU Stay

No of icu stay(days)	Dexmed		Propofol	
	Mean	SD	Mean	SD
	2.4	0.6	2.6	0.6
Mean difference	0.2			
T value	1.25			
P value	0.22, NS			

The mean ICU stay in Group D was 2.4 days and that of Group P was 2.6 days. There was no statistically significant difference in ICU stay between Group D and Group P. (p=0.22) (Table 3).

Discussion

Demographic Criteria

The mean age of the subjects in this study was 38.2 ± 12.9 years in Dexmedetomidine group and

39.1 ± 13.7 years in Propofol group. About 53% in Group D and 56% in Group P were males. The mean weight of patients were 60.93 Kgs and 66.47 Kgs in Group D and Group P, respectively. There was no statistically significant difference with regards to mean age, weight and sex. Hence the two groups were comparable.

Sedation Score

The level of sedation was assessed by Ramsay sedation score. The mean sedation scores were ranged from 2.3 to 3.5 in Group D and 2.6 to 3.7 in Group P. There was no significant difference in Ramsay sedation score between Group D and Group P during the study period. In a study conducted by R.M. Venn *et al.* [15]., there were no overall differences in the distribution of Ramsay sedation scores between the dexmedetomidine and placebo groups while intubated. However intubated patients receiving dexmedetomidine required significantly less midazolam than those receiving placebo. In a similar study by Samia Elbaradie *et al.,* [19] dexmedetomidine produced equivalent sedation as propofol and the patients who were received Dexmedetomidine, despite artificial ventilation and intubation, were easily aroused to co-operate without showing irritation.

Hemodynamic Parameters

In the present study, there was a significant bradycardia in Dexmedetomidine group compared to Propofol group. There was fall of 15 bpm after dexmedetomidine infusion and the fall in heart rate was sustained throughout the study period and did not require any treatment. In a similar study by Hussein M Agameya *et al.,* [20] heart rate showed significant reduction in dexmedetomidine group than in propofol group (p= 0.026).

In a study by Samia Elbaradie *et al.*, [19] also noted Patients who received dexmedetomidine infusion had significantly lower heart rates compared to patients who received Propofol infusion, (p=0.041), but did not need any intervention.

The mean systolic blood pressure in Propofol group were decreased about 6 mmHg from baseline value where as the fall in Dexmedetomidine group were 5 mmHg from baseline value, immediately after transfusion of study drugs, which was non-significant. The mean diastolic blood pressure were decreased by 4 mmHg and 3 mmHg in Dexmedetomidine and Propofol groups, respectively and it was not significant.

The mean arterial pressure was reduced by 3 mmHg and 4 mmHg in Dexmedetomidine and Propofol groups, respectively. The fall in MAP in patients received Propofol did not need any intervention and it was not significant. In a similar study by Samia Elbaradie *et al.,* [19] noted there was no significant difference in MAP between Dexmedetomidine and Propofol group. No patients in the 2 groups required inotropic support.

The mean oxygen saturation levels were within the optimal range in both groups during the study period of 24 hours. In a similar study by R.M. Venn and R.M. Grounds [3] noted that there was no significant difference between oxygen saturation and arterial blood gases in both Dexmedetomidine and Propofol groups.Similarly study done by R.M. Venn *et al.,* [15] showed no significant difference in respiratory rate and oxygen saturation between dexmedetomidine and placebo groups.

Analgesia

In the present study, visual analog scores were within the optimal range. VAS of 2-3 was achieved in both groups using Fentanyl analgesia. The total Fentanyl requirement was significant in Propofol group when compared with Dexmedetomidine group (p<0.00). In a similar study by Prerana N Shah *et al.,* [8] noted patients who received propofol infusions required significantly more analgesics than patients who received Dexmedetomidine infusions.

In a study by Herr D L *et al.* [16] noted requirement of morphine was significantly more in Propofol group compared to Dexmedetomidine group. Similarly study done by R.M. Venn *et al.,*[15] the requirement for morphine was reduced by half in the dexmedetomidine group while intubated.

ICU Stay

In the present study, there was no significant difference in length of ICU stay in both groups. In a similar study by R.M. Venn and R.M. Grounds [14] noted the recovery time and length of ICU stay were similar in both Dexmedetomidine and Propofol groups.

Conclusion

Dexmedetomidine and Propofol are safe sedative drugs for post-operative mechanically ventilated patients. To compare with Propofol, Dexmetomidine induces less sedation level with

the same duration of mechanical ventilation and awakening rate. Dexmetomidine provides its own analgesic effect and shortens the length of patient's stay in ICU. Bradycardia was noted more frequently in Dexmedetomidine while arterial hypotension, general malaise and delirium-in Propofol group.

References

1. Rashwan S, El moutaz Mahmoud H, Taha Z, *et al.* Safety and Efficacy of Dexmedetomidine, Ketofol, and Propofol for Sedation of Mechanically Ventilated Patients. J Intensive & Crit Care. 2018;4 (4):16.
2. Azrina Md Ralib, Saedah Ali, Mohd Nikman Ahmad, Ziyadi Mohd Ghazali, Nik Abdullah Nik Mohamad. A Comparative Study of Dexmedetomidine and Propofol for Sedation in The Cardiothoracic Intensive Care Unit. Int. Med J. 2007 Dec;6(2):1-17.
3. R.M. Venn and R.M. Grounds. Comparison between dexmedetomidine and propofol for sedation in the intensive care unit: patient and clinician perceptions, British Journal of Anaesthesia. 2001;87(5):684-90.
4. Curtis N. Sessler, Mark S. Gosnell, *et al.,* The Richmond Agitation–Sedation Scale Validity and Reliability in Adult Intensive Care Unit Patients. Am J Respir Crit Care Med. 2002 Nov 15;166(10):1338-44.
5. Riker RR, Shehabi Y, Bokesch PM *et al.* Dexmedetomidine vs Midazolam for Sedation of Critically Ill Patients: A Randomized Trial. JAMA. 2009;301(5):489-99.
6. T.J. McMurray, P.S. Collier, I.W. Carson, S.M. Lyons, P. Elliott. Propofol sedation after open heart surgery: A clinical and pharmacokinetic study. Anaesthesia. 1990;45:322-26.
7. Coursin DB, Coursin DB, Maccioli GA. Dexmedetomidine. Curr Opin Crit Care. 2001;7:221–6. [PubMed] [Google Scholar].
8. Prerana N Shah, Vaibhao Dongre, Vijay Patil, Sarla Pandya, Ashish Mungantiwar, Amol Choulwar. Comparison of post-operative ICU sedation between dexmedetomidine and propofol in Indian population. Indian Journal of Critical Care Medicine. 2014 May;18(5):265-66. DOI: 10.4103/0972-5229.132485.
9. Singh R, Batra YK, Bharti N, Panda NB. Comparison of propofol versus propofol–ketamine combination for sedation during spinal anesthesia in children: Randomized clinical trial of efficacy and safety. Paediatr Anaesth. 2010;20:439–44.
10. Yamauchi M, Asano M, Watanabe M, Iwasaki S, Furuse S, *et al.* Continuous low-dose ketamine improves the analgesic effects of fentanyl patient-controlled analgesia after cervical spine surgery. Anesth Analg. 2008;107:1041–44.
11. Camu F, Vanlersberghe C. Pharmacology of systemic analgesics. Best Pract Res Clin Anaesthesiol 2002;16:475–88.
12. Ramsay MA, Savege TM, Simpson BR, et al. Controlled sedation with alphaxalone- alphadolone. Br Med J. 1974;2(5920):656–9.
13. Simpson PJ, Eltringham RJ. Lorazepam in intensive care. ClinTher. 1981;4(3):150–63.
14. Penglin Ma, Jingtao Liu *et al.,* Practice of sedation and the perception of discomfort during mechanical ventilation in Chinese intensive care units. Journal of Critical Care. 2010;25:451–57.
15. R.M. Venn, C.J.Bradshaw *et al.*, Preliminary UK experience of dexmedetomidine, a novel agent for postoperative sedation in the intensive care unit. Anaesthesia. 1999;54:1136–42.
16. Mazzeo AJ. Sedation for the mechanically ventilated patient. Crit Care Clin. 1995;11:937-955.
17. Rowe K, Fletcher S. Sedation in the intensive care unit, Continuing Education in Anaesthesia, Critical Care & Pain. 2008;8(2):50-5.
18. Samia Elbaradie, Faten H El Mahalawy and Amira H Solyman. Dexmedetomidine vs Propofol for short term sedation of postoperative mechanically ventilated patients. Journal of Egyptian Nat Cancer Inst. 2000 Sep;16(3):153-58.
19. Hussein M Agameya, Ayman A. Mostafa *et al.,* Sedation for mechanically ventilated postoperative patients in the intensive care unit: comparative study between propofol and dexmedetomidine. Alexandria Journal of Anaesthesia and Intensive Care. 2005 June;8(2):20-26.

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Comparison of Recovery Profile of Sevoflurane and Desflurane in Patients Undergoing Elective Neurosurgical Procedures

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Abstract

Aim: The primary objective of the study was to compare the early post-operative recovery profile of Sevoflurane with Desflurane in adult patients undergoing elective neurosurgical procedures, with respect to emergence time, extubation time and the time taken to reach Aldrete score of 9. The secondary objectives were comparison of intra-operative hemodynamics, brain swelling, post-operative nausea and vomiting (PONV) and shivering. *Methodology:* After obtaining Institutional Ethical Committee (IEC) approval, 50 consenting adult patients posted for elective craniotomies were randomly allocated by computer generated random number technique into two groups, Group S (Sevoflurane) and Group D (Desflurane). Patients were preoxygenated and induced as per institution protocol. Patients were intubated with appropriate size endotracheal tube and anaesthesia was maintained with O_2: Air at 50%, chosen volatile anaesthetic that was age adjusted to obtain 1 MAC. Tidal volume and respiratory rate were adjusted to obtain an End tidal CO_2 ($EtCO_2$) of 30-35 mmHg. Normothermia was maintained with forced air warmer. When the duramater was opened, subjective assessment of brain swelling was done by the neurosurgeon, who was blinded to the study group. Infusions were stopped once the bone flap was secured and the volatile agent was discontinued after skin closure and detachment of Mayfield head holder. Patients were reversed and extubated after TOF ratio was > 0.9 and hemodyamics were stable. Intra-operative hemodynamics, brain swelling, emergence time, extubation time, time to reach Aldrete score of 9, PONV and shivering were recorded and patients were shifted to Post-Anaesthesia Care Unit (PACU) for monitoring. *Results:* Statistical analysis was done using SPSS software. Descriptive statistics of mean and standard deviation were arrived for the variables wherever appropriate and Paired 't' test, Chi-square test or Fischer's test were used wherever appropriate to compare the mean difference between the variables to derive the p-value. A p-value of <0.05 was considered statistically significant. The Emergence time (Group S 8.28 ± 3.75 minutes vs. Group D 8.44 ± 3.98 minutes; p-value 0.885), Extubation time (Group S 11.84 ± 4.13 minutes vs. Group D 11.92 ± 5.01 minutes: p-value 0.959), time to reach Aldrete score of 9 (Group S 7.72 ± 4.2 minutes vs. Group D 6.2 ± 3.74 minutes: p-value 0.618) were statistically and clinically comparable. The secondary objectives of the study like intra-operative hemodynamics (MAP with p-value 0.977, HR with p-value 0.431), brain swelling (p-value 1.00), PONV (p-value 0.307) and shivering (p-value 1.00) were also comparable between two groups. *Conclusion:* We conclude that there was no statistically significant difference in early recovery profile between Sevoflurane and Desflurane in neurosurgical procedures with respect to emergence time, extubation time and time to reach Aldrete score of 9. There was no significant difference in intra-operative hemodynamics, incidence of postoperative nausea and vomiting, shivering and brain swelling between both the groups.

Keywords: Desflurane; Sevoflurane; Emergence time; Extubation time.

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Introduction

Inhalational anaesthetics are the most common drugs used for maintaining anaesthesia in Neurosurgery due to ease of administration, end tidal volatile agent monitoring and predictable recovery characteristics. Isoflurane has been the gold standard volatile anaesthetic for neurosurgery [1] because of reduction of cerebral metabolism and intracranial tension. However, recovery from Isoflurane anaesthesia has been slightly prolonged because of its lipid solubility. Remarkable changes in recovery profile of patients undergoing neurosurgery has been noted after the introduction of less soluble volatile anaesthetic agents like Sevoflurane and Desflurane.

Both Sevoflurane (fluorinated methyl isopropyl ether) and Desflurane (fluorinated methyl ethyl ether) are fluorinated inhalational anaesthetic agents characterised by low Blood/Gas partition Coefficient. Though both these agents have favourable recovery characteristics, Desflurane is slightly better due to difference in Blood:Gas partition coefficients (0.42 vs 0.69) [2]. Use of these volatile anaesthetics for providing balanced anaesthesia for neurosurgical procedures results in better haemodynamic stability and faster recovery independent of the duration of administration. Faster recovery from anaesthesia enables earlier neurological assessment and detection of life threatening complications, thereby earlier appropriate interventions. Various studies have been published comparing Sevoflurane with Desflurane in ambulatory surgeries, with Desflurane having better recovery profile. However comparison of Sevoflurane with Desflurane in patients undergoing neurosurgical procedures are rare.

With this background, we devised a prospective, comparative single blinded and randomised study to compare the early recovery profile of Sevoflurane and Desflurane in patients undergoing neurosurgery with respect to Emergence time, Extubation time and Time required to reach modified Aldrete score 3 of 9 (Table 1). Secondary variables include Intra-operative Haemodynamics, Degree of brain swelling and post-operative vomiting and shivering were also noted.

Materials and Methods

After obtaining institutional ethical committee approval and informed consent, 50 adult patients admitted in tertiary care centre, posted for elective craniotomies were randomly allocated into Sevoflurane (S) and Desflurane (D) groups. All consenting patients with ASA Physical status 1 and 2 in age group 18-75 years with GCS 15/15 undergoing elective craniotomy were included in the study. Patient's with haemodynamic instability, GCS <15, patients exposed to General Anaesthesia within 7 days prior to surgery, allergy to volatile anaesthetics were excluded from the study. Patients were randomly allocated into 2 groups, Sevoflurane (S) and Desflurane (D) by computer generated random number technique. After initiating standard monitoring and preoxygenation, patients were induced with Inj. Thiopentone sodium 5mg/kg, Inj. Fentanyl 2 mcg/kg and Inj. Vecuronium 0.1mg/kg intravenously to facilitate intubation. Intravenous lignocaine 1.5 mg/kg was given to patients 90 seconds prior to intubation to blunt intubation response. Patients were intubated orally with flexometallic endotracheal tube as per their age and sex. Patients were ventilated with a mixture of Air:Oxygen (50:50%), with the volatile anaesthetic selected as per randomization using Datex-Ohmeda Avance®- GE Healthcare Anaesthesia Workstation. Tidal volume was set at 8 ml/kg and the respiratory rate was adjusted to an end tidal $EtCO_2$ of 30-35mmHg. $EtCO_2$, Airway pressure, Tidal volume and O_2/Volatile anaesthetic concentration (with Gas Analyser) was continuously monitored throughout surgery. Muscle relaxation was monitored using Organon TOF Watch using Train-of-four mode. Anaesthesia was maintained with intravenous infusion of Inj. Fentanyl at 0.5 mcg/kg/hr, Inj. Vecuronium at 0.02 mg/kg/hr, titrated to TOF count of 0 and with volatile anaesthetic as per study group. Inhalational anaesthetic concentration was age adjusted to obtain 1 MAC. All patients were infiltrated with 0.25% Inj. Bupivacaine at the site of fixation of Mayfield head holder into the patient's head and on the scalp over the surgical field. Arterial Blood Gas analysis was done prior to extubation and 6 hours after extubation. Intra-operatively, normothermia was maintained with forced air warming system and body temperature was monitored with an oesophageal probe. When duramater was opened, the neurosurgeon, who was blinded to the study group assessed the degree of brain swelling on a four point scale.

1. Relaxed brain
2. Mild brain swelling (acceptable)
3. Moderate brain swelling (no treatment required)
4. Severe swelling (treatment required)

At the end of surgery, patients were extubated after TOF ratio was > 0.9, respiratory function was

clinically adequate (tidal volume > 8 ml/kg, SpO_2 >96% with FiO_2 0.4) and hemodynamics was stable. Postoperative pain was managed with Inj.Ketorolac sodium and Intravenous Paracetamol.

The primary objectives of the study were defined as follows:

- Emergence time is time from the cessation of volatile anaesthetic till patient opened the eyes to verbal commands.
- Tracheal extubation time is time from the discontinuation of volatile anaesthetic to extubation.
- Modified Aldrete score: Target score of 9.

The secondary objectives were presence/absence of brain swelling, intra-operative hemodynamics (heart rate, blood pressure), Post-operative nausea and vomiting (which was treated with Inj. Ondansetron 4 mg intravenously) and shivering (which was treated with Inj. Tramadol 1 mg/kg intravenously.

Data Analysis

Descriptive statistics of mean and standard deviation were arrived for the variables: age, HR, MAP, emergence time, extubation time and time to reach Modified Aldrete score of 9, with 95% confidence interval. Paired 't' test, Chi square test and Fischer's test were used, wherever appropriate, to compare the mean difference between the variables to derive the p-value. p value <0.05 was considered as statistically significant. Data entry was done in Microsoft Excel 2007 and analyzed using SPSS version 16.

Results

The mean age in group S was 42.2 ± 15.3 years and 39.6 ± 16.1 years in Group D. The demographic profile showed no significant difference statistically, with the p-value being 0.561 for age and 0.400 for gender distribution between the two groups. The mean Emergence time was 8.28

Table 1: Modified aldrete score

	2	1	0
Respiration	Able to take deep breath and cough	Dyspnea/Shallow breathing	Apnea
Oxygen saturation	Maintains >92% on room air	Needs O_2 inhalation to maintain saturation >90%	Saturation < 90% even with O_2 supplementation
Consciousness	Fully awake	Arousable on calling	Not responding
Circulation	BP+/- 20mmHg preoperative	BP+/-20- 50mmHg preoperative	BP+/- 50mmHg preoperative
Activity	Able to move 4 extremities voluntarily or on command	Able to move 2 extremities voluntarily or on command	Able to move 0 extremities voluntarily or on command

Table 2: Comparison of parameters between Group S and Group D

		Group S (n=25) Mean ± SD	Group D (n=25) Mean ± SD	p-value (<0.05 statistically significant)
Age (in mean years ± SD)		42.2 ± 15.3	39.6 ± 16.1	0.561
Gender (Male/Female)		13/12	16/9	0.400
Mean Heart rate (beats/min)		77.7 ± 13.7	80.9 ± 14.8	0.431
MAP (mmHg)		82.2 ± 11.3	82.3 ± 11.2	0.977
Brain swelling	Yes	6	6	1.0
	No	19	19	
Mean Emergence Time		8.28 ± 3.75	8.44 ± 3.98	0.885
Mean Extubation Time		11.84 ± 4.13	11.92 ± 5.01	0.959
Mean Time to Aldrete score of 9		7.72 ± 4.2	6.2 ± 3.74	0.618
Shivering	Yes	2	2	1.0
	No	23	23	
PONV	Yes	1	3	0.307
	No	24	22	

± 3.75 minutes in Group S compared with 8.44 ± 3.98 minutes in Group D with p-value of 0.885. The mean Extubation time was 11.84 ± 4.13 minutes in group S and 11.92 ± 5.01 minutes in Group D with p-value of 0.959. The mean time to reach Modified Aldrete score of 9 was 7.72 ± 4.2 minutes in group S and 6.20 ± 3.74 minutes in group D (p-value 0.618). The mean emergence time and mean extubation time was shorter in group S compared to group D. However the time to reach Modifed Aldrete score of 9 was shorter in group D than group S. Statistical analysis revealed insignificant difference in early recovery profile between both the groups.

Out of the total 50 patients, 12 patients (6 in each group) had brain swelling. Only 2 patients in group D had moderate brain swelling, the rest had mild swelling. There was no significant difference in brain swelling between the groups. The mean pulse rate was 77.7 ± 13.7 in the group S and 80.9 ± 14.8 per minute in group D (p-value = 0.431). The mean MAP for the two groups S and D was 82.2 ± 11.3 and 82.3 ± 11.2 mmHg, respectively (p-value = 0.977). There was no significant difference in heart rate, mean arterial pressure between both groups. Shivering was observed in 2 patients in each group. PONV was observed in 1 out of 25 and 3 out of 25 in groups S and D respectively. There was no statistically significant difference in the incidence of PONV and shivering between Group S and D.

Discussion

In our study of comparison of recovery profile of Sevoflurane and Desflurane in patients undergoing elective neurosurgical procedures, using balanced anaesthetic technique, we compared the emergence time, extubation time and time to reach Aldrete score of 9. We also compared the intra-operative hemodynamics, degree of brain swelling, PONV and shivering in patients of both groups. Our study revealed clinically and statistically insignificant difference in early post-operative recovery outcome between Sevoflurane and Desflurane groups with respect to emergence time, extubation time and time to reach Aldrete score of 9.

The early post-operative recovery profile in our study was comparable with the study conducted by Halit Cobanoglu *et al.* [3]. Patients anaesthetized with Sevoflurane had shorter extubation time (7.3 ± 1.8 minutes in Sevoflurane group and 7.4 ± 2.4 minutes in Desflurane group), shorter time to eye opening and reached Modified Aldrete score of 9 earlier, than patients in Desflurane group, though without any statistical significance. Our results are also in accordance with the study by Giuseppina Magni *et al.* [2], which was conducted in patients undergoing craniotomy for supratentorial intracranial surgery, with comparable emergence time. However, extubation time was shorter in Desflurane group in their study (11.3 ± 3.9 minutes in Desflurane group versus 15.2 ± 3 minutes in Sevoflurane group). The difference may be attributed to the age adjusted target MAC of 1.2 used in the study compared to target MAC of 1 in our study. In the study done by Ayman A. Ghoneim, *et al.* [4], there was no significant difference in emergence time and extubation time between Sevoflurane and Desflurane. Our results are also similar to the study done by Surya Kumar Dube *et al.* [5], where there was no difference in emergence time (7.4 ± 2.7 minutes in Desflurane group versus 7.8 ± 3.7 minutes in Sevoflurane group, p-value = 0.65) and extubation time (11.8 ± 2.8 minutes versus 12.9 ± 4.9 minutes in Sevoflurane group, p-value = 0.28) in patients anaesthetized with Desflurane or Sevoflurane for neurosurgeries. There are few other studies too, where patients in Desflurane group have significant shorter emergence time and extubation time. However, these studies, to name a few, done by Nathanson *et al.* [7] was in outpatient surgeries, Heavner et al. [8] was in geriatric patients, Dupont *et al.* [9] was in pulmonary surgeries, Michael Tarazi's [10] was in laparoscopic tubal ligation and Kim's [11] was in minor ear, nose, throat surgeries. None of these studies were done in neurosurgeries. Hence, results were not comparable with our study. Prospective studies comparing Sevoflurane and Desflurane in neurosurgeries are very few.

Karamehmet, Yildiz *et al.* [12] compared Desflurane and Isoflurane in terms of hemodynamic stability, brain relaxation and postoperative recovery characteristics, with administration of 1 MAC of the volatile agent in patients undergoing craniotomy for supratentorial lesions and concluded that the Desflurane group had earlier post operative cognitive recovery, however with statistically significant higher intraoperative MAP. Alex Macario, *et al.* [13] did a meta-analysis of trials comparing the recovery profile of Sevoflurane and Desflurane. This study included 22 published reports of 25 studies. The meta-analysis revealed a faster recovery profile of Desflurane compared to Sevoflurane. The results of the metaanalysis was not comparable with our study since it included results from surgeries other than neurosurgery.

In our study, the mean time taken to reach Modified Aldrete score of 9 was shorter in Desflurane group (6.2 ± 3.74 minutes) compared to Sevoflurane group (7.72 ± 4.2 minutes) and was not statistically

significant (p-value 0.618). The study conducted by Ayman A. Ghoneim, *et al.* [4] in 2013 also revealed no significant difference between Sevoflurane and Desflurane in the time interval required to reach Aldrete score of ≥ 9. In the study done by Halit Cobanoglu *et al.* [3] Aldrete scores were compared between Sevoflurane and Desflurane groups, at 2nd minute (9.2 ± 0.4 in Sevoflurane group and 9.3 ± 0.4 in Desflurane group) and 5th minute (10 in both groups) after extubation and was statistically comparable between the two groups.

There was no statistically significant difference in incidence of brain swelling between Sevoflurane and Desflurane groups in our study. But two patients in Desflurane group had moderate brain swelling (which required no active intervention), when compared to none in Sevoflurane group and this can be attributed to the inherent cerebral vasodilating property of Desflurane contributing to a raised ICP. Our results were statistically comparable with the study conducted by Surya Kumar Dube *et al.* [5] with respect to incidence of intra-operative brain condition in Sevoflurane and Desflurane groups. In their study only 2 patients (4%), one in each group required treatment intraoperatively to reduce the brain bulge. Our findings are consistent with that of the study by Todd *et al.* [6] who detected 10% incidence in brain swelling in patients undergoing resection of brain tumours under inhalational anaesthesia. In our study, we did not measure ICP and the assessment of brain swelling was subjectively done by neurosurgeons. But in our study, none of the patients required active intervention to reduce brain swelling.

In our study there was no significant difference in intra-operative hemodynamic parameters between the two groups. Ayman A. Ghoneim, *et al.* [4] detected no difference in hemodynamic parameters including HR and MAP, between Sevoflurane and Desflurane groups. But their study shows significant reduction in MAP after induction in both the groups. Our results were comparable to the study done by Halit Cobanoglu *et al.* [6] where they statistically evaluated the intraoperative hemodynamic parameters, although for first 75 minutes only.

The number of patients involved in the study and allocated to both Sevoflurane and Desflurane groups in our study were comparable with the study conducted by Surya Kumar Dube *et al.* [3] PONV was observed in 4 patients (1 in Sevoflurane and 3 in Desflurane groups, with p-value 0.307) in our study and all the 4 patients were treated with Inj. Ondansetron 4mg i.v 15 patients had PONV (6 in Sevoflurane group and 9 in Desflurane group, with p-value 0.27) in their study. Postoperative shivering was observed in 4 patients (2 in each group) in our study and 2 patients (one in each group) in their study and there was no statistically significant difference. In our study, patients with shivering were treated with Inj. Tramadol 1mg/kg i.v. In the study done by Ayman A. Ghoneim, *et al.* [4], 10% of the patients in Sevoflurane group and 5% in Desflurane group had postoperative vomiting that required treatment with Inj. Ondansetron. In the same study, 20% of patients in the Sevoflurane group and 10% in Desflurane group required treatment with Inj. Nalbuphine for shivering.

Limitations of our study

Our study was designed to detect the early post-operative recovery profile after Sevoflurane or Desflurane administration in balanced anaesthetic technique. However, volatile anaesthetic agents have been shown to affect late cognitive function in adult patients, which was not assessed in our study.

Conclusion

In our study of comparison of recovery profile of Sevoflurane and Desflurane in patients undergoing elective neurosurgical procedures, patients anaesthetised with Sevoflurane had shorter emergence and extubation time compared to Desflurane, though not statistically significant. Patients anaesthetised with Desflurane had shorter time to reach Aldrete score of 9 compared to Sevoflurane, although not statistically significant. There was no significant difference in the other parameters like intra-operative hemodynamics, brain swelling, PONV and shivering. We conclude that both Sevoflurane and Desflurane provide comparable recovery profile in a balanced anaesthesia setting in neurosurgical procedures.

Key Message

There is no statistically significant difference in early recovery profile between Sevoflurane and Desflurane in neurosurgical procedures with respect to emergence time, extubation time and time to reach Aldrete score of 9. There is no significant difference in intra-operative hemodynamics, incidence of postoperative nausea and vomiting, shivering and brain swelling between both the groups.

References

1. James I, Walker I. Core topics in paediatric anaesthesia. Cambridge (UK): Cambridge University Press; 2013.p.258.
2. Magni G, Rosa IL, Melillo G, *et al.* A comparison between sevoflurane and desflurane anesthesia in patients undergoing craniotomy for supratentorial intracranial surgery. Anesth Analg. 2009; 109(2):567-571.
3. Cobanoglu H, Tavlan A, Topal A, et al. The effect of sevoflurane and desflurane on the early postoperative cognitive functions in geriatric patients. Eur J Gen Med. 2013;10:32-38.
4. Ghoneim AA, Azer MS, Ghobrial HZ. Comparative study between isoflurane, sevoflurane and desflurane in neurosurgical paediatric patients undergoing craniotomy for supratentorial tumour resection. Med J Cairo Univ. 2013;81:51-57.
5. Dube SK, Pandia MP, Chaturvedi A, *et al.* Comparison of intraoperative brain condition, hemodynamics and postoperative recovery between desflurane and sevoflurane in patients undergoing supratentorial craniotomy. Saudi J Anaesth. 2015;9(2):167-73.
6. Todd MM, Warner DS, Sokoll MD, *et al.* A prospective, comparative trial of three anesthetics for elective supratentorial craniotomy: Propofol/ fentanyl, isoflurane/nitrous oxide, and fentanyl/ nitrous oxide. Anesthesiology. 1993;78(6)1005-20.
7. Nathanson MH, Fredman B, Smith I, *et al.* Sevoflurane versus desflurane for outpatient anesthesia: A comparison of maintenance and recovery profiles. Anesth Analg. 1995;81(6):1186-90.
8. Heavner JE, Kaye AD, Lin BK, *et al.* Recovery of elderly patients from two or more hours of desflurane or sevoflurane anestheisa. Br J Anaesth. 2003;91(4):502-506.
9. Dupont J, Tavernier B, Ghosez Y, *et al.* Recovery after anesthesia for pulmonary surgery: Desflurane, sevoflurane and isoflurane. Br J Anaesth. 1999;82(3):355-59.
10. Yildiz K, Bicer C, Aksu R, *et al.* A comparison of 1 minimum alveolar concentration desflurane and 1 minimum alveolar concentration isoflurane in patients undergoing craniotomy for supratentotial lesions. Curr Ther Res. 2011;72(2):49-59.
11. Tarazi EM, Philip BK. A comparison of recovery after Sevoflurane or desflurane in ambulatory anesthesia. J Clin Anesth. 1998;10(4):272-77.
12. Kim JM, Lee JH, Lee HJ. Comparison of emergence time in children undergoing minor surgery according to anesthetic: Desflurane and sevoflurane. Yonsei Med J. 2013:1;54(3):732-38.
13. Macario A, Dexter F, Lubarsky D. Meta-analysis of trials comparing postoperative recovery after anesthesia with sevoflurane or desflurane. Am J Health-Syst Pharm. 2005;62(1):63-68.
14. Green MS, Green P, Neubert L, *et al.* Recovery following desflurane versus sevoflurane anesthesia for outpatient urologic surgery in elderly females. Anesth Pain Med. 2015;5(1).
15. Kaur A, Jain AK, Sehgal R, *et al.* Hemodynamics and early recovery characteristics of desflurane versus sevoflurane in bariatric surgery. J Anaesthesiol Clin Pharmacol. 2013;29(1):36-40.

Original Research Article

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Comparative Study of Haemodynamic Response to Intubation with McCoy laryngoscope, Intubating LMA and Vividtrac® Videolaryngoscope in Controlled Hypertensive Patients

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Abstract

Laryngoscopy and intubation can result in significant haemodynamic response which is even more exaggerated in hypertensive patients. The magnitude of cardiovascular response is directly related to the force applied and duration of laryngoscopy. Various airway devices and drugs have been tried to limit this pressor response. We conducted a prospective, randomized study to compare haemodynamic response to intubation using McCoy laryngoscope, Intubating Laryngeal Mask Airway (ILMA) and VividTrac® videolaryngoscope in patients with controlled hypertension requiring general anaesthesia for various surgeries. *Methods:* The study included 90 controlled hypertensive patients of either sex, belonging to ASA grade II, between age group of 40-60 years, requiring general anaesthesia were divided into three groups. In group M, patients were intubated with McCoy laryngoscope. In group L, patients were intubated with intubating LMA. In group V, patients were intubated using VividTrac® videolaryngoscope. Haemodynamic response following intubation were compared among all the three groups. Intubation time, the success rate of intubation and complications, if any, were also compared in all the three groups. *Results:* It was observed that VividTrac® videolaryngoscope produced significantly less haemodynamic response compared to intubation with ILMA and McCoy laryngoscope. Intubation using McCoy laryngoscope was found to be comparatively a faster method to secure tracheal intubation when compared to ILMA and videolaryngoscope. Complications, like oesophageal intubation and sore throat were more with intubating LMA, whereas injury to oropharyngeal mucosa was found to be observed with VividTrac® videolaryngoscope. *Conclusion:* VividTrac® videolaryngoscopy and intubation causes less haemodynamic changes compared to Intubating LMA and McCoy laryngoscopy.

Keywords: General anaesthesia; Intubation; Haemodynamic response; Controlled hypertension.

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Introduction

Endotracheal intubation is the gold standard in airway management to administer general anaesthesia. Laryngoscopy and intubation can result in significant haemodynamic response [1]. Mechanical stimulation of the respiratory tract induces reflex cardiovascular responses which

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is associated with increase in catecholamine levels [2]. The consequence of pressor response may cause tachycardia, hypertension and occasional dysrhythmias and in hypertensive patients it can lead to life threatening responses such as angina, myocardial infarction, pulmonary oedema and intracranial bleed [3]. Various drugs, laryngoscopes and airway devices have been compared for the haemodynamic responses during intubation [4,5,6]. Since there were not many studies done comparing VividTrac® videolaryngoscopes with intubating LMA and McCoy laryngoscopes in controlled hypertensive patients, we decided to conduct this randomized, comparative study.

Material & Methods

After obtaining Institutional ethical committee approval, this randomized, prospective study was conducted on 90ASA II adult patients aged between 40 to 60 years with controlled hypertension who were on antihypertensive medications with no clinical or laboratory evidence of new or worsening target organ damage undergoing various, elective surgical procedures with no anticipated difficulty requiring general anaesthesia with endotracheal intubation. Informed consent to participate in the study was taken in all patients enrolled in the study. Standard anaesthetic technique was followed in all patients. Patients were randomly allocated into either McCoy group (Group M), ILMA group (Group L) or VividTrac® video laryngoscope group (Group V) with 30 in each group by random number tables. Patients with uncontrolled hypertension, risk of gastric aspiration, anticipated difficult intubation, history of epilepsy or history of ischemic heart disease were excluded from the study. All the required parameters were collected by an independent observer anaesthesiologist. Tracheal intubation was performed in each patient by consultant anaesthesiologists who were experienced and who had performed at least 10 intubations with the new device in the clinical setting and who were not involved in the study.Thorough pre-anaesthetic evaluation was done. All antihypertensive drugs were continued till the morning of surgery with the exception of ACE inhibitors and angiotensin-receptor blockers which was stopped on the day of surgery. Baseline parameters, namely, heart rate (HR), systolic, diastolic and mean blood pressure (SBP, DBP and MBP), and arterial oxygen saturation (SpO_2) were recorded. Patients were premedicated with injglycopyrollate 5 mcg/kg, inj midazolam 1mg,inj fentanyl 1.5 /kg. After preoxygenation, induction was done with Inj propofol 2 mg/kg. All intubations were performed with appropriate sized cuffed endotracheal tube (ETT) using non-depolarising muscle relaxant Inj vecuronium 0.1 mg/kg. In group M, laryngoscopy was done with McCoy laryngoscope. In group L, intubation was done using intubating LMA. In group V, intubation was done using VividTrac® video laryngoscope. A failed intubation is defined as an attempt in which the trachea was not intubated even after three attempts or which required more than 120 sec to perform by the experienced anaesthesiologist. In such case, laryngoscopy and intubation was done by using Macintosh blade and case was excluded from the study. The time taken for the successful intubation attempt is the time taken from insertion of the blade or ILMA between the teeth until the position of the endotracheal tube was confirmed to be in the trachea by capnography. The heart rate, arterial blood pressure (systolic, diastolic, mean), SpO_2, end tidal carbondioxide ($EtCO_2$) were recorded at baseline, after anaesthetic induction (0 min), 1 min, 2 min, 3 min, 5 min, 7 min and 9 min after endotracheal intubation. $EtCO_2$ was maintained within 35 ± 5 to avoid the effects of hypercarbia on the haemodynamic variables. Complications of laryngoscopy and intubation like oropharyngeal trauma to lips, teeth, tongue, airway trauma and postoperative sore throat were noted.

Statistical methods

The statistical software namely SAS 9.2, SPSS 15.0, Stata 10.1, MedCalc 9.0.1, Systat 12.0 and R environment ver 2.11.1 were used for the analysis of the data and Microsoft word and excel have been used to generate graphs, tables. Quantitative data were expressed as mean ± Standard deviation. Qualitative data were expressed as frequency and percentage. ANOVA, when comparing between more than two means were used.

Results

Ninety patients were included in the current study. The demographic data of the group M, Land V are presented in Table 1. There was no statistically significant difference among groups with respect to demographic characteristics.All patients belonged to ASA II.

In our study, intubation was faster in Group M (22.5 ± 1.00 sec) than Group L (38.8 ± 1.51 sec) and Group V (31.5 ± 1.59 sec), which was statistically significant ($p<0.001$) as shown in table 2 and graph 1.

Differences in time may be due to unfamiliarity to handle the laryngoscope while looking at the screen instead of looking directly at the larynx and the time required for guiding of endotracheal tube through ILMA. Similar results were obtained by Bilgin H *et al.* [7] who documented that total intubation time was significantly longer in the ILMA group than in the C-Trach and McCoy group.

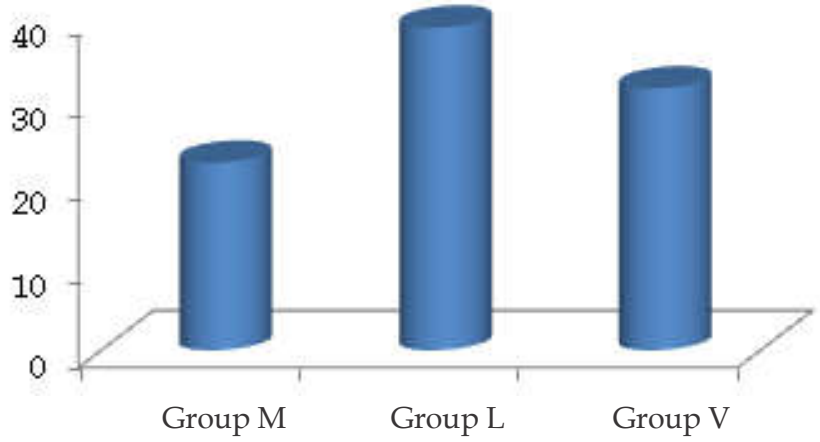
Haemodynamic variables i.e., heart rate, systolic blood pressure, diastolic blood pressure and mean arterial pressure were compared among the three groups which is shown in table 3 and graphs 2, 3, 4, 5. There was no statistical significane in the baseline haemodynamic parameters and immediately after IV induction p (>0.05) in all the three groups.

Table 1: Demographic characteristics

	Group M	Group L	Group V	p Value
Age(years)	48.875 ± 8.37	49.125 ± 7.34	47.875 ± 8.37	0.81
Weight (kg)	65.15 ± 5.91	64.325 ± 7.65	64.15 ± 5.91	0.81
Sex				
Male	18	17	17	0.95
Female	12	13	13	
Mallampati				
I	18	17	19	0.87
II	12	13	11	

Table 2: Time taken for first successful intubation and intubation success rate

	Mean(±SD)	Group M	Group L	Group V	p Value
Time for 1st successful intubation (in sec)		22.5 ± 1.00	38.8 ± 1.51	31.5 ± 1.59	<0.001
Intubation Success	1st attempt (%)	100%	80%(24)	86%(26)	
	2nd attempt (%)	Nil	13.3%(4)	10%(3)	
	3rd attempt (%)	Nil	6.6%(2)	3.3%(1)	

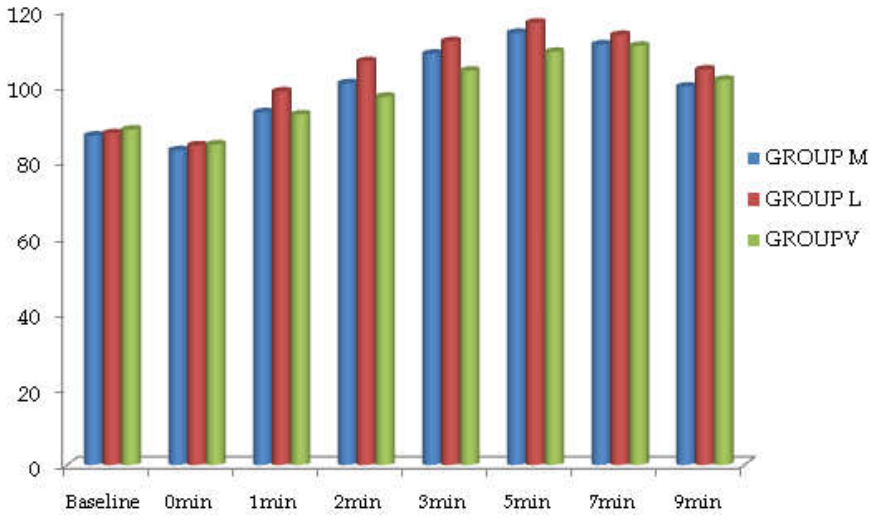


Graph 1: Time for 1st successful intubation in seconds between three groups

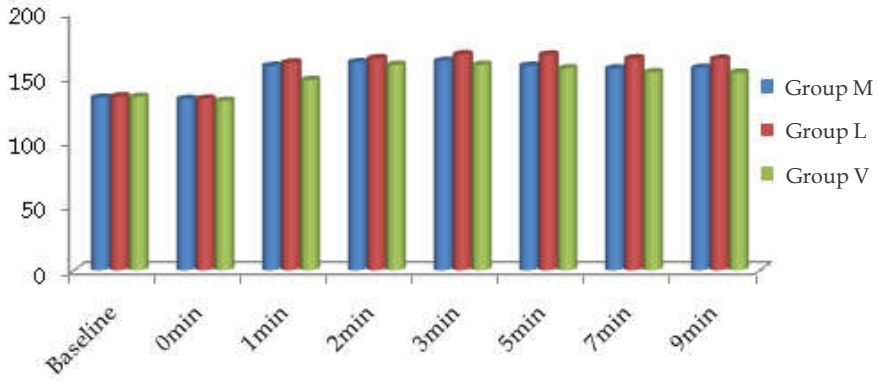
Table 3: Haemodynamic parameters

Vital Parameter	Group M	Group L	Group V	p Value
Baseline Heart Rate	86.7 ± 7.02	87.33 ± 5.68	88.3 ± 5.80	0.5
SBP	133.76 ± 5.55	134.73 ± 5.26	134.4 ± 5.31	0.7
DBP	80.66 ± 4.58	81.6 ± 4.82	81.53 ± 5.08	0.35
MAP	98.36 ± 3.54	99.311 ± 3.65	99.5 ± 4.11	0.45
T0 Heart Rate	82.83 ± 3.48	84.13 ± 5.89	84.36 ± 5.79	0.46
SBP	132.8 ± 4.88	133 ± 5.32	131.33 ± 3.83	0.33
DBP	79.73 ± 4.54	80.93 ± 4.57	79.66 ± 4.42	0.474
MAP	97.42 ± 3.44	98.28 ± 3.58	96.88 ± 3.28	0.28

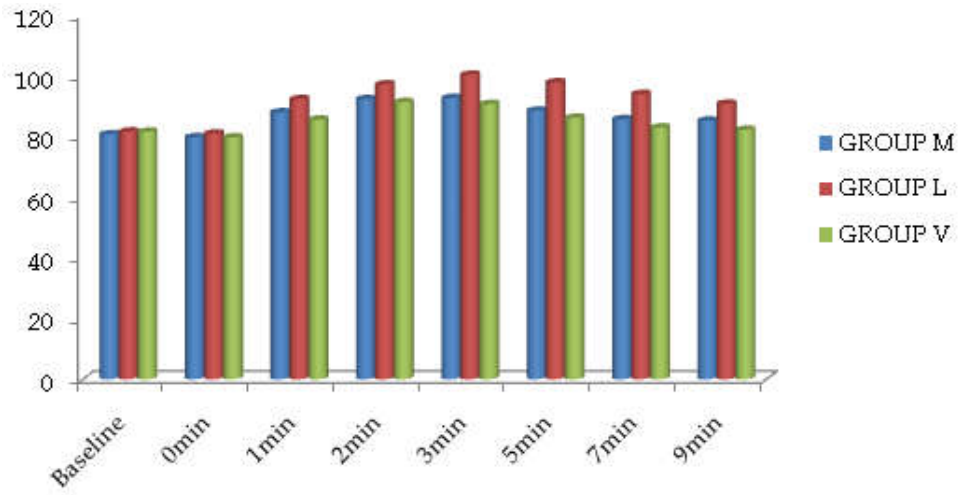
T1 Heart Rate	92.83 ± 3.48	98.33 ± 5.31	92.26 ± 5.98	<0.0001
SBP	158.46 ± 3.62	161 ± 3.62	147.53 ± 5.57	<0.0001
DBP	87.93 ± 2.70	92.26 ± 2.95	85.53 ± 3.04	<0.0001
MAP	111.44 ± 2.28	115.17 ± 1.84	106.2 ± 2.58	<0.0001
T2 Heart Rate	100.46 ± 3.78	106.3 ± 5.31	96.93 ± 5.93	<0.0001
SBP	161.26 ± 4.94	164.4 ± 3.16	159.26 ± 3.38	<0.0001
DBP	92.26 ± 5.29	97.13 ± 2.38	91.33 ± 2.48	<0.0001
MAP	115.26 ± 3.78	119.55 ± 2.13	113.97 ± 1.65	<0.0001
T3 Heart Rate	108.26 ± 4.01	111.56 ± 4.74	103.8 ± 5.75	<0.0001
SBP	162.33 ± 5.33	167.4 ± 2.04	159.33 ± 2.53	.000001
DPB	92.66 ± 4.67	100.3 ± 2.52	90.66 ± 1.98	<0.0001
MAP	115.88 ± 3.60	122.68 ± 1.99	113.55 ± 1.65	<0.0001
T5 Heart Rate	113.73 ± 3.92	116.43 ± 3.97	108.76 ± 5.23	<0.0001
SBP	158.53 ± 6.14	167.13 ± 1.79	156.53 ± 1.47	<0.0001
DBP	88.46 ± 5.05	97.8 ± 1.21	86.13 ± 2.22	<0.0001
MAP	111.82 ± 3.80	120.91 ± 1.19	109.6 ± 1.57	<0.0001
T7 Heart Rate	110.7 ± 3.74	113.2 ± 3.8	110.33 ± 4.72	0.015
SBP	156.46 ± 4.53	164.26 ± 2.39	153.53 ± 2.33	<0.0001
DBP	85.66 ± 4.03	93.93 ± 2.13	82.93 ± 2.39	<0.0001
MAP	109.26 ± 3.60	117.37 ± 1.90	106.466 ± 1.57	<0.0001
T9 Heart Rate	99.6 ± 3.58	104.1 ± 4.7	101.4 ± 4.58	0.0005
SBP	156.93 ± 5.91	163.93 ± 1.77	153.13 ± 2.55	<0.0001
DBP	85.2 ± 4.62	90.8 ± 1.789	82.2 ± 2.74	<0.0001
MAP	109.11 ± 4.02	115.17 ± 1.34	105.84 ± 1.88	<0.0001



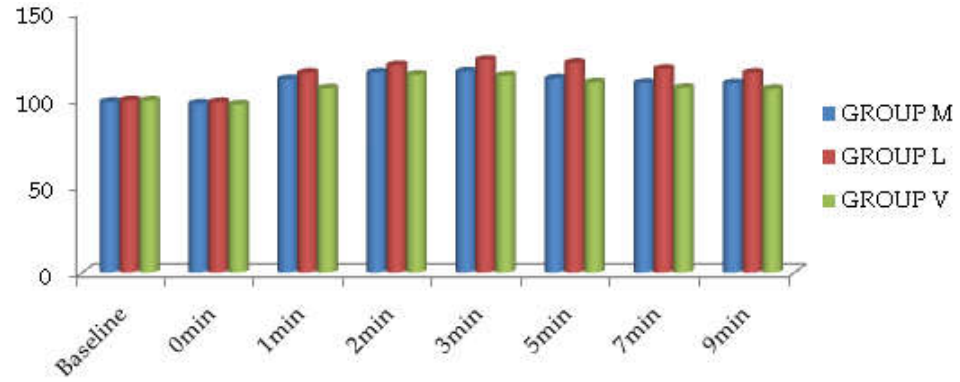
Graph 2: Graphical Representation of Heart Rate Between the Groups



Graph 3: Graphical Representation of Systolic Blood Pressure in mmHg Between the Groups



Graph 4: Graphical Representation of Diastolic Blood Pressure in mmHg Between the Groups



Graph 5: Graphical Representation of Mean Arterial Pressure in mmHg Between the Groups

Following intubation, there was statistically significant rise in HR, SBP, DBP and MAP in all the three groups(P<0.001) but significantly less in VividTrac® videolaryngoscope group indicating that videolaryngoscope maintained hemodynamic stability during intubation than McCoy and intubating LMA. Repeated oro-pharyngeal and tracheal stimulation resulting from ILMA probably induced greater pressor response than video laryngoscope. Upward lifting force required to expose the glottis is much less with Video laryngoscope.

Table 4: Complications

Complications	Group M	Group L	Group V
Oropharyngeal Injury	2 (6.6%)	nil	4 (13.3%)
Esophageal intubation	nil	3 (10%)	nil
Desaturation	nil	nil	nil
Sore Throat	2 (6.6%)	6 (20%)	nil

Discussion

Laryngoscopy and endotracheal intubation are associated with sympathetic stimulation that leads to haemodynamic changes. These haemodynamic changes are more exaggerated in hypertensive patients when compared to normotensive patients. This stress response can cause increase in blood pressure, heart rate and cardiac dysrrhythmias in the crucial period of anaesthetic induction [8]. So, it is important to attenuate the sympathetic response to laryngoscopy and endotracheal intubation.

The haemodynamic response is regulated by the hypothalamo-pituitary-adrenocortical and sympathetic adreno-medullary response. This response leads to secretion of cortisol, norepinephrine and epinephrine. The secretion reaches its peaks at approximately 30-45 seconds after intubation. Plasma adrenaline, noradrenaline

and vasopressin concentrations increase slightly in normotensive patients but there is three-fold increase in plasma noradrenaline inhypertensives. Further, an increase in plasma adrenaline level was observed in hypertensives, one minute after laryngoscopy.

Direct laryngoscopy involves stretching of the oropharyngeal tissues in order to straighten the angle between the mouth and the glottic opening. This stretch can cause pain and trigger a stress response.Though laryngoscopy and intubation separately result in sympathetic stimulation, the catecholamine rise and subsequent haemodynamic response with intubation exceeds that with laryngoscopy alone [9]. One of the major concerns during administration of general anaesthesia is to reduce the sympathetic stimulation by minimising the stretching of laryngopharyngeal structures. Various airway adjuncts, anaesthetic drugs, antihypertensives and analgesics have been used to blunt the level of stimulation and the stress response to the manipulation and stimulation of airway during laryngoscopy and intubation. McCoy levering laryngoscope has an adjustable hinged tip which improves the visualization of cords [6].

ILMA guidedoro-tracheal intubation does not directly stimulate the receptors of the larynx because it does not distort the base of the tongue [4]. A significant decrease in mean norepinephrine concentration was observed with ILMA guided intubation than in patients undergoing direct laryngoscopy [1]. VividTrac® video laryngoscope from Vivid Medical, Inc. is a rigid laryngoscope that can used to intubate patients with normal and difficult airways. Many studies have found that videolaryngoscopes cause less haemodynamic response [1].

McCoy blade has an adjustable tip which can be used to lift the epiglottis and decrease the force applied on the base of the tongue thereby reducing the pressor response [6].

ILMA is a device used to introduce the tracheal tube blindly which doesnot require exposure of glottis. So, theoretically causes less haemodynamic response. But the trial conducted by Sener *et al.* failed to attenuate the hemodynamic response with the use of ILMA, where, in contrary, there was higher response [4]. The longer duration, repeated airway manipulation, stimulation of supralaryngeal area which is rich in nociceptive receptors, removal of ILMA to advance the tracheal tube may have induced greater pressor response in these patients.

The video laryngoscope is a recent airway tool can reduce the degree of stretch on the airways. It incorporates video imaging into the bladewith LCD display and hence provides an improved glottis view without the need to alignoral, pharyngeal and laryngeal axis with minimal stretch. For the same reason these devices are useful in intubating patients with cervical injuries requiring immobilization. There is evidence to show that VLS caused less haemodynamic stimulation than the other laryngoscopes. Heart rate and blood pressure was not altered significantly with this device during intubation attempts [10].

In this randomized, prospective and comparative study, demographic characteristics, ASA grading and Mallampati grading were comparable. All patients had systemic hypertension and were on medications in whom blood pressure was well controlled.Following intubation, there was statistically significant rise in HR, SBP, DBP and MAP in all the three groups but significantly less in VividTrac® videolaryngoscope group indicating that videolaryngoscope maintained hemodynamic stability during intubation than McCoy and intubating LMA.

Our findings are similar to study done byPeirovifar A, et al. who documented that systolic blood pressure, mean blood pressure and heart rate during laryngoscopy as well as immediately and one minute after intubation was significantly lower in Glidescope group than Machintosh group [11].

A study done by Xue FS, *et al.* found that the hemodynamic responses to orotracheal intubation using a glidescope videolaryngoscope and Macintosh direct laryngoscopy were similar and they concluded that the glidescope videolaryngoscopy had no any special advantage over the direct laryngoscopy in attenuating the hemodynamic responses to orotracheal intubation [12].

Sener EB, *et al.* compared hemodynamic responses and upper airway morbidity following tracheal intubation via conventional laryngoscopy or intubating laryngeal mask airway in hypertensive patients. They postulated that the intense and repeated oropharyngeal and tracheal stimulation resulting from intubating laryngeal mask airway induces greater pressor responses than does stimulation resulting from conventional laryngoscopy in hypertensive patients [4].

A study was designed by Kavitha J, *et al.* who found direct laryngoscopy to be comparatively a faster method to secure tracheal intubation than Intubating Laryngeal Mask. In their study, ILMA offered no advantage in attenuating the

hemodynamic responses compared to direct laryngoscope. The success rate of intubation through Intubating Laryngeal Mask was comparable with that of direct laryngoscopy [13].

Grisdale, *et al.* found that there was no difference between the Glidescope (®) and the direct laryngoscope regarding successful first-attempt intubation or time to intubation, although there was significant heterogeneity in both of these outcomes [14].

Liu *et al.* argued that the failure in achieving an acceptable larynx view in a great number of patients compromises the clinical value of VividTrac® videolaryngoscope [15].

In our study, complications like oesophageal intubation and sore throat was more with intubating LMA, whereas injury to oropharyngeal mucosa was found to be obsverved with VividTrac® videolaryngoscope. Soliman R, et al. noted that incidence of oral trauma and bleeding related tointubation was higher with glidescope than with Macintosh laryngoscope [16].

Limitation of our study is that firstly, the anaesthesiologist cannot be blinded for device being used. Secondly the efficacy of these devices in comparision with other promising devises such as Airtraq, McGrathw, Bullard laryngoscopes etc have not been determined.

Conclusion

Video laryngoscopes provides greater haemodynamic stability and better view of glottis than McCoy during intubation. Other advantages are ease of insertion, less need of assist manoeuvres for intubation, with less complications. Thus, it is beneficial to use VLS for intubation in hypertensive patients. The improved view due to a magnified video image, anterior curvature of the blade leads to reduced need to align. The time taken for intubation was significantly longer in the VividTrac® videolaryngoscope group and it is postulated that if the time taken for laryngoscopy and intubation could be reduced, we might be able to realise the benefit of video laryngoscope in terms of haemodynamic response. The mean time taken to achieve endotracheal intubation with video laryngoscopy was longer in this study probably because of two reasons, namely, extra time taken in visualization of vocal cords and sliding the endotracheal tube though the groove of the video laryngoscope. Further studies are required to evaluate the utility of the device in hypertensivepatients with a Mallampatti score of ≥2, both form the point of view of ease of endotracheal intubation and haemodynamic response.

Conflict of Interest: nil

Financial assistance: nil

References

1. Sachidananda R, UmeshG, Shaikh SI. A review of hemodynamic response to the use of different types of laryngoscopes. Anaesth Pain & Intensive Care 2016;20(2):201–8.
2. Derbyshire DR, Smith G. Sympathoadrenal responses to anaesthesia and surgery. Br J of Anaesth. 1984;56:725–39.
3. Stone JG, Foëx P, Sear JW, Johnson LL, Khambatta HJ, Triner L. Risk of myocardial ischaemia during anaesthesia in treated and untreated hypertensive patients. Br J Anaesth. 1988;61:675–9.
4. Sener EB, Ustun E, Ustun B, Sarihasan B. Hemodynamic responses and upper airway morbidity following tracheal intubation in patients with hypertension: conventional laryngoscopy versus an intubating laryngeal maskairway. Clinics (Sao Paulo). 2012;67(1):49–54.
5. Kanchi M, Nair HC, Banakal S, and Murthy K, Murugesan C. Haemodynamic response to endotracheal intubation in coronary artery disease: Direct versus video laryngoscopy. Indian J Anaesth 2011;55:260-5.
6. McCoy EP, Mirakhur RK. The levering laryngoscope. Anaesthesia. 1993;48(6):516-9.
7. Bilgin H, Bozkurt M. Tracheal intubation using the ILMA, C-Trach or McCoy laryngoscope in patients with simulated cervical spine injury. Anaesthesia. 2006;61(7):685-91.
8. BD King, LC Harris, FE Greifenstein, JD Elder, R D Dripp. Reflex circulatory responses to direct laryngoscopy and tracheal intubation performed during general anesthesia. Anesthesiology. 1951; 12(5):556-66.
9. Kitamura T, Yamada Y, Chinzei M, Du HL, Hanaoka K.Attenuation of haemodynamic responses to tracheal intubation by the styletscope. Br J Anaesth. 2001;86(2):275-7.
10. Chrisen H. Maharaj, Elma Buckley, Brian H. Harte, John G. Laffey. Endotracheal Intubation in Patients with Cervical Spine Immobilization: A Co mparisonofMacintoshandAirtraqLaryngoscopes. Anesthesiology. 2007;107(1):53-59.
11. Peirovifar A., Mostafa Gharehbaghi M., Azarfarin R., Karimi L. Comparison of hemodynamic responses to orotracheal intubation in hypertensive

patients: laryngoscopy via Macintosh blade versus GlideScope video laryngoscope. European Journal of Anaesthesiology. 2012;29:235.

12. Xue FS, Zhang GH, Li XY, Sun HT, Li P, Li CW, Liu KP. Comparison of hemodynamic responses to orotracheal intubation with the GlideScope video laryngoscope and the Macintosh direct laryngoscope. J ClinAnesth. 2007;19(4):245-50.
13. Kavitha J, Tripathy DK, Mishra SK, Mishra G, Chandrasekhar LJ. Ezhilarasu PIntubating condition, hemodynamic parameters and upper airway morbidity: A comparison of intubating laryngeal mask airway with standard direct laryngoscopy. Anesth Essays Res. 2011;5(1):48-56.
14. Griesdale DE, Liu D, McKinney J, Choi PT. Glidescope® video-laryngoscopy versus direct laryngoscopy for endotracheal intubation: a systematic review and meta-analysis. Can J Anaesth. 2012;59(1):41-52.
15. Liu EH, Goy RW, Chen FG. The LMA CTrach, a new laryngealmask airway for endotracheal intubation under vision: evaluation in 100 patients. Br J Anaesth. 2006;96:396-400.
16. Soliman R, Mofeed M, Alamoudy O, Farouk A. A prospective randomized comparative study between Macintosh and Glide Scope in adult patients undergoing cardiac surgery. Egypt J Cardiothorac Anesth. 2015;9:8-13.

Original Research Article

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Effect of Dexmedetomidine Nebulization on Attenuation of Haemodynamic Responses to Laryngoscopy: Randomized Controlled Study

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Abstract

Introduction: Dexmedetomidine is a potent and highly selective alpha (2)-adrenoreceptor agonist. It has sympatholytic and antinociceptive effects which allow hemodynamic stability during stressful condition e.g. Laryngoscopy and surgical stimulation. This study has been done to assess the efficacy of nebulization of Dexmedetomidine to obtund the sympathetic response of laryngoscopy and tracheal intubation. *Material and Methods:* The present study was conducted on 70 patients of ASA physical status I and II, aged between 18 and 50 years of either sex, scheduled for elective surgeries under general anaesthesia. The preoperative vitals of each patient [HR, SBP, DBP and MAP] was recorded in waiting room of operation theatre. The patients were randomly divided into two groups. In preoperative room/ waiting area, Group-N (Normal saline group) patients were nebulized with normal saline (5 ml) and in Group-D (Dexmedetomidine group) patients were nebulized with Dexmedetomidine solution (2 mcg/kg) 30 minutes prior the induction of anaesthesia. All patients were induced with Inj. Fentanyl 2 mcg/kg, Inj. Propofol 2 mg/kg and paralyzed with Inj. Vecuronium 0.1 mg/kg. After confirming adequate neuromuscular blockade HR, SBP, DBP and MAP were recorded; Laryngoscopy was done [keeping laryngoscopy timing < 15 seconds] & patients were intubated with standard/ adequate size endotracheal tube. Heart rate and blood pressure were recorded after intubation at 1minute interval for 5 minutes. During this time no other stimuli were given to the patient (e.g. surgical drape, catheterization, Ryle's tube etc.). The comparison was made between hemodynamic parameters obtained at pre-laryngoscopy and post laryngoscopy time period. *Result:* We found that in Group- D, the parameters were lower than the baseline value at 3 min time after intubation. However, hemodynamic variables never reached the baseline by 5 minutes time in case of Group- N. Neither bradycardia nor hypotension was observed in any of the patients. The sedation score was more in Group- D when compared to Group- N. This indicates that nebulization with Dexmedetomidine in a dose of 2 mcg/kg is effective and safe in attenuating the laryngoscopy & tracheal intubation sympathetic response.

Keywords: Dexmedetomidine Nebulization; Laryngoscopy & Intubation; Sympathetic response.

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Introduction

Dexmedetomidine is a highly selective α_2 adrenoreceptor agonist. It has remarkable pharmacological properties including sedation, anxiolysis, and analgesia with the unique characteristic to cause no respiratory depression. In addition to this, it has sympatholytic and

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antinociceptive effects which allow hemodynamic stability during stressful conditions e.g. Laryngoscopy, tracheal intubation and surgical stimulation [1]. Bradycardia and hypotension are the most predictable, frequent and manageable side effects. Dexmedetomidine seems to be quite safer drug to be used.

Efficacy of intravenous Dexmedetomidine in various doses for attenuation of sympathetic response of laryngoscopy and tracheal intubation has already been established by various studies in past. There is paucity of available data showing the effect and efficacy of nebulisation by Dexmedetomidine in obtunding stress responses during laryngoscopy and intubation.

Aims and Objectives

- To assess the safety and efficacy of Dexmedetomidine, when administered via nebulization for attenuation of stress response to laryngoscopy and intubation in adult patients.

Materials and Methods

The present study was conducted on 70 patients of ASA physical status I and II, aged between 18-50 years of either sex, scheduled for elective surgeries under general anaesthesia. Approval of the institutional ethics committee was obtained. After obtaining informed written consent from all patients,

Exclusion criteria

- Patients of ASA physical status III and above
- Patients with predicted difficult airway as well as in whom laryngoscopy time may exceed 15 seconds
- Patients allergic to study drug Dexmedetomidine
- Patients addicted to narcotics; on long term therapy of beta blockers, anxiolytics, anticonvulsants, and antipsychotics were excluded from this study.

Using a computer-generated random numbers table, all patients were randomly allocated into two groups, Group- N and Group- D, with 35 patients in each group. Baseline hemodynamic parameters were recorded before nebulization like heart rate (HR), systolic blood pressure (SBP), diastolic blood pressure (DBP), mean arterial blood pressure (MAP) and oxygen saturation (SpO_2) in the patient waiting area of operation theatre. Group-N patients were nebulized with Normal saline (5 ml) and Group- D patients were nebulized with Dexmedetomidine solution (2 μg.kg-^{1}), 30 minutes before the induction & laryngoscopy. Study drugs were prepared in 5 ml of 0.9% normal saline. To achieve blinding, solutions were prepared in identical syringes by an independent investigator, who was not involved in the observation or the administration of anaesthesia.

All patients were nebulized for 10 to 15 minutes in sitting position in pre-operative area by nebulizer machine. Sedation was assessed at 2, 5 and 10 minutes using Modified Observers Assessment of Alertness/Sedation scale, just after completion of nebulization (Table 6).

Later patient was shifted to operation theatre. After attaching multipara monitor, baseline HR, SBP, DBP, MAP and SpO_2 were recorded. All patients were induced with Inj. Fentanyl 2 μg kg-^{1} and Inj. Propofol 2 mg kg-^{1} and paralysed with Inj. Vecuronium 0.1 mg kg-^{1}. All patients were ventilated by bag mask ventilation with 100% oxygen for 3 minutes. After confirming adequate neuromuscular blockade HR, SBP, DBP and MAP were recorded again. Then laryngoscopy was done, keeping laryngoscopy timing less than 15 seconds, patient was intubated. Time taken for laryngoscopy and intubation was monitored. If it exceeded more than 15 seconds in any case, patient was excluded from the study.

Heart rate and blood pressure were recorded after intubation at 1minute interval for 5 minutes. During this time, no other stimulus was allowed to the patient. Comparison was made between haemodynamic parameters obtained at pre-laryngoscopy and post-laryngoscopy time period. Maintenance of general anaesthesia was done with O_2 and N_2O [Ratio of 50:50%], Isoflurane and Inj. Vecuronium 0.02 mg/kg. After completion of surgery, patients were reversed, extubated and shifted to post-anaesthesia recovery room.

In case of hypotension episode, it was to be managed by incremental boluses of intravenous Mephentermine 3 mg (SBP fall >20% from the baseline) and bolus intravenous atropine 0.6 mg to reverse any incidence of bradycardia (HR < 50 beats). Statistical analyses of collected data were carried out by software SPSS latest version. Results on categorical measurements are presented in number (%) and results on continuous measurements are presented as mean ± SD. Significance was assessed at 5% level of significance.

Results

Both groups were comparable in their demographic parameters [Table 1]. The baseline HR, SBP, DBP and MAP were comparable in both the study groups. Sympathetic response to intubation i.e. increases in HR, SBP, DBP and MAP was recorded at 2 minutes post-intubation time period point in both the groups. In Group-D, vital parameters were back to near the baseline values by 3minutes. In Group- N [where patients were nebulized with normal saline] haemodynamic variables never reached the baseline by 5 minutes post intubation time period point. Patients in Group- N had statistically higher values of hemodynamic parameters like HR, SBP, DBP and MAP after intubation at all time intervals in comparison to patients of Group- D. [Table 2, 3, 4, 5]. The attenuation of haemodynamic response was better in Group- D when compared with Group- N. The hemodynamic variables reaching the baseline value at 3 min after intubation in Group- D clearly indicates that nebulization with dexmedetomidine in a dose of 2 $\mu g.kg^{-1}$ was effective in obtunding the sympathetic response of intubation. There were no incidence of bradycardia and hypotension in any of the patients after nebulization of Dexmedetomidine in the dose of 2 $\mu g.kg^{-1}$. Patients in group- N were not sedated (sedation score was 6). The sedation scores were always more in Group- D, at all time intervals when compared to Group- N. Sedation score was never < 3 in Group- D and patients were easily arousable [Table 7]. SpO_2 never fell below 95% in any of the patient of either group.

Table 1: Demography of Patients

Parameters	Group- D	Group- N
Total no. of patients	35	35
Age (yrs) Mean ± SD	36.50 ± 4.33	32.50 ± 6.12
Weight (Kg) Mean ± SD	63.23 ± 1.46	59.78 ± 3.81
Male (%)	37.14% (13)	51.42% (18)
Female (%)	62.85% (22)	48.57% (17)
ASA I (%)	48.57% (17)	42.85% (15)
ASA II (%)	51.42% (18)	57.14% (20)

Table 2: Comparison of Heart Rate

Time period of Heart Rate	Group- D Heart Rate	Group- N Heart Rate	p value
Baseline (Before nebulization)	80.40 ± 05.67	81.50 ± 05.30	0.4047
1 min	86.47 ± 13.46	94.17 ± 12.22	0.14
2 min	88.65 ± 13.45	98.11 ± 11.06	0.002
3 min	86.54 ± 13.51	98.40 ± 10.23	0.000
4 min	86.45 + 13.46	93.25 ± 10.11	0.020
5 min	84.48 ± 13.50	91.22 ± 9.89	0.020

Table 3: Comparison of Systolic Blood Pressure

Time period of SBP	Group- D SBP	Group- N SBP	p value
Baseline (Before nebulization)	114.28 ± 13.08	120.00 ± 13.17	0.73
1 min	124.60 ± 13.87	133.74 ± 11.24	0.003
2 min	126.80 ± 13.91	137.08 ± 10.68	0.001
3 min	124.60 ± 13.87	137.40 ± 09.81	0.000
4 min	124.60 ± 13.87	132.25 ± 09.70	0.009
5 min	122.57 ± 13.87	130.22 ± 09.44	0.009

Table 4: Comparison of Diastolic Blood Pressure

Time period of DBP	Group- D DBP	Group- N DBP	p value
Baseline (Before nebulization)	75.42+13.00	80.28+12.80	0.120
1 min	86.88 + 14.00	93.17 + 11.82	0.046
2min	89.08 + 14.01	97.11 + 10.70	0.009
3 min	86.88 + 14.00	97.40 + 09.81	0.001
4 min	86.88 + 14.00	92.25 + 09.70	0.066
5 min	84.88 + 14.03	90.22 + 09.44	0.066

Table 5: Comparison of Mean Arterial Pressure

Time period of MAP	Group- D MAP	Group- N MAP	p value
Baseline (Before nebulization)	88.77 + 13.07	91.80 + 12.39	0.323
1 min	100.22 + 14.16	104.40 + 11.77	0.184
2 min	102.57 + 14.02	108.62 + 10.14	0.043
3 min	100.28 + 14.15	108.80 + 09.46	0.004
4 min	100.25 + 14.14	103.77 + 09.22	0.223
5 min	098.22 + 14.17	101.45 + 08.93	0.258

Table 6: Modified Observer's Assessment of Alertness/Sedation Scale

Score	Description of Score
0	Does not respond to noxious stimulus
1	Does not respond to mild prodding or shaking
2	Responds only mild prodding or shaking
3	Responds only after name is called loudly or repeatedly
4	Lethargic response to name spoken in normal tone
5	Appear asleep but respond readily to name spoken in normal tone
6	Appear alert and awake, response readily to name spoken in normal tone

Table 7: Mean Modified Observer's Assessment of Alertness / Sedation Score

Mean Sedation score Alertness / Sedation Score	Group- D	Group- N
Baseline	6	6
At 2 min	5.77	6
At 5 min	4.51	6
At 10 min	3.45	6

Discussion

Laryngoscopy and tracheal intubation stimulates sympathetic system and manifest as wide range of stress responses such as tachycardia, hypertension, laryngospasm, bronchospasm, raised intracranial pressure and intraocular pressure due to activation of sympathetic system [1]. Reid and Brace had very well described the hemodynamic repercussions of laryngoscopy and intubation [2]. The hemodynamic response gets initiated within 5 seconds of direct laryngoscopy, peaks in 1-2 minutes and returns to baseline values by 5 minutes [3]. These changes are usually short-lived and well tolerated by healthy patients. In patients with co-morbidities like cardiovascular and cerebrovascular disease, it may lead to serious adverse events such as myocardial ischemia, ventricular dysrhythmias, cerebrovascular accidents and pulmonary edema. [4] Various drugs have been proved to be useful in attenuating the noxious response of laryngoscopy, such as Lignocaine, Opioids, Nitroglycerine, calcium channel blockers such as Diltiazem and β-blockers such Esmelol [5,6,7,8]. The α_2-receptor agonists like Clonidine and Dexmedetomidine are the latest addition in this list. The α_2-receptor agonists mediate their action through α_2A receptors located in locus caeruleus. Sedation and hypnosis are produced by inhibition of noradrenaline release due to presynaptic activation of α_2 A receptors in the locus caeruleus. Bradycardia and hypotension are caused by decreased sympathetic activity due to post-synaptic activation of α_2 receptors in central nervous system [9]. Dexmedetomidine is eight times more potent α_2 receptor agonist than Clonidine. The elimination half-time of Dexmedetomidine is 2 hours. Thus, action of Dexmedetomidine is short-lived [10,11].

Various studies have been done and published to study the efficacy of Dexmedetomidine in different doses, through various routes such as intravenous, intra-thecal, epidural, intra-nasal etc. Numerous studies have shown that Dexmedetomidine can be successfully used intra-nasally in paediatric patients for sedation and haemodynamic stability during intraoperative as well as postoperative period with smoother recovery. Sheta SA *et al.* has compared intra-nasal Dexmedetomidine versus Midazolam for premedication in children and found that intra-nasal Dexmedetomidine (1 μg.kg^{-1}) is an effective and safe alternative for premedication in children [12]. Zanaty OM *et al.* had done comparative evaluation of nebulized Dexmedetomidine, nebulized Ketamine, and their combination as premedication for outpatient paediatric dental surgery and concluded that nebulized Dexmedetomidine produced satisfactory sedation and smoother induction of general anaesthesia [13]. In a randomized trial, Gyanesh and colleagues compared intra-nasal Dexmedetomidine (1 μg.kg^{-1}), Ketamine (5 mg.kg^{-1}), and placebo (saline) in 150 children between 1 to 10 years undergoing MRI for intravenous cannula placement and documented that children of both nebulized Dexmedetomidine and Ketamine group were calm and co-operative while intravenous cannula placement [14]. Jia and colleagues studied the premedicant effects of various combinations of intra-nasal Dexmedetomidine combined with oral Ketamine in children and concluded that administration of 2 μg.kg^{-1} intranasal Dexmedetomidine and 3 mg.kg-^{1} oral Ketamine was the optimal combination to facilitate separation from parents and intravenous cannula placement or facemask acceptance [15].

The main disadvantage of the intra-nasal route of administration of drug is transient nasal irritation and sometimes coughs. To overcome this disadvantage, administering the drug via nebulization as atomized spray was a better idea. This resulted in maximum surface area coverage with a thin layer of drug, less drug loss to the oropharynx, better patient acceptability, and improved clinical effectiveness [16]. Studies had shown that nebulized Dexmedetomidine administration may allow rapid drug absorption through nasal, respiratory, and buccal mucosa, which allow bioavailability of 65% through nasal mucosa and 82% through buccal mucosa [17].

Numerous studies have been done to prove the efficacy of intravenous Dexmedetomidine in different doses for attenuation of stress response of laryngoscopy for intubation. Sulaiman S *et al.* has suggested in their study that administration of Dexmedetomidine 15minutes before laryngoscopy and intubation, in the dose of 0.5 μg.kg^{-1}, in patients with coronary artery disease posted for elective off pump coronary artery bypass surgery was effective in obtunding the laryngoscopic response [18]. Menda F *et al.* has also concluded that in attenuating hemodynamic response of endotracheal intubation in patients undergoing fast-track CABG, Dexmedetomidine in the dose of 1 μg.kg^{-1}, as an adjunct to anesthetic induction is very effective [19]. Sebastian B *et al.* has suggested that Dexmedetomidine in a dose of 0.75 μg.kg^{-1} intravenous is the optimal dose to obtund sympathetic response evoked by laryngoscopy and endotracheal intubation [20]. High sedation scores and episodes of apnea were documented in different

studies by various authors' after intravenous bolus administration of Dexmedetomidine in the dose of 1-2 $\mu g.kg^{-1}$ [21]. In our study, we have administered Dexmedetomidine in high dose i.e. 2 $\mu g.kg^{-1}$ but through nebulization rather than intravenous bolus. To eliminate confounding factor and to decrease noxious response to laryngoscopy, we have limited laryngoscopy time to 15 seconds in the study.

Conclusion

- Dexmedetomidine nebulization in dose of 2 $\mu g.kg^{-1}$, 30 minutes prior the laryngoscopy and intubation is effective in neutralizing sympathetic response of laryngoscopy and tracheal intubation.
- Dexmedetomidine nebulization in dose of 2 $\mu g.kg^{-1}$ is devoid of adverse effects like bradycardia and hypotension.

References

1. Shribman AJ, Smith G, Achola KJ. Cardiovascular and catecholamine responses to laryngoscopy with and without tracheal intubation. Br J Anaesth. 1987; 59:295-9.
2. Reid LC, Brace DE. Irritation of respiratory tract and its reflex effect on heart surgery. Surg GynaecolObstet. 1940;70:157-62.
3. Henderson J. Airway management in the adult. In: Miller RD, editor. Miller's Anaesthesia. 7th ed. Philadelphia: Churchill Livingstone; 2010. p.1573-610.
4. Prys-Roberts C, Greene LT, Meloche R, Foëx P. Studies of anaesthesia in relation to hypertension. II. Haemodynamic consequences of induction and endotracheal intubation. Br J Anaesth. 1971; 43:531-47.
5. Adachi YU, Satomoto M, Higuchi H, Watanabe K. Fentanyl attenuates the hemodynamic response to endotracheal intubation more than the response to laryngoscopy. AnesthAnalg. 2002;95:233-7.
6. Mikawa K, Hasegawa M, Suzuki T, Maekawa N, Kaetsu H, Goto R, et al. Attenuation of hypertensive response to tracheal intubation with nitroglycerin. J Clin Anesth. 1992;4:367-71.
7. Kumar S, Mishra MN, Mishra LS, Bathla S. Comparative study of the efficacy of I.V. esmolol, diltiazem and magnesium sulphate in attenuating haemodynamic response to laryngoscopy and tracheal intubation. Indian J Anaesth. 2003; 47:41-4.
8. Rathore A, Gupta GK, Tanwar GL, Rehman H. Attenuation of the pressure response to laryngoscopy and endotracheal intubation with different doses of esmolol. Indian J Anaesth. 2002; 46:449-52.
9. Aantaa R, Scheinin M. Alpha-2-adrenergic agents in anesthesiology. Acta Anaesthesiol Scand. 1993; 37:433-48.
10. Virtanen R, Savola J, Nyman L. Characterization of the selectivity, specifity and potency of Medetomidine as an alpha-2 adrenoceptor agonist. Eur J Pharmacol. 1988.pp.9-14.
11. Scheinin H, Virtanen R, MacDonald E, Lammintausta R. Medetomidine-a novel a-2-adrenoceptor agonist:A review of its pharmacological effects. Prog Neuro-Psychopharmacol Biol Psychiatry. 1989;13:635-51.
12. Sheta SA, Al-Sarheed MA, Abdelhalim AA. Intranasal Dexmedetomidine vs Midazolam for premedication in children undergoing complete dental rehabilitation: a double-blinded randomized controlled trial. Paediatr Anaesth. 2014 Feb;24(2):181-9.
13. Zanaty OM, El Metainy SA. A comparative evaluation of nebulized Dexmedetomidine, nebulized ketamine, and their combination as premedication for outpatient pediatric dental surgery. Anesth Analg. 2015 Jul;121(1):167-71.
14. Gyanesh P, Haldar R, Srivastava D, Agrawal PM, Tiwari AK, Singh PK. Comparison between intranasal Dexmedetomidine and intra-nasal Ketamine as premedication for procedural sedation in children undergoing MRI: a double-blind, randomized, placebo-controlled trial. J Anesth. 2014;28:12–8.
15. Jia JE, Chen JY, Hu X, Li WX. A randomized study of intranasal Dexmedetomidine and oral ketamine for premedication in children. Anaesthesia. 2013;68:944–9.
16. Mason KP, Lerman J. Dexmedetomidine in children: current knowledge and future applications. AnesthAnalg. 2011;113:1129–42.
17. Anttila M, Penttilä J, Helminen A, Vuorilehto L, Scheinin H. Bioavailability of Dexmedetomidine after extravascular doses in healthy subjects. Br J Clin Pharmacol. 2003;56:691–3.
18. Sulaiman S, Karthekeyan RB, Vakamudi M, Sundar AS, Ravullapalli H, Gandham R. The effects of Dexmedetomidine on attenuation of stress response to endotracheal intubation in patients undergoing elective off-pump coronary artery bypass grafting. Ann Card Anaesth. 2012; 15:39-43.
19. Menda F, Köner O, Sayin M, Türe H, Imer P, Aykaç B. Dexmedetomidine as an adjunct to anesthetic induction to attenuate hemodynamic response to endotracheal intubationin patients undergoing fast-track CABG. Ann Card Anaesth. 2010;13:16-21.

20. Sebastian B, Talikoti AT, Krishnamurthy D. Attenuation of haemodynamic responses to laryngoscopy and endotracheal intubation with intravenous Dexmedetomidine: A comparison between two doses. Indian J Anaesth. 2017;61:48-54.
21. Belleville JP, Ward DS, Bloor BC, Maze M. Effects of intravenous Dexmedetomidine in humans. I. Sedation, ventilation, and metabolic rate. Anesthesiology. 1992;77:1125-33.

Review Article

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Peri-Operative Considerations in Gout and Hyperuricemia: A Narrative Review

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Abstract

Gout is a chronic metabolic, inflammatory disease causing hyperuricemia with formation and deposition of monosodium urate crystals in joints, tissues and involving multiple systems. It has important anaesthetic and critical care implications. This review article aims to present an overview of gout and the effects of hyperuricemia along with its important peri-operative implications. The literature is sparse regarding its anaesthetic considerations.

Keywords: Tophi; Gouty Arthritis; Hyperuricemia; Excess Purines; Acute Kidney Injury; Cardiovascular disease; Lipidemia; Non-Steroidal Anti-inflammatory Drugs; Colchicine; Chronic renal failure; Anaesthesia.

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Introduction

Gout is a multisystem disorderin which metabolic and excretory abnormalities, often compounded by excessive purine intake, result in hyperuricemia which promotes the formation of monosodium urate crystals. These crystals either induce inflammation (acute gouty arthritis) or deposit in tissues leading to swelling (tophaceous gout), or both. It is the most common inflammatory arthritis in western countries and is characterized by deposition of monosodium urate crystals in joints and tissues resulting in patient having intermittent painful attacks which often require hospital visits and even admissions. These extremely painful and intermittent attacks are followed by long periods of remission.

Egyptians in *2640 BC* were the first to recognize the disorder which was then referred *aspodagra* (acute gout occurring in the first metatarsophalangeal joint) was later recognized by Hippocrates in the fifth century BC, who referred to it as 'the unwalkable disease' due the unbearable pain associated with it. The term Gout has it's etymological in anold French word *goute*, which is derived from the Latin word gutta (or 'drop'). The word refers to the prevailing medieval belief that an excess of one of the four 'humors'--which in equilibrium were thought to maintain health would, under certain circumstances, 'drop' or flow into a joint, causing pain and inflammation. As medicine advanced it was eventually identified

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the actual excess "humor" in gout to be uric acid. Gout has been associated with a protein rich food and excessive alcohol consumption, alifestyle that, at least in the past, could only be afforded by the affluent. It is for this reason gout was at one time referred to as the '*disease of kings*'. However, as the Western diet developed into one that is purine-rich and consumed by all regardless of economic status, there was a rise in the incidence of gout [1,2].

Risk Factors

Sustained hyperuricemia, which can be caused by overproduction or underexcretion of urate is a risk factor of significant importance. Pathological hyperuricemia has been defined as the serum uric acid concentration (408 µmol/L) above which monosodium urate crystals are formed in vitro at physiological pH and temperature. In most cases, it's the underexcretion of uric acid that is the main cause of hyperuricemia but there are other factors associated with the development of gout as well, which include drugs (such as diuretics, cyclosporin, and low dose aspirin), renal impairment and excessive consumption of red meat or seafood in the diet.

When over production or underexcretion of uric acid occurs, the serum urate concentration may exceed the solubility of urate (a concentration of approximately >6.8 mg/dL) which results in supersaturation of urate in the serum and other extracellular spaces. Sustained hyperuricemia increases the risk for urate crystal deposition from the supersaturated fluids into the tissues. Hyperuricemia which is defined as a serum uric acid level of more than 7.0 mg/dL in men or more than 6.0 mg/dL in women, is clearly associated with an increased risk for the development of gout, although most patients with hyperuricemia might not necessarily develop gout.

Epidemiology

About 3.9% population in the United States have gout, compared with about 2.7% in the early 1990s [2]. Hyperuricemia has been reported in 21% of the US population, correlating with a substantial rise in obesity and hypertension [3]. Risk of developing gout could be age-related; the recent epidemiologic data suggest that the typical age group at the time of diagnosis is between 40 and 69 years [3]. Within this age group, more men are affected than women [3]. This sex discrepancy in the incidence of Gout equalizes after women undergo menopause, suggesting that estrogen plays a role in uric acid regulation [4].

Genetics

Several DNA sequence variants that increase a patient's relative risk of developing hyperuricemia and gout have been indentified in genome-wide association studies [5-7]. The SLC2A9, SLC22A11, and SLC22A12 genes, which correspond with the Glut-9, OAT1, and URAT1 transporters, respectively, have been found to be highly associated with hyperuricemia [5,6]. Glut-9 which plays a role in urate reabsorption at the proximal tubules of the kidney may account for up to 3.7% of a patient's serum uric acid variance [6].

Pathophysiology

Sudden fluctuations in serum uric acid lead to acute flaring up of gout. The monosodium urate crystals begin to form and deposit into bursas, joints and tendons at serum uric acidlevels greater than 6.8 mg/dL [8].

On a cellular level, synovial cells phagocytize the monosodium uratecrystals, which then form an inflammasome. The inflammasome releases interleukin-1 beta (IL-1b) which in turn, leads to release of chemokines and inflammatory mediators to attract neutrophils. A very potent inflammatorystate in the joint or synovial tissues results from this cascade [10]. Tophi formation results from repetitive accumulation of monosodium urate crystals, and is referred to as tophaceous gout. Factors such as temperature,mechanical trauma, previous disease, and underlyingosteoarthritis make a joint susceptible to monosodiumurate crystal deposition and tophi formation [8,9].

Role of diet

A diet consisting of alcohol and excess proteins such as certain meats, seafood, and vegetables primarily associated with the disease. The data available indicates that intake of purinerichmeats and seafood are associated with increases in serum uric acid; whereas, intake of purine-rich vegetables was surprisingly not associated with increased risk of gout [10,11]. Alcohol consumption increases risk of gout and the risk depends on type of alcohol consumed, Beer intake is associated with a high risk of developinggout; whereas, liquor and wine consumption are associated with moderate and low

risks [10,11,12]. Certain food items such as cherries and dairy products have been linked to lower serum uric acid levels and their consumption could lower the incidence of gout [10,11,13]. The data available currently supports thatthe use of low-fat dairy items could be beneficial in reducing serum uric acid.

Associated Comorbidities

There is high association between Gout and hypertension, kidney disease, and cardiovascular disease [14,15,16,17,18]. Rennin angiotensin system stimulation by uric acid leads to vascular constriction, and renal inflammation and injury at microscopic level [16]. The use of uric acidlowering agents such as allopurinol in patients with both hyperuricemia and hypertension has shown a mild blood pressure lowering effect; this hemodynamic effect was reversed when allopurinol was discontinued [17]. Lowering serum uric acid also benefitted the patients by slowing the progression of renal disease [15,16]. As observed in the Multiple Risk Factor Investigative Trial (MRFIT), which was a study of primary prevention of coronary heart disease, gout could be an independent risk factor for myocardial infarction [18]. Antihypertensive such as losartan and antilipemic agents like fenofibrate, have modest uric acid–lowering effects and may be considered along with lifestyle modification specially in hypertensive patients with gout and hypercholesterolemia [19].

Presentation

Presentation of gout consist of spectrum of clinical and pathologic features built on a foundation of an excess burden of uric acid in the body, manifested in part by hyperuricemia, which is defined as a serum urate level greater than either 6.8 or 7.0 mg/dl. Most of the clinical features of gout are due to deposition of monosodium urate monohydrate crystals in supersaturated extracellular fluids of the joint, and certain other sites. Typically, the initial clinical presentation is acute episodic arthritis but patients can also present with chronic arthritis of one or more joints [20].

Suddenly, often in the middle of the night, an affected individual will develop severe, unbearable pain, most commonly in a toe, ankle, or knee. The gouty joint will exhibit a swollen, bluish red appearance and be very warm to the touch compared with the non-inflamed, contralateral joint or even the unaffected skin nearby. If patient presents with pain in single joint (acute monoarticular arthritis) then one should first rule out infection in the joint. The pathognomonic feature of gout is a swelling termed Tophi which is mainly found in periarticular, bursal, bone, auricular, and cutaneous tissues, these swellings are detectable by physical examination and/or by imaging and pathology examination. Renal manifestations of gout include urolithiasis, typically occurring with an acidic urine pH. An uncommon clinical manifestation of gout is, chronic interstitial nephropathy which occurs due to monosodium urate monohydrate crystal deposition in the renal medulla occurring mostly in severe disease [20].

The conditions that promote hyperuricemia, including hypertension, obesity, metabolic syndrome, type 2 diabetes mellitus and chronic kidney disease (CKD) are included in factors responsible for rising prevalence of gout and could be main presenting problems in patients of gout [20].

Diagnosis

Diagnosis of gout requires a detailed history regarding the onset, timeline, location, previous joint trauma or injury, other arthralgias, dietary intake, alcohol consumption, and certain medications. A thorough review of medications in case of acute gout is required since it can be caused byrecently implemented or chronic use of loop diuretics (and to a lesser degree, thiazide diuretics), niacin, or low-dose aspirin which are frequently prescribed these days in patients with cardiovascular disorders [22,23]. Cyclosporine and tacrolimus prescribed in patients who have undergone transplant surgeries have been strongly associated with precipitating gout [24].

The Gold standard for diagnosis of gout is joint aspiration and fluid analysis under microscope during episode of acute gout, in which we observe needle-shaped, negatively green birefringent crystals under polarized light microscope which are characteristic of gout [25,26,27]. Aspiration during the inter-critical or asymptomatic period may only show positive microscopy in about 70% of patients with diagnosed gout therefore the optimal time to make the definitive diagnosis by aspiration is during the acute stage [25,26,27]. Since simultaneous septic arthritis may occur in 4% of patients so to rule out septic arthritis, in addition to crystal examination, aspirated fluid should also be sent for gram stain and culture [27]. The usefulness of serum uric acid level in diagnosing gout remains poor since many patients with hyperuricemia remain asymptomatic and never develop gout. Hyperuricemia (serum

uric acid level greater than 6 mg/dL) indicates only an elevated serum uric acid level and is not diagnostic [26,27,28,29].

Imaging studies during acute gout episodes are useful only for ruling out trauma as no abnormality other than nonspecific soft tissue swelling occur in acute gout. Punched-out erosions and interosseous tophi are the hallmark signs seen in chronic gout. CT, MRI, and ultrasound have proven clinically useful in evaluating joints for tophi in cases with chronic gout. Advanced imaging methods are more typically used to monitor the success of disease treatment rather than for diagnosis.

Treatment

When patients with hyperuricemia experience multiple, frequent, disabling attacks, develop nodular disease that causes bone destruction, or have an illness involving injury to a major internal organ (such as the kidney), then the treatment with Allopurinol may be indicated to lower the level of serum uric acid, which in turn reduces the risk of tissue damage from further crystal deposition. Uric acid lowering therapy [21] which include, xanthine oxidase inhibitor (XOI) namely allopurinol or febuxostat, and uricosuric agents (probenecid, fenofibrate and losartan) are the main line of treatment in patients of gout. An important, but sometimes difficult step in the treatment is to stop theurate-elevating medications such as thiazide and loop diuretics, niacin, and calcineurin inhibitors, since these medications arebeing taken for other conditions such as cardiovascular diseases. An elevated uric acid level can occur even with low-dose acetylsalicylic acid (aspirin 325 mg daily), but it might not possible to recommend discontinuation of this modality as cardiovascular disease prophylaxis in gout patients. In such patients it becomes necessary to have a cardiologist opinion regarding alternative therapies for cardiac disorders. It is imperative to evaluate and manage the associated conditions and risk factors such as obesity, dietary factors, excessive alcohol intake, metabolic syndrome, type 2 diabetes mellitus, hypertension, hyperlipidemia, serum urate–elevating medications, history of urolithiasis chronic kidney, glomerular, or interstitial renal disease (e.g., analgesic nephropathy, polycystic kidney disease). After ruling out common causes, one must search for potential genetic or acquired cause of uric acid overproduction (e.g., inborn error of purine metabolism or psoriasis, myeloproliferative, or lymphoproliferative disease, respectively) and lead intoxication in rare cases [20].

Drugs used in Treatment of Gout

Nonsteroidal anti-inflammatory drugs (NSAIDs) such as naproxen, indomethacin, and sulindac are indicated for initial management in acute gout [30]. Some patients might show intolerance to traditional NSAIDs in such patients selective COX-2 inhibitors can be considered. The risks and benefits of NSAIDs should be carefully considered in each patient—adverse reactions to these drugs include an increased risk of bleeding, gastrointestinal (GI) distress, fluid retention, and hypertension which are become common with increased use of these drugs [30,31,32].

Physicians must show caution or avoid NSAIDs in patients with significant renal impairment, poorly controlled congestive heart failure, history of or active peptic ulcer disease, anticoagulation therapy, or hepatic dysfunction. There are many patients in whom NSAIDs and Colchicine are contraindicated or avoided, in such cases Corticosteroid injection forman effective alternative first-line therapy. Intra-articular approach with triamcinolone acetonidecan be considered in Gout involving fewer than three joints [27,30], otherwise intramuscular injection with triamcinolone acetonide can be given [30,32].

Colchicine is anotheranti-inflammatory drug used for managing acute gout, and should be started within the first 24 to 36 hours from the onset of symptoms [30,32,33]. The therapy might be discontinued due to the gastro-intestinal adverse reactions associated with higher dosages of the drug. Initiating colchicine before starting allopurinol therapy will prevent acute inflammatory episodes as the uric acid load in the body is only gradually eliminated by allopurinol [34]. Colchicine at high doses, is bone marrow–suppressant and in patients with renal insufficiency or patients taking cyclosporine or statins, it can cause neuromyopathy. It has a small benefit-to-toxicity ratio and should only be considered in patients if there is no alternative therapy. Lately subcutaneous injections of Canakinumab, which is a human monoclonal antiinterleukin-1 beta (IL-1b) antibody [31] are being considered in patients who are refractory to the first line drugs used in initial management and in patients whose treatment options are limited because of underlying conditions.

Causes of Hyperurecemia

Uric acid is the catabolic end product of purine nucleotides degradation and itsoverproduction

or under-excretion are leading causes of its accumulation in the body. Diet rich in purines such as organ meat (liver and spleen), red meat, and excessive consumption of alcohol and low alcoholic drinks such as beer is one of the reasons for hyperuricemia condition.

Over production may be caused due to genetic defect such as *Leschnyan syndrome* and health conditions such Multiple Myeloma, where there is high production of cellular nucleotides. Patients should be informed about the factors contributing to their hyperuricemia, such as obesity, a high-purine diet, regular alcohol consumption, and diuretic therapy, which may all be correctable.

Concerns Associated with Hyperurecemia

Cardiovascular Disease and Lipidemia

Hyperuricemia is becoming an important cause for metabolic diseases and CVD [35]. There are reports on hyperuricemia condition that it is associated with metabolic syndrome such as obesity, dyslipidemia and hypertension [36]. Lipid disorders like hypertriglyceridemia have frequently been observed to be linked with hyperuricemia [37]. Various studies have shown that elevated serum uric acid is also related to increased incidence of cardiovascular diseases [38]. Sedentary lifestyle and a diet rich in proteins and alcohol which are now very common in urban population makes them prone to hyperuricemia coupled with dyslipidemia which becomes a main CVD risk factor. Thus, it is of paramount importance that these patients restrict their high fat diet and bring lifestyle modifications to avoid the wave of CVD risk.

Association of Hyperuricemia with hypertension and Renal Injury

Uric acid has many effects on vasculature and renal tissue whichcan cause hypertension. Uric acid directly stimulates the renin-angiotensin system in the kidney [39-41]; inhibits the synthesis of vascular nitric oxide (NO), is a potent vasodilator [39,42]; stimulates the proliferation of smooth muscle cells to promote vascular narrowing and constriction [42-44]; and induce renal abnormalities like renal interstitial inflammation and tubular injury that can indirectly lead to hypertension [43,45]. Treatment with allopurinol blocks uric acid generation by inhibiting enzyme xanthine oxidase and has been found to be useful in correcting both the serum urate levels and the increase in blood pressure [43]. Allopurinol also results in a number of other effects, such as alterations of overall serum antioxidant levels [47-48], which could very well be the mechanism of action as opposed to urate lowering per se.

Hyperuricemia, Gout, Insulin Resistance, and Obesity

Studies done in past have shown that Metabolic syndrome is associated with higher incidence of gout, and individuals with hyperuricemia may also have an increased incidence of insulin resistance. One such study was by Yoo and colleagues [49], who observed that the incidence of insulin resistance in gout patients may be increased by as much as 35% over individuals without gout.

The oxidative stress caused by uric acid in adipocytes is a causative factor in insulin resistance as well as in cardiovascular disease. Sautin and coworkers [50] reported on the formation of NADPH (nicotinamide-adenine dinucleotide-phosphate) oxidase-dependent reactive oxygen species by uric acid. Stimulation with uric acid resulted in activation of MAP (mitogen-activated protein) kinases p38 and ERK1/2, a decrease in NO bioavailability, and an increase in protein nitrosylation and lipid oxidation in cultured mouse adipocytes. Study done by Choi and colleagues [51] observed that a diagnosis of gout conveyed a 35% to 65% increase in risk for future incidence of Type II diabetes.

Animal studies have observed that there is a possibility that urate-lowering may also have indirect benefits in reducing the expansion of the adipose compartment and treatment with allopurinol could reduce the rate and level of obesity [52].

Hyperurecemia and Renal Failure

There is a close association between hyperuricemia and chronic kidney disease (CKD) and elevated uric acid level isalso a risk factor for renal insufficiency in general populations. It is a poor prognostic factor of renal function in patients who also have IgA nephropathy. The treatment of hyperuricemia with allopurinol in patients suffering from CKD resulted in a fall in blood pressure and inhibition of the progression of renal damage. Conversely, the cessation of allopurinol treatment in CKD was followed by a rise in blood pressure and the development of renal damage but this was seen only in patients not receiving angiotensin converting enzyme inhibitor (ACEI) or angiotensin receptor blocker (ARB). The

protective effect of these drugs suggests that the renin angiotensin (RA) system plays an important role in the development of hypertension and renal damage from hyperuricemia.

Hyperurecemia in Tumor Lysis Syndrome and Kidney Injury

Tumor lysis syndrome refers to the metabolic disturbances that occurs when large numbers of neoplastic cells are destroyed rapidly during or more commonly 48-72 hours after chemotherapy, leading to the release of intracellular contents including various ions and metabolic byproducts into the systemic circulation. This release can inundate renal elimination and cellular buffering mechanisms, leading to numerous metabolic derangements. The cell breakdown during the chemotherapy releases nucleic acid purines, which are ultimately metabolized to their end product uric acid by hepatic enzyme xanthine oxidase. The excess conversion occurring in presence of high purine load following chemotherapy leads to hyperuricemia. Uric acid is a weak acid with a pKa of approximately 5.4. It is soluble in plasma and is freely filtered at the renal glomeruli, however it precipitates in renal tubular and collecting duct fluid due to the acidic pH of the media there. This decreased solubility at the level of tubules and collecting duct increases the formation of renal calculi. Since elimination of uric acid primarily occurs from the kidney and a preexisting volume depletion or any other renal dysfunction predisposes patients to worsening metabolic derangements and acute kidney injury (AKI).

Mechanical obstruction by uric acid crystals in the renal tubules leads to obstructive nephropathy which is the major cause of AKI. A high acidity and high concentration in the renal tubular fluid are factors leading to increaseduric acid precipitation. Renal medullary hemoconcentration and a decreased tubular flow rate also contribute to crystallization [54].

Significant Side Effects of Drugs used in Gout

Gout Medication	Side Effects
NSAIDS	indigestion, stomach pain, passing black tarry bowel motions, rash, mouth ulcers, swollen lips, difficulty breathing
Corticosteroids	indigestion, stomach pain, passing black tarry bowel motions, infections, mood changes, sleep problems, weight gain
Colchicine	nausea, vomiting, diarrhea, abdominal pain, blood in the urine
Allopurinol	rash, mouth ulcers, swollen lips, difficulty breathing, kidney stones (severe pain in your back or side), blood in the urine
Probenecid	rash, mouth ulcers, swollen lips, difficulty breathing, kidney stones (severe pain in your back or side), blood in the urine
Febuxostat	diarrhea, nausea, headache, rash, mouth ulcers, swollen lips, difficulty breathing

There is anincreased risk of bleeding, gastrointestinal (GI) distress, fluid retention, and increased BPin patients who are on anti-inflammatory drugs such as NSAIDs for a long period of time. They could also lead to analgesic nephropathy in these patients. NSAIDs should be used with caution or not at all in patients with any of the following: significant renal impairment, poorly controlled congestive heart failure, history of or active peptic ulcer disease, anticoagulation therapy, or hepatic dysfunction. In such scenarios it would be better to take the patients on corticosteroids and avoid NSAIDS.

Anaesthetic Considerations

Preoperative Considerations

As highlighted before gout is associated with many chronic medical conditions which require a thorough preoperative history and physical examination when such patient presents to us before surgery. The changing lifestyles and increased consumption of alcohol and excess proteins have made elevated uric acid a common finding. Detailed history including diet and substance abuse form an important part of preoperative questions and also guide the peri-operative physician to take complete history and order relevant investigations. All Co-morbidities and metabolic changes associated with gout such as disorders in cardiovascular disorders, gastrointestinal and endocrine diseases, obesity, renal dysfunction, renal stones and musculoskeletal disorders should be evaluated, and optimized preoperatively. These disorders have important implications for anesthetic management.Therefore, adequate information about each of the affected systems and ongoing treatment for preexisting problems is the key for giving safe anaesthesia. Excessive consumption of red meat or seafood and drugs (such as diuretics, ciclosporin, and low dose aspirin), renal impairment are some of the important risk factors associated with the development of gout and questions regarding them must be asked from these patients at the time of pre anesthetic check up of the patients. Since lowering serum uric acid also is associated with a slower

progression of renal disease and lowering of blood pressure therefore the patients should be asked during the preoperative visit to continue the uric acid lowering drugs before the surgeries. Special attention and care are needed in these patients regarding cardiovascular status. Assessing cardio pulmonary functional status in these patients could be challenging since they are often unable to perform any physical exercise as a consequence of pain or disability related to arthritisdue to severe pain. Dobutamine stress echocardiogram may be ordered in cases in which we are suspecting cardiac abnormality.

Evaluation of the co-morbidities such as hypertension, ischemic heart disease, pre-existing renal damage, signs of gastro intestinal bleed becomes important part of preoperative examination of these patients. Patients could present in the symptom free inter critical period of the disease so it is advisable to get uric acid levels done for patient with history of joint pain. The patients can be advised to restrict consumption of purine-rich meats and alcohol so as to prevent acute flare ups. A rheumatology work-up could be done in patients with such symptoms so as to start medication for acute flare ups or for review of ongoing medications. A gout patient requires a multidisciplinary approach in the perioperative period. However, there seems to be is no consensus on how to modify its treatment in the perioperative setting.

There is a high degree of association between hyperuricemia, hypertension, kidney disease, and cardiovascular diseasehence asking relevant history, examining the patient and getting ECG and KFT done to rule out associated problems becomes an important part of patient care in preoperative period. An X-ray KUB could be ordered to look for presence of urolithiasis.

According to the Multiple Risk Factor Investigative Trial (MRFIT) gout is an independent risk factor for myocardial infarction. Losartan and fenofibrate have modest uric acid–lowering effects hence they can be useful in patients having gout specially those who also have hypertension and hypercholesterolemia. Caution or complete avoidance should be observed with use of NSAIDS in patients with any of the following: significant renal impairment, poorly controlled congestive heart failure, history of or active peptic ulcer disease, anticoagulation therapy, or hepatic dysfunction. Corticosteroids are better than NSAIDS in such scenarios to prevent life threatening adverse drug effects.

Intraoperative considerations

Proper patient positioning is crucial for ease of surgery and preventing complication due to wrong position is one of the many responsibilities of anaesthesiogist. Positioning can be difficult in any case of arthritis due to pain, hence adequate analgesia and sedation are of extreme importance in these patients. All the standard ASA monitors are applied once the patient is inside Operation theatre (OT), including non-invasive blood pressure, temperature probe, pulse oximetry, ECG, and end-tidal capnography. Since many of these patients are already on long term steroids, a stress-dose corticosteroid should be considered in these patientsto prevent hemodynamic instability due to adrenal insufficiency. As corticosteroid use is a major risk factor for perioperative infection in these patients, therefore one must balance risks of adrenal insufficiency with infection before giving steroids [55]. As even low-dose corticosteroids can lead to disruption of the hypothalamic-pituitary axis, therefore no single cut-off dose can be used to determine which patients may be at risk of adrenal insufficiency [56]. Stress-dose corticosteroids required in the perioperative timeframe depends on the type of surgery and usually 50-75 mg of hydrocortisone or 10-15 mg methylprednisolone can be given intravenously on the day of the procedure. The dose then has to be tapered to the routine corticosteroid dose that patient was taking before the surgery over a period of 1-2 days postoperatively [57].

Gout can result in wide ranging involvement of the larynx including cricoarytenoid arthritis and tophi of laryngeal tissue, but such reports are exceedingly rare. A previously undiagnosed laryngeal arthritis can exacerbate with the use of laryngeal mask airway (LMA) or trauma during intubation, and this possibility must be kept in the list of differential diagnosis in a setting of acute upper airway obstruction, particularly following extubation.

Postoperative period

The important concerns included in the post operative period are adequate pain control, wound care, prevention of deep vein thrombosis, and maintenance of renal function fluid management. Extreme pain on movement of affected joints in these patients require use of multimodal pain control regimen. The multimodal approach may include acetaminophen, NSAIDs, intravenous opioids, local anesthetics injected

to wound or port site, tramadol and regional anaesthesia. A good pain control results in early mobilization and prevention of complications related to immobility such as thrombosis. Fluid management should be considered according to specific requirements of the patient and presence of associated comorbidities specially cardiac and renal dysfunction. A careful recording of input and output status must be done. In addition to all these factors a high quality nursing care is of extreme importance to ensure reduction in complications and faster recovery.

Conclusions

Gout and hyperuricemia form important risk factors for surgery and anaesthesia. It can lead to diseases of the musculo-skeletal, cardiovascular and renal systems. The adverse effects of drugs used to treat gout and hyperuricemia should also be considered in the peri-operative period. Maintenance of end organ perfusion, evaluation of renal function tests, assessment of cardio-pulmonary exercise testing and padding of pressure points and joints is of paramount importance. Hyper-uricemic emergencies like tumor lysis syndrome may require admission to the intensive care unit and renal replacement therapy.

References

1. Nuki G, Simkin PA. A concise history of gout and hyperuricemia and their treatment. Arthritis Res Ther. 2006;8(suppl 1):S1.
2. Zhu Y, Pandya BJ, Choi HK. Prevalence of gout and hyperuricemia in the US general population: The National Health and Nutrition Examination Survey 2007-2008. Arthritis Rheum. 2011;63(10):3136-41.
3. Zhu Y, Pandya BJ, Choi HK. Prevalence of gout and hyperuricemia in the US general population: The National Health and Nutrition Examination Survey 2007-2008. Arthritis Rheum. 2011;63(10):3136-41.
4. Dirken-Heukensfeldt KJ, Teunissen TA, van de Lisdonk H, Lagro-Janssen AL. Clinical features of women with gout arthritis. A systematic review. Clin Rheumatol. 2010;29(6):575-82.
5. Reginato AM, Mount DB, Yang I, Choi HK. The genetics of hyperuricaemia and gout. Nat Rev Rheumatol. 2012;8(10):610-21.
6. Yang Q, Köttgen A, Dehghan A, *et al.* Multiple genetic loci influence serum urate levels and their relationship with gout and cardiovascular disease risk factors. Circ Cardiovasc Genet. 2010;3(6):523-530.
7. Mount DB. The kidney in hyperuricemia and gout. CurrOpinNephrolHypertens. 2013; 22(2):216-223.
8. Schumacher HR Jr. The pathogenesis of gout. Cleve Clin J Med. 2008;75(suppl 5):S2-S4.
9. Roddy E, Zhang W, Doherty M. Are joints affected by gout also affected by osteoarthritis? Ann Rheum Dis. 2007;66(10):1374- 1377.
10. Schumacher HR Jr. The pathogenesis of gout. Cleve Clin J Med. 2008;75(suppl 5):S2-S4.
11. Roddy E, Zhang W, Doherty M. Are joints affected by gout alsoaffected by osteoarthritis? Ann Rheum Dis. 2007;66(10):1374-1377.
12. Choi HK, Atkinson K, Karlson EW, *et al.* Purine-rich foods, dairy and protein intake, and the risk of gout in men. N EnglJMed. 2004;350(11):1093-1103.
13. Zaga L, Theodoratou E, Kyle J, *et al.* The association of dietaryintake of purine-rich vegetables, sugar-sweetened beverages anddairy with plasma urate, in a cross-sectional study. PLoS One. 2012;7(6):e38123.
14. Zhang Y, Neogi T, Chen C, *et al.* Cherry consumption anddecreased risk of recurrent gout attacks. Arthritis Rheum. 2012;64(12):4004-11.
15. Dirken-Heukensfeldt KJ, Teunissen TA, van de LisdonkH,Lagro-Janssen AL. Clinical features of women with gout arthritis.A systematic review. Clin Rheumatol. 2010;29(6):575-82.
16. Mount DB. The kidney in hyperuricemia and gout. Curr Opin Nephrol Hypertens. 2013;22(2):216-23.
17. Pillinger MH, Goldfarb DS, Keenan RT. Gout and its comorbidities. Bull NYU Hosp Jt Dis. 2010;68(3):199-203.
18. Agarwal V, Hans N, Messerli F. Effect of allopurinol on bloodpressure: a systematic review and meta-analysis. J Clin Hypertens (Greenwich). 2013;15(6):435-42.
19. Krishnan E, Baker JF, Furst DE, Schumacher HR. Gout and therisk of acute myocardial infarction. Arthritis Rheum. 2006;54(8):2688-96.
20. Schumacher HR Jr, Chen LX. Newer therapeutic approaches:gout. Rheum Dis Clin North Am. 2006;32(1):235-44.
21. American College of Rheumatology Guidelines for Management of Gout. Part 1: Systematic Nonpharmacologic and Pharmacologic Therapeutic Approaches to Hyperuricemia. Arthritis Care & Research. 2012 Oct;64(10):1431-46 DOI 10.1002/acr.21772 © 2012, American College of Rheumatology.
22. Agudelo CA, Wise CM. Gout: diagnosis, pathogenesis, and clinical manifestations. CurrOpinRheumatol. 2001;13:234-39.
23. Eggebeen AT. Gout: an update. Am Fam Physician. 2007;76(6):801-808.

24. Pascual E, Perdiguero M. Gout, diuretics and the kidney. AnnRheum Dis. 2006;65(8):981-82.
25. Ning TC, Keenan RT. Unusual clinical presentations of gout.CurrOpinRheumatol. 2010;22(2):181-87.
26. Schumacher HR Jr. The pathogenesis of gout. Cleve Clin J Med.2008;75(suppl 5):S2-S4.
27. Tausche AK, Jansen TL, Schröder HE, *et al.* Gout—currentdiagnosis and treatment. DtschArztebl Int. 2009;106(34-35):549-55.
28. Zhang W, Doherty M, Pascual E, *et al.* EULAR evidence-basedrecommendations for gout. Part I: diagnosis. Report of a taskforce of the Standing Committee for International Clinical Studies Including Therapeutics (ESCISIT). Ann Rheum Dis. 2006;65(10):1301-1311.
29. Zhu Y, Pandya BJ, Choi HK. Prevalence of gout and hyperuricemiain the US general population: The National Health and Nutrition Examination Survey 2007-2008. Arthritis Rheum. 2011;63(10):3136-41.
30. Reginato AM, Mount DB, Yang I, Choi HK. The geneticsof hyperuricaemia and gout. Nat Rev Rheumatol. 2012;8(10):610-21.
31. Khanna D, Khanna PP, Fitzgerald JD. American College of Rheumatology guidelines for management of gout. Part 2: therapyand anti-inflammatory prophylaxis of acute gouty arthritis. Arthritis Care Res (Hoboken). 2012;64(10):1447-61.
32. Burns CM, Wortmann RL. Latest evidence on gout management:what the clinician needs to know. Ther Adv Chronic Dis. 2012;3(6):271-86.
33. Winzenberg T, Buchbinder R. Cochrane Musculoskeletal Groupreview: acute gout. Steroids or NSAIDs? Let this overview fromthe Cochrane Group help you decide what's best for your patient. J Fam Pract. 2009;58(7):E1-E4.
34. Terkeltaub RA, Furst DE, Bennett K, *et al.* High versus lowdosing of oral colchicine for early acute gout: twenty-fourhoursoutcome of the first multicenter, randomized, double-blind, placebo-controlled, parallel-group, dose-comparison colchicinestudy. Arthritis Rheum. 2010;62(4):1060-68.
35. Borstad GC, Bryant LR, Abel MP, *et al.* The efficacy of colchicine when initiating allopurinol for chronic gouty arthritis. Program and abstracts of the American College of Rheumatology 66th Annual Scientific Meeting; October 25-29, 2002; New Orleans, Louisiana. Abstract 285.
36. C. Bengtsson, L. Lapidus, C. Stendahal, J. Waldenstrom. Hyperuricemia and risk of cardiovascular disease and overall deat. Acta Med Scand. 1988:224:549-55.
37. Z. Cai, X. Xu, X. Wu, C. Zhou, D. Li. Hyperuricemia and the metabolic syndrome. Asia Pac J Clin Nutr 2007:18: 81-87.
38. K.A. Barlow. Hyperlipidemia in primary gout Metabolism. 1968:17:289-299. http://dx.doi.org/10.1016/0026- 0495(68)90132-7.
39. F.N. Brand, D.L. McGee, W.B. Kannel, J. Stokes, W.P. Castelli. Hyperuricemia as a risk factor of coronary heart disease: The Framingham Study. Am J Epidemiol. 1985;121:11-18.
40. Mazzali M, Hughes J, Kim YG, *et al.* Elevated uric acid increases blood pressure in the rat by a novel crystal-independent mechanism. Hypertension. 2001;38(5):1101-6.
41. Saito I, Saruta T, Eguchi T, *et al.* Role of renin-angiotensin system in the controls of blood pressure and aldosterone in patients with cirrhosis and ascites. Jpn Heart J. 1978;19(5):741-7.
42. Saito I, Saruta T, Kondo K, *et al.* Serum uric acid and the renin-angiotensin system in hypertension. J Am Geriatr Soc. 1978;26(6):241-7.
43. Sanchez-Lozada LG, Soto V, Tapia E, *et al.* Role of Oxidative Stress in the Renal Abnormalities Induced by Experimental Hyperuricemia. Am J Physiol Renal Physiol. 2008;295(4):F1134-41; Epub 2008 Aug 13.
44. Nakagawa T, Mazzali M, Kang DH, *et al.* Hyperuricemia causes glomerular hypertrophy in the rat. Am J Nephrol. 2003;23(1):2-7.
45. Kang DH, Han L, Ouyang X, *et al.* Uric acid causes vascular smooth muscle cell proliferation by entering cells via a functional urate transporter. Am J Nephrol. 2005;25(5):425-33.
46. Sanchez-Lozada LG, Tapia E, Avila-Casado C, *et al.* Mild hyperuricemia induces glomerular hypertension in normal rats. Am J Physiol Renal Physiol. 2002;283(5):F1105-10.
47. Takano Y, Hase-Aoki K, Horiuchi H, *et al.* Selectivity of febuxostat, a novel non-purine inhibitor of xanthine oxidase/xanthine dehydrogenase. Life Sci. 2005;76(16):1835-47.
48. Butler R, Morris AD, Belch JJ, *et al.* Allopurinol normalizes endothelial dysfunction in type 2 diabetics with mild hypertension. Hypertension. 2000;35(3):746-51.
49. Farquharson CA, Butler R, Hill A, *et al.* Allopurinol improves endothelial dysfunction in chronic heart failure. Circulation. 2002 Jul 9;106(2):221-6.
50. Yoo HG, Lee SI, Chae HJ, *et al.* Prevalence of insulin resistance and metabolic syndrome in patients with gouty arthritis.Rheumatol Int. 2011;31(4):485-91.
51. Sautin YY, Nakagawa T, Zharikov S, Johnson RJ. Adverse effects of the classic antioxidant uric acid in adipocytes: NADPH oxidase-mediated oxidative/ nitrosative stress. Am J Physiol Cell Physiol. 2007; 293(2):C584-96.
52. Choi HK, De Vera MA, Krishnan E. Gout and the risk of type 2 diabetes among men with a high cardiovascular risk profile. Rheumatology (Oxford) 2008;47(10):1567-70.

53. Nakagawa T, Hu H, Zharikov S, *et al*. A causal role for uric acid in fructose-induced metabolic syndrome. Am J Physiol Renal Physiol. 2006;290(3):F625-31.

54. Ohno I. Relationship between hyperuricemia and chronic kidney disease. Nucleosides Nucleotides Nucleic Acids. 2011;30(12):1039-44.

55. Abu-Alfa AK, Younes A. Tumor lysis syndrome and acute kidney injury: evaluation, prevention, and management. Am J Kidney Dis. 2010;55(5 Suppl 3):S1-13; quiz S14-9.

56. Smitten AL, Choi HK, Hochberg MC, Suissa S, Simon TA, Testa MA, Chan KA. The risk of hospitalized infection in patients with rheumatoid arthritis. J Rheumatol. 2008;35:387–93.

57. Kirwan JR, Hickey SH, Hällgren R, Mielants H, Björck E, Persson T, Wollheim FA. The effect of therapeutic glucocorticoids on the adrenal response in a randomized controlled trial in patients with rheumatoid arthritis. Arthritis Rheum. 2006;54:1415-21.

58. Coursin DB, Wood KE. Corticosteroid supplementation for adrenal insufficiency. JAMA. 2002; 287:236-240.

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[2] Twetman S, Axelsson S, Dahlgren H, Holm AK, Källestål C, Lagerlöf F, et al. Caries-preventive effect of fluoride toothpaste: A systematic review. Acta Odontol Scand 2003; 61: 347-55.

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[3] Fleischer W, Reimer K. Povidone iodine antisepsis. State of the art. Dermatology 1997; 195 Suppl 2: 3-9.

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[4] American Academy of Periodontology. Sonic and ultrasonic scalers in periodontics. J Periodontol 2000; 71: 1792-801.

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[5] Garoushi S, Lassila LV, Tezvergil A, Vallittu PK. Static and fatigue compression test for particulate filler composite resin with fiber-reinforced composite substructure. Dent Mater 2006.

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[6] Hosmer D, Lemeshow S. Applied logistic regression, 2nd edn. New York: Wiley-Interscience; 2000.

Chapter in book

[7] Nauntofte B, Tenovuo J, Lagerlöf F. Secretion and composition of saliva. In: Fejerskov O,

Kidd EAM, editors. Dental caries: The disease and its clinical management. Oxford: Blackwell Munksgaard; 2003. p. 7-27.

No author given

[8] World Health Organization. Oral health surveys - basic methods, 4th edn. Geneva: World Health Organization; 1997.

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[9] National Statistics Online—Trends in suicide by method in England and Wales, 1979-2001. www. statistics.gov.uk/downloads/theme_health/HSQ 20.pdf (accessed Jan 24, 2005): 7-18. Only verified references against the original documents should be cited. Authors are responsible for the accuracy and completeness of their references and for correct text citation. The number of reference should be kept limited to 20 in case of major communications and 10 for short communications.

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