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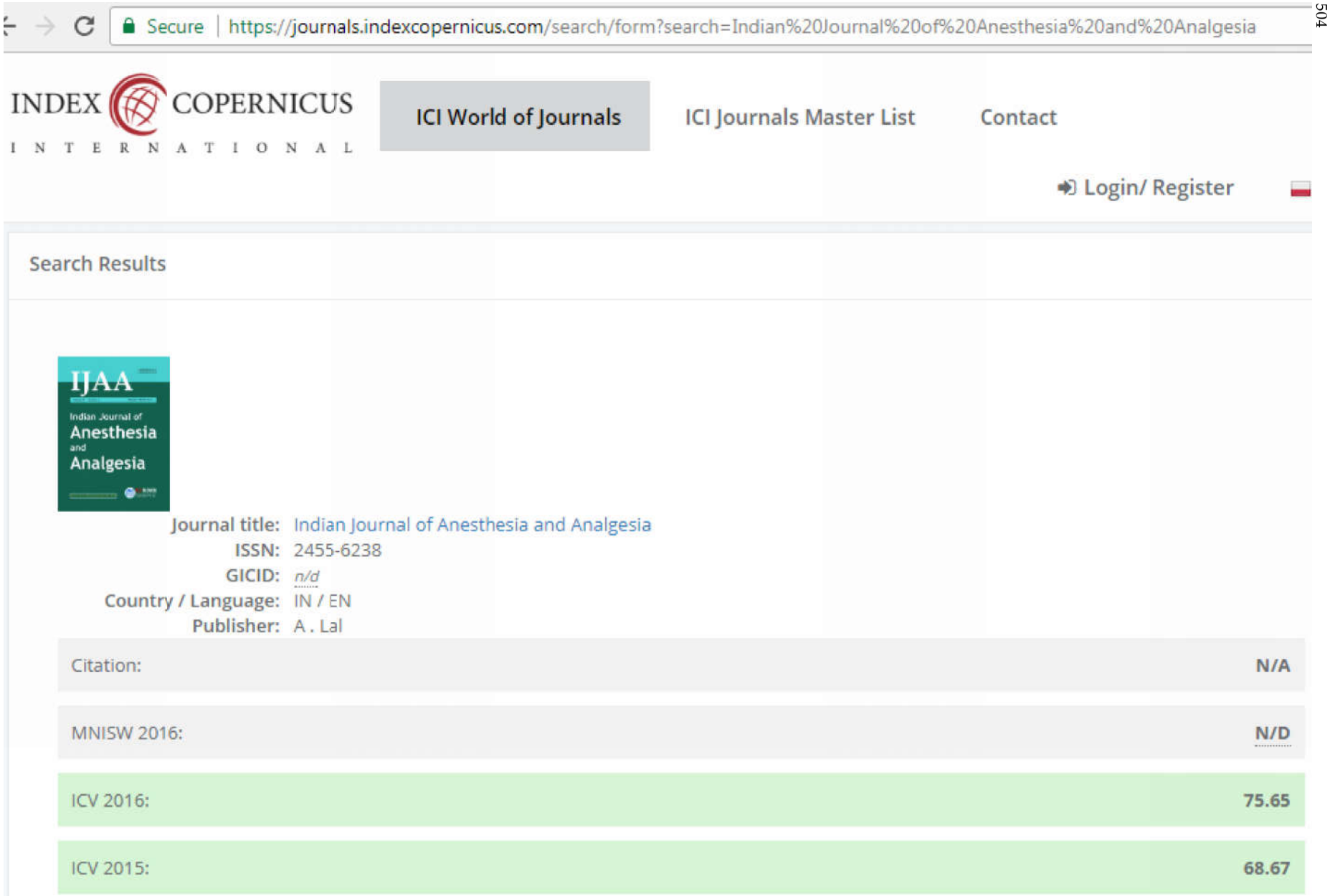
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Comparative Clinical Study of 0.5% Hyperbaric Bupivacaine Alone and 0.5% Hyperbaric Bupivacaine with Midazolam Intrathecally for Lower Limb and Lower Abdominal Surgeries

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Abstract

Aim: The present study was conducted to evaluate the efficacy and analgesic effect of mixture of midazolam-bupivacaine as compared to bupivacaine alone in patients undergoing lower limb and lower abdominal surgeries under subarachnoid block. *Materials and Methods:* The present study was conducted on 100 patients aged between 18 to 60 years belonging to ASA Grade I and II of both the sexes posted for lower limb and lower abdominal surgeries. *Results:* In 100 patients duration of sensory blockade in both group B and group M. the mean duration of sensory blockade in group B is 89.1±2.95 minutes were as in group M, it is 118.94±10.83 minutes, $p<0.05$, hence statistically significant. ($t = 18.5918$, $p= 0.000$, statistically significant). The mean duration of maximum motor blockade in B is 163.3±16.6 with a range being 135 to 210 minutes. In group M, the mean duration of maximum motor blockade is 180.24±27.40 minutes with a range being 152 to 245 minutes. As p value is 0.0004 it is statistically significant. (T=3.693, P value-0.0004, highly significant). In group B, the mean duration of analgesia is 125.46±7.18 minutes with a range of 110 to 142 minutes. In group M, the mean duration of analgesia is 243.26±24.41 minutes with a range of 173 to 273 minutes. In group B, the mean VAS score is 3.98±1 and in group M, it is 3.6±0.6. The t value is 2.869 and the p value is 0.005, hence there is statistical significance between them. *Conclusion:* It can be inferred that inj. midazolam 1 mg in combination with inj.bupivacaine 0.5% hyperbaric can be safely administered intrathecally for better postoperative analgesia.

Keywords: Bupivacaine; Midazolam; Intrathecal; Lower Abdominal Surgeries.

Introduction

Regional anesthesia for lower limb and lower abdominal surgeries surgery is held generally to be safer than general anaesthesia. It avoids general anesthesia related problems such as poly-pharmacy, airway manipulation, misplacement of end tracheal tube, hypo or hyperventilation, vomiting, pulmonary aspiration. It reduces surgical stress and attenuates increase in plasma catecholamine and other hormones. Regional anaesthesia gives intra and postoperative pain relief with full preservation of mental status and normal reflexes. The subarachnoid blockade is the common form of centrineuraxial blockade performed for lower limb surgeries. The ensuing nerve block ensures the patient well being, while motor block facilitates the surgeon's work. The 0.5% hyperbaric bupivacaine is the most commonly used drug. It produces longer duration of anaesthesia with good muscle relaxation. It provides effective pain relief in initial post-operative period. In order to maximize post operative analgesia, a number of adjuvants have been added to spinal local anaesthetics. Morphine prolongs the post -operative analgesia but is associated with major side effects, in particular delayed respiratory depression [1]. The other

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adjuvants like clonidine, ketamine have also been tried but none has become established in regular clinical practice because of their adverse effects. The subarachnoid midazolam was originally shown to have anti-nociceptive properties in studies performed in animals in early 1980's [2]. The subarachnoid midazolam is being used in humans since 1986 and doses up to 2 mg have been described [3]. It abolishes pain of somatic origin, produces selective sensory block and blocks somatosympathetic reflexes without any neurotoxicity.

The subarachnoid midazolam potentiates the blocking actions of local anaesthetics. It improves the quality of sensory and motor block, without prolonging the recovery. It also provides prolonged post-operative pain relief without producing sedation [4,5].

The subarachnoid midazolam is also devoid of complications such as, bradycardia, hypotension, post-operative nausea and vomiting, pruritus, urinary retention and neurotoxicity. The present study was conducted to evaluate the efficacy and analgesic effect of mixture of midazolam-bupivacaine as compared to bupivacaine alone in patients undergoing lower limb and lower abdominal surgeries under subarachnoid block.

Methodology

The present study was conducted on 100 patients aged between 18 to 60 years belonging to ASA Grade I and II of both the sexes posted for lower limb and lower abdominal surgeries. The study was conducted at Konaseema institute of medical sciences and research foundation, Amalapuam, Andhra Pradesh during the period of December 2014 to October 2016.

Inclusion Criteria

Patients belonging to ASA grade I and II, Patients of either sex aged 18 to 60 years, patients undergoing lower limb and lower abdominal surgeries.

Exclusion Criteria

Patients with ASA grade III and IV physical status, Patients in extreme age, who had undergone chronic analgesic therapy, with gross spinal abnormality, localized skin sepsis, haemorrhagic diathesis, neurological involvement or disease, patients with peripheral neuropathy.

Pre-Anaesthetic Evaluation

A detailed history was taken from each patient subjected for study. The data such as age, sex, weight, hospital registration number, date of admission were noted. The general physical examination was performed and baseline data i.e., general condition, pulse rate, blood pressure, respiratory rate were recorded. The cardiovascular, respiratory and central nervous system were thoroughly examined clinically.

The back and vertebral column of the patients were examined to rule out any spinal deformity and infection. Laboratory investigations were performed. Tablet Alprazolam 0.5mg on the night before surgery to relieve anxiety. Tablet Ranitidine 150mg on the night before surgery. Informed written consent was taken from the patient. A minimum of 6 hours Nil per oral status was confirmed. The patients were randomly allocated by simple randomization in to control Bupivacaine group(B) and Midazolam (group M) + Bupivacaine group(B), each group consisting of 50 patients.

The monitoring was established with electrocardiography display, pulse oximetry, and non invasive blood pressure. The baseline pulse rate, blood pressure, rate of respiration, oxygen saturation and ECG were recorded in each patient before subarachnoid block.

Intra-Operative Period

After the subarachnoid blockade, all the patients were monitored for pulse rate, blood pressure, respiratory rate, oxygen saturation at 2, 4, 6, 8, 10, 15, 30, 45, 60,90, 120, 150, 210, 240 and 270 minutes intra-operatively and every hour till 4 hours post-operatively until the effect of subarachnoid block was disappeared.

During the procedure all the patients were infused with appropriate quantity of intravenous fluids. Any untoward side effects were noted.

Bradycardia: A pulse rate of less than 60 beats per minutes was considered as bradycardia and, if any was treated with injection atropine 0.6 mg intravenously.

Hypotension: A systolic blood pressure of less than 90mm Hg or decrease in 30% below the baseline blood pressure was considered as hypotension. It was corrected with rapid infusion of IV fluids, oxygen with face mask, foot end elevation and injection mephentemine 6mg IV was given. Any untoward effects like nausea and vomiting were noted and treated appropriately.

Post-Operative Analgesia

The patients were monitored in post anaesthesia care unit. Duration of sensory blockade, duration of maximum motor blockade, total duration of analgesia.

Sedation Score

0: Wide awake,

1: Sleeping comfortably responding to verbal commands,

2: Deep sleep arousable,

3: Deep sleep not arousable.

The effectiveness of pain relief in the post operative period was assessed by Visual Analogue Score. The patient makes a mark on a 10cm scale horizontal or vertical one end of which is marked as 'No pain' and the other end as 'The worst pain one can image.

The position of the mark on the line measures how much pain the patient experiences. The patients were observed for 24 hours and any post-operative side effects such as nausea, vomiting, head ache, respiratory depression, drowsiness urinary retention and Neurological deficits were noted. The interval data were expressed as Mean and Standard Deviation.

The Student's t- test was used for comparing two groups. Chi-Square test was used for analysis of statistical data. A 'p' value less than 0.05 was considered significant for statistical difference.

Results

The present clinical study was conducted on 100 patients of either sex belonging to different age group. These patients belonged to ASA grade I or II and underwent lower limb orthopaedic surgeries under subarachnoid anaesthesia. The study was undertaken to evaluate the efficacy of intrathecally administered Inj. Midazolam (preservative free) and 0.5% hyperbaric bupivacaine in improving the quality of anaesthesia and providing post operative pain relief.

The following observations were made during the study. Group B consisted of 50 patients and the drug administered is 3 ml of 0.5% hyperbaric bupivacaine, Group M consisted of 50 patients and the drug administerd is 3 ml of 0.5% hyperbaric bupivacaine and 0.2 ml (1 mg) midazolam.

Age wise distribution in both group b and group M. The minimum age was 19 years and maximum age was 60 years. The mean age in group B is 40.14±11.6023 and group M is 49.72±11.708 years. This table shows sex distribution of the study population. There were 34 male patients and 16 female patients in group B. The group M had 33 male patients and 17 female patients (Table 1).

Time of onset of Sensory Block. t value is 8.3512 and p value being 0.000($p<0.05$), hence statistically significant. Duration of sensory blockade in both group B and group M. the mean duration of sensory blockade $p<0.05$ hence statistically significant. ($t = 18.5918$, $p= 0.000$, statistically significant). The mean duration of maximum motor blockade p value is 0.0004 it is statistically significant. (T=3.693, P value-0.0004, highly significant). The duration of analgesia in both the groups p value is 0.000 ($p<0.05$), hence statistically highly significant. (t=32.4063, P value-0.000, Significant) (Table 2).

Table 1: Demographic distribution

Age in years	Group B	Group M
Below 30	13	18
31-40	14	14
41-50	12	12
51-60	11	6
Mean age in years ± SD	40.14±11.6023	49.72±11.708
Sex (Group)		
Male	34	33
Female	16	17
Maximum Sensory level		
T6	2	9
T7	9	17
T8	25	21
T9	10	3
T10	4	0

Table 2: Variables in study

Onset of Sensory Blockade	Range	Mean	SD
Group –B	4-6	4.62	0.62
Group –M	2-6	3.26	1.01
Duration of sensory blockade (mins)			
Group –B	86-98	89.1	2.95
Group –M	106-140	118.94	10.83
Duration of motor blockade (mins)			
Group –B	135-210	163.32	16.6
Group –M	148-250	180.24	27.40
duration of analgesia			
Group –B	110 to 142	125.46	7.18
Group –M	173 to 273	243.26	24.41

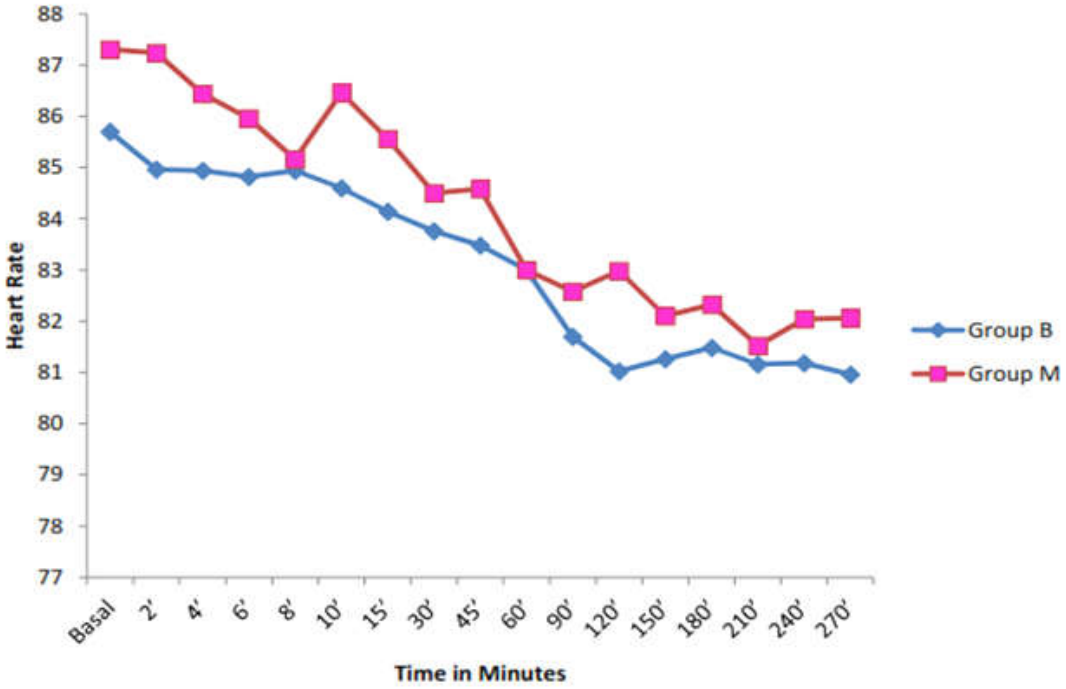

Fig. 1: Heart rate in both groups

Heart rate is not significant in comparision in both groups

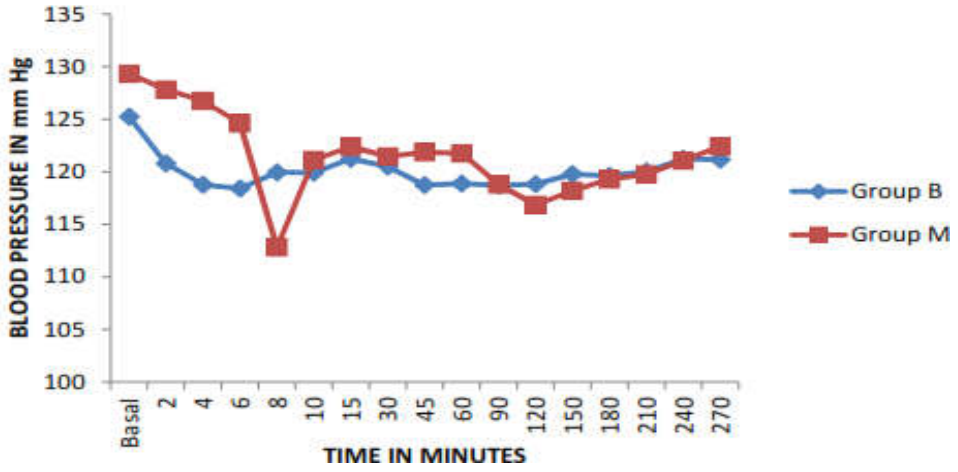

Fig. 2: Mean Systolic blood pressure (mm of Hg).

Systolic blood pressure is not significant in comparision in both groups

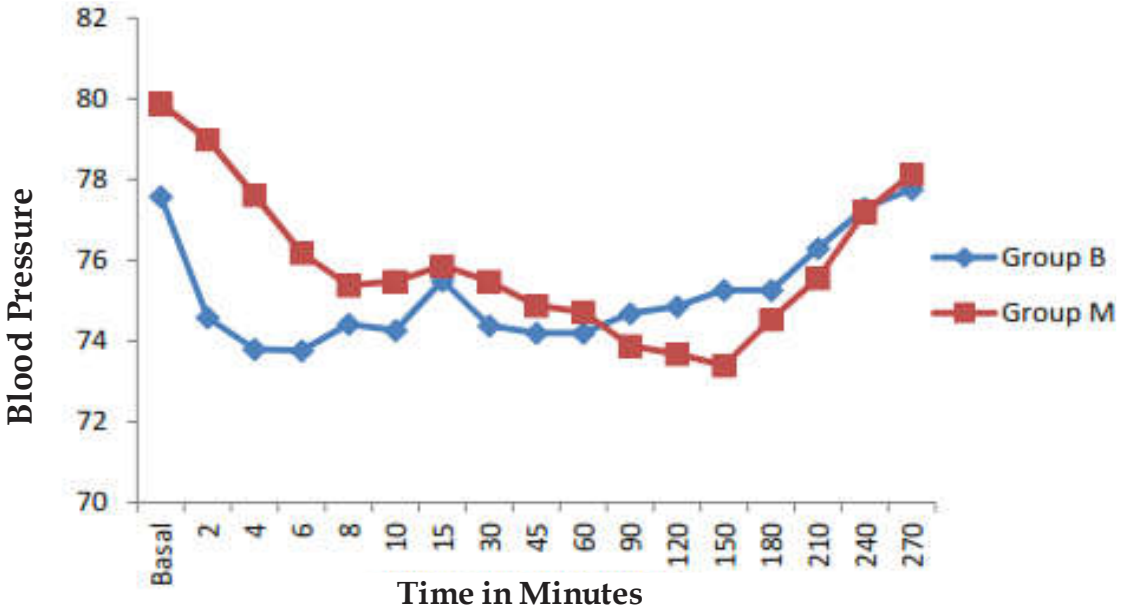

Fig. 3: Mean Diastolic blood pressure (mm of Hg).

Mean Diastolic blood pressure is not significant in comparision in both groups

Table 3: Time of first voiding and VAS score

Group	Duration of first voiding (mins) Range	Mean	SD
B	225-400	285.56	38.10
M	236-410	295.06	55.74
VAS (Scores)			
B	3-5	3.98	1
M	3-5	3.6	0.6

The mean duration of first voiding time is 285.56 ± 38.1 minutes in group B and 295.06 ± 55.74 in group M. Since p value is >0.05, this is statistically not significant. (t=0.98473, p=0.3275, not significant). The Visual Analogue score for effectiveness of pain relief is shown in the table. In group B, the mean VAS score is 3.98 ± 1 and in group M, it is 3.6 ± 0.6. The t value is 2.869 and the p value is 0.005, hence there is statistical significance between them. The complications (side effects) encountered in the group B and M. In group B, 3 patients had bradycardia, 3 patients had hypotension, and 2 patients had nausea and vomiting. In group M, 2 patients had bradycardia, 3 had hypotension, and 3 patients had nausea. Here p= 1.86 and hence there is no statistical difference between the groups. (Table 3).

Discussion

The subarachnoid blockade is the common form of centrineuraxial blockade performed for lower limb and lower abdominal surgeries. The ensuing nerve block ensures the patient well being, while motor block facilitates the surgeon's work. 0.5% hyperbaric bupivacaine produces longer duration of anaesthesia with good muscle relaxation. It provides effective pain relief in initial post-operative period. In order to maximize post operative analgesia, a number of adjuvants have been added to spinal local anaesthetics. Midazolam is a newer water soluble imidazo-benzodiazepine derivative which has been tried since early 1980's. It had been tried widely and antinociceptive effect with neurological safety had been well established in animals and humans. The present clinical study is a randomized prospective study in 100 patients belonging to age group 18 to 60 years of both the sexes and of ASA Grade I and II who were scheduled to undergo various elective lower limb orthopaedic surgeries under subarachnoid anaesthesia. The patient group B received 3.0mL of 0.5% hyperbaric bupivacaine and the patient Group M received 3.0mL of 0.5% hyperbaric bupivacaine with 0.2mL (1mg preservative free) midazolam intrathecally. The result of the present clinical study were discussed under the following headings.

Time of Onset of Sensory Blockade

In present study, the time for onset of sensory blockade for the two groups was not statistically significant when compared. In Group B, it was 4.62±0.62 minutes were as in Group M it was 3.26±1.06 minutes, Were p value 0.000 p<0.05) significant. So the addition of the midazolam to bupivacaine has made apparent difference with regard to time of onset.

Vaswani et al [6] have reported that the addition of midazolam intrathecally has reduced the onset of sensory blockade from 3'41''±0.41 minutes in control group (groupI) to 2.00±0.25 minutes in midazlam group (Group II) (p<0.001). The results of present study are consistent with Vaswani et. al. [6] with regards to onset time.

Duration of Sensory Blockade

The study conducted by Batra Y. K et. al. [7] showed that the duration of sensory blockade being increased from 229.8±41.4 minutes in bupivacaine group to 267.6±67.38 minutes in midazolam group with p value<0.05 and thus, being statistically significant. In present study the duration of sensory blockade was prolonged from is 89.1±2.95 minutes in group B to 118.94±10.83 minutes in Group M and it was found to be statistically significant as p<0.05. It can be attributed to the lipophilicity of midazolam and its synergism with local anaesthetics. The benzodiazepines and exert their antinociceptive effect at the spinal cord by different mechanism. Midazolam excerts its action through GABA on getting bound, opens ligand gated chloride channels. Chloride conductance is increased leading to hyperpolarisation and presynaptic inhibition of afferent terminal in spinal cord and hence reduction in neuronal activity [4]. Our study consistent with both Batra et. al. [7] with regards to duration of sensory blockade.

Duration of Maximum Motor Blockade

The study of Batra et. al. [8]on the patients undergoing knee arthroscopy, reported that the mean ambulation time as a measure of complete recovery from motor blockade was 242±30.9 minutes in the bupivacaine group and 258.3±25.4 minutes in Midazolam group (p >0.05). This study shows that intrathecal midazolam has no significant effect on motor blockade. In present study, the duration of maximum motor blockade in group B is 163.3±16.6 with a range of 135 to 210 minutes, and 180.24±27.40 minutes in group M with a range being 152 to 245 minutes. As p value is 0.0004 it is statistically not significant. The results of our study are consistent with that of Batra et al [7] with respect to maximum duration of motor blockade.

Duration of Analgesia

Midazolam is a potent short acting benzodiazepine in aqueous solution has been reported to provide antinociceptive effect in animals and in humans. M.H Kim and Y.M. Lee [8] Anjana Sen. et. al. [9], Batra Y.K et. al. [7], Nidhi Agarwal et al [10] and Bharti N et. al. [11] and Vaswani et. al. [6] showed that the mean duration of analgesia significantly prolonged in patients receiving intrathecal midazolam. In present the duration of analgesia was prolonged from 125.46±7.18 minutes in bupivacaine group to 243±24.41 minutes in midazolam group. This is statistically highly significant as p value is 0.000.

Time of First Voiding

The early trials conducted by Goodchild and Nobel [3] showed that the intrathecal administration of midazolam causes depression of sympathetic nervous system activity in humans. The study of Batra et. al. [7] showed no difference in the time of first voiding in control group (252±29.8minutes) and in study group (258.8±25.4) (p>0.05). Kim et. al. [8] reported that time to the episode of first self-voiding (control group:4.99h, BM1 group:4.95h, MB2 group:5.31h), was similar in all groups. The analgesic effect of intrathecal midazolam was segmental, with no alteration in sympathetic tone or reflexes.

In present study, the time of first voiding, when compared with two groups were statistically not significant. The time of first voiding is 285±38.10 minutes in group B and 295.06±55.74 minutes in group M (p= 0.3275) (p<0.05 to be statistically significant). The results of our study are consistent with the study of Batra et. al. [7] and Kim et. al. [8]. In the present study the sedation score ranged from 0 to 1 in both the groups.

Most of the patients in group M were calm and sleeping comfortably were as most of the patients in the group B were awake and alert. Midazolam is used in a variety of clinical setting for pre and post operative settings for sedation. The studies of have shown that the sedation scores were higher in the patients receiving midazolam the epidural or intrathecal route. Vaswani et. al. 6 reported that sedation was earlier with maximum sedation level of short duration if midazolam is given

intravenously. The sedation scores were less but more sustained when the midazolam is administered intrathecally. Anjana Sen et. al. [9] also reported the higher sedation scores with intrathecal midazolam.

Conclusion

It can be inferred that inj. midazolam 1 mg in combination with inj.bupivacaine 0.5% hyperbaric can be safely administered intrathecally for better postoperative analgesia.

References

1. Cousins MJ, Mathes LE. Intrathecal and epidural administration of opioids. Anaesthesiology 1984;61: 276-310.
2. D. Niv, J.G Whitwam and L. Loh. Depression of nococeptive sympathetic reflexes by the intrathecal administration of midazolam. Br J Anaesth 1983;55: 541-46.
3. C.S Good Child, Noble J. The effects of intrathecal midazolam on sympathetic nervous system reflexes in man - A pilot study. J clin pharmacol, 1987 Mar;23(3):279-285.
4. M.Edwards, J.M Serro and C.S Good Child. On the Mechanism by which Midazolam Causes Spinally Mediated Analgesia. Anaesthesiology, 1990;73: 273-277.
5. Juliet M. Serro, Ray L. Marks, Stephen J. Morley and Colin S. Goodchild. Intrathecal midazolam for the treatment of chronic mechanical low back pain: a controlled comparision with epidural steroid in pilot study. Pain, 1992 Jan;48(1):5-12.
6. RK Vaswani, Lalit Kumar Raiger, Richa Purohit and Pramila Bajaj. The Effect of Intrathecal Midazolam on Postoperative Pain Relief in Orthopaedic Surgery. Hospitals Today. 2002;4:150-153.
7. Y.K. Batra, K Jain, P Chari, M.S. Dhillon, B.Shaheen and G.M Reddy. Addition of intrathecal midazolam to bupivacaine produces better post -operative analgesia without prolonging recovery. Int. J .Clin Pharmacol Ther. 1999 Oct;37(10):519 -23.
8. M.H. Kim and Y.M. Lee. Intrathecal midazolam increases the analgesiceffects of spinal blockade in patients undergoing haemorrhoidectomy. Br J Anaesth, 2001;86(1):77-9.
9. Anjana Sen, A.Rudra, santhosh Kumar Sarkar, B Biswas. Intrathecal Midazolam for Postoperative Pain Relief in Caesarian Section Delivery. J Indian med; Assoc, 2001;99(12):683-86.
10. Nidhi Agarwal, A. Usmani, R Sehgal, Rakesh Kumar and Poonam Bhadoria. Effect of intrathecal midazolam bupivacaine combination on post operative analgesia. Indian J Anaesth 2005;49(1):37-39.
11. Bharti N, Madan R, Mohanty PR, Kaul HL. Intrathecal midazolam added to Bupivacaine improves the duration and quality of spinal anaesthesia. Acta Anaesthesiol Scand 2003;47(9):11101-5.

Original Research Article

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To Study the Prognostic Value of Shock Index in Patients Presenting with Severe Sepsis and Septic Shock

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Abstract

Objective: Sepsis is a problem that presents a management challenge and its early recognition and intervention clearly improves the outcome. Development of cost effective clinical parameters that would effectively prognosticate the outcome of sepsis would be invaluable. Shock Index, defined as ratio of heart rate (HR) and systolic blood pressure (SBP) may be a good non invasive measure of haemodynamic instability than HR and SBP alone. We conducted a study-

1. To calculate shock index in patients with severe sepsis and septic shock at 0, 2 and 6 hours of admission .

2. To assess whether shock index (SI) at 0,2 and6 hours has any prognostic significance in patients of severe sepsis and septic shock.

Methods: Records of 57 patients from August 2015 to January 2016 were collected from Medical Records Department of the hospital and clinical data recorded. Shock index (SI) was calculated at 0, 2 and 6 hours. The patients were divided into two groups according to their outcome as Survival or Death. Mann Whittney test , Pear on coefficicent and Kaplan Mieir Survival analysis curve were used for calculations.

Results: SI at 2 and6 hours significantly predicts mortality with pvalue of 0.001 and 0.0014 respectively. The best predictor of mortality is where SI at 2 hours or 6 hours is greater than their cut off points .

Conclusion: From the present study, it may be concluded that SI at 2,6 hours was clinically relevant and easily calculated predictor of mortality.

Keywords: Sepsis; Prognosis; Shock Index.

Introduction

Sepsis is a major cause of mortality and morbidity throughout the world. Sepsis patients represent only 2% hospital admission but lead to an estimated 17% of in hospital deaths [1]. It is projected that sepsis patients in USA will increase by 1.5% per annum indicating an increase of additional 1 million sepsis patients by the year 2020 in USA alone [2]. The increasing number of sepsis patients imposes a financial burden to not only developing countries but also developed nations like USA. Average treatment cost of sepsis patient in a general intensive care unit in United Kingdom was USD$10,622 in the year 1998 [3].

Development of cost effective and easily available clinical parameters that would effectively prognosticate the outcome of sepsis would be invaluable. The shock index (SI) is defined as heart rate divided by systolic blood pressure with a normal range of 0.5 to 0.7 in healthy adults.This index was first introduced by Allgower and Buri [4] in 1967 as simple and effective tool in gauging hypovolemia in haemorrhagic and infectious shock state. Birkhan [5]

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studied shock index to identify ectopic pregnancy. And Rady et al [6] used it for evaluation of clinical shock in emergency department. There is paucity of data in role of of Shock Index in sepsis. We have conducted a retrospective observational study to prognosticate the value of shock index in patients presenting with severe sepsis and septic shock

Aims and Objectives

1. To calculate shock index in patients aged 12 to 70 years with severe sepsis and septic shock at 0, 2 and 6 hours of admission to emergency department.
2. To assess whether shock index (SI) at zero,two and six hours has any prognostic significance in patients of severe sepsis and septic shock.

Study Design

Retrospective observational pilot study. Records of 57 patients from August 2015 to January 2016 were collected from Medical Records Department of the hospital and data with respect to Demography, Clinical values, Laboratory values. The patients were divided into two groups according to their outcome as Survival or Death.

Materials and Methods

A retrospective observational study was conducted. Records of 57 patients from August 2015 to January 2016 were collected from Medical Records Department and data with respect to Demography, vitals, Laboratory values was observed. Shock index (SI) was calculated at zero (S1), two (S2) and six (S3) hours.

Inclusion Criteria

1. Patients aged 12 years to 70 years
2. Patients who had at least two of the four SIRS criteria and fulfilled requirements for either severe sepsis or septic shock.

SIRS Criteria's

- Body temperature less than 36°C or greater than 38°C
- Heart rate greater than 90 beats per minute
- Respiratory rate greater than 20 breaths per minute or, an arterial partial pressure of carbon dioxide less than (32 mmHg).
- White blood cell count less than 4000 cells/mm^3 (4 x 109 cells/L) or greater than 12,000 cells/mm^3 (12 x 109 cells/L), or the presence of greater than 10% immature neutrophil band forms.

Requirements for Severe Sepsis Patients

i. Fulfilling at least 2 or more of SIRS criteria

ii. Has an associated or suspected source of infection

iii. Has one or more of the following

- Evidence of end organ damage (eg. Elevated creatinine levels, > 120 µmol/L or altered mental status, GCS < 14)
- Serum lactate levels of equal or > 4mg/dL)
- Episode of hypotension (<90/60 mmHg), which responds to initial fluid resuscitation

Requirements for Septic Shock Patients

i. Fulfilling at least 2 or more of SIRS criteria.

ii. Has an associated or suspected source of infection.

iii. Has persistent hypotension (<90/60 mmHg) which does not respond to adequate fluid resuscitation (adequate fluids referred to as CVP 8-12 cmH20).

Exclusion Criteria's

1. Patients aged < 12 years old.
2. Patients taking medications that have significant atriaventricular blockage effect. (Beta blockers, calcium channel blockers, digoxin and amiodarone).
3. Patients with end-stage malignancie
4. Patients with internal pacemakers.
5. Patients with associated diagnosis of acute coronary Syndrome or with atrial fibrillation.
6. Patients presenting with associated upper gastrointestinal bleeding (having presenting complaints of hematemesis or diagnosed by an OGDS).
7. Patients with imuno-compromised states (on chronic steroid therapy or retroviral disease).

Data was collected manually from case records of medical record department of the hospital as the case records in the hospital are not computerized. Heart rate and systolic blood pressures on arrival, that is, O hour, 2 hour and 6 hour was noted and SI at 0 (S 1), 2 hour (S 2) and 6 hour (S 3), was calculated. Demograhic profile, total leucocyte count, haemoglobin, and diagnosis of the patients included in the study were also recorded.

Statistical Analysis

The patients were divided into two groups according to their outcome as Survival or Death. ROC curve was used to calculate the cut off point of shock index for predicting mortality. Mann Whittney test was used to compare qualitative variables. Pearso on coefficicent and Kaplan Mieir Survival analysis curve were used for calculation of correlation and OS respectively.

Sample Size

Formula used is:

		Disease +	
Test	+	*a*	*b*
		e	*d*
		(a+c)	*(b+d)*

$$n = \frac{Z^2 \quad P(1 \quad P)}{2} \qquad (1)$$

n will be *(a+c)* if we use Sensitivity ad *P*, and n will be *(b+d)* if we use Specificity as *P* in formula (1).

$$N = \frac{(a+c)}{Prevalence} \qquad (2)$$

$$N = \frac{(b+d)}{(1 \quad Prevalence)} \qquad (3)$$

Where Zis value of Z at two sided alpha error of 5% and is desired precision.

Result

A total of 57 patients were studied. Demographic profile of the patients is as follows:

1. *Males*: Females	26 : 31
2. Age Range	12 to 70
3. Median Age	35

In our study group, 18 patients were admitted under Obstetrics and Gynaecology, 24 patients underMedicine and 15 patients under Surgery department. There were 20 (35.08%)patients with gastrointestinal causes, 12 (21.05%) patients of pneumonia and chest infections, 10 (17.54%) patients of different types of abortion, 8 (14.03%) patients of other obstetric and gynaecological diagnosis and 7 (12.28%) other infections. There were 28 deaths and 29 survivors.

Shock index was calculated at 0 hour (S1), 2 hours (S2) and 6 hours (S3) and it was found that s1 does not predict mortality whereas s2 and s3, that is Shock Index at 2 hours and 6 hours significantly predicts mortality. P<0.001 and p<0.0014 respectively (Table 2). Haemoglobin and total leukocyte count (WBC) was correlated with shock index and it was observed that Only Shock index at 6 hours is significantly positively correlated with WBC as WBC Increases, Shock index also increases with correlation coefficient of .2972 (Table 1).

Figures 1, 2, 3 and 4 show ROC curves against S1, S2 and S3. ROC analyses sensitivity reflecting an objective measure of performance for a diagnostic test. It analyses sensitivity , compares true positive versus false positive rate.

Pearson co-efficicent and Kaplan Mieir Survival analysis curve were used for calculation of correlation and OS respectively.

Table 3 and Figures 5, 6 and 7 show Kaplan Mier Survival analysis and Table 4 shows logistic regression. We observed that S2, S3 and S2+S3 are the significant predictors of mortality.

Only Shock index at 6 hours is significantly positively correlated with WBC as WBC Increases, Shock index also increases with correlation coefficient of .2972.

Shock Index at 0 hour does not predict mortality with non significant p value

Shock Index at 2 hours and 6 hours significantly predict mortality.

Table 1: Correlation of Parameters with shock index

	Correlation coefficient r	P value	95% Confidence interval for r
S1(Log) with Hb	-0.1622	0.228	-0.4056 to 0.1027
S1(Log) with WBC(Log)	0.1493	0.2676	-0.1158 to 0.3945
S2(Log) with Hb	0.078	0.5641	-0.1864 to 0.3318
S2(Log) with WBC(Log)	0.2566	0.054	-0.004210 to 0.4848
S3(Log) with Hb	-0.04111	0.7614	-0.2985 to 0.2218
S3(Log) with WBC(Log)	0.2972	0.0248	0.03967 to 0.5177

The best predictor of mortality is when any of shock index at 2 hours or 6 hours is greater than cut off point with minimum standard error. 053 and maximum AUC. Figure 1 Figure 2 Figure 3.

The risk of mortality in S2 (>1), S3 (>.8491) and S2 (>1) or S3 (>.849) are significantly higher with odds ratio of 9.6, 8.5 and 13.3 respectively.

Table 2:

	Area under the ROC curve (AUC)	Standard Error	95% Confidence interval	P value	Cut off point	Sensitivity	Specificity
S1	0.624339	0.0813	0.486123 to 0.749164	0.1261	>1.2	57.14	69.44
S2	0.732804	0.0706	0.599027 to 0.841333	0.001	>1	76.19	75
S3	0.734127	0.0733	0.600449 to 0.842410	0.0014	>0.8491	80.95	66.67
S2(>1) or S3(>.849)	0.744048	0.053	0.611156 to 0.850441	<0.0001		90.48	58.33

Table 3:

	OS for 1 month	Mean of survival time	Median of survival time	P value
Shock Index at 0 hours				
S1>1.2	0.00%	13.97	15	0.201
S1<=1.2	45.15%	17.63	15	
Shock Index at 2 hours				
S1>1	0.00%	11.30	8	0.003
S1<=1	36.28%	19.36	19	
Shock Index at 6 hours				
S1>.849	0.00%	13.20	10	0.016
S1<=.849	0.00%	16.38	19	

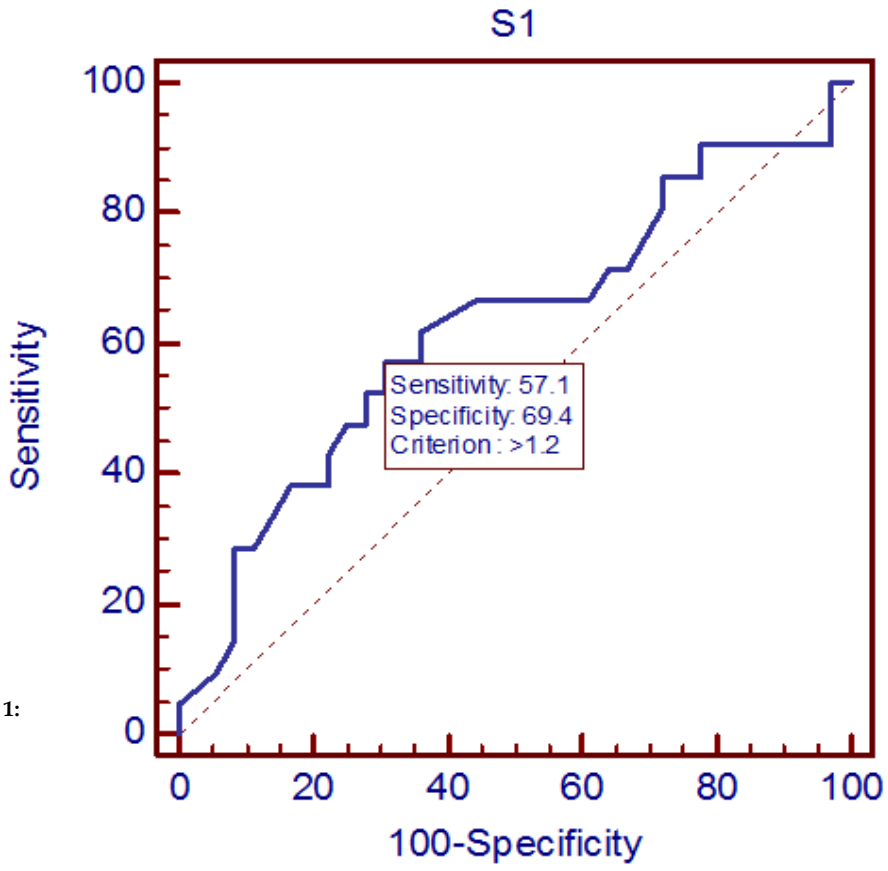

Fig. 1:

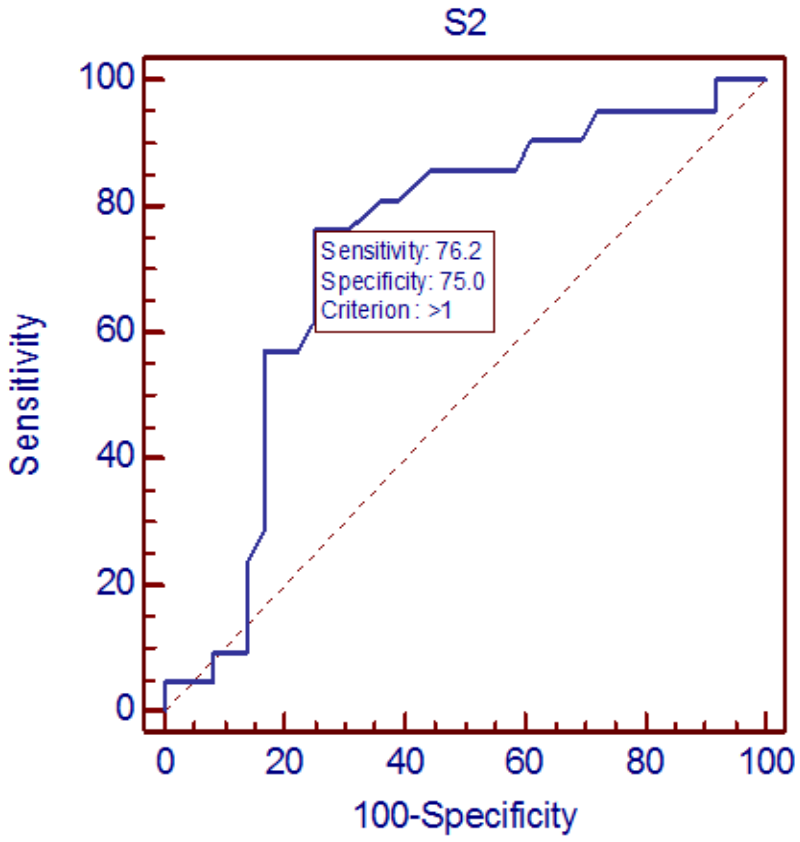
S2
Sensitivity: 76.2
Specificity: 75.0
Criterion : >1
Sensitivity
100-Specificity
0
20
40
60
80
100

Fig. 2:

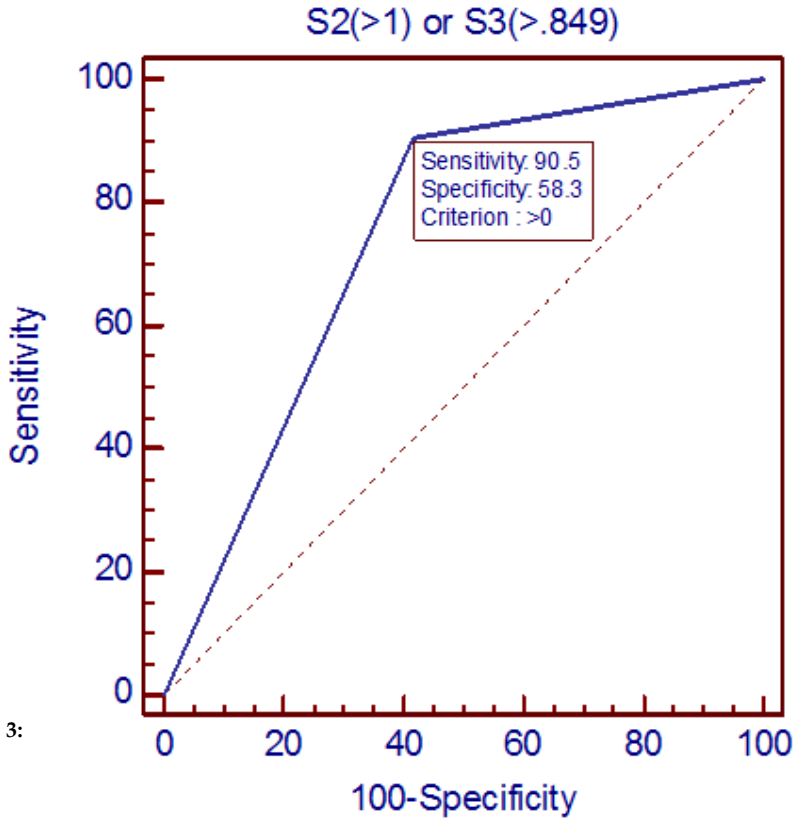
S2(>1) or S3(>.849)
Sensitivity: 90.5
Specificity: 58.3
Criterion : >0
Sensitivity
100-Specificity
0
20
40
60
80
100

Fig. 3:

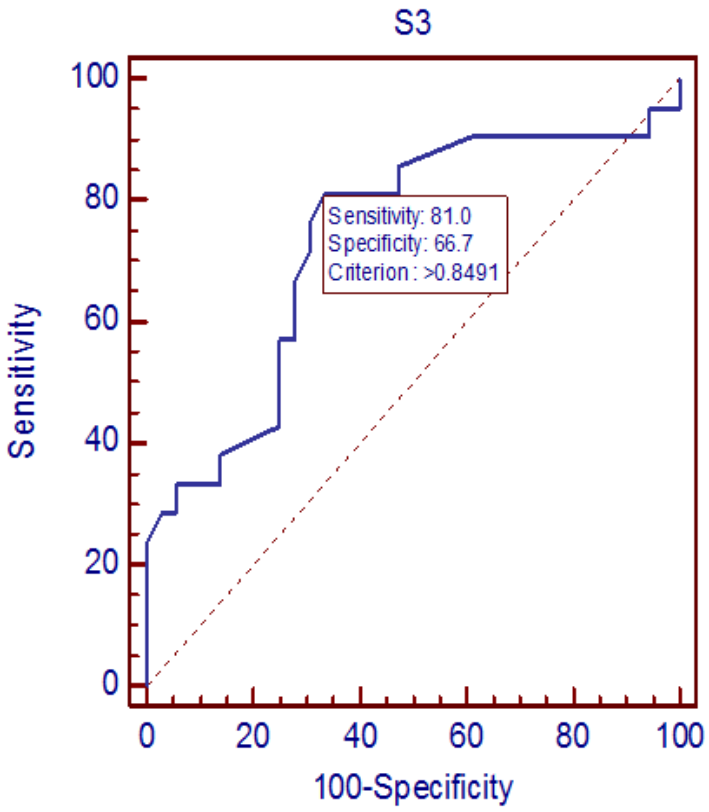
S3
Sensitivity: 81.0
Specificity: 66.7
Criterion : >0.8491
Sensitivity
100-Specificity
0
20
40
60
80
100

Fig. 4:

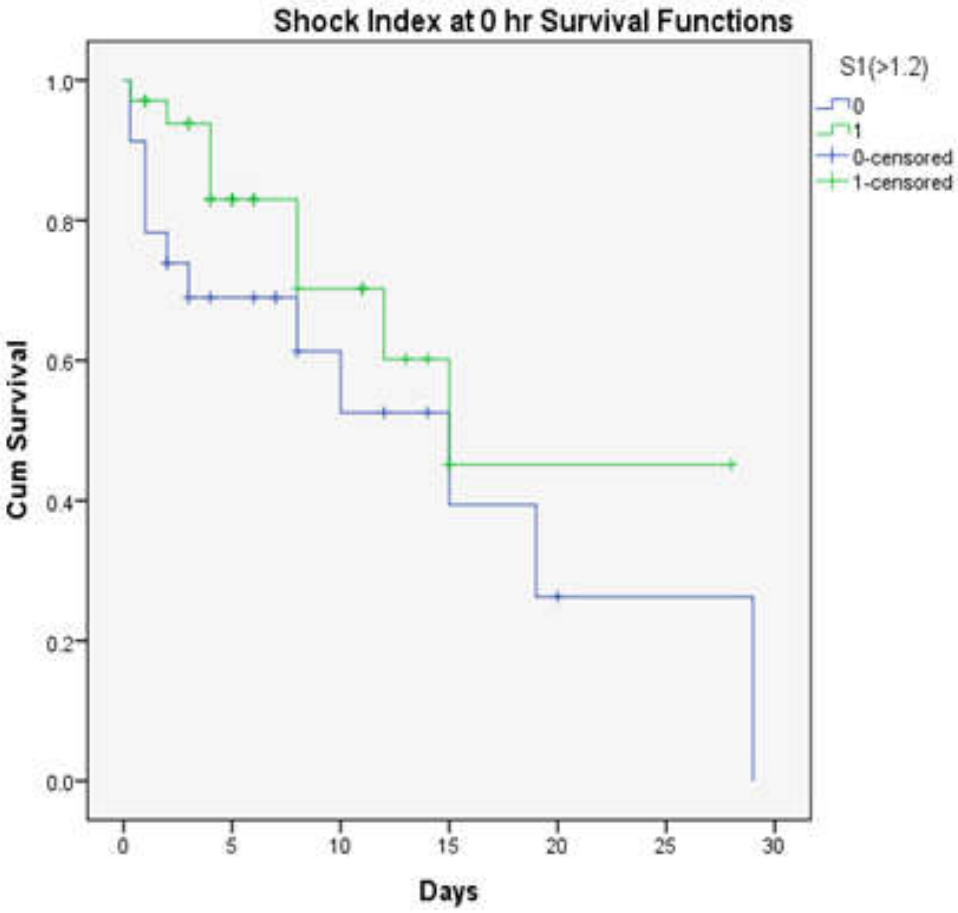
Shock Index at 0 hr Survival Functions
S1(>1.2)
0
1
0-censored
1-censored
Cum Survival
Days
0.0
0.2
0.4
0.6
0.8
1.0
0
5
10
15
20
25
30

Fig. 5:

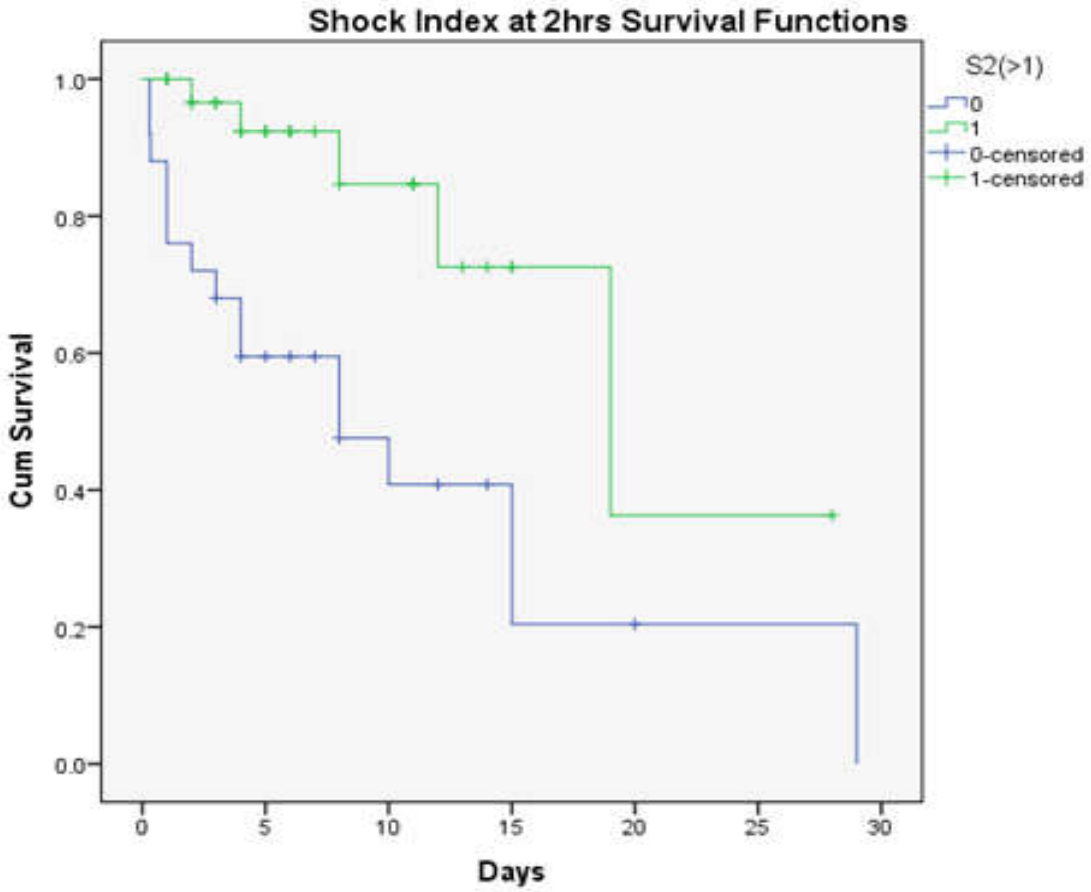
Shock Index at 2hrs Survival Functions
S2(>1)
0
1
0-censored
1-censored
Cum Survival
1.0
0.8
0.6
0.4
0.2
0.0
0
5
10
15
20
25
30
Days

Fig. 6:

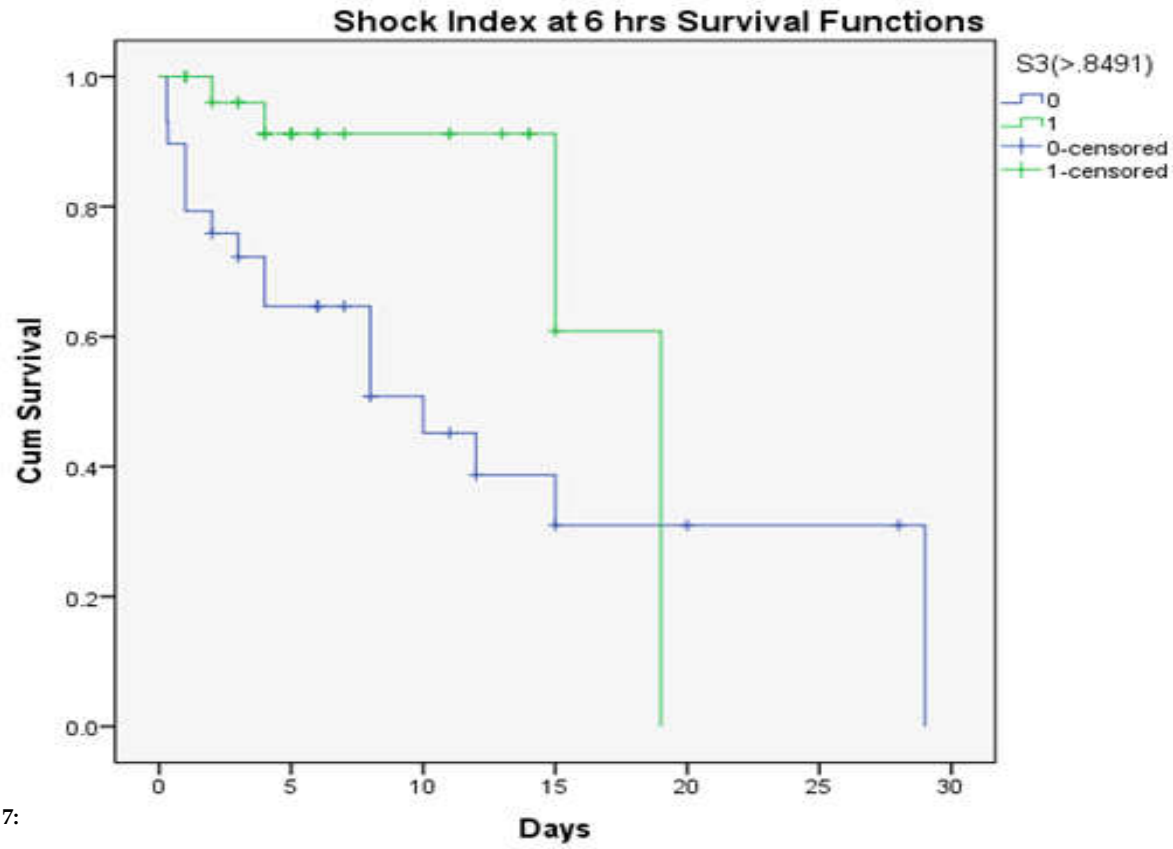
Shock Index at 6 hrs Survival Functions
S3(>.8491)
0
1
0-censored
1-censored
Cum Survival
1.0
0.8
0.6
0.4
0.2
0.0
0
5
10
15
20
25
30
Days

Fig. 7:

Table 4: S2, S3 and S2+S3 are the significant predictors of mortality

	B	S.E.	P value	Odds ratio	95% C.I. for odds ratio Lower	Upper
S2(>1) or S3(>.849)	2.588	.817	.002	13.300	2.684	65.915
S3(>.8491)	2.140	.659	.001	8.500	2.338	30.908
S2(>1)	2.262	.641	.0004	9.600	2.734	33.708
S1(>1.2)	1.109	.570	.052	3.030	.991	9.269

Discussion

Sepsis is a cause of high mortality among admitted patients [1]. It has increased financial burden in developed and developing nations [3]. Need of the hour is to effectively manage these patients and cut down the cost of treatment without compromising the health of patients. Shock Index is easy to use, accurate, cost effective bedside tools for early diagnosis of sepsis [7].

We observed that Shock index at 2 hours and 6 hours significantly predicts mortality in a patient with sepsis or septic shock whereas SI at 0 hour does not predict mortality. Our findings were consistent with Mohd Yusuf et. al. [8]. They tested seven clinical parameters to prognosticate the outcome in sepsis, namely, Shock index at presentation, shock index at 2 hours, Age, gender Temperature, Heart Rate and Respiratory Rate. They found that shock index at presentation and shock index at two hours were significant variables but shock index at 2 hours is more sensitive predictor as compared to shock index at presentation.

Utility of SI in predicting mortality among community acquired pneumonia was studied by Myint et al [9] but they did not include serial readings and based their findings on single finding, that is, SI at 0 hour. Zarzaur et al [10] also included single reading of shock index in their study involving mortality in trauma patients.

Isaac B et. al. [11] collected vital signs at 4 hourly interval from admission to discharge from ICU. They defined a "sustained SI elevation" as having an SI greater than 0.7 for at least 50% of the readings and concluded that sustained elevation of the SI is associated with increased morbidity and mortality in patients admitted to the ICU with severe sepsis.

In the present study we correlated WBC count and haemoglobin with shock index and found Only Shock index at 6 hours is significantly positively correlated with WBC as WBC Increases, Shock index also increases with correlation coefficient of .2972. Tony B(2013) [12] repored that an elevated shock index(0.7) performed identically to full SIRS criteria (including WBC) and low risk patients with normal SI may forgo (or not urgently need) routine triage laboratory screening for sepsis, especially from triage and before full evaluation.

These results taken together confirm that SI can be applied in clinical practice and the immediate clinical relevance of our findings is that SI, Shock Index, is cost effective and easily available clinical parameter which can prognosticate sepsis.

Conclusion

From the present study, it may be concluded that SI at 2, 6 hours was clinically relevant and easily calculated predictor of mortality. It should be added to heart rate and systolic blood pressure, allowing for early recognition of severe sepsis and septic.

References

1. Hall MJ, Williams SN, DeFrances CJ, et. al. Inpatient Care for Septicemia or Sepsis: A Challenge for Patients and Hospitals. U.S. Department of Health and Human Services - National Center for Health Statistics. 2011;62:1–7.
2. Angus DC, Linde-Zwirble W, Lidicker J, et. al. Epidemiology of Severe Sepsis in the United States: Analysis of Incidence, Outcome, and Associated Costs of Care. Crit Care Med. 2001;29:1303–10. [PubMed].
3. Edbrooke DL, Hibbert CL, Kingsley JM, et. al. The patient-related costs of care for sepsis patients in a United Kingdom adult general intensive care unit. Crit Care Med 1999;27:1760-7.
4. Allgöwer M, Buri C. Schockindex. Deutsche Medizinische Wodenschrift. 1967;46:1–10.
5. Birkhahn Robert H, Theodore J Gaeta, Shawn K Van Deusen, John Tloczkowski. The ability of traditional vital signs and shock index to identify ruptured ectopic pregnancy. American Journal of Obstetrics and Gynecology 2003;189(5):1293.
6. Rady M, Nightingale P, Little R, et al. Shock Index: A Re-evaluation in Acute Circulatory Failure. Resuscitation. 1992;23:227–34. [PubMed].

7. Haas H. Outils de triage aux urgencies pédiatriques. Archives de Pédiatrie. 2005;12:703–05. [PubMed].
8. Mohd Yussof SJ, Zakaria MI , Mohamed FL, Bujang MA, Lakshmanan S, Asaar AH Value of Shock Index in Prognosticating The Short Term Outcome of Death for Patients Presenting With Severe Sepsis and Septic Shock in The Emergency Department Med J Malaysia, 2012;6(4):406-12.
9. Myint, Phyo K. Patrick Musonda, Prasanna Sankaran, Deepak N. Subramanian, Hannah Ruffell, Alexandra C. Smith, Philippa Prentice, Syed M. Tariq, Ajay V. Kamath. Confusion, Urea, Respiratory Rate and Shock Index or Adjusted Shock Index (CURSI or CURASI) criteria predictmortality in community-acquired pneumonia. European Journal of Internal Medicine 2010;21(5):429-33.
10. Zarzaur Ben L., Martin A. Croce, Peter E. Fischer, Louis J. Magnotti, Timothy C. Fabian. New Vitals After Injury: Shock Index for the Young and Age x Shock Index for the old. Journal of Surgical Research 2008;147(2):229-36.
11. Isaac B, April SJoylene T Alem M. Shock Index and Outcomes in Patients Admitted to the ICU With Sepsis. Chest. 2015;148(4)supplement:337A.
12. Tony B, Jeffrey G, Timothy H, Yolanda H, Nidhi G, Alison S, Edward P, Nathan S. Shock Index and Early Recognition of Sepsis in the Emergency Department: Pilot Study. West J Emerg Med 2013Mar;14(2):168-74.

Original Research Article

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Comparison of Bupivacaine 0.375% and Ropivacaine 0.375% in Supraclavicular Block under Ultrasound Guidance for Upper Limb Surgeries

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Abstract

Background: Regional anesthesia is comparatively safer than general anesthesia. Regional anesthesia can be safely used in outpatient anesthesia, patients with full stomach, diabetic patients, associated cardiac, pulmonary, hepatic or renal damage and polytrauma. Bupivacaineroutinely used has side effects relatedto cardiovascular and central nervous system. Ropivacaine a recent addition has the ability to produce differential blockade with less motor blockade and reduce cardiovascular and neurological toxicity. Ultrasound imaging has increased the success rate and has helped in reducing the complications as it gives real time visual image.

Materials and Methods: A prospective, randomized single blinded study was undertaken in patients posted for upper limb surgeries under Supraclavicular block under ultrasound guidance. 60 patients of ASA class I and II were randomly grouped into two groups. Group R will receive 30ml Ropivacaine 0.375% and Group B will receive 30ml of Bupivacaine 0.375% in supraclavicular brachial plexus blockade. Onset of motor and sensory blockade, duration of motor, sensory blockade and duration of post-operative analgesia were studied. Hemodynamic changes over time were recorded.

Results: Group R patients had earlier onset of sensory and motor block compared to Group B patients. There was no difference in duration of sensory and motor block and duration of analgesia between both the groups.

Conclusion: Ropivacaine is a safer alternative to Bupivacaine with earlier onset of both sensory and motor block and if used along with ultrasound guidance has a higher success rate and lowers the incidence of complications

Keywords: Brachial Plexus; Bupivacaine; Ropivacaine; Ultrasound.

Introduction

Regional anesthesia is comparatively safer than general anesthesia. Regional anesthesia has some advantages over general anesthesia such as it can be used in outpatient anesthesia, for patients with full stomach, for diabetic patients, associated cardiac, pulmonary, hepatic or renal damage and polytrauma. Regional nerve blocks are based on the concept that pain is conveyed by nerve fibers, and the transfer of pain can be interrupted along their pathway. Other important advantages are postoperative analgesia, early ambulation, no airway manipulation, early resumption of oral feeding and decreased postoperative pulmonary, gastrointestinal and thrombo-embolic complications [1]. More over regional anesthesia offers ideal operating conditions by producing complete muscle relaxation, stable intraoperative hemodynamics and the associated sympathetic block.

Brachial plexus blocks are among the most commonly performed peripheral neural blocks for upper extremity surgeries. Supraclavicular blocks are the most commonly performed brachial plexus blocks

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as the typical feature of these blocks include rapid onset, predictable and dense anesthesia, along with its high success rate [2]. Bupivacaine which is routinely used nowadays is known for its wide and unpredictable latency of nerve block when small volume of local anesthetic solution is injected and associated with a number of side effects, including cardiovascular and central nervous system toxicity. Ropivacaine which is a recent addition has the ability to produce differential blockade with less motor blockade and reduced cardiovascular and neurological toxicity [3].

The first supraclavicular brachial plexus block was performed in 1912 by Kulen Kampff. The conventional paresthesia technique being a blind technique may be associated with higher failure rate and injury to nerves and surrounding structures. Ultrasound (US) visualization of anatomical structure is the only method offering safe blocks of superior quality by optimal needle positioning. US allows direct visualization of peripheral nerves, the block needle, and local anesthetic distribution

The first literature description of the use of ultrasound for supraclavicular block was by La Grange and colleagues in 1978 for needle positioning. In the conventional technique the insulated needle is advanced near to the nerve blindly and the anesthetic delivered. It has the disadvantage of vascular and nerve injury and pulmonary complications such as pneumothorax. Ultrasound guidance provides real time images and the advantage to minimize complications. After skin and transducer preparation, a linear 38 mm, high frequency 10-15 MHz transducer is placed firmly over the supraclavicular fossa. Nerves in supraclavicular region appear hypo-echoic and are round or oval. The brachial plexus is identified as a compact group of nerves similar to a bunch of grapes located over the first rib. The needle is advanced along the long axis of the transducer in the same plane as the ultrasound beam. Local anesthetic is injected so as to cause hydro dissection of the nerve [4].

Methods

Sixty patients belonging to ASA I or II, with age between 18 and 65 years were recruited for randomized study. Hospital ethics committee approval and written informed from all patients were taken. The patients posted for surgeries around elbow, forearm and hand were randomized into two groups Group B: 30 subjects will receive 30ml Bupivacaine 0.375% and Group R: 30 subjects will receive 30ml of mixture of Ropivacaine 0.375. Patients who are known to have hypersensitivity reaction to local anaesthetics, patients with coagulopathies, patient who has local infection at the site of proposal puncture for supraclavicular block, pregnant or lactating women are exclude from study. Detailed history, general physical examination and routine investigations were done prior to the day of surgery. Patients were premedicated with Tab. Ranitidine 150mg and Tab.Metoclopramide 10mg and Tab.Alprazolam 0.5mg previous night of surgery orally.

After patient shifted to operation room, large bore IV line secured. Standardmonitoring like ECG, SpO_2, and NIBP were connected and recorded. Thepatient is positioned supine and made to face the contralateral side. After skin and transducer preparation, a linear 38-mm, high frequency 10-15 MHz transducer is placed firmly over the supraclavicular fossa in the coronal oblique plane to obtain the best possible transverse view of the subclavian artery and brachial plexus. Nerves in the supraclavicular region appear hypo-echoic and are round or oval. The brachial plexus is located lateral and superficial to the pulsatile subclavian artery and superior to the first rib. The subclavian artery is identified first the subclavian vein lies more medially. The first rib is identified as a hyper-echoic structure lying deep to the vessels, and giving a bony shadow. The brachial plexus is consistently found lateral and superficial to the subclavian artery and above the first rib. The needle is advanced along the long axis of the transducer in the same plane as the ultrasound beam. This way, the needle shaft and tip can be visualized in real time as the needle is advanced towards the target nerves. Local anaesthetic solution is injected so as to cause hydro dissection of the planes around the plexus. The volume of local anaesthetic used is 30 ml. The onset of anesthesia was evaluated by the pin prick with a 23 gauge needle. The time of onset was defined as the time between injection and complete loss of pinprick sensation. The temperature was tested by using the spirit soaked cotton on the skin. The time of onset of complete sensory blockade was recorded.

Heart rate, noninvasive blood pressure and oxygen saturation were monitored at an interval of 0 min, 5 min, 10 min, 15 min, 30 min, 45 min, 60 min, 90 min, and 2 hrs during the surgery. Duration of sensory block which is the time elapsed between the injection of drug and appearance of pain requiring analgesia and duration of motor block was also recorded.

Sensory block will be graded asGrade 0: Sharp pin felt, Grade 1: Analgesia, dull sensation felt, Grade 2: Anaesthesia, no sensation. Motor blockwill be

determined according to a modified Bromage scale for upper extremities on a 3-point scale. Grade 0: Normal motor function with full flexion and extension of elbow, wrist and fingers

Grade 1: Decreased motor strength with ability to move the fingers only,

Grade 2: Complete motor block with inability to move the fingers.

Duration of motor block is from onset of motor blockade (Grade II) to the time patient could first move their fingers. Duration of sensory block is from onset of sensory blockade (Grade II) to the time of sensory recovery (pin prick). Duration of analgesiais from Grade I sensory block to the first demand of analgesia.

Postoperatively all the patients will be asked to mark their postoperative pain on 0-10 numerical scale [VAS], Where 0=no pain, 1-3=mild pain, 4-6=moderate pain, 7-9=severe pain, 10=worst imaginable pain. Diclofenac sodium intra muscular injection will be used as rescue analgesic whenever patients complained of pain. (First demand for analgesia).

Statistical Analysis

The data thus obtained was compiled and analyzed using Statistical Package for Social services. (SPSS version 20). Quantitative data was analyzed by using student't' test. Qualitative data was analyzed using Chi – Square test. A p value of less than 0.05 was considered as statistically significant.

Results

Time of onset of sensory block

There was significant difference in onset of sensory block between the group B (11.4 ± 2.71) and group R (9.53 ± 2.64) by t test (p = 0.009)

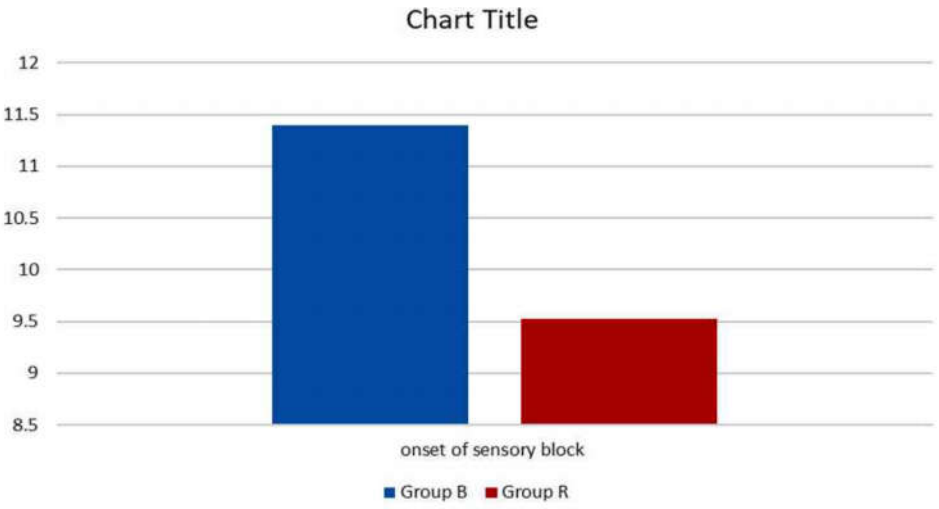

Fig. 1: Comparison onset of sensory block in minutes

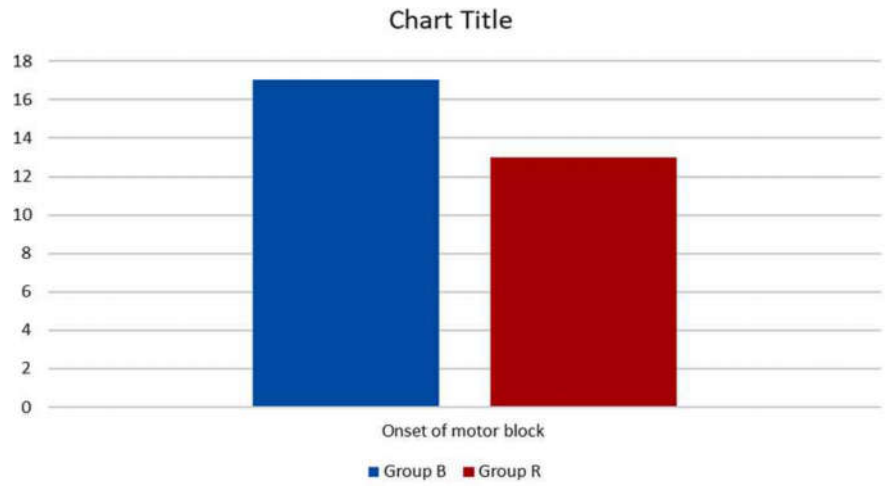

Fig. 2: Comparison of onset of motor block in minutes

Comparison of Motor block onset in minutes (Mean ± SD)

There was significant difference in onset of motor block between the group B (17.03±3.21) and group R (13±3.23). (p = 0.0001).

Duration of Sensory Block in two groups (min) (Mean ± SD)

There was no significant difference in duration of sensory block between the group B (444.5±21.47) and group R (434.67±29.969) by student t test (p = 0.149).

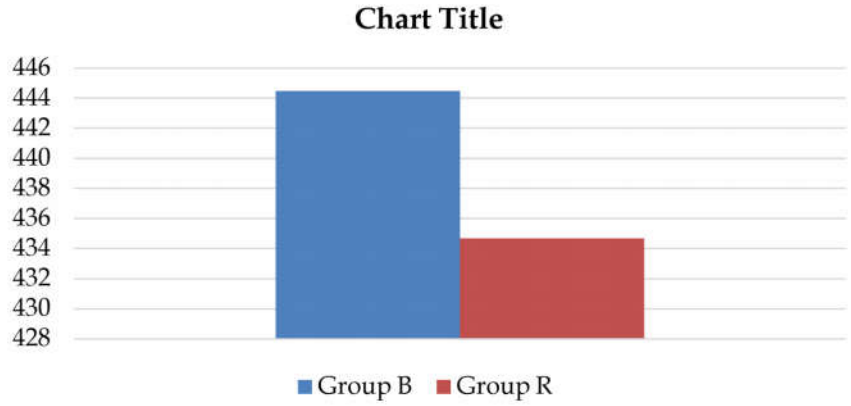

Fig. 3: Mean values of duration of sensory block in two groups

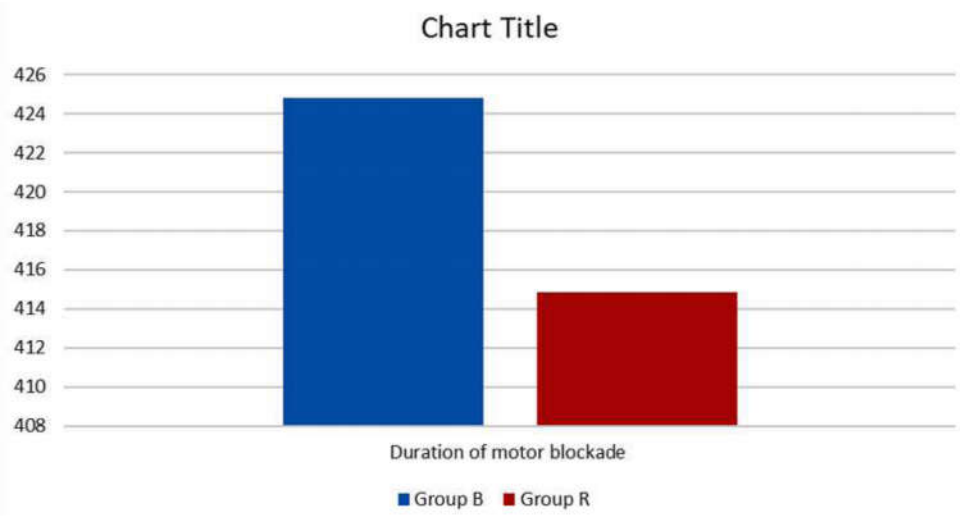

Fig. 4: Mean values of duration of motor block in two groups

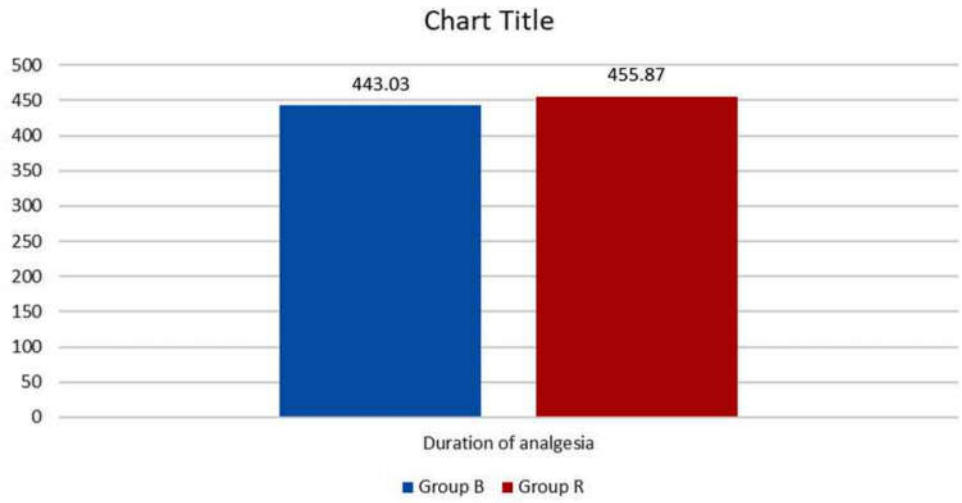

Fig. 5: Mean values of duration of Analgesia in two groups

Duration of Motor Block in two groups (min) (Mean ± SD)

There was no significant difference in duration of motor block between the group B (424.83±19.453) and group R (414.83±24.371). (p = 0.084).

Comparison of Duration of Analgesia in study groups

There was no significant difference in duration of Analgesia between the group B (455.87 ± 15.62) and group R (443.03 ± 33.54). (p = 0.06)

Discussion

Brachial plexus block has been emerged as a popular technique among the anesthesiologists for upper limb surgeries. This type of anesthesia avoids the untoward effects of general anesthesia like complications related to upper airway instrumentation. The research has also shown that this approach is very attractive approach and effective.

This study was taken up to evaluate the efficacy of Bupivacaine and Ropivacaine and the advantage in using ultrasound guidance to avoid complications and block failure. A randomized single blinded study was taken up

In a study by Sreeharsha Sirigeri comparing 0.5% Bupivacaine and 0.75% Ropivacaine in supraclavicular brachial plexus block by perivascular approach were randomly divided into Group B and Group R, which received 30ml of 0.5% Bupivacaine and 0.75% Ropivacaine respectively. The onset time of sensory block was faster in Group R compared to Group B having a mean value of 16.13±3.05 minutes and 17.70±2.35 minutes respectively. The onset time of motor block was faster in Group R compared to Group B having a mean value of 23.90±1.83 minutes and 25.43±2.22 minutes respectively. The duration of sensory and motor block was 480.3 and 472.8 in group R and 472.1 and 460.2 in group B. The duration of post-operative analgesia was 504.2 minutes in Group R and 499.6 minutes in Group B [5].

In this study the onset time for sensory and motor block in Bupivacaine (Group B) was 11.4 minutes and 17.03 minutes respectively and the onset time of sensory and motor block in Ropivacaine (Group R) was 9.53 and 13 respectively. The duration of sensory and motor block in Bupivacaine group was 444.5 minutes and 424.83 minutes respectively while in the Ropivacaine group it was 434.67 minutes and 414.83 minutes respectively. The onset of sensory and motor block was faster in Group R than in Group B which was significant.

In a study by Chandni M Soni et. al. the motor and sensory block by Ropivacaine and Bupivacaine in combination with lignocaine in supraclavicular block was compared in sixty patients scheduled for upper limb orthopedic surgeries who were randomly divided into two groups. Group R received Ropivacaine 0.75% 20 ml plus Xylocaine 2% 10 ml while Group B received Bupivacaine 0.5% 20 ml plus Xylocaine 2% 10 ml via supraclavicular route. Sensory onset of group R is nearly 6.6 minutes while in Group B it is 7.4 minutes, and motor onset in group R is 12.9 minutes while that in Group B is 11.5 minutes. There is no significant difference in intra-operative pulse, SBP and DBP. The duration of sensory block in Group R is nearly 9.13 hours while that in Group B is 9.81 hours, the duration of motor block in Group R is 8.9 hours while in Group B it is 9.93 hours and total duration of analgesia in Group R is 9.2 hours while that in Group B is 9.86 hours. Group Bupivacaine showed prolonged duration of sensory and motor block and prolonged duration of analgesia compared to Group Ropivacaine but the difference was statistically insignificant [6].

Whereas in this study onset time for sensory and motor block in Bupivacaine (Group B) was 11.4 minutes and 17.03 minutes respectively and the onset time of sensory and motor block in Ropivacaine (Group R) was 9.53 and 13 respectively. The duration of sensory and motor block in Bupivacaine group was 444.5 minutes and 424.83 minutes respectively while in the Ropivacaine group it was 434.67 minutes and 414.83 minutes respectively. The onset of sensory and motor block was faster in Group R than in Group B which was significant. There was no significant difference in duration of sensory and motor block between the group B and Group R and there is no significant difference in intraoperative pulse, SBP and DBP.

In another study by Hetal rathod et. al. the effects of 0.375% Bupivacaine and 0.375% Ropivacaine in supraclavicular brachial plexus block was compared in sixty patients scheduled for upper limb orthopedic surgeries who were randomly divided into Group B and Group R who received 0.375% Bupivacaine and 0.375% Ropivacaine respectively. The sensory and motor onset (mean-minutes) was 21.13 and 25.87 in group B and was 13.3 and 21.37 in group R respectively. The duration of sensory and motor block (mean- minutes) was 480.3 and 472.8 in group R, and 472.1 and 460.2 in group B The duration of post-operative analgesia was 504.2 minutes in Group R and 499.6 minutes in Group B. Group R provided statistically significant & rapid onset of sensory and motor blockade than Group B for upper limb surgeries.

There were no significant differences in duration of sensory and motor blockade [1].

In this study the onset time for sensory and motor block in Bupivacaine (Group B) was 11.4 minutes and 17.03 minutes respectively and the onset time of sensory and motor block in Ropivacaine (Group R) was 9.53 and 13 respectively. The duration of sensory and motor block in Bupivacaine group was 444.5 minutes and 424.83 minutes respectively while in the Ropivacaine group it was 434.67 minutes and 414.83 minutes respectively. The duration of post-operative analgesia was 443.03 minutes in Group R and 455.87 minutes in Group B .The onset of sensory and motor block was faster in Group R than in Group B which was significant.

In a study by Tarek atef tawfic 60 patients aged between 17 and 61 years with chronic renal failure (CRF) for arterio-venous fistula (AVF) creation were compared with 0.25% Ropivacaine (group I) and 0.25% Bupivacaine (group II) for supraclavicular block. Both groups were comparable as regards onset time of motor block as well as duration of sensory and motor block. However, the mean onset time of sensory block was more delayed in the Ropivacaine group. There was significantly higher incidence of complications in Bupivacaine group especially respiratory distress and Horner's syndrome. Therefore, these results suggest that Ropivacaine 0.25% is a better local anesthetic than Bupivacaine 0.25% for use in a supraclavicular approach for brachial plexus block in high risk patients with CRF [7].

In this study the onset time for sensory and motor block in Bupivacaine (Group B) was 11.4 minutes and 17.03 minutes respectively and the onset time of sensory and motor block in Ropivacaine (Group R) was 9.53 and 13 respectively. The duration of sensory and motor block in Bupivacaine group was 444.5 minutes and 424.83 minutes respectively while in the Ropivacaine group it was 434.67 minutes and 414.83 minutes respectively. The duration of post-operative analgesia was 443.03 minutes in Group R and 455.87 minutes in Group B .The onset of sensory and motor block was faster in Group R than in Group B which was significant. There were no complications in either of the groups because of the use of ultrasound.

Conclusion

Supraclavicular approach to the brachial plexus is an alternative to general anesthesia for surgeries around the elbow, forearm and hand. Complications including vascular puncture, local anesthetic toxicity, pneumothorax, and patient discomfort have made the technique undesirable. With the advent of ultrasound, all these complications are minimized and the drug can be deposited under direct vision. Ultrasound guidance with real-time needle visualization in relation to anatomic structures and target nerves makes regional anesthesia safer and more successful. With ultrasound guidance in experienced hands, brachial plexus blockade can lead to decreased block performance and onset time, increased success rate and decreased rate of complications [8].

Bupivacaine is a long acting local anesthetic with long duration of action with a number of side effects, including motor weakness, cardiovascular and central nervous system toxicity. Ropivacaine a similar long acting amide local anesthetic with better safety margin because of its structural properties and hence is associated with less CNS, CVS toxicity and local neurotoxicity. It also has the advantage of faster onset of sensory and motor blockade; longer duration of analgesia and anaesthesia [9].

Reference

1. Hetal Rathod, Hetal Parikh, R.M Upadhayaya. Comparative study of 0.375% Bupivacaine and 0.375% Ropivacaine in brachial plexus block via supraclavicular approach. International Journal of Biomedical Research 2015:6(02):77-82.
2. Bhatia R, Kaeley N, Sarkar D. Clinical Evaluation of Ropivacaine Versus Ropivacaine with Lignocaine and Adrenaline in Supraclavicular Brachial Plexus Block: A Randomized Double Blind Study. National Journal of Medical and Allied Sciences 2015;4(1):33-37.
3. D Tripathi, K Shah, C Shah, S Shah, E Das. Supraclavicular Brachial Plexus Block for Upper Limb Orthopedic Surgery: A Randomized, Double Blinded Comparison Between Ropivacaine and Bupivacaine. The International Journal of Anesthesiology. 2012 Nov;30(4).
4. Singh G, Saleem MY. Comparison between Conventional Technique and Ultrasound Guided Supraclavicular Brachial Plexus Block in Upper Limb Surgeries. Int J Sci Stud 2014;2(8):169-176.
5. Sirigeri S, Patil VV. A comparative study of 0.5% Bupivacaine and 0.75% Ropivacaine in supraclavicular brachial plexus block by perivascular approach: Prospective randomized study. J. Evolution Med. Dent. Sci. 2016;5(13):568-571, DOI: 10.14260/JEMDS/2016/130.
6. Chandni M Soni, Hetal Parikh. Comparison of motor and sensory block by Ropivacaine and Bupivacaine in combination with Lignocaine in supraclavicular block. Natl J Med Res. 2013;3(4): 353-357.

7. Tarek Atef Tawfic. A clinical and pharmacokinetic comparison of Ropivacaine and Bupivacaine for Supraclavicular Brachial Plexus Block in patients with Chronic Renal Failure, AJAIC 2006 June;9(2):23-28.
8. Farheen Mirza. Ultrasound-Guided Regional Anesthesia for Procedures of the Upper Extremity Anesthesiology Research and Practice Volume 2011, Article ID 579824, 6 pages. doi:10.1155/2011/579824.
9. Modak S, Basantwani. Comparative study of 0.5% Ropivacaine and 0.5% Bupivacaine for bronchial plexus block by supraclavicular approach for upper limb surgeries. Int J Basic Clin Pharmacol. 2016 Aug;5(4):1205-1209.

Original Research Article

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Effect of Inj. Dexmedetomidine and Inj. Clonidine on Haemodynamic Changes during Laryngoscopy &Tracheal Intubation: A Comparative Study

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Abstract

Aim and Objectives: 1. To evaluate the effects of dexmedetomidine and clonidine on haemodynamic changes during Laryngoscopy and tracheal intubation. 2. To compare the effect of dexmedetomidine and clonidine on haemodynamic changes during Laryngoscopy and tracheal intubation. 3. To compare the side effects.

Materials & Methods: After approval of the institutional ethical committee, this prospective observational study was conducted on 60 patients of ASA Grade I & II , undergoing elective surgeries under general anesthesia.

Group A: Injection Dexmedetomidine 1mcg/kg diluted to 20ml with normal saline were given over 10 minutes.

Group B: Injection. Clonidine 2mcg/kg diluted to 20ml with normal saline were given over 10 minutes.

All patient received Injection Pentazocine 0.3mg/kg and were pre-oxygenated for 3minute Anaesthesia was induced with thiopantone sodium (5mg/kg intravenous) till loss of eyelashreflex over 30 second and mask ventilation was confirmed. Injection succhinylcholine 1.5mg/kg was given to facilitate laryngoscopy and intubation. anaesthesia was maintained with oxygen nitrous oxide, halothane with intermittent use of injection Atracurium and controlled ventilation. At the end of surgery the neuromuscular blockade was antagonized with injection Glycopyrolate (.01mg/kg) Intavenou. and injection Neostigmine (.05mg/kg) i.v. and patient were extubated.

Result: Dexmedetomidine is more effective than Clonidine in attenuation of haemodynamic changes during laryngoscopy and intubation.

Conclusion: Dexmedetomidine significantly attenuates the haemodynamic changes during laryngoscopy and intubation. Clonidine also significantly attenuates the haemodynamic changes during laryngoscopy and intubation.Thus we conclude that Dexmedetomidine is a better drug to attenuate the haemodynamic response during laryngoscopy and intubation.

Keywords: Dexmedetomidine; Clonidine; Hemodynamic Response; Laryngoscopy and Orotracheal Intubation.

Introduction

Since the time of introduction of endotracheal intubation in anaesthesia in the last quarter of the 19th century it has become one of the frequently performed procedures in the practice of anaesthesia.

Endotracheal intubation is the translaryngeal placement of a tube into the trachea via nose or mouth. The technique of laryngoscopy and intubation induces noxious stimuli that lead to extreme haemodynamic stress which is associated with intense sympathetic activity marked by tachycardia and hypertension [1].

The increase in pulse rate and blood pressure are usually transitory, variable & unpredictable. Normal, healthy persons tolerate this response, but in susceptible and high risk individuals, this transient

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sympathetic response can evoke life-threatening conditions.

Various non-pharmacological & pharmacological methods have been used to attenuate the haemodynamic response to laryngoscopy & endotracheal intubation.

Alpha-2 agonists have been used for attenuating the sympathetic response and among alpha-2 agonist both Clonidine and Dexmedetomidine appear to fulfil all the above criteria. Both drugs have actions on both alpha-1 and alpha-2 receptors but dexmedetomidine is highly specific and selective alpha-2 adrenoceptor agonist with alpha2:alpha1 binding selectivity ratio of 1620:1 compared to 220:1 for clonidine.

Aims and Objective

1. To evaluate the effects of dexmedetomidine and clonidine on haemodynamic changes during Laryngoscopy and tracheal intubation.
2. To compare the effect of dexmedetomidine and clonidine on haemodynamic changes during Laryngoscopy and tracheal intubation.
3. To compare the side effects, if any.

Material and Method

The study was conducted on patients undergoing laryngoscopy and tracheal intubation in elective surgeries under general anesthesia.

After approval of the institutional ethical committee, this prospective observational study was conducted on 60 patients in the age group of 20 to 50 years, ASA Grade I & II of either sex, undergoing elective surgeries under general anesthesia.

Patients were divided in to two groups comprising 30 patients each:

Group (D) Dexmedetomidine Group were given injection Dexmedetomidine 1mcg/kg diluted to 20ml with normal saline over 10 minutes

Group (C) Clonidine group were given injection Clonidine 2mcg/kg diluted to 20ml with normal saline over 10 minutes.

Material

The study includes drugs dexmedetomidine hydrochloride 100mcg/ml 1ml vial and injection clonidine hydrochloride 150mcg/ml 1ml ampoule.

Patient Exclusion Criteria

1. Stenosis, Left ventricle failure, Atrioventricular conduction block, asthma, chronic obstructive pulmonary disease, any liver or renal disease
2. Patient taking antihypertensives, analgesics, sedatives, beta-blockers.

On the day prior to surgery pre anesthetic evaluation was done and patients were explained about the procedure and technique and written informed consent was taken.

All routine investigations like Complete blood count, Urine (r &µ), Blood urea, creatinine, Blood sugar, Electrocardiogram were done prior to surgery.

Pre-Medication

All patient were given Injection glycopyrolate 0.2mg Intravenous, and injection Ondensetran 4mg intravenous, Injection Ranitidine Hydrochloride 50mg intravenous before infusion.

Technique and Method

On the day of surgery, Anaesthesia machine and circuits were checked, resuscitation equipments were kept ready.

After confirmation of Nill per oral status, patients were shifted to the operating room and connected to monitor.

Preoperative base line parameters, were recorded after 5 minute of settling in the operative room and also after infusion of Dexmedetomidine./Clonidine (T1).

All patient received Injection Pentazocine 0.3mg/kg and were pre-oxygenated for 3min. Anaesthesia was induced with thiopantone sodium (2.5% 5mg/kg intravenous) till loss of eyelash reflex over 30 second and mask ventilation was confirmed. Injection succhinylcholine 1.5mg/kg was given to facilitate laryngoscopy and intubation. At the onset of apnea using laryngoscope, intubation was done with a well lubricated appropriate size cuffed endotracheal Tube and anaesthesia was maintained with oxygen nitrous oxide, halothane with intermittent use of inj. Atracurium and controlled ventilation.

At the end of surgery the neuromuscular blockade was antagonized with inj. Glycopyrolate (.01mg/kg) intravenous and injection Neostigmine (.05mg/kg) intravenous and patient were extubated after complete reversal of neuromuscular blockade.

Data Collection

Sequence	TIME	SBP	DBP	HR
Basal reading when pt.is shifted to OT(T0)	-	-	-	-
After Induction (T1)	-	-	-	-
After intubation(T2)	-	-	-	-
At 2 min after intubation(T3)	-	-	-	-
At 6 min after intubation(T4)	-	-	-	-
At 10 min after intubation(T5)	-	-	-	-

Statistical Analysis Plan

Statical analysis was done using statistical package for social sciences version 15.0. chi-square test, Unpaired t-test were used.

Observations and Results

Observation duly recorded, have been tabulated and statistically analyzed in this section. Comparison of quantitative data between groups was done by unpaired t-test. A $p<0.05$ was considered clinically significant.

Inference (Table 2): The Tables 2 show age wise distribution in both the groups. The minimum age in Dexmedetomidine and Clonidine groups were 26 and 25 years respectively. the maximum age in Dexmedetomidine and Clonidine groups were 44 and 45 years respectively. There was no significant difference in the age of patients between the group-D and group-C. both group were similar with respect to age distribution.

Table 1: Demographic profile of patients

Demographic profile	Dexmedetomidine-GP Mean ± SD	Clonidine-GP Mean ± SD	p-value
Age(yrs)	32.06±4.96	32.13±5.34	>0.05
Gender(M:F)	17:13	18:12	>0.05
Weight(kg)	48.13	48.06	>0.05

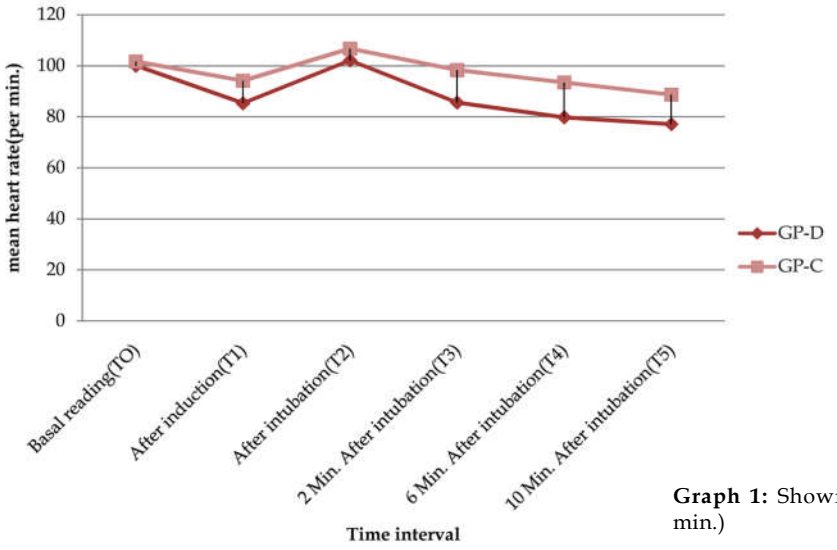
Inference (Table 1): Demographic profile in term of age, sex, weight were comparable in both the groups.
P-values
p>0.05- Statistically not significant (NS),
p<0.05- Statistically significant (S),
p<0.01- Statistically highly significant (HS),
p<0.001- Very highly significant.

Table 2: Age distribution in two groups

Age Group (in years)	Dexmedetomidine-Group		Clonidine-Group	
	No. of Pts.	%	No. of Pts.	%
20-29	11	36.66	10	33.33
30-39	15	50	15	50
40-49	04	13.33	05	16.66
Mean age and SD of Patients	32.06±4.96		32.13±5.34	
	p value >0.05			

Table 3: Showing Mean Heart rate of patients in both the groups

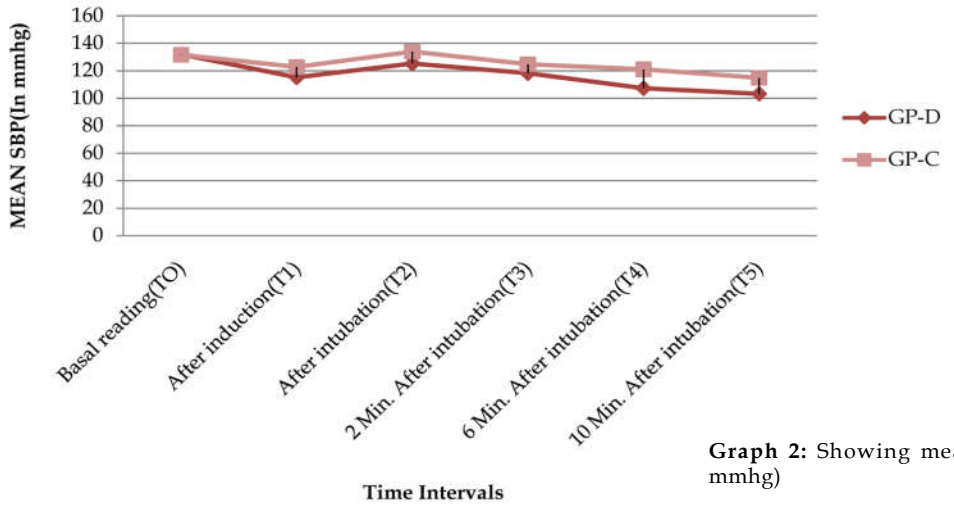
Time	Dexmedetomidine-Group mean ±SD	% Change from baesline	Clonidine-Group mean ±SD	% Change from baseline	P-Value
Basal reading when pt. is shifted to OT(T0)	100.06 ±4.56	-	101.66 ±1.74	-	>0.05
After induction(T1)	85.33 ±3.30	14.72	94.13 ±1.67	7.40	<0.05
After intubation(T2)	102.13 ±3.30	2.06	106.73 ±2.11	3.01	<0.01
At 2 min after intubation(T3)	85.63 ±3,03	14.42	98.93 ±1.36	3.30	<0.05
At 6 min after intubation(T4)	79.83 ±4.21	20.21	93.43 ±1.38	8.09	<0.05
At10min after intubation (T5)	77.16 ±2.90	22.88	88.66 ±1.39	12.78	<0.05



Graph 1: Showing mean Heart rate(per min.)

Table 4: Showing mean systolic blood pressure (in mmHg) of patients in both the groups

Time	Dexmedetomidine-Group		Clonidine-Group		P-value
	Mean ± SD	% Change from baseline	Mean ± SD	% Change from baseline	
Basal reading when pt.is shifted to OT(T0)	132±1.72	-	131.73±2.54	-	>0.05
After induction(T1)	115.2±2.73	12.72	122.8±5.24	6.77	<0.05
After intubation(T2)	125.26±3.58	5.10	133.96±2.49	1.69	<0.01
At 2 Min.after intubation(T3)	118.26±3.87	10.15	124.8±3.54	5.48	<0.05
At 6 min after intubation(T4)	107.36±2.93	18.66	121.13±4.94	8.04	<0.05
At10 min after intubation(T5)	103.26±1.85	21.77	114.862.82	12.80	<0.05



Graph 2: Showing mean SBP (In mmhg)

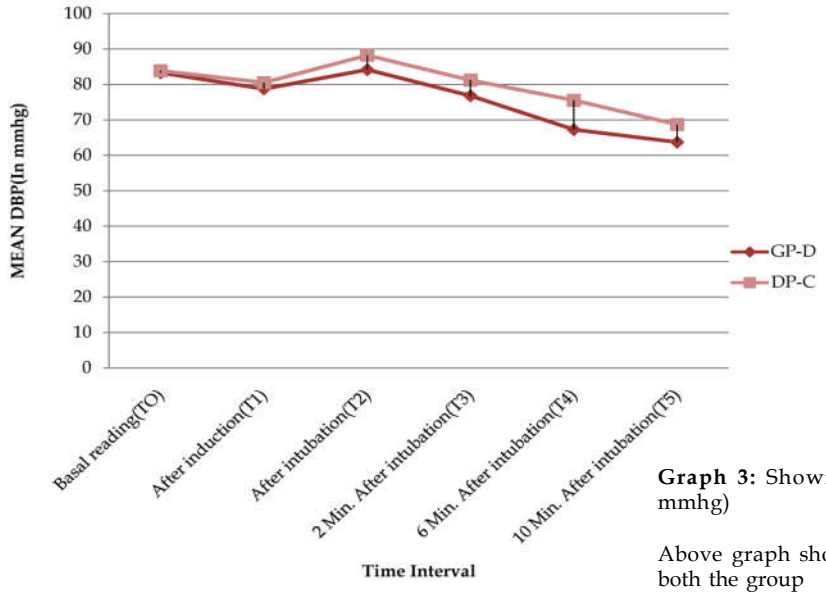
Inference (Table 3): The baseline heart rate was comparable in both the group (p>0.05).

At the time of laryngoscopy and intubation, heart rate increased in both Dexmedetomidine & Clonidine group but more in Clonidine group (p<0.01). There was continuous decrease in heart rate at 2, 6, 10 minutes after intubation in both groups, but the mean heart rate at any time was lower in the Dexmedetomidine group than in the Clonidine group which was statistically significant (p<0.05).

Inference (Table 4): The baseline SBP were comparable in both the group (p>0.05). At time of laryngoscopy and intubation, SBP increased in both Dexmedetomidine & Clonidine group but more in Clonidine group (p<0.01). There was continuous decrease in SBP at 2, 6, 10 minutes after intubation in both groups but the mean SBP at any time was lower in the Dexmedetomidine group than in the Clonidine group which was statistically significant (p<0.05).

Table 5: Showing mean Diastolic blood pressure (in mmHg) of patients in both the groups

Time	Dexmedetomidine-Group		Clonidine-Group		P-value
	Mean ± SD	% Change from baseline	Mean ± SD	% Change from baseline	
Basal reading when pt. shifted to OT (T0)	83.33±3.74	-	83.93±4.50	-	>0.05
After induction(T1)	78.76±2.62	8.02	80.53±5.30	4.05	<0.05
After intubation(T2)	84.20±4.00	1.33	88.26±4.37	5.32	<0.01
At 2 Min. after intubation(T3)	76.83±4.15	10.09	81.26±4.85	3.18	<0.05
At 6 Min. after intubation(T4)	67.26±2.51	21.29	75.56±7.36	9.97	<0.05
At 10 Min.after intubation (T5)	63.73±2.65	25.42	68.73±7.30	18.11	<0.05



Graph 3: Showing mean DBP (In mmhg)

Above graph showing mean dbp of both the group

Inference (Table 5): The baseline DBP were comparable in both the group (p>0.05). At time of laryngoscopy and intubation, DBP increase was seen in both Dexmedetomidine & Clonidine group but more in Clonidine group (p<0.01). There was continuous decrease in DBP at 2,6,10 minutes after intubation in both groups, but the mean DBP at any time was lower in the Dexmedetomidine group than in the Clonidine group which was statistically significant (p<0.05).

Inference (Table 6): The table 6 showing that in Dexmedetomidine Group 1 patient had bradycardia intraoperatively which was statistically insignificant. it was immediately corrected with atropine 0.6 mg. In the Clonidine group 2 patients developed hypotension. it responded with 500ml of intravenous ringers lactate administration within 10 minutes . 1 patient had bradycardia it was immediately corrected with atropine 0.6 mg. it was also statistically insignificant.

Table 6: Showing complication of patients in both the groups

Complication	Dexemedetomidine - group	Percentage (%)	Clonidine-group	Percentage (%)
Hypotension	-	-	2	6.66
Bradycardia	1	3.33	1	3.33

Result

Both groups were comparable in their age, gender and body weight distribution (p>0.05).

The basal mean HR±SD in the present study Group D and Group C was 100.06±4.56 and 101.66±1.74 bpm respectively.

Both groups had rise in HR after intubation that was 2.06% in group D and 3.01% in group C and difference was statistically highly significant (p<0.01).

Difference in HR between two groups remained statistically significant at 2, 6 and 10 min after intubation (p<0.05).

The basal mean SBP in the present study in, Group D and Group C were 132±1.72, 131±2.54 mmHg respectively.

Both group had maximum rise in SBP after intubation that was 5.10% in group D and 1.69% in group C which was statistically highly significant ($p<0.01$).

Difference in SBP between two groups remained statistically significant at 2, 6 and 10 min after intubation ($p<0.05$).

The basal mean±SD, DBP in the present study in Group D and Group C were 83.46±3.74, 83.93±4.50 mmHg respectively.

Both group had maximum rise in DBP after intubation that was 1.33% in group D and 5.32% in group C which was statistically highly significant ($p<0.01$).

Difference in DBP between two groups remained statistically significant at 2, 6 and 10 min after intubation ($p<0.05$).

In Dexmedetomidine group no any patients had hypotension and one patient had bradycardia, while in Clonidine group 2 patients had hypotension and 1patient had bradycardia.

Discussion

Laryngoscopy and tracheal intubation are considered as the most critical events during administration of general anaesthesia as they provoke transient but marked sympatho-adrenal response manifesting as hypertension and tachycardia. Many drugs have been tried by various authors for blunting haemodynamic responses to laryngoscopy and intubation like Recently α-2 agonists like clonidine and dexmedetomidine have been tried for suppressing the response to intubation and have been found to have better effects compared to all the drugs mentioned above, without any of the side effects like respiratory depression or increased incidence of post operative nausea and vomiting.

Demographic Criteria

Two groups were comparable and there was no statistically significant Difference between the mean ages, sex and weight .

In this study optimal age range was 20 to 50 years. The mean values of age with standard deviations are 32.06±4.96 and 32.13±5.34 for Dexmedetomidine and Clonidine groups respectively. there were no significant difference between two groups. (P>0.05)

Dr A Venkateswara et al found mean values of age with standard deviations are 32.1±8.8, 35.8±9.6, and 33.4±9.2 for normal saline, Dexmedetomidine and Clonidine groups respectively. there is no statistically significant difference between three groups. (P=0.28)

Heart Rate Changes

The basal mean HR±SD in the present study Group D and Group C was 100.06±4.56 and 101.66±1.74 bpm respectively.

After intubation in Group D there was only 2.06%(102.13±3.30) increase in mean HR was observed from its basal value(100.06±4.56), whereas in Group C there was 3.01% (106.73±2.11) increase in mean HR was observed from its basal value (101.66±1.74), which was statistically highly significant compared to Group-D (P<0.01).

At 2,6 minutes after intubation in Group D there was only 14.42% (85.63±3.03), 20.21%(79.83±4.21) respectively decrease in mean HR was observed from its basal value(100.06±4.56), whereas in Group C there was 3.30% (98.93±1.36), 8.09% (93.43±1.38) respectively decrease in mean HR was observed from its basal value(101.66 ±1.74), which was statistically significant compared to Group-D (P<0.05)

Shrisendu *et al*, has also found statistically significant rise in HR during intubation in clonidine group compare to dexmedetomidine. In his study this statistically significant higher HR in clonidine group last upto 3 min after intubation.

Scheinin *et al* reported that use of α-2 agonist leads to bradycardia. During intubation there was rise in heart rate in both the groups which was more in group C compare to group D and this rise in HR in group C was statistically significant ($p< 0.05$)

Systolic Blood Pressure Changes

The basal mean SBP in the present study in, Group D and Group C were 132±1.72, 131±2.54 mmHg respectively. After intubation in Group D there was 5.10% (125.26±3.58) increase in mean SBP was observed from its basal value (132±1.72), in Group C there was 1.69% (133.96±2.49) increase in mean SBP was observed from its basal value (131.73±2.54), which was statistically highly significant compared to Group-D (P<0.01).

At 2, 6,minutes after intubation in Group D there was 10.15%(118.26±3.87), 18.66(107.36±2.93) respectively decrease in mean SBP was observed from its basal value (132±1.72). whereas in Group C there was 5.48% (124.8±3.54), 8.04% (121.13±4.94)

respectively decrease in mean SBP was observed from its basal value (131.73±2.54), which was statistically significant compared to Group-D (P<0.05).

Shirsendu et al found that the changes in the SBP and their statistical comparisons indicates that though there was an increase in SBP in all three groups, measured 1 min after drug administration, the difference was not significant. The attenuation of the SBP was highly significant in the dexmedetomidine group as compared to that in the clonidine group (p<0.05 at intubation, 1 and 3 min and p<0.001 at 5 and 10 min).

Sameer Arora et al, also found that during intubation both groups had maximum rise in SBP but this was more in Group C than in Group D. There was 6% (133.1±0.9132) rise in SBP in Group D from baseline (126.1±1.281) SBP whereas Group C had 15% (140.3±1.283) rise from its baseline (122.5±1.189), which was statistically highly significant (pÂ0.001).

Similar to our Study; Celik et al. found fall in BP after infusion of Dexmedetomidine and Gupta et al. found fall in BP with Clonidine .

Diastolic Blood Pressure Changes

The basal mean±SD, DBP in the present study in Group D and Group C were 83.46±3.74, 83.93±4.50 mmHg respectively.

After intubation in Group D there was 1.33% (84.33±4.00) increase in mean DBP compared to basal value (83.46±3.74), Group C there was 5.32% (88.4±4.37) increase in mean DBP compared to basal value (83.93±4.50), which was statistically highly significant from compared to Group-D (P<0.05).

At 2, 6 minutes after intubation in Group D there was 10.09% (76.83±4.15), 21.29%(67.26±2.51) respectively decrease in mean DBP was observed from its basal value (83.46±3.74), in Group C there was 3.18% (81.26±4.85), 9.97% (75.56±7.36) respectively decrease in mean DBP compared to basal value (83.93±4.50), which was statistically significant compared to Group-D (P<0.05).

Sameer Arora et al., has also found during intubation both groups had maximum rise in DBP but this was more in Group C than in Group D. There was 8.90% (88.07±1.27) rise in DBP in Group D from baseline (80.87±1.67) DBP whereas Group C had 12.84% (92.00±0.99) rise from its baseline (81.53±1.04), which was statistically highly significant (p<0.001).

N K kalra et al., observed that the DBP of the group recieving 1.5µgm/kg of clonidine was significantly lower than the group receiving clonidine 1 µgm/kg.

Conclusion

Following conclusion are drawn from the present study

- Dexmedetomidine and Clonidine significantly attenuates the haemodynamic changes during laryngoscopy and intubation.
- Dexmedetomidine is more effective than Clonidine in attenuation of haemodynamic changes during laryngoscopy and intubation.
- Thus we conclude that Dexmedetomidine is a better drug to attenuate the haemodynamic response during laryngoscopy and intubation.

References

1. Fox EJ, Sklar GS, Hill CH, Villanueva R, King BD. Compilation related to the pressor response to endotracheal intubation, Anaesthesiology. 1977:47: 524-5.
2. Karl et al Insertion of LMA in place of endotracheal intubation to attenuate the cardiovascular response. IJA, 1999;43:30-35.
3. Kumar et al- Blocking Glossophryngeal & superior laryngeal nerve to attenuate the cardiovascular response to laryngoscopyv& endotracheal intubation. IJA,1993;41:20-25.
4. King BD, Harris LC Jr, Greifenstein FE, Elder JD Jr, Dripps RD. Reflex circulatory responses to direct laryngoscopy and tracheal intubation performed during general anesthesia. Anesthesiology. 1951 Sep;12(5):556–566.
5. Denlinger JK, Ellison N, Ominsky AJ. Effects of intratracheal lidocaine on circulatory responses to tracheal intubation. Anesthesiology. 1974 Oct;41(4): 409–412.
6. Stoelting RK. Blood pressure and heart rate changes during short duration laryngoscopy for tracheal intubation. Influence of viscious or intravenous lidocaine. Anaesthesia analgesia. 1978;57:197-9.
7. Dahlgreen N,Messeter K. Treatment of the stress response to laryngoscopy and intubation with Fentanyl. Anaesthesia. 1981;36:1022.
8. Fuji Y, Tanaka H, Saitoh Y, Toyooka H. Effects of Calcium channel blockers on circulatory response to tracheal intubation in hypertensive patients: Nicardipine vs Diltiazem. Canadian Journal of Anaesthesia. 1995;42:785-8.
9. Martin DE, Rosenberg H, Aukburg SJ, Bartkowski RR, Edwards MW Jr, Greenhow DE, et al. Low-dose fentanyl blunts circulatory responses to tracheal intubation. Anesth Analg 1982;61:680-4.
10. Ebert JP, Pearson JD, Gelman S, Harris C, Bradley EL. Circulatory responses to laryngoscopy:The

comparative effects of placebo, fentanyl, and esmolol. Can J Anaesth 1989;36:301-6.

11. Prys-Roberts C, Foex P, Biro GP. Studies of anaesthesia in relation to hypertension versus adrenergic â receptor blockade. British Journal of Anaesthesia. 1973;45:671-80.
12. McCammon RL, Hilgenberg JC, Stoelting RK. Effect of Propranolol on circulatory responses to induction of diazepam- nitrous oxide anesthesia and to endotracheal intubation. Anesthesia analgesia, 1981 Aug;60(8):579-83.

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Ultrasound-Guided Transverse Abdominis Plane Block Using Bupivacaine 0.25% vs Ropivacaine 0.2% For Post-Operative Analgesia in Caesarean Section

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Abstract

Introduction: Present study was conducted to compare the analgesic efficacy of 0.25% Bupivacaine and 0.2% Ropivacaine in Transverse Abdominis Plane (TAP) block under ultrasound guidance as a part of a multimodal analgesia regimen for post caesarean delivery pain management. *Materials & Methods:* This prospective study was conducted at IMS and SUM Hospital, Bhubaneswar in 100 pregnant women (ASA grade II and III parturient) undergoing either elective or emergency LSCS under spinal anaesthesia by ultrasound guided transverse abdominis plane block randomised in two groups – 0.25% bupivacaine and 0.2% ropivacaine, given 10 ml on each side. The patients were assessed at post anesthesia care unit (PACU) and at 2, 6, 12, 24, 48 hours postoperatively in the obstetric ward for time of first request for analgesia, pain score of the patients analyzed during rest and movement using visual analogue scale (VAS) and side effects during first 48 hours. *Results:* The two groups were comparable in demographics and baseline characteristics. The time of full regression of block (p=0.731), time required for 1st analgesia (p=0.699) and total consumption of analgesia (p=0.833) were comparable in the two groups. The VAS score at rest and movement at multiple time intervals during follow-up period was similar in both groups. *Conclusion:* Analgesic efficacy and safety of bupivacaine 0.25% and ropivacaine 0.2% is similar in TAP block under ultrasound guidance.

Keywords: Analgesia; Transverse Abdominis Plane; Caesarean; Ultrasound.

Introduction

The ideal postcaesarean section (CS) analgesic regime should be efficacious without impacting the ability of mother to take care of the neonate and with minimal drug transfer through breast milk. However, observational data from country that these goals are far from being achieved because of limited availability of drugs, equipment and expertise are the major issues in providing adequate post-CS analgesia [1].

Though different approaches have been introduced for proper pain relief, these multimodal approaches are still inadequate and unsatisfactory in many patients [2].

The transverse abdominis plane (TAP) is the fascial plane between the internal oblique and transverseabdominis muscle containing the thoracolumbar nerves T10 to L1.

The introduction of local anaesthetic in this plane blocks these nerves (T10 to L1). With the widespread availability of ultrasound guidance for more accurate localization of TAP (than the 'blind' technique), the TAP block is now established as an important technique for reduction of post-operative pain following all abdominal surgeries including CS [3].

Various long acting amide linked LA agents including ropivacaine [3] and bupivacaine [4] have been utilised for post-operative analgesia with ultrasound-guided TAP block. They share a similar

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pKa and plasma protein binding property. Bupivacaine is a racemic molecule while, ropivacaine is a pure enantiomer which has been developed to reduce the potential toxicity and improve the relative sensory and motor blocks [5].

The present study was planned to compare the analgesic efficacy of 0.25% Bupivacaine and 0.2% Ropivacaine in TAP block under ultrasound guidance as a part of a multimodal analgesia regimen for post caesarean delivery pain management.

Materials & Methods

This prospective study was conducted at IMS and SUM Hospital, Bhubaneswar from January 2016 to August 2017. Institutional Ethics Committee permission was obtained. 100 pregnant women (ASA grade II and III parturient) undergoing either elective or emergency LSCS under spinal anaesthesia by ultrasound guided transverse abdominis plane block were randomised in two groups – 0.25% bupivacaine and 0.2% ropivacaine, given 10 ml on each side.

Patients refusing consent, with allergy to opioids or amide group local anaesthetics of NSAIDs, coagulation derangement or bleeding disorders, infection at the site of block, cardiovascular, pulmonary or neurological diseases and those converted to general anaesthesia after giving sub arachnoid block were excluded from the study. Demographic details of the patients were noted.

All patients received subarachnoid block by 25 G Quinckie's needle at L 3-4/L2-3 interspace with a total volume of 2 ml in the same syringe using a standard midline approach. Both Groups received 10 mg of 0.5% of hyperbaric bupivacaine (2 ml). Supplemental O2 was delivered by face mask at 5L/min throughout surgery and during their stay in the post anaesthetic care unit.

Monitoring was done of all patients using the following: a- ECG. b. Pulse oximetry. c- Non Invasive blood pressure monitoring. Surgery was allowed to proceed after T4 to T6 sensory blockade to pin prick sensation was established. IV crystalloids and ephedrine were administered as needed to treat hypotension. All patients received an IV infusion of oxytocin 10 IU after delivery. IV ondansetron 4 mg was administered intra-operatively if nausea and vomiting was not corrected by vasopressor for treatment of hypotension or occurred unrelated to hypotension. At end of surgery, a linear ultrasound probe was placed in the anterior abdominal wall as the three layers are distinct here. After identifying the TAP which was between internal oblique and transverse abdominis muscle the probe was moved postero-laterally to lie along the mid-axillary line. Under all aseptic precautions the block was given with 22 G hypodermic needle attached to a 20 ml syringe containing the drug as per the group allocation. Then the drug was deposited in the fascial plane after aspiration, check aspiration was done every 5 ml to rule out intravascular injection.

The patient was observed for 15 minutes and then shifted to post-anaesthesia care unit. In one group, 10 ml of 0.25% of Bupivacaine injected on either side while other received 10 ml of 0.2% of Ropivacaine injected on either side.

The outcome variables compared in the two groups were time of first request for analgesia, pain score of the patients analyzed during rest and movement using visual analogue scale (0 – no pain and 10 – worst pain) and side effects during first 48 hours.

The presence and severity of pain, nausea, vomiting and any other side effects were assessed in the post anesthesia care unit (PACU) and at 2, 6, 12, 24, 48 hours postoperatively in the obstetric ward.

Data was analysed using SPSS version 21 software. Data with normal distribution between two groups was compared using independent samples t test while data which was not normally distributed was compared using Mann-Whitney test. Chi square test was used to compare categorical data between the two groups. Level of significance in the study was 0.05.

Results

Hundred patients were randomized to bupivacaine 0.25% (n=49) and ropivacaine 0.2% (n=51) groups. Demographics and baseline characteristics of patients have been described in Table 1. Patients in the two groups were comparable in age, weight, height and gravida status. The duration of surgery in both groups was similar (p=0.606).

The outcome variables have been described in Table 2. The time of full regression of block (p=0.731), time required for 1st analgesia (p=0.699) and total consumption of analgesia (p=0.833) were comparable in the two groups. The VAS score at rest and movement at multiple time intervals during follow-up period was similar in both groups.

Postoperative nausea and vomiting was noted in 5 patients in bupivacaine and 6 patients in ropivacaine group.

Table 1: Demographics and Baseline characteristics

	Bupivacaine (n=49)	Ropivacaine (n=51)	P value
Age (in years)	25.7±3.1	26.4±3.1	0.233
Weight (kg)	75.7±8.3	74±9.5	0.347
Height (cm)	157.9±2.3	158±2.7	0.748
Previous status			
G1	23 (46.9%)	26 (51%)	0.506
G2	22 (44.9%)	18 (35.3%)	
G3	4 (8.2%)	7 (13.7%)	
Duration of surgery (min)	44.7±5.7	45.3±5.9	0.606

Table 2: Outcome variables

	Bupivacaine (n=49)	Ropivacaine (N=51)	P value
Time of full regression of block (in min)	128.9±13.9	129.8±13	0.731
Time required for 1st analgesia (in min)	456±30.2	453.3±37.4	0.699
Total consumption of analgesia	406.1±42.9	404.4±38	0.833
VAS at rest (median)			
0 hrs	0 (0-0)	0 (0-0)	1
2 hrs	0 (0-0)	0 (0-0)	1
6 hrs	0 (0-0)	0 (0-0)	0.047
12 hrs	0 (0-2)	2 (0-2)	0.504
24 hrs	0 (0-2)	2 (0-2)	0.635
48 hrs	0 (0-0)	0 (0-0)	0.486
VAS at movement (median)			
0 hrs	0 (0-0)	0 (0-0)	1
2 hrs	0 (0-0)	0 (0-0)	1
6 hrs	0 (0-0)	0 (0-0)	0.29
12 hrs	2 (2-2)	0 (0-2)	0.144
24 hrs	2 (0-2)	0 (0-2)	0.823
48 hrs	2 (0-2)	0 (0-2)	0.647

Discussion

Rafi introduced the TAP block in 2001, while the USG guided approach was described by Hebbard et al in 2017 [6,7]. TAP block has been shown to benefit by providing good analgesia in the anterior abdominal wall. Owing to poor vascularity in TAP, the action of LA is prolonged and is devoid of major complications. Use of USG guided technique further reduces complications associated with blind approach [8]. This property has been used in post Caesarean section (CS) analgesia. Accordingly, 0.25% Bupivacaine [4] and 0.5% Ropivacaine [3] have been demonstrated effective post CS analgesia in TAP. A TAP block with lower concentration of 0.375% for analgesia post CS was demonstrated by Chansoria et al [9].

A number of studies have compared bupivacaine 0.25% and ropivacaine 0.5% in different types of abdominal surgeries [10-12]. In all these studies, 0.5% ropivacaine has been shown to provide longer duration of analgesia compared to 0.25% bupivacaine. In the present study, a lower concentration of ropivacaine (0.2%) has been used to compare the post CS analgesia with bupivacaine 0.25%. Such lower dose comparison of the ropivacaine has been done by Jalil et al in TAP block for postoperative analgesia after appendectomy, and they found comparable efficacy in the two groups [13]. However, head-to-head comparisons between these two drugs in post CS analgesia are lacking.

Bupivacaine being a potential cardiotoxic and CNS toxic agent, led to development of newer molecules like ropivacaine [5]. The present study demonstrated comparable efficacy in bupivacaine 0.25% and ropivacaine 0.2% in providing post-CS analgesia by TAP block. The adverse events occurrence was similar in the two groups. However, the inherent toxicity with ropivacaine is less and advocates its use over bupivacaine in TAP block.

In current study, the mean time for first analgesic request was 453.3±37.4 minutes in the ropivacaine group. This was lower compared to Chansoria et al [9] in the ropivacaine group (12.36±2.57 hours). Similarly, in study by Srivastava et al [4] the median time for request for analgesia was 12 hours in Bupivacaine group, which was higher than the current study. This difference can be explained as both these studies had a standard postoperative analgesic regimen on shifting to the recovery room.

Present study did not include any such regimen and the exact time to analgesia without any additional factors was observed in the present study. Mankikar et al [3] also did not give additional analgesic regimen in their study and found the mean time to first rescue analgesic as 9.53 hours in the group receiving ropivacaine 0.5%. Higher dose in their study may explain the slightly longer time than the present study.The present study also overcame the limitations of the previous studies, as the patients were observed for > 24 hours till 48 hours. Srivastava et al [4] and Chansoria et al [9] used blind procedures for giving TAP while Mankikar et al [3] practiced USG guided technique similar to that in the present study.

Conclusion

The analgesic efficacy and safety of bupivacaine 0.25% and ropivacaine 0.2% is similar in TAP block under ultrasound guidance as a part of a multimodal analgesia regimen for post caesarean delivery pain management.

References

1. Kerai S, Saxena KN, Taneja B. Post-caesarean analgesia: What is new? Indian J Anaesth. 2017;61(3): 200-214.
2. Snell P, Hicks C. An exploratory study in the UK of the effectiveness of three different pain management regimens for post-caesarean section women. Midwifery. 2006;22(3):249-261.
3. Mankikar MG, Sardesai SP, Ghodki PS. Ultrasound-guided transverse abdominis plane block for post-operative analgesia in patients undergoing caesarean section. Indian J Anaesth. 2016;60(4):253-257.
4. Srivastava U, Verma S, Singh TK, et al. Efficacy of trans abdominis plane block for post cesarean delivery analgesia: A double-blind, randomized trial. Saudi J Anaesth. 2015;9(3):298-302.
5. Kuthiala G, Chaudhary G. Ropivacaine: A review of its pharmacology and clinical use. Indian J Anaesth. 2011;55(2):104-110.
6. Rafi AN. Abdominal field block: a new approach via the lumbar triangle. Anaesthesia. 2001;56(10): 1024-1026.
7. Hebbard P, Fujiwara Y, Shibata Y, Royse C. Ultrasound-guided transverse abdominis plane (TAP) block. Anaesth Intensive Care. 2007;35(4):616-617.
8. Farooq M, Carey M. A Case of Liver Trauma With a Blunt Regional Anesthesia Needle While Performing Transverse Abdominis Plane Block. Reg Anesth Pain Med. 2008;33(3):274-275.
9. Chansoria M, Hingwe S, Sethi A, Singh R. Evaluation of Transverse Abdominis Plane Block for Analgesia after Cesarean Section. J Recent Adv Pain. 2015;1(1): 13-17.
10. Patel D, Patel B, Patel H, Shah D, Vachhrajani P. Transverse Abdominis Plane Block for Post Operative Analgesia in Lower Abdominal Surgery/: A Comparison of Bupivacaine and Ropivacain. Int J Sci Res. 2016;5(12):446-450.
11. Fuladi N, Deshmukh S, Bhure A. Comparative Study of Bupivacaine 0.25% Versus Ropivacaine 0.5% in Transverse Abdominis Plane Block for Postoperative Analgesia in Lower Abdominal Surgeries/: a Randomised Controlled Trial. J Evol Med Dent Sci. 2014;3(17):4569-4576.
12. Sharma N, Mehta N, Sharma S. An evaluation of (0.25%) Bupivacaine Vs (0.5%) Ropivacaine for postoperative analgesia using ultrasound guidedtransverse abdominis plane block for abdominal surgeries: A comparative study. Indian J Clin Anaesth. 2016;3(4): 635-639.
13. Abdul Jalil RM, Yahya N, Sulaiman O, et al. Comparing the effectiveness of ropivacaine 0.5% versus ropivacaine 0.2% for transabdominis plane block in providing postoperative analgesia after appendectomy. Acta Anaesthesiol Taiwanica. 2014;52(2):49-53.

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To Evaluate Hemodynamic Effect of Propofol and Etomidate as Induction Agents in Elective Surgeries

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Abstract

Introduction: One of the major concerns of the anaesthetist during induction of anesthesia is maintenance of haemodynamic stability. Various induction agents have been used during induction like thiopentone, propofol, ketamine and etomidate.

Aim: The aim of this study was to evaluate the hemodynamic effect ofPropofoland Etomidate as induction agents in elective surgeries undergeneral anesthesia.

Material and Methodology: Sixty (60) patients of age group (18-60 years) of ASA grade I and II were randomly divided into two groups of thirty patients each, as follows:

Group I: Propofol 2 mg/kg was given intravenously as induction agent.

Group II: Etomidate 0.3 mg/kg was given intravenously as induction agent. The various haemodynamic parameters were recorded and compared.

Result: A significant difference inhaemodyanamic parameters seen between both the groups. In group I (Propofol) HR, SBP, DBP, MBP significantly decrease at the time of induction and upto 60 minutes ($p<0.05$) whereas in group II (Etomidate) lesserfall in hemodynamics parameters seen as compared to group I ($p>0.05$).

Conclusion: Induction with etomidate is associated with lesser fall in haemodynamic parameters as compared to propofol .

Keywords: Induction; Haemodynamic; Parameters; Propofol; Etomidate.

Introduction

Hemodynamic stability at the time of induction of anaesthesia and during surgery has been a major concern for the anaesthetist. It depends not only on the basal tone of the autonomic nervous system but is also importantly influenced by baroreceptor reflex regulation of autonomic outflow influencing cardiac function and peripheral vascular resistance[1]. Pressor response to laryngoscopy and intubation is a documented fact in patients, under a variety of anaesthetic techniques [2-3]. These changes are due to stimulation of receptors at the base of the tongue which leads to hypertension, tachycardia and other arrhythmias in proportion to magnitude of the stimulus. There is an increase in the concentration of catecholamines like adrenaline and nor- adrenaline in response to the stimulus of laryngoscopy [5] and subsequent intubation stimulates the receptors in larynx and trachea withenhancement of hemodynamic and epinephrine response. The mean increase in arterial pressure due to laryngoscopy and intubation may be upto 20-25 mmHg and the peak response occurs approximately 30-35sec after laryngoscopy. These cardiovascular changes are

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transient, variable and unpredictable and usually well tolerated by healthy individuals, but may be fatal in patients with hypertension, coronary artery disease or raisedintracranial tensions. Laryngoscopy produced the major contribution to the stresss response whereas tracheal intubation on its own contributed only a little. Various drugs and techniques have been utilized to blunt this response with variable degree of success. Thiopentone, propofol, etomidate, ketamine andetofol (admixture of propofol and etomidate) are used as induction agents induction to lower the stress response to laryngoscopy and intubation and to maintain better hemodynamic stability.

Induction of anaesthesia with propofol is smooth and decreases airway reflexes but is associated with significant blood pressure reduction and hemodynamic instability. Propfolis commonly used in outpatient anaesthesia for its rapid and smooth onset of action, short recovery period and minimal per operative side effects [6] but it decreases the cardiac parasympathetic tone in a dose dependent manner [1]. Etomidate as an intravenous induction agent has minimal cardiovascular side effects making it especially suitable for cardiac compromised patients and for those in whom hypotension must be avoided during induction and surgery.

Although etomidate provides stable hemodynamics and minimal respiratory depression, it is associated with several side effects when used for induction of anaesthesia or continuous infusion , including nausea and vomiting [7].

In this study, we aim to evaluate the hemodynamic effects of propofol and etomidate during induction, laryngoscoy, intubation and during surgery under general anaesthesia in elective surgeries.

Aims and Objectives

To evaluate and compare the efficacy of propofol and etomidate as induction agents in maintaining haemodynamic stability in elective surgery under general anesthesia.

Material and Methods

This randomized double blind clinical study was conducted in the department of anaesthesiologyat a tertiary care centre in India, after approval from Institutional Ethical Committee on 60 ASA grade I and II patients aged 18 to 60 years, of either sex, undergoing elective surgery lasting for approximately 2 hrs undergeneral anesthesia.

Patient having cardiac disease, hypertension, respiratory disease, cerebello vascular disease, Mallampati grade III-IV, epilepsy and pregnant patients were excluded from the study. All patients were kept nil per oral for 8 hours. Written informed consent was taken from all patients. On arrival in the operation theatre standard anaesthesia monitors including pulse oxymetry, electrocardiogram, non invasive blood pressure (NIBP) were attached and hemodynamic parameters were recorded. An 18 G intravenous cannula was secured and Ringer Lactate infusion was started. Midazolam 0.025 mg/kg i/v and Nalbuphine 0.1mg/kgi/v were given 2 minutes before induction. The patients were randomly divided into two groups. Randomization was done by computer generated random numbertables. Group I received Propofol 2mg/kg i/v and group II Etomidate 0.3mg/kg i/v for induction. All study drugs were prepared by an anesthesiologist who was blinded to the details of the study. Volume of medication and speed of injection were equal in both the groups. Injection Rocuronium 1.2mg/mg i/v was given as muscle relaxant. Laryngoscopy and endotracheal intubation was done by experienced anesthesiologist and the duration of laryngoscopy was keptto less than 10 seconds. Proper placement of ETT was confirmed by capnography and bilateral auscultation of chest. Anesthesia was maintained by Isoflurane 1-1.5% and equal mixture of Oxygen-Nitrous Oxide (4 L/min) along with intermittent bolus of injection Rocuronium as required throughout the surgery. Heart rate (H.R), systolic blood pressure(SBP), diastolic blood pressure (DBP), mean arterial blood pressure (MBP)and oxygen saturation were continuously monitored and recorded before induction, at induction and after induction at 1, 2, 5,10, 20, 30 and 60 minutes by an anaesthesiologist who wasblinded to the study .

Statistical Analysis

Data was analysed by computer software package Statistical Package for Social Sciences (SPSS) version 20.0 for windows. Categorial data like gender was presented as number. Age, weight, heart rate and blood pressure were presented as Mean±standard deviation (S.D). Inter group comparison of blood pressure and heart rate was done using ANOVA. p value of <0.05 was considered significant.

Results

The *patient's characteristics* i.e. age, sex and weight were statistically similar in both the groups. [Table 1]. The mean baseline heart rate, SBP, DBP,

MBP in both the groups were comparable to each other and statistically non significant. The heart rate in groupI at 1 minute decreased to 69.2±10.5 and in group II to74.8±8.7 and the difference in heart rate betweenboth the groups was statistically significant ($p<0.05$). No significant difference in heart rate was observed at 0 minute, and from 2 minutes till 60 minutes. (p-value>0.05) of induction. Statistically significant fall in *SBP* was observedin group I at 0 minute (at time of induction), and from1 minute, 2minute, 5minute, 10minute, 30minute, 60 minutes ($p=0.000$) of induction [Table 3]. Statistically significant fall in DBP was observed in group I at 0 minute (at time of induction) and at 1minute, 2 minute, 5 minute, 10 minute, 30 minute and 60 minutes (p-value=0.000) after induction [Table 4]. Statistically

Table 1: Comparison of Demographic variables of patients in both the groups

Variables	Group I(n=30)	Group II(n=30)	p value	Statistical significance
Age (years)	37.62±9.06	37.60±9.64	0.265	NS
Gender (male/female)	20/10	18/12	0.279	NS
Weight (kg)	58.1±1.8	57.5±1.6	0.232	NS

Table 2: Comparison of Heart rate between both the groups

Time	Group I (N=30)	Group II (N=30)	P value	Statistical Significance
Baseline	81.5±12.3	84.5±9.8	**0.310**	**NS**
O minute	73.0±11.4	76.7±8.3	0.144	NS
1 minute	69.2±10.5	74.8±8.7	0.024	S
2 minute	79.0±8.5	80.8±10.2	0.452	NS
5 minute	76.5±9.0	79..6±9.6	0.167	NS
10 minute	75.2±10.2	78.4±9.2	0.175	NS
30 minute	74.5±10.3	78.5±10.5	0.113	NS
60 minute	74.6±9.7	78.5±10.0	0.102	NS

Table 3: Comparison of Systolic blood pressure (SBP) between both the groups

Time	Group I (N=30)	Group II (N=30)	P value	Statistical Significance
Baseline	137±4.3	131.1±8.7	0.167	NS
O minute	102.2±8.1	118.6±14.4	0.000	S
1 minute	94.2±9.4	112.9±17.1	0.000	S
2 minute	94.8±7.4	127.3±10.9	0.000	S
5 minute	95.7±6.4	125.4±9.2	0.000	S
10 minute	96.7±6.5	124.3±7.7	0.000	S
30 minute	98.5±5.3	124.4.±9.6	0.000	S
60 minute	99.6±5.5	124.9±7.8	0.000	S

Table 4: Comparison of Diastolic blood pressure between both the groups

Time	Group I (N=30)	Group II (N=30)	P value	Statistical Significance
Baseline	87.4±4.0	86.4±4.5	0.317	NS
O minute	58.1±6.2	74.7±10.6	0.000	S
1 minute	56.2±5.7	69.7±12.0	0.000	S
2 minute	57.7±5.5	80.4±7.6	0.000	S
5 minute	57.0±4.6	80.2±6.2	0.000	S
10 minute	56.5±4.2	79.6±5.9	0.000	S
30 minute	58.5±5.1	79.9±5.9	0.000	S
60 minute	58.0±4.4	80.2.±6.7	0.000	S

Table 5: Comparison of Mean blood pressure between both the groups

Time	Group I (N=30)	Group II (N=30)	p value	Statistical Significance
Baseline	104.3±3.9	102.1±4.9	0.057	NS
O minute	72.4±6.4	89.0±11.5	0.000	S
1 minute	68.4±6.3	84.2±13.4	0.000	S
2 minute	69.6±5.1	96.0±8.2	0.000	S
5 minute	69.5±4.7	95.2±6.8	0.000	S
10 minute	69.6±4.1	94.6±5.6	0.000	S
30 minute	70.9±4.7	95.1±6.1	0.000	S
60 minute	71.6±3.8	95.3±5.8	0.000	S

significant fall in MBP was observed in group I at 0minute (at time of induction), and after 1minute, 2minute, 5minute, 10minute, 30minute and 60 minutes (p-value=0.000) of induction [Table 5].

Discussion

General anesthetic induction agents may decrease arterial blood pressure via cardio vascular depression and attenuation of autonomic nervous system activity. On the other hand laryngoscopy and endotracheal intubation elicit vasopressor responses such as hypertension and tachycardia. Various attempts have been made to attenuate hemodynamic instability duringinduction, larynoscopy, and intubation. In many studies induction agents, eitheralone or in combination have been used to achieve minimumcardiovascular effects. Propofol is widely used as an intravenous induction agent but induction with propofol alone causes remarkable reduction in blood pressure. Various studies show that etomidate provides better hemodynamic profile during induction but for its adverse effects like myoclonus and adrenal suppression.

Patients in both the groups were comparable with respect to age, sex and mean weightconsistent with findings of K Meena et. al. who also hadcomparable age group and comparable gender distribution [8].

In our study significant difference in heart rate was seen at 1minute in group I vs II after induction (p = 0.024). No significant difference in heart rate was observed at 0 min, after 1min till 60 mintues. (p>0.05) Masoudifar M et al concluded there were no significant difference among groups I (Propofol) and II (Etomidate) in terms of HR (P = 0.47) [9]. Whereas Singh R et. al. found a significant increase from baseline in heart rate (P = 0.001) at 1 minute after intubation in their study. This statistically significant difference can be due to ASA grade III patients with coronary artery diseaseand left ventricular dysfunction [10].

In our study statisticallysignificant fall in SBP was observed in group I at 0min which persisted till 60 minutes. A significant fall in SBP was observed in group I vs II at 2min, 5min,10min, 30min and 60 minutes (p=0.000).

Geeta Karki et al concluded that Etomidate offers superior hemodynamic stability during induction compared to thiopentone and propofol, similar to our study [11].

Stastically significant fall in DBP was found in group I vs group II at 0 minute, 1minute, 2minute, 5minute, 10minute, 30minute and 60 minutes (p-value 0.000) of induction. In 2015 Ozgur Yagan et. al. measured the haemodynamic responses using etomidate, propofol and combination of etomidate-propofol. In all 3 groups, a significant decrease in MAP values were seen at T2 and T3 compared to the baseline values, and this decrease was greater in group P compared to that in group E and PE ($P < 0.001$, $P<0.01$)[12] Findings of our study are comparable with, Ozgur Yagan et. al.

Statistically significant difference was found in MBP in both the groups at 0 min (at the time of induction) and after 1 minute of induction. Significant change (fall in MBP) was observed in group I vs II at 2minute, 5minute,10minute, 30minute and 60 minutes (p-value 0.000). Bendel SI et. al. found that MBP decreased to a greater extent in patients receiving propofolthan in those receiving etomidate ($P = 0.006$) [13]. Erdil F et. al. concluded that MBP were lower at T3 and T4 in the propofol group than in the etomidate group ($P < 0.05$) [14]. Findings of our study are consistent with the study of Bendel et. al. and Erdil et. al.

Conclusion

Induction with etomidate provides stable hemodynamic parametersas compared to propofol which causes noteworthy hypotension when used for' induction of anesthesia.

References

1. Ebert TJ, Muzi M, Berens R, Goff D, Kampine JP. Sympathetic responses to induction of anaesthesia in humans with propofol or etomidate. Anaesthesiology 1992;76:725-33.
2. King BD, Harris LC, Griefenstein FE et. al. Reflex circulatory response to direct layrngoscopy andintubation performed during anesthesia Anaesthesiology 1951;12:556-66.
3. Wycoff CC. Endotracheal intubation effects on blood pressure and pulserate. Anaesthesiology 1960;21:153-8.
4. Burnstien CL, Pinto Lo FJ and Newman W. Electro-cardiographic studiesduring tracheal intubation. I: effect during usual routine technics. Anaesthesiology 1950;11:224-37.
5. Russel W J, Morris RG, Frewin D B et .al. Changes in plasma catecholamine concentrations during endotracheal intubation. Br J Anaesth 1981;53:837-9.
6. Ghabash M, Matta M & Kehhaleh J,Depression of excitatory of propofol induction by fentanyl,Middle East J Anaesthesiol, 1996;13(4):419-25.

7. St Pierre M, Dunkel M, Rutherford A, Hering W. Does etomidate increase postoperative nausea? A double-blind controlled comparison ofetomidatein lipid emulsion with propofol for balanced anaesthesia.Eur J Anaesthesiol 2000;17:634-641.
8. Meena K, Meena R, Nayak SS, Prakash S, Kumar A . A Comparative Study of Effect of Propofol, Etomidate and Propofol Plus Etomidate Induction on Hemodynamic Response to Endotracheal Intubation: A RCT. J AnesthClin Res 2016;(7):622. doi: 10.4172/2155-6148.1000622.
9. Masoudifar M1, BeheshtianE.Comparison of cardiovascular response to laryngoscopy and tracheal intubation after induction of anesthesia by Propofol and Etomidate.J Res Med Sci.2013;18(10):870-4.
10. Singh R, Choudhury M, Kapoor PM, Kiran U. A randomized trial of anesthetic induction agents inpatients with coronary artery disease and left ventricular dysfunction. Ann Card Anaesth. 2010; 13:217-23.
11. Geeta Karki, Vishwadeep Singh, Abhishek Barnwal, Lalit Singh. A Comparative Evaluation of Hemodynamic Characteristics of the Three Induction Agents – Etomidate, Thiopentone and Propofol. Journal of Evolution of Medical and Dental Sciences 2014 Aug 11;3(34):9133-41.
12. Yagan O, Tas N, Kucuk A, Hanci V, Yurtlu BS. Haemodynamic Responses to Tracheal Intubation Using Propofol, Etomidate and Etomidate-Propofol Combination in Anaesthesia Induction. J Cardiovasc Thorac Res 2015(7):134-40.
13. Bendel SI, Ruokonen E, Pölönen P, Uusaro A. Propofol causes more hypotension than etomidate in patients with severe aortic stenosis: Adouble-blind, randomized study comparing propofol andetomidate. ActaAnaesthesiol Scand 2007;51:284-9.
14. Erdil FL, Demirbilek S, Begec Z, Ozturk E, Ersoy MO. Effects of propofol or etomidate on QT interval during electroconvulsive therapy. J ECT. 2009Sep;25(3): 174-7.

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Effect of Premedication with Intravenous Clonidine in Modulating the Haemodyanamic Responses during Laparoscopic Surgeries

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Abstract

Context: Pneumoperitoneum during laparoscopic surgeries leads to adverse effects on cardiovascular physiology which in turn compromises tissue perfusion.

Aims: To study the effect of premedication with intravenous clonidine in modulating the haemodyanamic responses during laparoscopic surgeries.

Settings and Design: Prospective randomised double blinded study.

Methods and Material: The study was conducted in a group of sixty patients undergoing laparoscopic surgeries who were randomly allocated into two groups each having thirty patients namely group green who received 2µg/kg of intravenous clonidine in 100 ml normal saline 15 minutes prior toinduction and group red who received 100 ml of plain saline 15 minutes prior to induction. Haemodyanamic parameters during induction, intubation, pneumoperitoneum and extubation were monitored. The postoperative pain scores and time to first analgesic request were documented.

Statistical Analysis used: Student's t test was used for the haemodyanamic parameters. Chi square test was used for non parametric values and corresponding p was computed. P value of <0.05 was considered statistically significant.

Results: There was a 20 to 27% increase in heart rate in group red during haemoperitoneum whereas the increase in group green (clonidine group) was 16%. The mean systolic BP varied from 134±17.75 to 95.23± 9.93 in green group whereas in red group it varied from 144±14.57 to 129.93±13.44. Postoperative visual analogue score was 3.36 in group green as compared to 7.36±1.54 in red group.

Conclusions: Patients receiving intravenous clonidine as premedication showed stable haemodyanamics and better analgesia and sedation as compared to those who didn't receive clonidine.

Keywords: Laparoscopy; Haemodyanamics; Pneumoperitoneum; Clonidine; Analgesia.

Introduction

The creation of capnoperitoneum during laparoscopic surgeries leads to adverse cardiovascular effects such as an increase in mean arterial pressure, decrease in cardiac output and increase in systemic vascular resistance which in turn compromise tissue perfusion [1,2]. Clonidine is a cost effective centrally acting alpha2 selective partial adrenergic agonist; alpha2:alpha1 selectivity ratio being 220:1. It inhibits the release of catecholamines and vasopressin [3]. The primary outcome of this study was to study the haemodynamics after premedication with intravenous clonidine in patients undergoing laparoscopic surgeries. The secondary outcome was to study the other actions of clonidine i.e pain and sedation scores and time to analgesic request.

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Materials and Methods

After approval from the hospital ethics and research committee, a prospective randomised double blinded comparative study was conducted on 60 adult patients undergoing laparoscopic surgeries for a period of nine months. The criteria for enrolling the patients in the study were as follows:

Inclusion Criteria

Patients undergoing laparoscopic surgeries under general anaesthesia, age between twenty and sixty years, ASA grade 1 and 2, elective surgeries with a duration of approximately two to three hours.

Exclusion Criteria

Ischaemic heart disease, aortic stenosis, left ventricular failure, atrioventricular block, patients on beta blockers, MAO inhibitors and benzodiazepines, laparoscopic surgeries that got converted to open surgeries.

After preoperative assessment patients fulfilling the study criteria were selected and preoperative orders to be nil orally for six hours before surgery was given. Patients were randomly assigned to one of the two groups (green or red) each having having thirty patients according to a random table created by a personal computer. Two batches of similar looking one ml ampoules which were colour coded as green and red were secured from pharmacy. The green ampoules contained 150µg/ml of clonidine and red ampoules contained saline. The content of the colour coded ampoules was known only to the pharmacist. The patients in group green were given 2µg/kg of clonidine in 100ml saline 15 mintes before induction and the patients in group red were given 100 ml of saline 15 minutes before induction. On the day of the surgery intravenous access was secured and after checking the anaesthesia machine and equipments and noting the name, age, weight and sex, the patient was shifted to the operation theatre. Monitors were connected and baseline parameters namely pulse oximeter, non invasive blood pressure and ECG were recorded. Premedication with the study drug was administered as an infusion at a dose of 2µg/kg in 100ml saline over 15minutes prior to induction. Intravenous glycopyrrolate 0.2 mg and i.v fentanyl 1.5µg/ml was given to all patients. Patient was induced with 2mg/kg of intravenous propofol and endotracheal intubation facilitated with atracurium (0.5mg/kg). Patient was maintained on isoflurane 1%, oxygen and nitrous oxide (total flow 3L/min) and relaxation was maintained with i.v atracurium. The minute ventilation was controlled and adjusted to end tidal carbondioxide between 32-45 mm of Hg. The intraabdominal pressure (IAP) was maintained at less than 14 mm of Hg. Bradycardia, defined as heart rate less than 20% of baseline or absolute heart rate less than 50 per minute whichever is less was treated with 20µg/kg of atropine. Hypotension, defined as BP less than 25% of baseline or systolic BP less than 90 mm of Hg was treated with 5-10 mg bolus ephedrine IV. Intr operatively the haemodyanamics were monitored as:

- Baseline
- 5 minutes after premedication
- 15 mintes after premedication (T0)
- Immediately after intubation (T1)
- 3 minutes after intubation (T2)
- Before pneumoperitoneum (PNO) (T3)
- 15 minutes after PNO (T4)
- 30 minutes after PNO (T5)
- 10 minutes after release of PNO (T6)
- 10 minutes after extubation (T7)

In addition the $ETCO_2$ and SpO_2 was monitored. Towards the end of the surgery, all patients were given ondansetron 0.15mg/kg and were reversed with iv neostigmine 5µ/kg and glycopyrrolate 10µg/kg. After extubation the patients were shifted to PACU and vitals monitored for 60 minutes. The Ramsay sedation score was assessed postoperatively after shifting to PACU.

Degree of sedation (Ramsay scale)

1. Awake and agitated
2. Awake and comfortable
3. Asleep but arousable
4. Asleep but sluggish response
5. No response to call or touch

Ten point visual analogue scale (VAS) was noted at the end of 60 minutes postoperatively before shifting the patient to the ward. The time to first analgesic request; TAR (period elapsed between the end of surgery to the time when the first analgesic was administered at patient's request) was noted. The results obtained in the study were recorded in a tabulated proforma. Descriptive and inferential statistical analysis were used in the study. Results on continuous measurements are presented on Mean±SD (Min-Max) and results on cateogorical

measurements are presented in Number (%). Significance is assessed at 5% level of significance. The following assumptions on data is made .Student T test (two tailed, independent) has been used to find the significance of study parameters on continuous scale between 2 groups. Chi-square/Fisher Exact test has been used to find the significance of study parameters on categorical scale between two or more groups.

Significant Figures

+ suggestive significance (P value: 0.05<P<0.10)

*Moderately significant (P value: 0.01<P≤ 0.05)

*** Strongly significant (P≤0.01)

Sample size estimation

Proportion known population

$n = [(z^2 * p * q) + ME^2] / [ME^2 + z^2 * p * q / N]$

Proportion unknown population:

$n = [(z^2 * p * q) + ME^2] / (ME^2)$

ME: is the margin of error, measure of precision.

and Z is 1.96 as critical value at 95%CI

N: population size

n: Sample size

σ: Standard deviation

Z: Critical value based on Normal distribution at 95% Confidence Interval

Standard deviation: $SD = \sqrt{\frac{\sum (x - \bar{x})^2}{n-1}}$

Statistical Software

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 etc.

Results

The patients were randomised into the intravenous clonidine group/test group (green) group and intravenous saline/control (red) group. The two groups were comparable in respect to age [Table 1], sex [Table 2], weight [Table 3], duration [Table 4] and ASA physical status.

The mean heart rate varied from 88.07±17.30 to 73.5±18.14 in clonidine group.it varied from 132±18.3 to 89.3±14.40 in control group. The heart rate after 15 minutes of infusion (T0) of clonidine was significantly lower when compared to that in control group (p<0.05). Immediately after intubation (T1) and 3 minutes after intubation (T2), the increase in heart rate, to the respective baseline, was 8.3% and 10.3% respectively in the control group whereas in clonidine group the increase was only by 6% and 10% respectively. Before pneumoperitoneum (T3) the heart rates had a statistically significant difference in both the the groups (p<0.01). After 15 minutes (T4) and 30 minutes (T5) of pneumoperi-toneum there was a significant difference in heart rates between the two groups (<0.001). There was a 20 to 27% increase in heart rates between in the control group during pneumoperitoneum whereas the increase in clonidine group was 16% and 10%. At all points the heart rates in clonidine group in comparison to control group was lower which was statistically significant [Figure 1]. The mean systolic BP varied from 134.67±17.75 to 95.23±9.93 in clonidine group whereas in control group it varied from 144±14.57 to 129.93±13.44. Although there was no significant difference in systolic BP between both groups after 5 minutes of infusion, systolic BP after 15 minutes (T0) of clonidine was significantly lower when compared to control group (p<0.01). After intubation the systolic BP (T1) decreased in clonidine group by 20% and increased in the control group by 3% when compared to the respective baseline values, which was statistically significant. Before pneumoperitoneum (T3), 15 minutes and 30 minutes after pneumoperitoneum the

Table 1: Age distribution of patients studied

Age in years	Test group		Control group	
	No	%	No	%
21-30	3	10.0	4	13.3
31-40	7	23.3	6	20.0
41-50	11	36.7	13	43.3
51-60	8	26.7	5	16.7
>60	1	3.3	2	6.7
Total	30	100.0	30	100.0
Mean ± SD	45.50±11.25		44.77±11.38	

Samples are age matched with p=0.803

Table 2: Gender distribution of patients studied

Gender	Test group		Control group	
	No	%	No	%
Male	7	23.3	15	50.0
Female	23	76.7	15	50.0
Total	30	100.0	30	100.0

Samples are gender matched with p=0.060

Table 3: Comparison of weight (kg) in two groups of patients studied

Weight (kg)	Test group		Control group	
	No	%	No	%
<50	7	23.3	4	13.3
51-60	12	40.0	10	33.3
61-70	5	16.7	12	40.0
>70	6	20.0	4	13.3
Total	30	100.0	30	100.0
Mean ± SD	58.43±13.26		62.60±8.66	

Mean weight is statistically similar with P = 0.155

Table 4: Comparison of Duration (hrs) of surgery in two groups of patients studied

Duration (hrs)of surgery	Test group		Control group	
	No	%	No	%
1-2 hours	1	3.3	4	13.3
2-4 hours	28	93.3	25	83.3
>4 hours	1	3.3	1	3.3
Total	30	100.0	30	100.0
Mean ± SD	3.16±0.55		3.03±0.76	

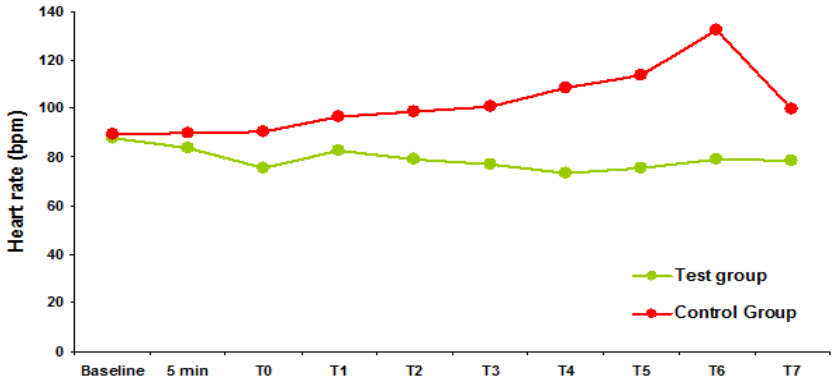

Fig. 1: Comparison of heart rate (bpm) in two groups of patients studied

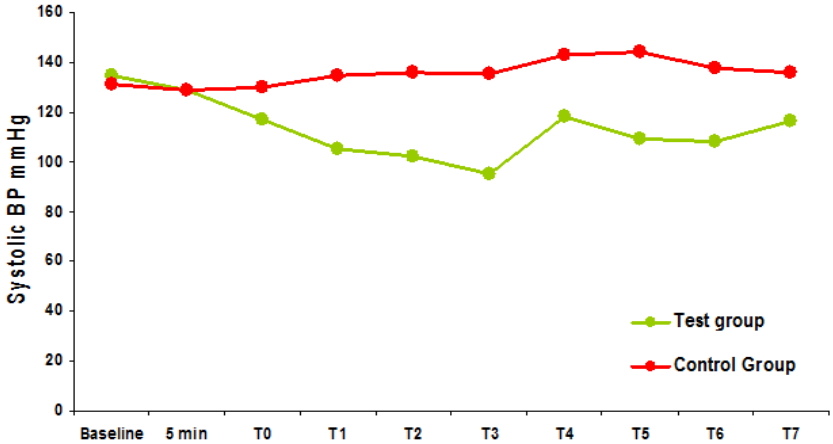

Fig. 2: Comparison of Systolic BP mmHg in two groups of patients studied

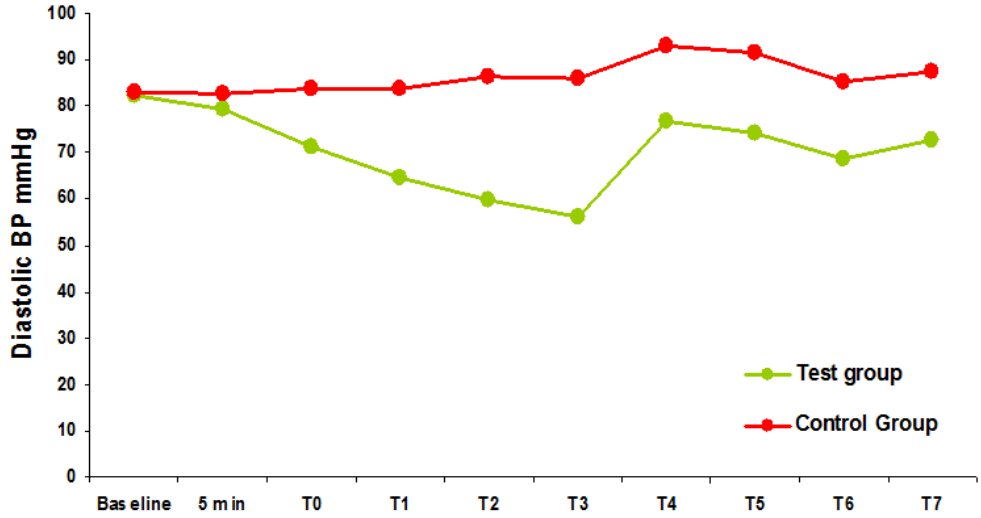

Fig. 3:

Fig. 4:

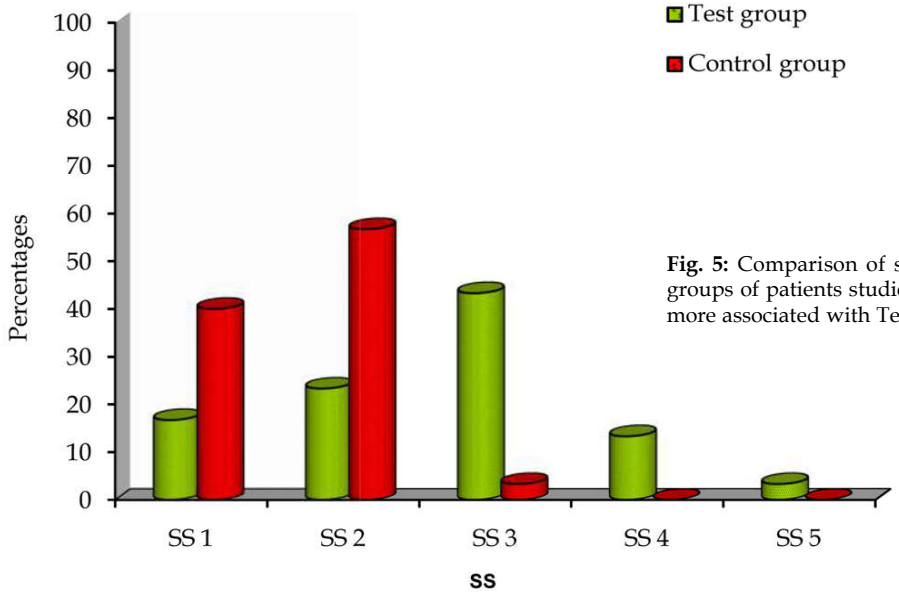

Fig. 5: Comparison of sedation scale (SS) in two groups of patients studied SS score is significantly more associated with Test group with P = <0.001**

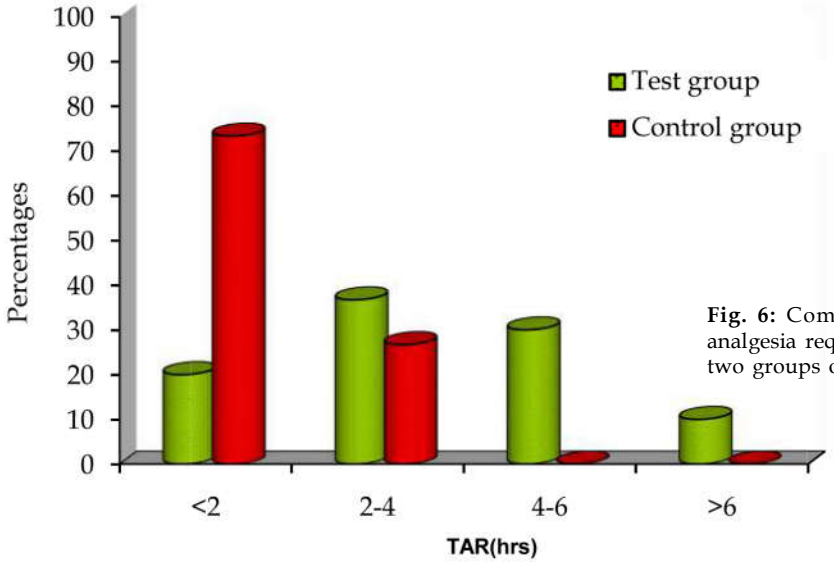

Fig. 6: Comparison of time to analgesia request (TAR) in hrs in two groups of patients studied

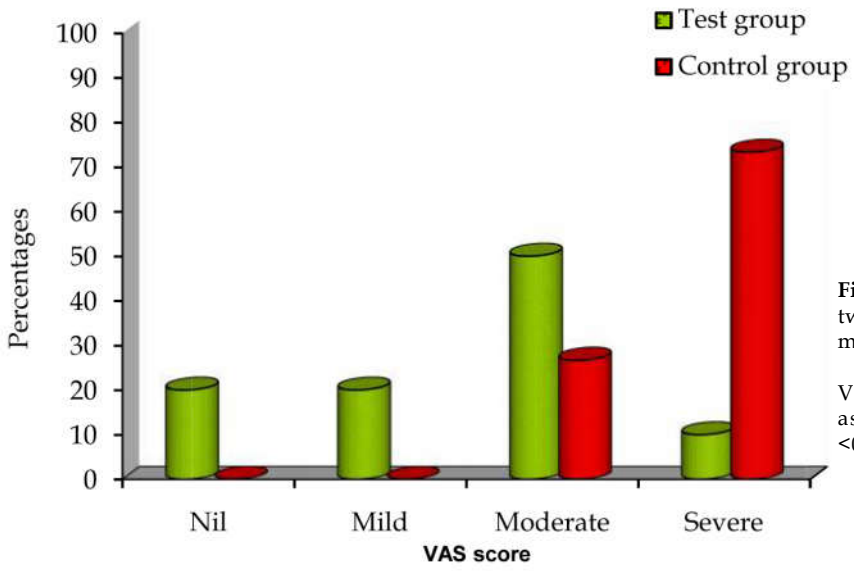

Fig. 7: Comparison of VAS score in two groups of patients studied at 60 minutes post operatively

VAS score is significantly less associated with Test group P = <0.001**

systolic pressures were significantly lower in clonidine group than control group . In the clonidine group there was a decrease of 12.45% and 18.8% after 15 minutes and 30 minutes of pneumoperitoneum respectively. In the control group there was increase in systolic BP after 15 and 30 minutes of pneumoperitoneum by 9-10%. At all points of time the systolic BP in clonidine group compared to the control group was lower which was statistically significant (p<0.001)[Figure 2]. Although 5 minutes after infusion of the drug there was no statistically significant difference in diastolic BP in both groups, post intubation and immediately thereafter at all points of time the diastolic BP was significantly lower in clonidine group than the control goup (p<0.001) [Figure 3]. Since mean arterial pressure is derived from systolic and diastolic pressures, it followed the same trends. It was seen to be significantly lower in clonidine group as compared to the control group [Figure 4]. Patients in clonidine group were significantly more sedated when compared to the patients in control group [Figure 5]. Mean TAR (hours) is significantly more in test group with P=<0.001** [Figure 6]. VAS score is significantly less associated with test group P=<0.001** [Figure 7].

Discussion

Laparoscopic surgeries have the advantage of reduced postoperative pain due to smaller incisions and less haemorrhage and shorter recovery times and significant cost savings. They involve the creation of carbondioxide pneumoperitoneum which causes

increases in intraabdominal pressure(IAP). IAPs higher than 10 mm of Hg induces significant alterations in haemodyanamics. Dexter et al [1] randomised patients to insufflation pressures of either 7 or 15 mm of Hg during laparoscopic cholecystectomy. Heart rate and mean arterial pressure in both groups increased but stroke volume and cardiac output were significantly more depressed in the high pressure group. In a study by Mc Laughlin et. al. [2] intraabdominal pressures of 15 mmof Hg caused a 30% decrease in cardiac output (CO) and stroke volume (SV) and a 60% increase in mean arterial pressure (MAP) from preinsufflation levels, and these changes were determined to be statistically significant. Considering all these facts the IAP was kept below 14 mm of Hg in the present study. The alpha 2 adrenergic agonists like clonidine have a central sympatholytic action. They improve haemodyanamic stability during surgery and are known to reduce the anaesthetic and opiod consumption by causing sedation, anxiolysis and analgesia. Decreased sympathetic nervous system activity is manifested as peripheral vasodilatation and a decrease in systolic blood pressure, heart rate and cardiac output [3]. The ability of clonidine to modify the potassium channels in the CNS and thereby hyperpolarize the cell membranes may be the the mechanism for profound decrease in anaesthetic requirements produced by clonidine [4]. Studies using oral clonidine administered 60 to 90 minutes before induction of anaesthesia have shown good results in minimising the haemodyanamic changes during laparoscopic surgery [5].

Although the bioavailability of clonidine is 90% after oral administration , it requires 2 to 4 hours to reach its peak effect [6], necessitating its ingestion at least 2 hours prior to induction to achieve the desired clinical effect. Intravenous clonidine has its onset of action within 15 minutes. Therefore its administration 15 minutes before the surgery by the intravenous route was preferred in this study. Various doses of iv clonidine have been used in the past to maintain haemodyanamics during laparoscopy. The dose of i.v clonidine in the present study is similar to the dose used in the study by Tripathi D C et. al. [7] who have compared two doses of i.v clonidine namely 1µg/kg and 2µg/kg in modulating the haemodyanamic stress response during laparoscopic surgery. They found that with a dose of 2µg/kg , there is a decrease in HR, SBP, DBP and MAP from baseline within 15 minutes of premedication ($p<0.05$), but at no time this decrease was more than 20% from baseline. This finding is comparable to our study where there was a fall in SBP by 13% after premedication with clonidine which was not significant. Marco P Zalunaedr et. al. [8] used 3µg/kg of i.v clonidine immediately before induction and compared it with a placebo. It was observed that MAP, post–intubation was significantly lower in clonidine group as compared to placebo ($p<0.05$). in our stud , we used 2µg/kg clonidine 15 minutes before induction and observed that MAP, post–induction was lower in the clonidine group when compared to control group and this difference was statistically strongly significant ($p=0.001$) immediately after intubation and $p< 0.001$ 3 minutes after intubation. In the study by Tripati D C et. al., the patients who received 2µg/kg of iv clonidine there was an increase in HR and DBP ($p>0.05$) and MAP remained comparable to the baseline. These changes were statistically not significant. These findings are comparable with the findings in our study except for the DBP. , which showed a decrease in our study.

Following institution of pneumoperitoneum , there was significant increase in HR, SBP,DBP and MAP in the control group as compared to the clonidine group ($p<0.001$) in our study (143±17.63 vs 117±18.56 for BP; 76.67±15.69 for DBP and 109±11.04 vs 87.00±15.27 for MAP). This finding is comparable is comparable to the study by Tripathi D C et. al.[7] who showed a statistically significant difference in HR, SBP, DBP and MAP, 20 minutes and 40 minutes after institution of pneumo-peritoneum ($p<0.05$) in the present study, 10 minutes after release of pneumoperitoneum, the HR in the control and clonidine group were similar (p+0.129). 10 minutes post extubation and 10 minutes after release of pneumoperitoneum, the HR, SBP, DBP and MAP were lower in clonidine group as compared to the control group and this difference was statistically significant in our study ($p<0.001$) in the present study, 2 patients in the clonidine (6.7%) had bradycardia. They responded well to intravenous atropine 0.6 mg. Clonidine related bradycardia has rarely been described as a side effect in commonly prescribed doses. it is more commonly associated with clonidine poisoning or overdose.

The patients who are more susceptible to bradycardia are the ones with clinical sinus node dysfunction and those already receiving sympatholytic agents. 3 patients (10%) in the clonidine group developed hypotension which was treated with ephedrine 6mg iv. Ray M et .al. [9] in their study used 3µg/kg of iv clonidine 15 minutes before induction and as infusion at 1µg/kg/min. The incidence of bradycardia and hypotension was high in their study.

The incidence of bradycardia was not significant in our study as we used a lower dose of clonidine. In the study by Kalra NK et. al. [10] there was no

bradycardia and hypotension as they used a dose lower than our study i.e 1.5µg/kg i.v. 15 minutes before induction. The analgesic effect of clonidine has been a subject to research in recent times. Mechanisms of analgesic effect either during acute pain or chronic pain management have been recently discovered and these still remain as active fields of research [4,11].

In this study we have tried to compare the time of first requirement of analgesia postoperatively in both the groups. The 1 hour postoperative 10 point VAS score was significantly lower in the patients who received clonidine (VAS 3.86±2.45 in clonidine group vs 7.36±1.54 in control group). It was observed that most of the patients who received clonidine were sleeping comfortably in the PACU but when aroused and assessed for VAS they had mild to moderate pain. The time to analgesia request was significantly higher in clonidine group (4.17±1.79 hours vs 1.65±0.95 hours) 36.7% of patients who received clonidine requested analgesia in 2- 4 hours post-operatively whereas 73.3% of patients in control group requested analgesia within 2 hours post-operatively.

Singh S et. al. [7] have used oral clonidine and have shown a decrease in postoperative analgesic requirement. The mean sedation score in clonidine group was 2.63±1.03 as compared to 1.63± 0.55 in the control group. 43.3% of the patients who received clonidine had a sedation score of 3. In spite of the high sedation scores , none of the patients in the clonidine group had respiratory depression.

In the study by Tripathi et. al. [9] a similar iv dose was used and the meam sedation scores were 2 as compared to 2.63±1.03 in the present study.

Conclusion

From the results of our study we arrived at the following conclusions.

1. Premedication with 2µg/kg intravenous clonidine, 15 minutes before surgery in ASA 1 and 2 patients was found to be relatively safe and effective in providing stable haemodyanamics intraoperatively and as protection against stress response to pneumoperitoneum.
2. Intravenous clonidine offers additional advantage of providing post-operative analgesia and sedation.
3. Intravenous clonidine at a dose of 2µg/kg can be recommended as premedication for laparoscopic surgeries in patients without cardiovascular diseases.

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Conflict of Interest: None

Abbreviations

BP- Blood pressure
CO_2- Carbon-dioxide
DBP- Diastolic blood pressure
ECG- Electrocardiogram
$ETCO_2$- End – tidal carbondioxide
IV- Intravenous
IM- Intramuscular
MAP- Mean arterial pressure
PNO- Pneumoperitoneum
SBP- Systolic blood pressure
SpO_2- Oxygen saturation
SVR- Systemic vascular resistance
TAR- Time to analgesia request

References

1. Dexter SP, Vucevic M, Gibson J, McMahon MJ. Haemodyanamic consequences of high and low pressure capnoperitoneum during laparoscopic cholecystectomy. Surg Endosc. 1999;13(4):376-81.
2. Mc Laughlin JG, Scheeres DE, Dean RJ, Bonnell BW. The adverse hemodynamic effects of laparoscopic cholecystectomy. Surg Endosc. 1995;9(2):121-4.
3. Baskar S, Singh G, Jacob R . Clonidine in paediatrics-A Review. Indian Journal of Anaesthesia 2009;53(3) 270-280.
4. Kawahito Shinji, Kawano Takashi, Kitahata Hiroshi, Oto Jun, Takahashi Akira, Takaishi Kazumi et al. Molecular mechanism of inhibitory effects of clonidine on vascular adenosine triphosphate sensitive potassium channels. Anesth Analg. 2011;113(6): 1372-1380.
5. Singh S, Arora K. Effect of oral clonidine premedication on perioperative haemodyanamic response and postoperative analgesic requirement for patients undergoing laparoscopic cholecystectomy. Indian J Anaesth 2011;55(1):26-30.

6. John L Reid. The clinical pharmacology of clonidine and central antihypertensive agents. Br J Clin Pharmac. 1981;(12)295-302.
7. Tripathi DC, Shah KS, Dubey SR, Doshi SM, Raval PV. Haemodyanamic stress response during laparoscopic cholecystectomy: Effect of two different doses of intravenous clonidine premedication. J Anaesthesiol Clin Pharmacol. 2011Oct;27(4):475-80.
8. Zalunardo MP, Zollinger A, Spahn DR, Seifert B, Pasch T. Preoperative clonidine attenuates stress response during emergence from anaesthesia. J Clin Anesth 2000A UG;12(5):343-9.
9. Ray M, Bhattacharjee DP, Hajra B, Pal R, Chatterjee N. Effect of clonidine and magnesium sulphate on anaesthetic consumption, haemodyanamics and postoperative recovery: A comparative study. Indian J Anaesth. 2010;54:137-41.
10. Kalra NK, Verma A, Agarwal A, Pandey HD. Comparative study of intravenously administered clonidine and magnesium sulphate on haemodyanamic responses during laparoscopic cholecystectomy. J Anaesthe Clin Pharmacol 2011;27:344-8.
11. Dabbagh A. Clonidine: An old friend newly discovered Anesth Pain Med 2011;1(1)8-9.

Original Research Article

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Comparison of Dexmedetomidine with 0.5% Levobupivacaine and 0.5% Ropivacaine in Supraclavicular Brachial Plexus Block

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Abstract

Background and Aims: Dexmedetomidine as an adjuvant to local anaesthetic in supraclavicular plexus block. We compared the onset time of sensory and motor block and postoperative analgesia.

Methods: Sixty patients scheduled for upper limb surgeries were divided into two equal groups, group LD and RD, randomly. The patients received brachial plexus block via supraclavicular route with the help of nerve stimulator. In group LD (n=30) 30cc of 0.5% levobupivacaine with 1µg/kg dexmedetomidine and in group RD (n=30) 30cc of 0.5% ropivacaine with 1µg/kg dexmedetomidine was given. Onset of motor and sensory block and time to first rescue analgesia were recorded.

Results: Sensory and motor onset time was significantly early in Group LD compared with RD ($P< 0.05$). Duration of post operative analgesia was significantly longer in Group LD compared to Group RD ($P<0.05$).

Conclusion: Addition of Dexmeditomidine to Levobupivacaine for supraclavicular brachial plexus block shorthens the onset times for sensory and motor blocks and significantly prolonged the duration of analgesia.

Keywords: Analgesia; Dexmedetomidine; Levobupivacaine; Ropivacaine; Sensory; Motor.

Introduction

Peripheral nerve block as an anesthetic technique plays an important role in modern regional anesthesia. Upper limb surgeries below the shoulder joint are mostly performed under peripheral blocks such as the brachial plexus block. Peripheral nerve blocks not only provide intra-operative anesthesia, but also extend analgesia in the post-operative period without major systemic side-effects by minimizing stress response and using minimal anesthetic drugs [1].

Its increased popularity is because of advancements in regional anesthesia techniques in terms of local anesthetics drugs, newer adjuvant and use of pheripheral nerve stimulator or ultra sound for safe and successful conduct of block.

Levobupivacaine and ropivacaine are long-acting local anesthetics used for peripheral nerve blocks to provide prolonged postoperative analgesia. Levobupivacaine has been reported to have a longer duration of analgesic effect compared with ropivacaine when used for spinal and epidural anesthesia [2-5].

Studies on animals revealed that compared with ropivacaine, levobupivacaine had similar or more pronounced nerve blocking effects, depending on the concentration. Clinical studies have shown that levobupivacaine and ropivacaine have fewer adverse affects on the cardiovascular system and central nervous system (CNS) than does bupivacaine making

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them more advantageous in regional anesthetic techniques that require large volumes of local anesthetics [6-8].

Adding dexmedetomidine to local anesthetics during peripheral nerve blockade [9] and regional anesthesia [10] procedures may also prove efficacious for the surgical patients. In human study, dexmedetomidine has also shown to prolong the duration of the block and post-operative analgesia when added to local anesthetic in various regional blocks [11,12].

Hence the present study is aimed to compare the effectiveness of 0.5% levobupivacaine and 0.5% ropivacaine with 1μg/kg of dexmedetomidine in supraclavicular brachial plexus block in terms of onset of sensory and motor blockade,duration of analgesia and complications,if any.

Materials and Methods

The present study is a prospective, randomized, double blinded comparative study including 60 patients with ASA grade I, II of either sex, aged between 20 and 60 years scheduled for upper limb surgeries of fracture radius ulna, post burn contracture release, debridment and tendon repairs were included in the study. Exclusion criteria were patients not giving consent, existence of peripheral neuropathy, bleeding disorders, local cutaneous infections, and patient with hypersensitivity to either of the drugs used in the study and pregnant women and lactating mothers.

After obtaining approval from institutional ethical committee and informed consent from patients fulfilling the inclusion criteria, cases were divided randomly into two groups: Group LD: received Inj. levobupivacaine hydrochloride 0.5% 30cc and 1μ/kg dexmedetomidine and Group RD: received Inj. ropivacaine hydrochloride 0.5% 30cc and 1μ/kg dexmedetomidine. Each individual was allocated to respective group by computer generated randomization chart. Neither patients nor observer were told about the drug injected .

A thorough preoperative evaluation was performed. After the patient was taken on to operation table, and was monitored using pulseoximeter, ECG and noninvasive blood pressure monitors. An intravenous access was secured using an in-dwelling cannula of appropriate size on the normal limb. Oxygen supplementation was given with nasal cannula at 2 litres/min. Brachial plexus block was performed by supraclavicular approach using pheripheral nerve stimulator.

Patient was positioned supine with head turned about 30 degree to contralateral side. After palpating the interscalene groove and tracing it to the most inferior point, which is just posterior to the subclavian arterial pulse, the latter can be felt in the plane just medial to the midpoint of the clavicle.

Then local infiltration with 2cc of 2% plain lignocaine was given to minimize needle pain. A 22G, 50 mm stimuplex needle with the nerve stimulator was directed just above and posterior to the subclavian arterial pulse and directed caudally at a very flat angle against the skin. The needle was advanced until the flexion of finger was noted.

If contraction was still observed with the intensity of stimulating current decreased to 0.5mA, then following protocol was followed: Group LD received 30 cc of 0.5% injection levobupivacaine hydrochloride and 1μ/kg dexmedetomidine and Group RD received 30 cc of 0.5% injection ropivacaine hydrochloride and 1μg/kg dexmedetomidine. If the rib was encountered without paraesthesia or if blood was encountered, the needle was withdrawn and the landmarks as well as the plane of needle insertion path were re-evaluated.

Patients were evaluated to determine the loss of arm abduction (deltoid sign as sign of successive motor blockade). Sensory block was assessed by pin prick over the surgical site. Failure of loss of arm abduction or pain at surgical site after 30 min was considered to be block failure and hence general anaesthesia was given to those patients and thus was excluded from the study. After evidence of successful motor and sensory block, surgery was performed.

Patients were monitored every hourly for 10 hours for heart rate, blood pressure, SpO_2, onset of sensory block, onset of motor block, and complications if any, then after 10 hours patients were shifted to ward and the time of requirement of first rescue analgesic was noted.

Post-operative pain was also assessed by using visual analog scale (VAS) and VAS less than 4 was given rescue with intravenous diclofenac 1-2mg/kg.

Statistical Analysis

Student t test (two tailed, independent) has been used to find the significance of study parameters on continuous scale between two groups (Inter group analysis) on metric parameters. Chi-square/Fisher Exact test has been used to find the significance of study parameters on categorical scale between two or more groups, Non-parametric setting for Qualitative data analysis

Results

After studying 60 cases, the observation and results were summarized in tabulated form. Table 1 shows the distribution of patients according to mean age with standard deviation and Table 2 shows sex incidence of patients in both the groups with no significant difference. Table 3 shows the mean onset time of sensory blockade and motor blockade in minutes in both the groups. Sensory onset time was calculated from time of injection of drug to onset of dull sensation on any of the nerve distribution.

Motor onset time was calculated from time of injection of drug to when patient felt heaviness on abduction of arm at shoulder. The mean sensory onset time in Group LD was 8.77±1.33 mins and mean motor onset time was 12.93±1.76 mins and Group RD the mean sensory onset was 10.30±2.04 mins, mean motor onset time being 14.80±1.71 mins. Sensory and motor onset time was earlier in Group LD when compared to Group RD, and it was statistically significant (P<0.001).

Table 4 shows the duration of analgesia with standard deviation in hours. Duration of sensory block was calculated from the time between the peak effect time and feeling of dull sensation in any of the nerve distributions.

The duration of effective analgesia was calculated from the time between the end of local anesthetic administration to the time when VAS was less than 4 and rescue analgesic was administered when VAS score was equal to or greater than 4.

Table 1: Age distribution of patients studied (Samples are age matched with P=0.266)

Age in years	Ropivacaine+dexmedetomidine	Levobupivacaine+dexmedetomidine	Total
21-30	11(36.7%)	8(26.7%)	19(31.7%)
31-40	10(33.3%)	10(33.3%)	20(33.3%)
41-50	5(16.7%)	5(16.7%)	10(16.7%)
51-60	4(13.3%)	7(23.3%)	11(18.3%)
Total	30(100%)	30(100%)	60(100%)
Mean ± SD	35.93±10.51	39.20±11.96	37.57±11.29

Table 2: Gender distribution of patients studied (Samples are gender matched with P=0.118)

Gender	Ropivacaine+dexmedetomidine	Levobupivacaine+dexmedetomidine	Total
Female	10(33.3%)	16(53.3%)	26(43.3%)
Male	20(66.7%)	14(46.7%)	34(56.7%)
Total	30(100%)	30(100%)	60(100%)

Table 3: Onset of sensory and Motor (In Mins) in two groups studied

Onset (mins)	Ropivacaine+dexmedetomidine	Levobupivacaine+dexmedetomidine	Total	P value
Sensory	10.30±2.04	8.77±1.33	9.53±1.87	0.001**
Motor	14.80±1.71	12.93±1.76	13.87±1.96	<0.001**

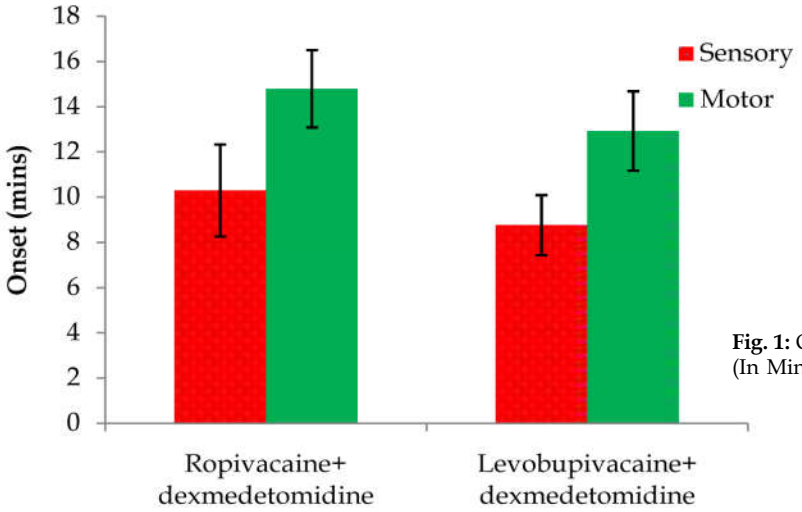

Fig. 1: Onset of sensory and Motor (In Mins) in two groups studied

Table 4: Duration of Analgesia (hrs) in two groups of patients studied

Duration of Analgesia (hrs)	Ropivacaine+dexmedetomidine	Levobupivacaine+dexmedetomidine	Total
<12	3(10%)	0(0%)	3(5%)
12-18	27(90%)	11(36.7%)	38(63.3%)
18-24	0(0%)	19(63.3%)	19(31.7%)
Total	30(100%)	30(100%)	60(100%)
Mean ± SD	13.97±2.03	19.30±2.71	16.63±3.58

P<0.001**, significant, Student t test

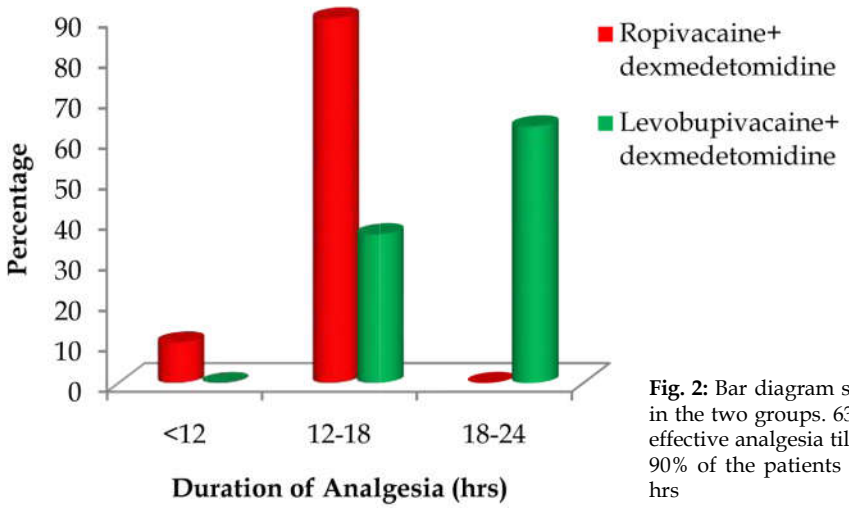

Fig. 2: Bar diagram showing the duration of analgesia in the two groups. 63.3% of patients in Group LD had effective analgesia till 18-24 hrs where as in Group RD 90% of the patients had effective analgesia till 12-18 hrs

Table 4 shows the duration of analgesia in the postoperative period in the two groups in hours.The mean duration of analgesia in Group LD (19.30± 2.71 hrs) was significantly longer than Group RD (13.97±2.03 hrs), both the duration of effective analgesia and the time for rescue analgesia were statistically significant ($P < 0.05$). At VAS score ≥ 4, rescue analgesia was given (Inj. Diclofenac, 1–2 mg/kg i.v.). No significant changes was found in hemodynamic parameters between both the groups.

Discussion

The supracla-vicular approach performed at trunk level provides the most complete and reliable anesthesia as it provides anesthesia of the entire upper extremity in the most consistent, time-efficient manner of many brachial plexus techniques for elbow, forearm, and hand surgery [13].

Dexmedetomidine, a highly selective, α -adrenergic agonist, has analgesic, sedative, anesthetic sparing effects when used in systemic route [14]. Use of dexmedetomidine as an adjuvant mixed with local anesthetics has been performed with neuraxial anesthesia in both adult and pediatric patients [15,16]. Peripherally, α2 agonists produce analgesia by reducing release of norepinephrine and causing α2 receptor independent inhibitory effects on nerve fiber action potentials. Centrally, α2 agonists produce analgesia and sedation by inhibiting substance P release in the nociceptive pathway at the level of the dorsal root neuron and by activating α2 adrenoceptors in the locus coeruleus [17,18].

A study by Brumett et al [19] showed that dexmedetomidine enhances duration of bupivacaine anaesthesia and analgesia of sciatic nerve block in rats without any damage to nerve.

Kousugi et al in their study found high concentrations of dexmedetomidine inhibit compound action potentials in frog sciatic nerves without α2 adrenorecptors activation in a concentration dependent manner and reversibly [20].

In this prospective, randomized, and double-blinded trial, we compared the effect of 1 microgram/kg of dexmedetomidine as an adjuvant with 30 ml 0.50% ropivacaine and 30 ml of 0.5% levobupivacaine in supraclavicular brachial plexus block, on the onset time of sensory and motor block as well as on the postoperative rescue analgesic.

The statistically significant mean onset of sensory and motor blockade was observed earlier in group LD compared to group RD. Similar results were

observed by Mageswaran and Choy [21]. On the contrary, Nodulas et al found that both 0.5% Levobupivacaine and 0.5% ropivacaine had similar onset of action [22]. Similarly in the study conducted by Deshpande et al, they found the onset of sensory and motor block early with levobupivacaine 0.5% with a statistically high significance [23]. Esmaoghu et al found that adding dexmedetomedine to levobupivacaine for an axillary brachial plexus block shortens both the sensory and motor block onset time, extends the block duration, and the analgesia period which was also similar to our study [11].

There was a significant difference ($P < 0.05$) in time of rescue analgesia, viz. prolonged for levobupivacaine with dexmedetomidine (19.30±2.71 h) than for ropivacaine with dexmedetomidine (13.97±2.03h).

Liisanantti et. al. [24] reported that the duration of analgesia when using levobupivacaine for brachial plexus block was the same asthat when using ropivicaine. Casati et. al. [25] reported that there were no difference in postoperative pain scores comparing levobupivacaine and ropivacaine.

However, Cline et. al. [26] showed a longer analgesic effect of levobupivacaine compared with ropivacaine. Mankad et. al. [13] did a study on 60 patients found that Levobupivacaine, a novel long-acting local anesthetic agent, having better profile in terms of duration of analgesia, with a considered disadvantage of delayed wearing off of motor blockade, offers an alternative to ropivacaine for brachial plexus block in upper limb surgeries. Biswas et. al. [27] concluded in their study that dexmedetomidine(1 microgram/kg) added to levobupivacaine in supraclavicular brachial plexus block prolongs the duration of block and the duration of postoperative analgesia. kulkarni et. al. [28] in their study compared 0.5% levobupivacaine and 0.5% ropivacaine in supraclavicular brachial plexus block for upper limb surgeries and concluded that 0.5% levobupivaine provides rapid onset of sensory and motor blockade and prolonged duration of analgesia which is similar to our study.

To conclude, in our study we found that dexmedetomidine when added to levobupivacaine for supraclavicular brachial plexus block shortens the onset times for sensory and motor blocks and prolongs their duration. The significantly prolonged duration of analgesia obviates the need for any additional analgesics. The added advantage of conscious sedation, hemodynamic stability, and minimal side effects makes it a potential adjuvant for nerve blocks.

References

1. Bruce BG, Green A, Blaine TA, Wesner LV. Brachial plexus blocks for upper extremity orthopaedic surgery. J Am Acad Orthop Surg. 2012;20:38–47. [PubMed].
2. Sia AT, Goy RW, Lim Y, et al. A comparison of median effective doses of intrathecal levobupivacaine and ropivacaine for labor analgesia. Anesthesiology 2005;102:651–6.
3. Kopacz DJ, Allen HW, Thompson GE. A comparison of epidural levobupivacaine 0.75% with racemic bupivacaine for lower abdominal surgery. Anesth Analg 2000;90:642–8.
4. Egashira T, Fukasaki M, Araki H, et al. Comparative efficacy of levobupivacaine and ropivacaine for epidural block in outpatients with degenerative spinal disease. Pain Physician 2014;17:525–9.
5. Perotti L, Cusato M, Ingelmo P, et al. A comparison of differences between the systemic pharmacokinetics of levobupivacaine and ropivacaine during continuous epidural infusion: a prospective, randomized, multicenter, double-blind controlled trial. Anesth Analg 2015;121:348–56.
6. Leone S, Di CS, Casati A, Fanelli G. Pharmacology, toxicology, and clinical use of new long acting local anesthetics, ropivacaine and levobupivacaine. Acta Biomed 2008;79:92-105.
7. Scott DB, Lee A, Fagan D, Bowler GM, Bloomfield P, et al. Acute toxicity of ropivacaine compared with that of bupivacaine. Anesth Analg 1989;69:563-569.
8. Gristwood RW, Greaves JL. Levobupivacaine: a new safer long acting local anaesthetic agent. Expert Opin Investig Drugs 1999;8:861-876.
9. Kettner SC. Dexmedetomidine as adjuvant for peripheral nerve blocks. Br J Anaesth. 2013;111:123. [PubMed].
10. Ammar AS, Mahmoud KM. Ultrasound-guided single injection infraclavicular brachial plexus block using bupivacaine alone or combined with dexmedetomidine for pain control in upper limb surgery: A prospective randomized controlled trial. Saudi J Anaesth. 2012;6:109–14. [PMC free article] [PubMed].
11. Esmaoglu A, Yegenoglu F, Akin A, Turk CY. Dexmedetomidine added to levobupivacaine prolongs axillary brachial plexus block. Anesth Analg. 2010;111:1548–51. [PubMed].
12. Obayah GM, Refaie A, Aboushanab O, Ibraheem N, Abdelazees M. Addition of dexmedetomidine to bupivacaine for greater palatine nerve block prolongs postoperative analgesia after cleft palate repair. Eur J Anaesthesiol. 2010;27:280–4. [PubMed].
13. Mankad PP, Makwana JC, Shah BJ. A comparative study of 0.5% ropivacaine and 0.5% levobupivacaine in supraclavicular brachial plexus block. Int J Med Sci Public Health 2016;5:74-79.
14. Huang R, Hertz L. Receptor subtype and dose dependence of dexmedetomidine-induced accumulation

of [14C] glutamine in astrocytes suggests glial involvement in its hypnotic-sedative and anesthetic-sparing effects. Brain Res. 2000;873:297–301. [PubMed].

15. Al-Ghanem SM, Massad IM, Al-Mustafa MM, Al-Zaben KR, Qudaisat IY, Qatawneh AM, et al. Effect of adding dexmedetomidine versus fentanyl to intrathecal bupivacaine on spinal block characteristics in gynaecological procedures: A double blind controlled study. Am J Appl Sci. 2009;6:882–7.
16. El-Hennawy AM, Abd-Elwahab AM, Abd-Elmaksoud AM, El-Ozairy HS, Boulis SR. Addition of clonidine or dexmedetomidine to bupivacaine prolongs caudal analgesia in children. Br J Anaesth. 2009;103:268–74. [PubMed].
17. Eisnach JC, De Kock M, Klimscha W. Alpha2adrenergic agonists for regional anesthesia. A clinical review of clonidine (1984–1995) Anesthesiology. 1996;85:655–674. [PubMed].
18. Guo TZ, Jiang JY, Buttermann AE, Maze M. Dexmedetomidine injection into locus corelus produces antinociception. Anesthesiology. 1996;84:873–881. [PubMed].
19. Brummett CM, Norat MA, Palmisano JM, Lydic R. Perineural administration of dexmedetomidine in combination with bupivacaine enhances sensory and motor blockade in sciatic nerve block without inducing neurotoxicity in rat. Anesthesiology. 2008;109:502–511. [PMC free article] [PubMed].
20. Kosugi T, Mizuta K, Fujita T, Nakashima M, Kumamoto E. High concentration of dexmedetomidine inhibit compound action potential in frog sciatic nerve without adrenoreceptor activation. Br J Pharmacol. 2010;160:1662–1676. [PMC free article] [PubMed].
21. Mageswaran R, Choy YC. Comparison of 0.5% ropivacaine and 0.5% levobupivacaine for infraclavicular brachial plexus block. Med J Malaysia 2010;65(4):300–3.
22. Nodulas N, Kaliakmanis D, Graikiotis A, Kouvalakidou A. Comparison of Levobupivacaine 0.5% and Ropivacaine 0.5% for digital nerve block in ambulatory surgery. European Journal of Anaesthesiology. 2011;28:120.
23. Deshpande JP, Ghodaki PS, Sardesai S.Comparative clinical study Between Racemic Bupivacaine and Levobupivacaine in Supraclavicular brachial plexus block. Indian journal of applied research. 2014; 4(5):451-4.
24. Liisanantti O, Luukkonen J, Rosenberg PH. High-dose bupivacaine, levobupivacaine and ropivacaine in axillary brachial plexus block. Acta Anaesthesiol Scand 2004;48(5):601–6.
25. Casati A, Borghi B, Fanelli G, Montone N, Rotini R, Fraschini G, et. al. Interscalene brachial plexus anesthesia and analgesia for open shoulder surgery: arandomized, double-blinded comparison between levobupivacaine and ropivacaine. Anesth Analg 2003;96:253–9.
26. Cline E, Franz D, Polley RD, Maye J, Burkard J, Pellegrini J. Analgesia and effectiveness of levobupivacaine compared with ropivacaine in patientsundergoing an axillary brachial plexus block. AANA J 2004;72(5):339–45.
27. Saumya Biswas, Ratan Kumar Das, Gauri Mukherjee, Tapas Ghose. Dexmedetomidine an Adjuvant to Levobupivacaine in Supraclavicular Brachial Plexus Block: A Randomized Double Blind Prospective Study. Ethiop J Health Sci. 2014 Jul;24(3):203–08.
28. Shantanu B. Kulkarni, Meena Pimpare, Balasaheb T. Govardhane. Comparison of levobupivacaine with ropivacaine for supraclavicular brachial plexus block. Int J Res Med Sci. 2016 Sep;4(9):3789-3796.

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Oral Premedication in Paediatric Surgeries under General Anaesthesia with Ketamine versus Midazolam: A Comparative Study

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Abstract

Background: Pre-operative anxiety (anxiety regarding impending surgical experience) in children is a common phenomenon that has been associated with a number of negative behaviors during the surgical experience (e.g. agitation, crying, spontaneous urination and the need for physical restraint during anaesthetic induction). Pre-operative anxiety has also been associated with the display of a number of maladaptive behaviourspost surgery, including post-operative pain, sleep disturbances, parent-child conflict and separation anxiety [1]. The risk factors associated with high incidence of perioperative anxiety in children include shy and inhibited nature, previous poor quality medical encounters, poor social adaptability and increased parental anxiety [1]. If children are less anxious during the peri-operative period, not only will they often exhibit less behavioral disturbances post-operatively, but they may face subsequent medical care more easily [2]. Thus, there are several compelling reasons to treat children's anxiety preoperatively. The aim of our study was to compare the efficacy and safety of oral midazolam versus oral ketamine for pre-medication in paediatric surgeries under general anaesthesia.

Materials and Methods: Sixty children belonging to ASA physical status I as outlined by the American Society of Anaesthesiologists (ASA) of either gender were included in the study. They were randomly divided into two groups of 30 children in each group, group A and group B. Group A patients received 0.5mg/kg of oral midazolam as a premedicant 45 minutes before induction and Group B patients received 6mgs/kg of oral ketamine as a premedicant 45 minutes before induction. Time of onset of sedation and sedation score at 30 minutes were noted. Anxiety score at separation from parents, room air saturation, response to pre-oxygenation, side effects, if any, preoperatively and postoperatively were also noted.

Results: In our study, the mean time of onset of sedation was lower with ketamine group (19.48 minutes) as compared to the midazolam group (25.63). The sedation score at 30 minutes and anxiety score at separation from parents were also satisfactory. In our study we found that the mean sedation score at 30 minutes was 1.9 with ketamine group and 3.03 in midazolam group.The mean anxiety score at separation was 1.8 with ketamine group and 2.53 in midazolam group. All patients allowed calm separation from parents.

Conclusion: It is concluded that ketamine at a dose of 6 mgs/kg orally provides better sedation and anxiolysis in children with minimal side effects than oral pre-medication with midazolam at the dose of 0.5 mg/kg.

Keywords: Preoperative Anxiety; Ketamine; Midazolam; Paediatric Population; Oral Premedication.

Introduction

Children suffer from varying degrees of stress while facing the prospects of surgery depending upon the age, developmental maturity and past surgical experiences. They are principally worried about pain and separation from their parents. Pre-operative anxiety in children is a common phenomenon. It has been associated with a number of negative behaviors

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such as agitation, crying, spontaneous urination and the need for physical restraint during anaesthetic induction. Pre-operative anxiety is also associated with the display of a number of maladaptive behaviors post surgery, including post-operative pain, sleep disturbances, parent-child conflict and separation anxiety [1].

Younger children, previously anaesthetized children and children who experience turbulent anaesthetic inductions are at risk of developing behavioral disturbances [2].

The risk factors associated with high incidence of perioperative anxiety in children include shy and inhibited nature, previous poor quality medical encounters, poor social adaptability and increased parental anxiety. Children younger than 5 years of age or living in a one parent family appear to have a higher incidence of problematic behavior in a two week follow-up after anaesthesia [3].

Interventions like sedative pre-medication, parental presence during anaesthetic induction, behavior preparation programs, music therapy and acupuncture have been sought to treat or prevent childhood pre-operative anxiety and possibly decrease the development of negative behaviours post-operatively [1].

If children face less stress during the peri-operative period, then they will often exhibit less behavioural disturbances post-operatively, but they may face subsequent medical care more easily.[2] Hence it is very important to treat children's anxiety preoperatively.

The aims of premedication in children is to alleviate the stress and fear of surgery as well as to ease parent – child separation and promote a smooth induction of anaesthesia thereby reducing the post-operative behavioral disturbances associated with bad pre-operative experience. Almost all sedative pre-medicants are effective in this regard. Children six months to four years of age have been reported to experience the greatest negative post-operative behaviour changes and pre-medication is very useful in them.

Midazolam is the most commonly used sedative pre-medicant followed by ketamine, transmucosal fentanyl and meperidine. All possible routes have been described–oral, intranasal, intramuscular, rectal etc. The oral route has several advantages as it is painless, quick and reliable.

An ideal sedative pre-medicant should be cheap, easily available,have rapid onset of action, able to reduce anaesthetic and analgesic requirements and with no side effects during induction, emergence or discharge from the post-anaesthetic care unit.

Materials and Methods

This is a prospective comparative study conducted between July 2007 and November 2008 in which 30 paediatric patients in each group received oral pre-medication.

This study was conducted after obtaining approval from the departmental dissertation committee. Informed consent was obtained from the parents.

Sixty children of either gender participated in the study belonging to ASA physical status 1. They were randomly divided into two groups, 30 children in group A and 30 children in group B.

The study was conducted in children undergoing surgeries from various specialities under general anaesthesia. The duration of surgeries were between 60 and 90 minutes. Inclusion Criteriawere age between 10 months and 10 years and weight between 8 and 20 kgs. Exclusion Criteria were age below 10 months and above 10 years, ASA physical status III (or) higher, children allergic to Benzodiazepines and ketamine, epilepsy (or) raised intracranial pressure, cardio vascular anomalies, respiratory tract infections and children with anticipated difficult intubation.

Preoperative evaluation for all the children was doneon the day before surgery and instructed for nil per oral for the anticipated six hours before surgery.

On the day of Surgery, 45 minutes before induction, Group A children received 0.5 mg/kg oral midazolam and Group Bchildren received 6 mgs/kg oral ketamine.

Parenteral formulations (ketamine vial 50 mgs/ml and midazolam ampoule 5mgs/ml) of both the drugs were made palatable by mixing with sugar solution and were administered to children orally in the pre-operative holding area. The child was then monitored constantly to see changes in mood, behaviour and appearance. Onset of sleepiness, closure of eyes and any side effects like nausea, vomiting, increased salivation, hallucination, nystagmus, hiccough were noted.

Subsequently, the following observations were made and recorded:

1. Time of onset of sedation when the sedation score was 3 or less
2. Level of sedation at 30minutes after pre-medication
3. Level of anxiety at the time of separation from the parents
4. Room air SP02
5. Response to pre-oxygenation/mask application

6. Post-operative recovery time

7. Side effects - Pre-operative

- Post-operative

Level of sedation was noted on a five-point scale as per Table 1 and level of anxiety was noted on a four-point scale as per Table 2.

After premedication, the children were transferred to the operation theatre. Appropriate monitors were applied. Pulse oximeter was applied and room air SpO_2 was noted.

Now, the response to pre-oxygenation with the mask was noted, that is whether the child showed signs of refusal or remained calm.

All the children were induced with intravenous Thiopentone sodium at a dose of 6mgs/kg and Atracurium at a dose of 0.5 mgs/kg was used to facilitate endo tracheal intubation. Ventilation was controlled and anaesthesia was maintained with oxygen, nitrous oxide and sevoflurane. For intra operative analgesia, fentanyl was used at a dose of 1 microgram/kg. Towards the end of the surgery, all children received paracetamol suppositories for post-operative pain relief. The recovery time was noted between the end of surgery and the spontaneous eye opening. After ensuring adequate recovery of muscle power, children were extubated and transported to the recovery room. Children were closely monitored until transferred to the post-operative ward and any unwanted effects during the period were noted.

For the purpose of data analysis, sedation scores of 1 and 2 were taken as satisfactory and scores 3 and 4 were taken as unsatisfactory. Similarly anxiety scores of 1 and 2 were taken as satisfactory and scores of 3 and 4 were taken as unsatisfactory induction.

Statistical Analysis

Data analysis was done with the help of computer using Epidemiological Information Package (EPI 2002). Using this software, frequencies, percentage, mean, standard deviation, x2 and 'p' values were calculated. A 'p' value less than 0.05 is considered as significant.

Results

Our study was conducted on 60 patients divided into two groups. Group A – 30 patients and Group B – 30 patients. Group A patients received 0.5mg/kg of oral midazolam as a premedicant 45 minutes before induction.Group B patients received 6mgs/kg of oral ketamine as a premedicant 45 minutes before induction.

Table 1: Level of sedation on five point scale

Score	Sedation Level
1.	Barely arousable (Fully asleep)
2.	Eyes closed (Light sleep)
3.	Eyes opened but looks drowsy
4.	Awake
5.	Agitated

Table 2: Level of anxiety on four point scale

Score	Anxiety Level
1.	Calm and Sleepy
2.	Apprehensive but withdrawn from surroundings
3.	Crying
4.	Agitated and difficult to control

Table 3: Time of onset of sedation

Time of sedation in minutes	Group A (Midazolam) No	%	Group B (Ketamine) No	%
< 15 minutes	4	13.3	13	43.3
16 – 30	16	53.3	13	43.3
31 – 45	4	13.3	3	10
Not sedated	6	20	1	3.3
Total	30	100	30	100
Mean	25.63 minutes		19.48 minutes	
S.D	6.96		8.7	
'p'	0.0018 (Significant)			

Table 4: Sedation score in 30 minutes

Sedation Score in 30 minutes	Group A (Midazolam)		Group B (Ketamine)	
	No	%	No	%
1	1	3.3	11	36.7
2	6	20	13	43.3
3	15	50	5	16.7
4	7	23.3	-	-
5	1	3.3	1	3.3
Total	30	100	30	100
Mean	3.03		1.9	
S.D	2.5		0.9	
'p'	0.0001			

Table 5: Anxiety Score at separation

Response to Pre-oxygenation	Group A		Group B	
	No	%	No	%
Refused	10	33.3	20	66.7
No refusal	20	66.7	10	33.3
'p'	0.0201 (Significant)			

Table 6: Response to Pre-oxygenation (Face mask application)

Response to Pre-oxygenation	Group A		Group B	
	No	%	No	%
Refused	10	33.3	20	66.7
No refusal	20	66.7	10	33.3
'p'	0.0201 (Significant)			

Table 7: Side Effects

Side Effects	Group A (Midazolam)		Group B (Ketamine)	
	No	%	No	%
Pre operative				
Hiccoughs	3	10	-	-
Laughing	2	6.7	-	-
Salivation	-	-	6	20
Sighing	1	3.3	-	-
Sweating	-	-	2	6.7
Total side effects	6	20	8	26.7
No side effects	24	80	22	73.3
Total	30	100	30	100
Post Operative				
Crying	11	36.7	4	13.3
Irritable	1	3.3	-	-
Nausea	-	-	5	16.7
Total side effects	12	40	9	30
No side effects	18	60	21	70
Total	30	100	30	100

The mean and standard deviation for the time of onset of sedation were 25.63±6.96 and 19.48±8.7 minutes in the groups A and B respectively.The mean time of onset of sedation is lower in group B which is statistically significant (Table 3).

The mean sedation score at 30minutes is lower (1.9) in ketamine group which is statistically significant. The mean and standard deviation for the time of onset of sedation were 25.63±6.96 and 19.48± 8.7 minutes in the groups A and B respectively. The mean time of onset of sedation is lower in group B which is statistically significant.

The mean sedation score at 30minutes is lower (1.9) in ketamine group. This is statistically significant.

The mean anxiety score at separation from parents is lower (1.8) in the ketamine group. This is statistically significant (Table 5). Only 1/3 of children in group A refused pre- oxygenation with mask whereas 2/3 of children in group B refused. This is statistically significant (Table 6).

Increased salivation and sweating were noted in 20% and 6.7% of patients in group B respectively. Hiccoughs (10%), laughing (6.7%) and sighing (3.3%) were noted in group A. Post-operatively, 36.7%of

children in group A remained crying and 3.3% irritable. 16.7% of children in group B had nausea and 13.3% remained crying.

Discussion

Anaesthesia for children presents major challenges as it deals with the most psychologically vulnerable age group. Anaesthesia during surgery prevents children from recalling actual surgical events. They are subjected to stress while preparing for surgery. Most of the children experience significant anxiety before anaesthetic induction. Pre-operative anxiety is a global concern for health care providers [4]. Main aim ofanaesthesiologist is ensuring adequate reduction of preoperative anxiety and there by reducing occurrence of postoperative negative psychological and behavioral changes.

There are many pharmacological (pre-medication) and behavioral methods (parental presence during induction of anaesthesia) to treat pre-operative anxiety in children [5], but none of these methods have been satisfactorily effective and practicable. Use of an effective sedative pre-medicant significantly minimizes the emotional trauma associated with perioperative anxiety and its sequelae. Currently oral midazolam and oral ketamine are the most commonly used pre-medicants. Use of opiods for pre-medication has been declining owing to concerns for respiratory depression.

An ideal pre-medicant for children should be easily available, palatable, have both rapid onset and short duration of action, be able to reduce anaesthetic and analgesic requirements and possess minimal side effects without significant delay in recovery period.

In our study children aged between 10 months and 10 years were chosen for the study. Sixty healthy children awaiting elective surgery who didn't meet the exclusion criteria were randomly assigned into two groups of 30 each. Group A received 0.5 mgs/kg of midazolam and Group B received 6mgs/kg of ketamine orally in the preoperative room. Palatability was ensured by mixing with sugar solution. Time of onset of sedation and sedation score at 30 minutes were noted. Anxiety score at separation from parents, room air saturation, response to pre-oxygenation, side effects, if any, preoperatively and postoperatively were also noted.

In our study, the mean time of onset of sedation was lower with ketamine group (19.48 minutes) as compared to the midazolam group (25.63). The sedation score at 30 minutes and anxiety score at separation from parents were also satisfactory.

These results coincide with the studies conducted earlier by several others. JA Kulkarni [6] points out that ketamineorally is an effective pre-medicant in paediatric patients. The study found that ketamine was well accepted by all children. All patients allowed calm separation from parents.

Granry et. al. [7] conclude that ketamine is an unique anaesthetic, analgesic and sedative drug.

Guidelines for ketamine sedation in Emergency Departments from British Association quote that ketamine is a powerful anaesthetic agent with anxiolytic, analgesic and amnesic properties with a wide safety margin.

Dr. Suranjit Debnath and Dr. Yash Pande [8] in their comparative study of premedication in children with oral ketamine and midazolam, conclude that sedation and anxiolysis were better in ketamine than in the midazolam group, during separation from parents and at intravenous cannulation. Recovery was also smooth in ketamine group.

In our study, the mean sedation score at 30 minutes was 1.9 with ketamine group and 3.03 in midazolam group. Similarly the mean anxiety score at separation was 1.8 with ketamine group and 2.53 in midazolam group.

However, 66.7 per cent of children in ketamine group refused pre-oxygenation with mask while only 33.3 per cent of children in midazolamgroup refused pre-oxygenation.

There was no significant difference in the recovery time between the groups.

Preoperatively excessive salivation (6 children) and sweating (2 children) were noted in ketamine group. Few children in midazolam group had hiccoughs (3 children) and sighing (1 child). Postoperatively 16.7 per cent of children in ketamine group had nausea and few children (12) in midazolam group were irritable and crying. Postoperatively recovery was smooth in ketamine group.

Main goal of anaesthesiologists in treating paediatric patients has always been to provide access to care for all children especially those with behavioral issues. The introduction of oral ketamine and midazolam provides safe, effective method of sedating the uncooperative paediatric patients.

Conclusion

It is concluded that pre-medication with ketamine at a dose of 6 mgs/kg orally provides better sedation and anxiolysis in children with minimal side effects

when compared with oral pre-medication with midazolam at the dose of 0.5 mg/kg.

References

1. Wright KD, Stewart SH, et. al., Prevention and intervention strategies to alleviate preoperative anxiety in children: a critical review. Behav Modif 2007 Jan;31(1) 52-79.
2. Goresky GV, Whitsett SF., Psychological preparation of children for surgery. Can J Anaesth. 1994 Nov;41 (11):1033-5.
3. Karling, M. and Hägglöf, B. Child behaviour after anaesthesia: association of socioeconomic factors and child behaviour checklist to the post-hospital behaviour questionnaire. Acta Paediatrica, 2007;96: 418–423.
4. Dreger, Victoria A. et. al. Management of preoperative anxiety in children AORN Journal, 2008;84(5):796-799.
5. Hatice K et. al. The effects of maternal presence during anesthesia. Paediatric Med Chir 2004 May-June;26(3) 169-174.
6. Kulkarni J.A., Oral Ketamine for Pre-medication in Children, Bombay Hospital Journal (BHJ).
7. Granry J.C., Dube L., et. al., Ketamine: New Uses for an Old Drug. Current Opinion in Anaesthesiology 2000 July;13(3):299-302.
8. Suranjit Debnath and Yash Pande., A Comparative Study of Oral Pre-medication in Children with Ketamine and Midazolam, Indian Journal Anaesthesia, 2003;47(1):45-47.
9. Andrea Messeri, Simona Caprilli and Paolo Busoni., Anaesthesia induction in children: a psychological evaluation of the efficiency of parents' presence Paediatric Anaesthesia 2004 July;14(7):551-556.
10. Damle SG, Gandhi M, Laheri V. Comparison of oral ketamine and oral midazolam as sedative agents in pediatric dentistry. J Indian SocPedodPrev Dent 2008;26:97-101.

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How Efficacious Intrathecal Dexmedetomidine with Levobupivacaine in Lower Limb Surgeries: A Comparative Study

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Abstract

Background and Aim: Studies and research are ongoing to find appropriate adjuvants to intrathecal local anaesthetic agents to make them more effective and economical. In view of the same we undertook a study with Levobupivacaine, being a newer agent with more cardiac stability and compared the outcomes with 3 adjuvants (REF).

Settings and Design: After approval from hospital ethical committee a randomized double blind study was conducted among 60 healthy American Society of Anesthesiologist ASA I and II patients, scheduled for lower limb surgeries. The study was conducted over 1 year at SRMSIMS.

Materials and Methods: Spinal block was administered in L3 and L4 intervertebral space, using 0.5% Levobupivacaine 12mg. Adjuvants were added in group 1, Dexmedetomidine 5mcg, and in group 2, Dexmedetomidine 10 mcg. Anaesthetic level achieved was T10. Onset time to achieve sensory, motor blockade, their regression time was noted. Hemodynamic changes and requirement for other analgesic drug was also noted.

Results: 60 patients were enrolled in our study, the data was recorded and analyzed using statistical analysis.

Conclusion: To conclude, Levobupivacaine with Dexmedetomidine, gives better result for intra as well as for postoperative regional anaesthesia without any adverse effects.

Keywords: Adjuvants; Intrathecal; Levobupivacaine; Dexmedetomidine Clonidine.

Introduction

Subarachnoid blockadeis the commonly used regional anaesthetic technique for lower limb surgery, because of the advantages of being economical and easy to administer. Its dis-advantages of short duration of action and lack of post-operative analgesiahas started new researches for the search of such intrathecal compounds, which can provide good relaxation, least hemodynamic disturbances and prolonged analgesia. Surgical anaesthesia requires dense sensory block and usually moderate to dense motor block. To achieve this, concentrated local anaesthetic preparations are required. Levobupivacainea long-acting local anaesthetic, pharmacological structure similar to that of Bupivacaine with larger safety margin and less neurotoxic and cardiotoxic side effects, is new in the list of local anaesthetic. Intrathecal α-2 agonistsprolong the duration of action of local anaesthetics and reduce the required dose. Clonidine, an α2-agonist, produces vasoconstriction and antinociception from α2 stimulation of receptors in dorsal horn cells of spinal cord, widely accepted as adjuvant for spinal anaesthesia. Dexmedetomidine, a highly selective α2 adrenergic agonist, α2/α1 selectivity 8 times higher than that of Clonidine is the new drug to be used as the adjuvant.

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Aims & Objectives

To investigate the influences of Dexmedeto-midine added to Levobupivacaine ononset and duration of sensory and motor block, duration of analgesia, hemodynamic changes, adverse effect of drugs, if any.

Material & Methods

After approval from hospital's ethical committee, we took 60 patients for our study in our institute aged 18 years – 55 years, ASA I-II from Oct 13 - Feb14 for lower limb surgeries for interlocking of tibia. It was designed in the form of a prospective randomized double blind study. We excluded ASA III / IV, patients with BMI > 30 and <20, patients withuncontrolled or labile hypertension, Heart block, dysarrythmia, on cardiac medication therapy (adrenergic receptor antagonist, Beta blocker, CCB or ACE inhibitor), Addiction to narcotics, Any contraindication to spinal anaesthesia and H/O drug allergy to the drugs, we are using.

After full general physical and laboratory examination, Complete Blood Count, Fasting Blood Sugar, S. Urea, S. Creatinine, S. electrolytes, PT/PTT, ECG and CXR, the patients were admitted a day prior to surgery. We counseled the patients about the regional anesthesia and informed consent was taken.

Anxiolysis was done with Tab Alprazolam 0.25 mg night before and at 6 AM with sips of water.

In O.T, standard monitor's i.e. ECG, SpO_2, NIBP, HR were attached to the patients. All patients were preloaded with RL 500 ml. Ensuring all aseptic precautions, under local anaesthesia Lumbar Puncture was done with 27G Quincke spinal needle at L3-L4 space.

We injected the drug after ensuring free flow of clear CSF. O_2 through facemask was given to each patient. After following exclusion criteria, 60 patients were randomized into 2 groups by a computer generated list.

In group 1, we used Levo Bupivacaine 0.5%, 12 mg + Dexmedetomidine 5 mcg, and in group 2, we used Levo Bupivacaine 0.5%, 12mg + 10mcg Dexmedetomidine. In group 2-0.3 ml, preservative free normal saline to make volume in all groups constant. The drug was prepared by a third observer, who was unaware about the study.

After the block, we assessed the time of sensory block up to T10 and grade 3 Bromage motor block before surgery. Zero was started at the time of subarachnoid block. Bromage 0-The patient has free movement of legs and feet. Bromage 1- The patient is just able to flex knee with free movement of feet. Bromage 2- The patient is unable to flex knee, but free movement of feet. Bromage 3-The patient is unable to move the leg and feet [3]. Vital signs (Pulse, B.P, ECG, SpO_2) were recorded preoperatively, then at 5 min interval intra-operatively until the end of surgery, then every 15 min, then 30 min.

Hypotension [SBP fall > 30%, from baseline or < 90mm Hg] and bradycardia [HR<50 bpm] were noted. The other adverse effects e.g. nausea, vomiting, shivering, pruritus, sedation and respiratory depression were noted.

We noted the time of recovery of S_1 dermatome and use of rescue analgesic drug.

Inj. Diclofenac 75 mg i.m. was administered for postoperative analgesia. We noted vital signs, response to pain and nausea. For nausea, Inj. Metoclopramide 10 mg i.v. was used, as a rescue drug.

Results

SPSS statistical software (16.0) was usedfor data analysis. In this study p value <0.05 have been considered as statistically significant. To calculate the sample size, a power analysis of α=0.05 and beta=0.80, showed that 30 patients per study group were needed. Data are expressed as mean and standard deviation. For comparing the three main groups Student t test was applied. For qualitative assessment chi square test was done. Demographic data's in both groups are comparable because p value is not significant (Table 1).

Table 1:

	Group-1 (N=30)	Group-2 (N=30)	P value
Hypotension	0	3	0.492
Bradycardia	3	2	1.00
Nausea	1	1	1.00
Vomiting	1	1	1.00

Table 1:

	Groups		
	Group1	**Group 2**	**p value**
Age in years(Mean ± SD)	46.6±6.91	39±15.47	0.403
Height in cm(Mean ± SD)	166.5±3.30	165±4.35	0.650
Weight in Kg(Mean ± SD)	68.25±3.11	63.5±2.72	0.086
BMI [Kg/M²]	24.57±0.165	23.35±0.65	0.176

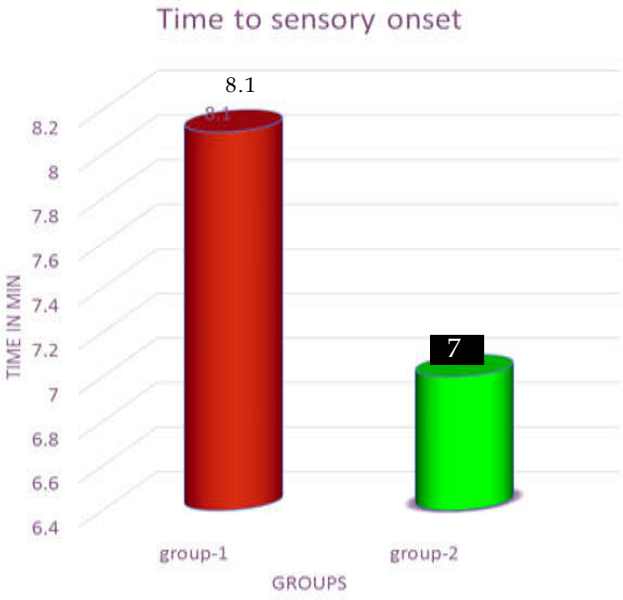

Fig. 2:

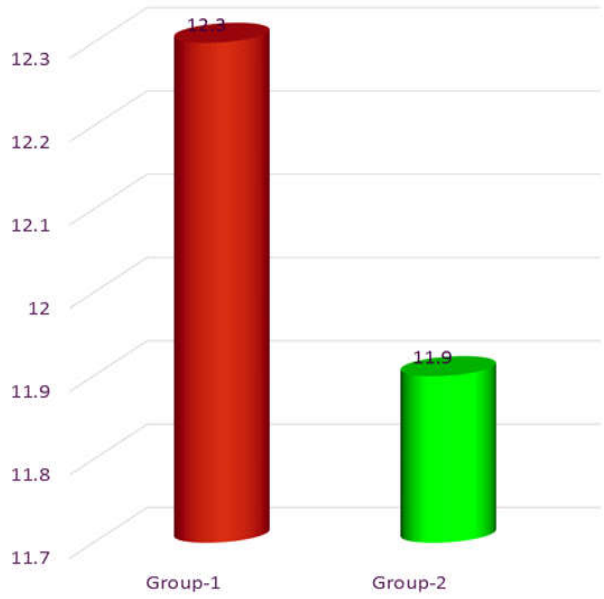

Fig. 3:

Table 2:

Groups	Group-1	Group-2	p value
Mean ± SD	8.1 ± 0.99	7.0 ± 1.05	<0.05
No of cases	30	30	

Table 3:

Groups	Group-1	Group-2	p value
Mean ± SD	12.3± 4.8	11.9 ± 3.4	<0.05
No of cases	30	30	

Demographic Data

All patients (n=60) completed the study. There was no statistically difference in patients demo-graphics.

Time to Sensory Onset

- The time to sensory onset in group-1 was 8.1± 0.99 min and in group-2 was 7.0±1.05 min
- Thus, the time of sensory onset was shortest in group-2 compared to group-1, which was statistically significant (p<0.05).

Time to motor block

- The time to motor block in group-1 was 12.3± 4.8 min and in group-2 was 11.9±3.4 min.
- Thus, the time of motor block was shortest in group-2 compared to group-1. (p value <0.05)

Table 4:

Groups	Group-1	Group-2	p value
Mean ± SD	11.2 ± 1.13	9.5 ± 1.08	0.00
No of cases	30	30	

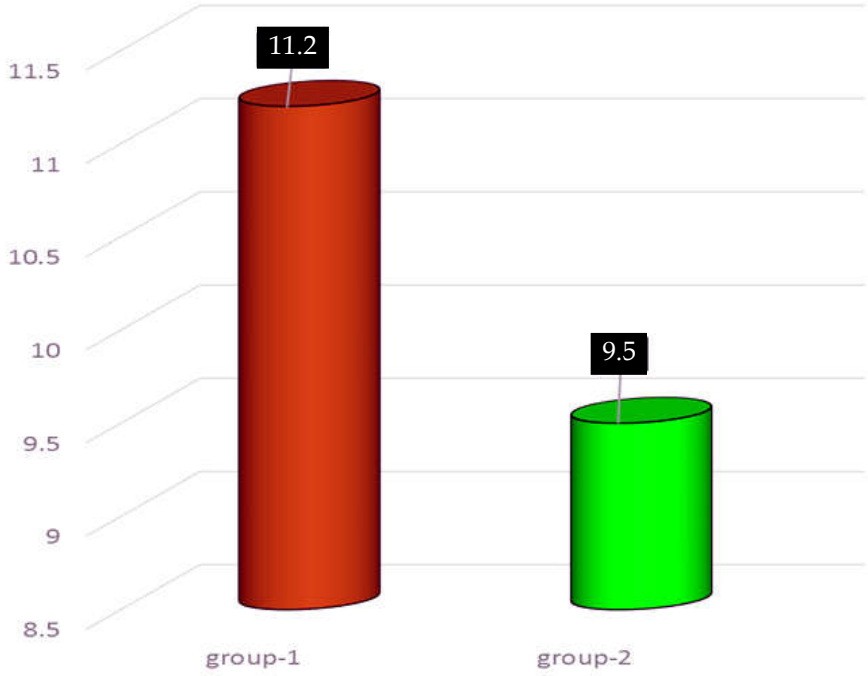

Fig. 4:

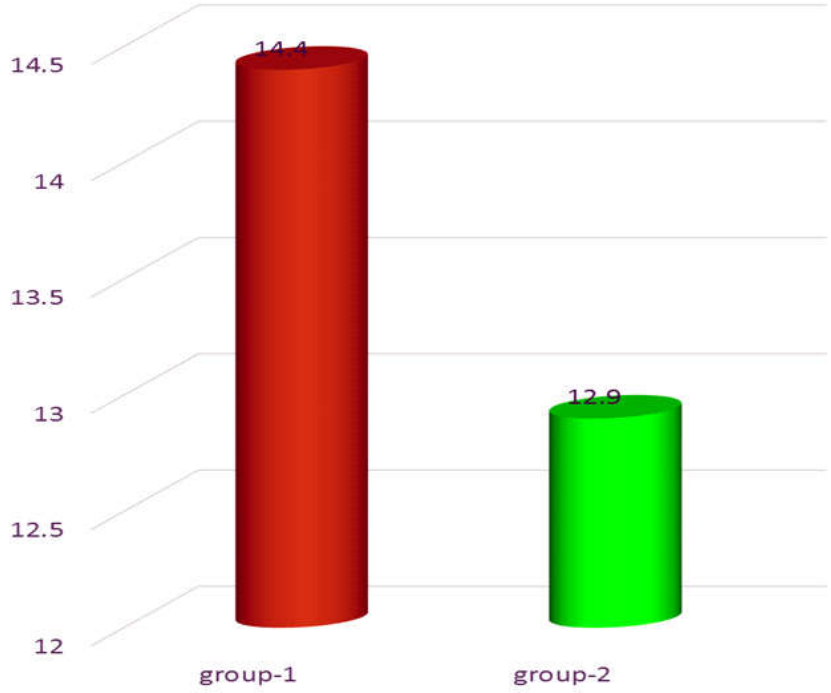

Fig. 5

Table 5:

Groups	Group-1	Group-2	p value
Mean ± SD	14.4 ± 1.83	12.9 ± 1.79	0.071
No of cases	30	30	

Time to achieve sensory level up to T10

- The time to achieved sensory level up to T10 in group-1 was 11.2±1.13 min and in group-2 was 9.5±1.08 min
- Thus, time to achieved sensory level up to T10 was shortest in group-2 compared to group-1, which was statistically significant.($p<0.05$)

Time to Achieve Bromage 3

- The time to achieved bromage3 in group-1 was 14.4±1.83 min and in group-2was 12.9±1.79 min
- Thus, time to achieved bromage3 was shortest in group-2 compared to group-1, which was statistically non-significant ($p>0.05$).

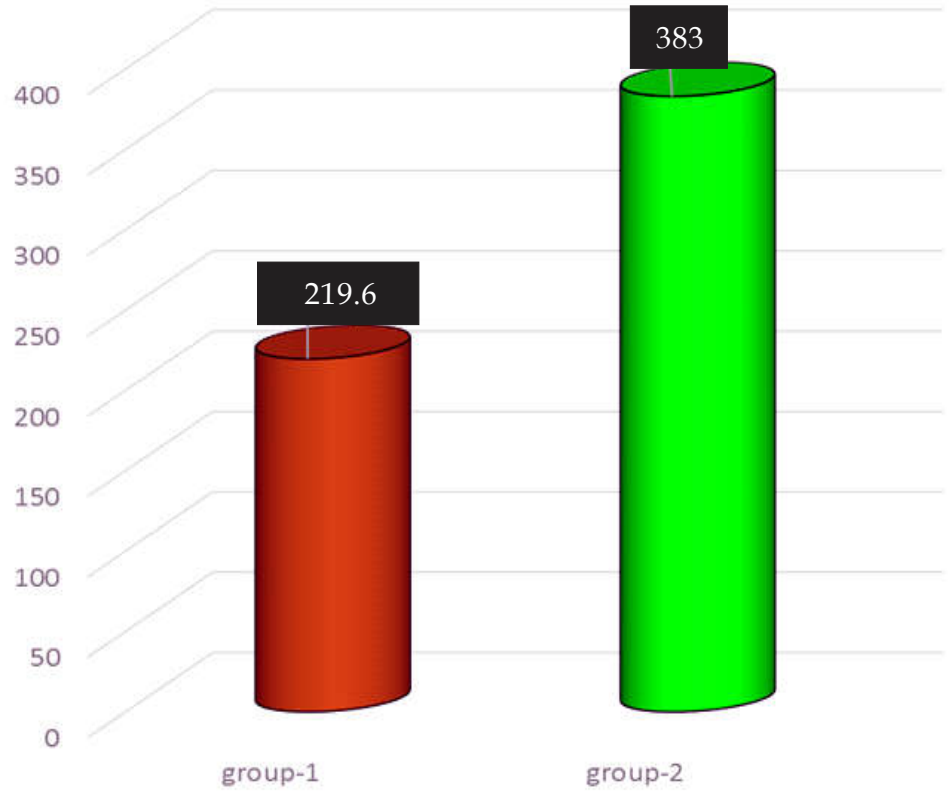

Fig. 6:

Table 6:

Groups	Group-1	Group-2	p value
Mean ± SD	297.9 ± 13.5	473.7 ± 15.2	0.000
No of cases	30	30	

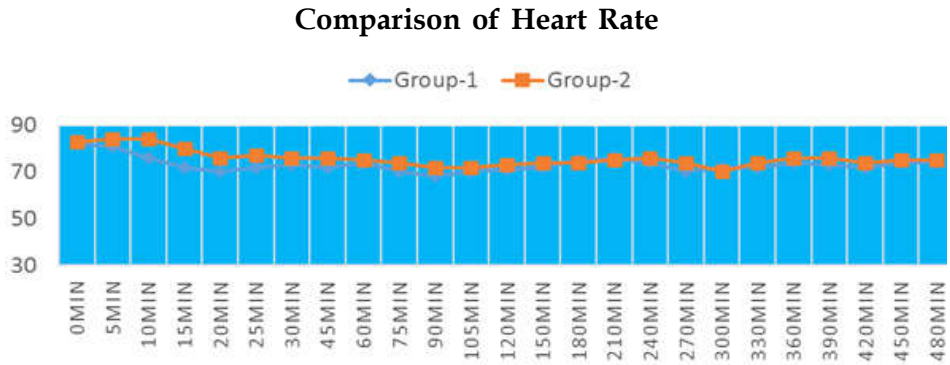

Fig. 7:

Time to Regression to S1

- The time to Regression to S1 in group-1 was 297.9± 13.5 min and in group-2 was 473.7± 15.2 min.
- Thus, the Regression to S1 was greater in group-2 compared to group-1, which was statistically significant. ($p<0.05$).

Time to achieve Bromage

- The time to achieved Bromage 0 in group-1 was 219.6±7.35 min and in group-2 was 383.8 ± 7.85 min.
- Thus, the time to achieved Bromage 0 was greater in group-2 compared to group-1, which was statistically significant ($p<0.05$).

Heart Rate

There was no statistically significant difference ($p \geq 0.05$) in heart rate amongst the groups.

Mean Arterial Blood Pressure

Mean Arterial Blood pressure started falling after 5min in both groups, but was no statistically significant difference in between groups.

Oxygen Saturation

- Oxygen saturation was similar in all the two groups
- There was no statistically significant difference

Table 7:

Groups	Group-1	Group-2	p value
Mean ± SD	219.6 ± 7.35	383.8 ± 7.85	0.00
No of cases	30	30	

Comparison of Mean Arterial Pressure

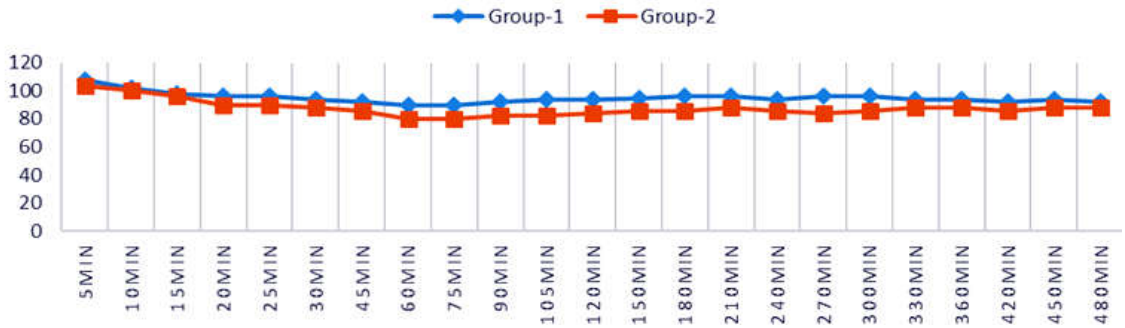

Fig. 7:

Table 8:

Adverse Effects	Group-1 (n=30)	Group-2 (n=30)	p value
Hypotension	0	3	0.492
Bradycardia	3	2	1.00
Nausea	1	1	1.00
Vomiting	1	1	1.00

Side Effects

- Among the side effects, hypotension was common in group-2 than in group-1
- Bradycardia was seen in both groups
- Nausea and vomiting was less in both groups

The characteristics of spinal block were summarized in Table 2. Time to reach T6 and Time to reach Bromage grade 3 were significantly late in Dexmedetomidine group. Regression time to S1 and Bromagein these patients who received supplemental anaesthesia was analyzed. This requirement was mainly at the time of puncture, $p<0.05$. So a significant number of patients in group 1 received supplemental anesthesia.6 patients in group 1 and 9 patients in group 2 developed hypotension. It was managed with Inj. Mephenteramine and ivfluids [$p >0.05$].

Two patients in group 1 and 3 patients in group 2 had persistent hypotension. Five patients in group 1 and 4 patients in group 2 developed bradycardia. It responded well to inj. Atropine 0.6 mg [p>0.05]. Only patients of group 1 had pruritus, which is absent in Dexmedetomidine group. It was found to be significant [p>0.05]. Incidence of nausea in both groups are almost very low and non-significant.

Discussion

Levobupivacaine is a longer acting with pharmacological structure similar to Bupivacaine with larger safety margin. Levobupivacaine had less inotropic effect and produced less prolongation of QTc interval than Bupivacaine. It also had less depressant effect on AV conduction and QRS duration. Feyzi Celik et. al. compared the anaesthetic and hemodynamic effects of intrathecally administered Levobupivacaine and Bupivacaine in combination with Fentanyl in hip surgery. They found the onset of sensory block and the time to two segment regression wassimilar between the two groups. In the Levobupivacaine group, the time to onset of motor block was longer and the motor block regression time was shorter than that of Bupivacaine group. They proposed that Levobupivacaine may be a good alternative to Bupivacaine.

Glacer C. compared it with Racemic Bupivacaine in elective hip replacement cases and demonstrated that Levobupivacaine is less cardiotoxic and neurotoxic [4].

Studies of adding intrathecal adjuvants in Levobupivacaine are very less. Dexmedetomidine, a novel α2 agonist is on its way to be added in the list of adjuvants. It potentiates local anaesthetic action, prolongs postoperative analgesia and has dose dependent sedative effect. The stimulation of α2 receptors decreases calcium entry into nerve terminals, which may contribute to its inhibitory effect on neurotransmitter release, leading to its various effects such as hypotension, bradycardia, sedation and analgesia [6,7,8]. Vidhi Mahendru et. al. found significantly longer sensory and motor block times, when 5 μg Dexmedetomidine was added to Bupivacaine than Fentanyl and Clonidine was added.

Studies have shown that prolongation of spinal block by intrathecal 5mcg and 10mcg Dexmedetomidine with no effect on hemodynamics. Hala et. al. opined that addition of 5mcg and 10 mcg Dexmedetomidine to intrathecal Bupivacaine, prolonged the analgesic effect of drug in dose dependent manner. With 5mcg Dexmedetomidine, the mean duration of analgesia achieved was 240 min and with 10 mcg Dexmedetomidine the mean duration of analgesia was 520 min.

No hemodynamic instability or other side effects were noted in either group. Keshav et. al. used 5 and 10 mcg Dexmedetomidine with intrathecal Bupivacaine. It showed dose dependent shortening of onset of block and prolongation of block accordingly.

In our study we used 5mcg and 10 mcg of spinal Dexmedetomidine without premedication with any type of Benzodiazepines. Onset of sensory block was also shortened which was dose dependent. Addition of Dexmedetomidine to Levobupivacaine prolonged the sensory andmotor block duration in patients subjected to lower limb surgery under spinal anaesthesia.

Aliye Esmaoglu et. al. found sensory and motor block onset times were shorter and regression of the sensory block to S1 dermatome and Bromage 0 were longer, when 3 μg Dexmedetomidine was added to Levobupivacaine, no statistically significant differences between groups in terms of blood pressure and heart rate.

Feroz Ahmad Dar et. al. investigated the effect of adding Dexmedetomidine to intrathecal Bupivacaine on the onset time and duration of motor and sensory blocks and found sensory and motor block onset times were similar but durations were prolonged without any significant adverse effects.

Dipak L. Raval, Minaxi Chaudhary compared intrathecal Bupivacaine with either Dexmedetomidine or Clonidine, found onset time of sensory and motor block is decreased in Dexmedetomidine.

Conclusion

Levobupivacaine, which has similar anaesthetic properties to Bupivacaine, being more cardio stable, may be a good alternative anaesthetic to Bupivacaine.

Dexmedetomidine precipitated the onset time of sensory and motor block and it prolonged duration of sensory and motor block significantly when used with Levobupivacaine in spinal anaesthesia in a dose dependent manner.

Because of the absence of significant adverse effect, we endorse the addition of Dexmedetomidine to spinal anaesthesia with Levobupivacaine when prolongation of spinal anaesthesia is desired.

References

1. Cuvas O, Er AE, Ongen E, Basar H. Spinal anaesthesia for transurethral resection operations: Bupivacaine versus Levobupivacaine. Minerva Anestesiol.; 2008;74(12):697-01.
2. Al-Ghanem SM, Massad IM, Al-Mustafa MM, Al-Zaben KR, Qudaisat IY, Qatawneh AM and Abu-Ali HM. Effect of Adding Dexmedetomidine versus Fentanyl to Intrathecal Bupivacaine on Spinal Block Characteristics in Gynaecological Procedures: A Double Blind Controlled Study. Am J ApplSci 2009;6:882-7.
3. Al-Mustafa MM, Abu-Halaweh SA, Aloweidi AS, Murshidi MM, Ammari BA, Awwad ZM, et. al. Effect of Dexmedetomidine added to spinal Bupivacaine for urological procedure. Saudi Med J 2009; 30:365-70.
4. Bromage PR. A comparison of the hydrochloride and carbon dioxide salts of Lidocaine and Prilocaine in epidural analgesia. ActaAnaesthesiolScandSuppl 1965;16:55-69.
5. Feyzi Celik, Haktan Karaman, Adnan Tufek, Gonul Olmez Kavak, Zeynep Baysal Yildirim, Orhan Tokgoz, Abdulmenap Guze Lz drav. Comparison of the effectiveness of intrathecal Bupivacaine and Levobupivacaine in hip surgery; Vestn 2013 Nov;82: 732–8
6. Vidhi Mahendru, Anurag Tewari, Sunil Katyal, Anju Grewal, M Rupinder Singh, Roohi Katyal. A comparison of intrathecal Dexmedetomidine, Clonidine, and Fentanyl as adjuvants to hyperbaric Bupivacaine for lower limb surgery: A double blind controlled study: Journal of Anaesthesiology Clinical Pharmacology. 2013 October-December;29(4):496-02.
7. Aliye Esmaoglu, Sumeyra Turk, Adnan Bayram, Aynur Akýn, Fatihugur, Ay°eulgey. The Effects of Dexmedetomidine Added to Spinal Levobupivacaine for Transurethral Endoscopic Surgery: Balkan Med J 2013;30:186-90.
8. Feroz Ahmad Dar, Hilal Ahmad Bhat, Tasaduq Javeed, Mohd. Rafiq Najar. The Effects of Dexmedetomidine Added to Spinal Bupivacaine for lower limb surgery: IOSR Journal of Dental and Medical Sciences. 2014 April;13(4):17-20.
9. Dipak L. Raval, Minaxi Chaudhary. 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 January– March; 2(1):77-83.

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Four Segments Versus two Segments Paravertebral Block for Inguinal Hernia Repair

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Abstract

Background: Paravertebral block (PVB) has been successfully used to provide good analgesia with fewer side effects in inguinal herniorrhaphy. So, the present study was conducted to compare the characteristics of two segments with four segments PVB for anaesthesia and postoperative analgesia.

Material & Methods: Fifty patients of ASA grade I and II, aged between 18-80 years scheduled for inguinal herniorrhaphy of a tertiary care teaching hospital were randomly selected in two groups of 25 each; Group F [Four segment block – T_{10}, T_{11}, T_{12}, L_1 (5ml 0.75% plain ropivacaine with 1:400000 epinephrine per segment)] and Group T [Two segment block – T_{10}, and L_1 (15ml 0.75% plain ropivacaine with 1:400000 epinephrine at T_{10} and 5 ml at L_1)]. Onset, duration of surgical anaesthesia, duration of complete analgesia and effective analgesia were recorded. Postoperative pain was assessed at predetermined time intervals using visual analogue scale (VAS).

Results: The mean duration of application was 14.94±3.30 minutes in group F and 6.16±1.57 minutes in group T. ($p<0.001$) The mean duration of surgery start time in group F and group T was 27.40±2.55 minutes, 22.79±3.55 minutes respectively. ($p<0.01$) Group T showed 84% satisfaction level while group F showed 76%. VAS score in both the groups was found statistically insignificant at 0, 6, 12, 24, 36, 48Hrs interval.

Conclusion: Two segments technique of PVB can be a viable alternative to the four segments technique for inguinal hernia surgery because it is less time consuming, provides similar analgesia as compared to the four segment technique. Furthermore, decreasing the number of injections in the two segment block technique may further increase patient comfort and satisfaction.

Keywords: Paravertebral Block; Inguinal Herniorrhaphy; Analgesia; Visual Analogue Scale.

Introduction

Inguinal herniorrhaphy is commonly performed under various techniques viz. general anaesthesia, infiltration anaesthesia, central neuraxial anaesthesia, nerve-blocks and paravertebral blocks [1]. The choice of anaesthesia for inguinal hernia remains a controversial topic [2]. The regional technique of paravertebral block has been successfully used for inguinal herniorrhaphy. Its attributes are prolonged unilateral sensory block with minimization of postoperative pain, reduction of nausea and vomiting, shortened hospital stay, patient satisfaction and rapid return to normal activities [1,3].

Paravertebral nerve block is an old technique and was initially utilized as an alternative to spinal anesthesia in order to minimize the cardiovascular and respiratory effects of central neuraxial blockade [4]. However, after its initial description paravertebral nerve block was sparingly used to provide anesthesia and analgesia. More recently, there has been renewed

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interest in this technique for the treatment of acute and chronic pain. Paravertebral nerve block involves injection of local anesthetic in a space immediately lateral to where spinal nerves emerge from the intervertebral foramina [5]. Because of the multiple neurologic structures confined within paravertebral space local anesthetic introduced here can produce unilateral motor, sensory and sympathetic block [6]. The resultant anesthesia or analgesia due to paravertebral block is conceptually similar to a unilateral epidural anesthesia. Higher or lower levels can be chosen to accomplish a band like segmental blockade at the desired level [7]. Conventionally the desired effect achieved by paravertebral nerve block is by giving the drug or local anesthetic at each nerve root level. Radiographic dye studies using methylene blue have demonstrated that if the anesthetic is deposited in excess volume, then a multisegmental longitudinal spread typically results [8].

Paravertebral nerve block has been an established technique for providing analgesia to the chest and abdomen for many years. It has multiple applications and may serve as the primary anesthetic for chest trauma, chest tube insertion, breast surgery, herniorrhaphy, soft tissue mass excision, bone harvesting from the iliac crest, as an adjunct in laparoscopic surgery, cholecystectomy, nephrectomy and other abdominal and thoracic surgeries [8]. Effective pain control during operation and postoperative period is essential for optimal care of surgical patients. Thus satisfactory analgesia is essential not only to keep up the morale of the patients but also to avoid harmful effects. In the current cost-conscious environment, it is important to examine the impact of anaesthetic techniques on recovery process after ambulatory surgery because proposed recovery times and perioperative complications increase the cost of patient care. In addition patient satisfaction is improved when the anaesthetic technique choosen for the procedure is associated with lesser incidence of post-operative side-effects [9]. Paravertebaral block provides good analgesia with fewer side-effects in inguinal herniorrhaphy patients [10]. The present study was conducted to compare the characteristics of two segment paravertebral block with four segment paravertebral block for anaesthesia and postoperative analgesia for inguinal hernia repair surgeries.

Materials & Methods

The present study was conducted in the department of Anaesthesiology and Critical Care of a tertiary care teaching hospital. After getting approval from Institutional ethics committee patients of ASA grade I and II, aged between 18-80 years scheduled for inguinal herniorrhaphy were included in this study. All patients were thoroughly examined and informed consent was taken. Patients allergy to local anesthetic, coagulopathy, blood dyscrasias, anticoagulant therapy, infection at the site of needle insertion, empyema, tumour occupying the paravertebral space were excluded from the study. Patients were randomly selected in two groups:

Group F: Four segment block – T_{10}, T_{11}, T_{12}, L_1 (5ml 0.75% plain ropivacaine with 1:400000 epinephrine per segment)

Group T: Two segment block – T_{10}, and L_1 (15ml 0.75% plain ropivacaine with 1:400000 epinephrine at T_{10} and 5 ml at L_1)

All the monitoring equipments (Non-invasive blood pressure cuff, pulse oximetry probe, ECG) were attached to the patient and base line values of heart rate, blood pressure, SpO_2 and respiratory rate were recorded.

After cleansing the skin with an antiseptic solution, 6-8 ml of dilute local aesthetic was infiltrated subcutaneously alongside the line where the injections would be made. The injection was carried out slowly to avoid pain on injection and new needle reinsertions were made through already anesthetized skin. The needle was inserted perpendicular to the skin with constant attention to the depth of needle insertion and the medial-lateral needle orientation. Drug was injected after aspiration. Iliac crest (corresponds to L3-4 or L2-3), spinous processes (midline) and tips of scapulae (corresponds to T7) were helpful to identify spinal levels and to estimate the position of the transverse processes. After contacting the transverse process of the individual vertebrae and noting the depth of the bony contact, the needle was hold at 1cm finger backstop and withdrawing the needle almost upto skin level and was reinserted with a 10^0 caudal angulation to a depth till 1cm finger backstop; then the drug was injected after aspiration.

Onset and duration of surgical anaesthesia was assessed by pinprick method. Pain was evaluated using standard 10 cm linear visual analogue scale (VAS) with, 0 corresponding to no pain and 10 to worst pain possible. Duration of complete analgesia (time from onset to first report of pain) and effective analgesia (from onset to first dose of rescue analgesic) was recorded. In failed block, general anesthesia was induced with propofol 2 mg/kg and fentanyl (50-100 μg) intravenously.

Blood pressure, heart rate and respiratory rate were recorded immediately prior to skin incision (baseline), 60s after skin incision, during sac traction and on closure of the wound. Postoperative pain at rest was assessed during the first two postoperative days at predetermined time intervals (0, 6, 12, 24, 36 and 48 h) using VAS score. The analgesic used was oral tablet paracetamol 650 mg 3 times a day to be given after the period of effective analgesia of the procedure, if VAS score was >3.

Data were analysed using SPSS Statistics software. The qualitative data between two groups were compared using chi square test and for comparison of the continuous variable, student t-test were used. $p<0.05$ was considered statistically significant at 95% confidence interval.

Results

Fifty male patients of ASA grade I and II, aged between 18-80 years scheduled for inguinal herniorrhaphy were randomly allocated into two groups of 25 each. The mean age, weight, height and body mass index (BMI) of the patients in both the groups was comparable and the p value between the groups was >0.05 i.e. statistically insignificant.

The mean duration of surgery in group F and group T was 87.60+10.21 minutes, 92.20+12.50 minutes respectively. The p value between the two groups was >0.05 i.e. statistically insignificant. The mean duration of application in group F was 14.94±3.30 minutes and in group T, it was 6.16±1.57 minutes.

The p value in both the group was <0.001 i.e. statistically significant. The mean duration of surgery start time in group F and group T was 27.40±2.55 minutes, 22.79±3.55 minutes respectively. The p value between the two groups was $p<0.01$ i.e. statistically significant (Table 1).

Group T showed 84% satisfaction level while group F showed 76%. Contra-lateral spread was found only in 2 (8%) cases of group F and 1 case (4%) of group T. Failure of block was 20% in group F and 28% in group T which was statistically insignificant (Table 2).

VAS score in both the groups was found statistically insignificant at 0, 6, 12, 24, 36, 48 Hrs interval. (Table 3) Paracetamol rescue was given in 3

Table 1: Comparison of demographic characteristics and other variables in both the groups

	Group-F (Mean ± SD)	Group-T (Mean ± SD)	
Age(yrs)	47.84 ±5.12	48.16±8.63	p>0.05
Height (cms)	154.8 ± 4.44	156.92 ± 3.96	p>0.05
Weight (kgs)	54.7 ± 4.36	56.36 ± 3.63	p>0.05
Body Mass Index (kg/m2)	23.13 ± 1.68	22.89 ± 1.36	p>0.05
Duration of surgery period (min)	87.60± 10.21	92.20±12.50	p>0.05
Duration of application (min)	14.94±3.30	6.160±1.57	**p<0.001**
Surgery start time (min)	27.40±2.55	22.79±3.55	**p<0.01**
Duration of sensory block (hours)	12.84±2.04	13.44±1.66	p>0.05

Table 2: Contra-lateral spread, patient satisfaction, success of block and motor block in both the groups

	Group-F N (%)	Group-T N (%)	
Contra-lateral spread			
Yes	2 (8.0%)	1 (4.0%)	p>0.05
No	23 (92.0%)	24 (96.0%)	
Patient satisfaction			
Yes	19 (76.0%)	21 (84.0%)	p>0.05
No	6 (24.0%)	4 (16.0%)	
Success of block			
Yes	20 (80.0%)	18 (72.0%)	p>0.05
No	5 (20.0%)	7 (28.0%)	
Motor block			
Yes	3 (15.0%)	1 (5.6%)	p>0.05
No	17 (85.0%)	17 (94.4%)	

Table 3: Comparison of Visual Analogue Score at 0, 6, 12, 24, 36, 48 Hrs in both the groups

Time interval	VAS score	Group-F N=20	Group-T N=18	
0 Hr	VAS 0	20 (100.0%)	18 (100.0%)	
6 Hr	VAS 0	20 (100%)	17 (94.44%)	p>0.05
	VAS 1	0 (0%)	1 (5.55%)	
12 Hr	VAS 0	19 (95.0%)	16 (88.88%)	p>0.05
	VAS 2	1 (5%)	2 (11.12%)	
24 Hr	VAS 0	18 (90.0%)	16 (88.9%)	p>0.05
	VAS 3	2 (10.0%)	2 (11.1%)	
36 Hr	VAS 0	17 (85.0%)	15 (83.33%)	p>0.05
	VAS 3	3 (15.0%)	3 (16.66%)	
48 Hr	VAS 0	17 (85%)	14 (77.77%)	p>0.05
	VAS 3	3 (15.0%)	4 (22.22%)	

cases (15%) of group F and 4 cases (22.22%) of group T. There was no significant difference in HR, SBP, DBP, MAP, SpO2 and respiratory rate during the intra/post operative period (p>0.05).

Discussion

Paravertebral block was first described by Hugo Sellheim in 1905 [8]. It was initially utilized as an alternative to spinal anaesthesia. More recently, this block has been successfully used to provide analgesia for multiple thoracic and abdominal procedures in both children and adults [11].

In present study the demographic data of patients was comparable in both the groups. This study found that time taken for the block was shortened when a two segment paravertebral block was used as compared with a four segment paravertebral block. Both methods gave similar anesthetic success. Satio et al used a single injection paravertebral block technique with 12 ml local anesthetic in inguinal hernia surgeries with a success rate of 60% [12]. In Satio et al cadaver study where anatomic borders of paravertebral block were investigated, fluid shift occurred between thoracic and lumbar paravertebral areas [13]. For successful inguinal hernia surgery, ilioinguinal, iliohypogastric and genitofemoral blocks have to be performed. In the present study, paravertebral block was applied at L^1 level beside T^{10}, to cover ilioguinal, iliohypogastric and the genitofemoral nerves [11,14]. In previous studies, it was reported that multiple segment paravertebral block injections were not comfortable for patients and they may increase the risk of pleural puncture (1.1%) and Penumothorax (0.5%) [11,14]. There was no pleural puncture or pneumothorax in any patient of either groups in present study.

The present study found that the shorter injection time in the two segment paravertebral block was reported to be more comfortable by the patients, but that patient satisfaction showed no significant difference between the two groups. In present study the sensory block lasted for approximately 12 hrs which is in accordance with the Weltz et al study [3]. This may be due to slow local anesthetic uptake due to the avascular structure of the paravertebral area.

In present study the time taken to perform the block was significantly more in group F as compared to group T. The surgery start time was significantly more in groups F as compared to group T. The sensory block duration was comparable in both study groups. This suggests that both methods are good choices with regard to analgesic comfort during the post operative period. These finding are in agreement with the study conducted by Ozkan et al [15].

In the literature, there are epidural and intrathecal spreads in 1% and contralateral spread in 1.1% for paravertebral block [11,16]. In present study, contralateral spread occurred in 8% of patient in Group F and 4% in Group T. Motor blockade of the ipsilateral lower limb measured in terms of knee flexion occurred in 15% in group F and 22.22% in group T, which was statistically not significant. However, larger studies would be necessary to confirm these finding; since the sample size in present study was underpowered to determine disadvantages of paravertebral block.

Prolonged postoperative analgesia and absence of motor blockade which are the key features of paravertebral block, lead to decreased opioid consumption and enable early ambulation. In present study analgesia was present even after 48 hours of surgery. The shorter hospital stay and early discharge observed in present study was in accordance with the Hadzic et al study [17].

The failure rate in present study for four segment paravertebral block was 20% and for 2 segments

paravertebral block was 28% which was higher than the 12% failure rate reported by Cheema et al [18]. Since the success rate was lower when the study began and progressively increased with the number of cases, it could be attributed to improvement of expertise in performing the block with experience. Furthermore, the use of nerve stimulator for confirmation of correct needle placement along with ultasound guidance may add objectivity to this procedure and may further decrease failure.

Conclusion

Paravertebral block can provide ideal anesthesia conditions such as prolonged postoperative analgesia, unilateral blockade, early ambulation, intraoperative hemodynamic stability, faster recovery and early discharge from the hospital. Furthermore, decreasing the number of injections in the two segment block technique may further increase patient comfort and satisfaction and perhaps decreases complications. The two segment technique is less time consuming, provides similar analgesia as compared to the four segment technique but the success rate is dependent on experience of the person performing the block. So, two segments technique of paravertebral block can be a viable alternative to the four segments technique for inguinal hernia surgery.

References

1. Isil CT, Cinar ASO, Oba S, Isil RG. Comparison of spinal anaesthesia and paravertebral block in unilateral inguinal hernia repair. Turk J Anaesth Reanim 2014;42:257-63.
2. Lim SL, Ng Sb A, Tan GM. Illioinguinal and iliohypogastric nerve block revisited: Single shot versus double shot technique for hernia repair in children. Paediatric Anaesthesia 2002;12:255-60.
3. Weltz CR, Klein SM, Arbo JE, Greengrass RA. Paravertebral block anesthesia for inguinal hernia repair. World J Surg 2003;27:425-9.
4. Baumgarten RK, Greengrass RA, Wesen CA. Paravertebral block: the holy grail of anesthesia for hernia surgery? Anesth Analg 2007;104:207.
5. Tsuchiya N, Ichizawa M, Yoshikawa Y, Shinomura T. Comparison of ropivacaine with bupivacaine and lidocain for illioinguinal block after ambulatory inguinal hernia repair in children. Paediatric Anaesthesia 2004;14:468-70.
6. Ivani G, Gonio A, De Negri P, Eksborg S, Lonnqvist PA. Spinal versus peripheral effects of adjunct clonidine; comparison of the analgesic effect of a ropivacaine-clonidine mixture when administered as a caudal or illioinguinal-iliohypogastric nerve blockade for inguinal surgery in children. Paediatric Anaesthesia 2002;12:680-4.
7. Li C, Song C, Wang W, Song C, Kong X. Thoracic paravertebral block versus epidural anesthesia combined with moderate sedation for percutaneous nephrolithotomy. Med Princ Pract 2016;25(5):417–22.
8. Batra RK, Krishnan K, Agarwal A. Paravertebral Block. J Anaesthesiol Clin Pharmacol. 2011; 27(1):5–11.
9. Ernst E, Pittler MH. The effectiveness of acupuncture in treating acute dental pain. A systemic review. Br Dent J 1998;184:443-7.
10. Klein SM, Pietrobon R, Nielsen KC, Steele SM, Warner DS, Moylan JA et al. Paravertebral somatic nerve block compared with perip-heral nerve blocks for outpatient inguinal herniorrhaphy. Reg Anesth Pain Med 2002;27:476–80.
11. Karmakar MK. Thoracic paravertebral block. Anesthesiology 2001;95:771–80.
12. Satio T, Gallagher ET, Cutler S, Tanuma K, Yamada K, Saito N et al. Extended unilateral anesthesia: new technique or paravertebral anesthesia? Reg Anaesth 1996;21:304-7.
13. Satio T, Den S, Tanuma Y, Carney E, Carlsson, C. Anatomical bases for paravertebral an esthetic block; fluid communication between the thoracicand lumbar paravertebral regions. Surg Radiol Anat 1999; 21:359-63.
14. Lonnqvist PA. Entering the paravertebral space age again? Acta Anaesth Scand 2001;45:1-3.
15. Ozkan D, Akkaya T, Comert A. Balkc N, Ozdemir E, Gumus H et al. Anesth Pain Med 2009;34(4):312-5.
16. Karmakar MK, Kwok WH, Kew J. Thoracic paravertebral block: radiological evidence of contralateral spread anterior to the vertebral bodies. Br J Anaesth 2000;84:263-5.
17. Cheema S, Richardosn J, Mc Gurgan P. Factors affecting the spread of bupivacaine in the adult thoracic paravertebral space. Anaesthesia 2003; 58:684-711.
18. Hadzic A, Kerimogla B, Loreio D, Kanca PE, Claudio RE, Yufa M et al. Paravertebral blocks provide superior same day recovery over general anesthesia for patients undergoing inguinal hernia repair. Anesth Analg 2006;102:1076-81.

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Comparison of the Effect of Ketamine, Tramadol, 1.5% Saline and Normal Saline Gargle on Post-Operative Sore Throat after Endotracheal Intubation

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Abstract

Postoperative sore throat (POST) is a frequent complaint following endotracheal intubation with incidence rates varying from 14.4% to 61%. Regardless of the incidence or duration, POST is rated as a patient's 8th most undesirable outcome in the postoperative period, and is certainly an opportunity to improve patient outcomes.

Background and Objectives: Various non-pharmacological and pharmacological trials have been used for attenuating POST with variable success. The aim of the present study was to compare the effect of ketamine, tramadol and 1.5% saline gargle in prevention of post-operative sore throat.

Methods and Material: Following institutional ethical committee approval and written informed consent, a prospective randomized double-blinded study was conducted in 100 cases divided into four groups of 25 patients in each group. Patients included in the study were of age group 18- 60 years, ASA grade I-II, undergoing elective surgeries with duration of surgery approximately 2 hrs or more requiring tracheal intubation. Patients were allocated randomly to four groups, Group A, Group B, Group C and Group D. After shifting patient to operation theatre 5 mins prior to induction of anesthesia, Group A received 30ml of normal saline, Group B preservative free ketamine 1ml (50 mg) in 29 ml of normal saline, Group C received tramadol 1ml(50 mg) in 29ml normal saline and Group D received 30ml of 1.5% saline to gargle for 30 seconds. Postoperatively presence of sore throat was noted at rest and on swallowing immediately after extubation, at 2 h, 4 h, and 24 h.

Statistical Analysis Used: IBMSPSS_21 was used for statistical analysis.

Results: There was no significant difference in POST at rest (Figure 1) at 0 hr, 4 hr and 24 hr postoperatively among the four groups. Incidence of POST at rest at 2hr was significantly lower in ketamine group. Ketamine caused significant reduction in POST at swallowing (Figure 2) at 2 & 4hrs. Tramadol caused significant reduction at 2 & 4 hrs. 1.5% saline caused significant reduction in POST at swallowing at 2hrs.

Conclusions: Among all the groups ketamine was found to be most effective in prevention of POST followed by tramadol. Based on the risk estimate analysis even 1.5% saline reduces incidence of POST.

Keywords: Postoperative; Complication; Endotracheal Intubation.

Introduction

Postoperative sore throat (POST) is a frequent complaint following endotracheal intubation with incidence rates varying from 14.4% to 61%. It ranks along nausea as the most common complaint after endotracheal intubation for general anaesthesia [1]. Regardless of the incidence or duration, POST is rated as a patient's 8th most undesirable outcome in the postoperative period, [2] and is certainly an opportunity to improve patient outcomes [3].

Various non-pharmacological and pharmacological trials have been used for attenuating POST with variable success. Among the non-pharmacological

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methods, smaller-sized endotracheal tubes, lubricating the endotracheal tube with water-soluble jelly, careful airway instrumentation, intubation after full relaxation, gentle oropharyngeal suctioning, minimizing intracuff pressure (<20mmhg), and extubation when the tracheal tube cuff is fully deflated have been reported to decrease the incidence of POST [4]. The pharmacological methods include inhalation of beclomethasone, fluticasone and gargling with azulenesulphonate, aspirin and licorice [5-7].

Preemptive application of locally active anti-inflammatory and analgesic agents may reduce the discomfort associated with airway inflammation. In this regard ketamine(phencyclidine derivative) and benzydine hydrochloride (topical NSAID) have been used independently as preoperative gargle and have been noted to decrease the incidence and severity of POST [7]. Role of n-methyl-d-aspartate (NMDA) in nociception and inflammation is already known [8,9]. NMDA receptors are found in peripheral nerves and in the central nervous system [10,11]. Hence NMDA antagonists such as ketamine and tramadol act on peripheral nerve endings in pharyngeal mucosa and can reduce the incidence of sore throat [12]. Although no literature is available about role of hypertonic saline for reducing POST. It has been hypothesized that similar to its role for providing symptomatic relief in acute bronchiolitis and sore throat due to upper respiratory tract infections it may be beneficial in POST too [13]. In view of making it palatable we diluted hypertonic saline to 1.5% saline. In our study we plan to compare the efficacy of ketamine, tramadol, 1.5% saline and normal saline gargles to reduce the incidence of POST.

Aim of the Study

Primary aim is to compare the effect of ketamine, tramadol, 1.5% saline and normal saline gargle in prevention of post-operative sore throat.

Materials and Methods

Following institutional ethical committee approval and written informed consent, a prospective randomized double-blinded study was conducted in 100 cases divided into four groups of 25 patients in each group.

With the level of significance (alpha) = 0.05, and power of 80%, sample size required was 20 per group. To accommodate any exclusion, 25 patients from each group were selected.

Patients included in the study were of either gender, 18 to 60 years age belonging to physical status (American Society of Anesthesiologist) ASA grade 1 or 2, undergoing elective surgery of duration of approximately 2 h or more and requiring tracheal intubation. Patients with neuromuscular disease, allergy or hypersensitivity of drugs, on steroid therapy, undergoing oral cavity and pharynx surgeries with use of nasogastric tube were excluded.

Patients who required more than two attempts at intubation or had bucking or coughing during intubation were also excluded.

Patients were allocated randomly to four groups, Group A, Group B, Group C and Group D.

Simple randomization was done using SPSS software (IBM, SPSS Statistics 21).

All patients were kept fasting overnight and premedicated with oral alprazolam 0.5 mg and ranitidine 150 mg on night before surgery and on the morning of surgery. After shifting patient to operation theatre Group A received 30ml of normal saline, Group B received preservative free ketamine 1ml (50 mg) in 29 ml of normal saline, Group C received tramadol 1ml (50 mg) in 29ml normal saline and Group D received 30ml of 1.5% saline to gargle for 30 seconds, 5 mins prior to induction of anesthesia.

The solution for gargling was administered by anaesthesiologist not associated with the management of the case. The anaesthesiologist anesthetizing the case and those recording the scores were blinded to it. In the operation theatre, after connecting the patient to standard monitoring intravenous access was secured. Anesthesia was induced with fentanyl 2 mcg/kg and thiopentone 5 mg/kg. Tracheal intubation was facilitated by atracurium 0.6 mg/kg, and the trachea intubated with soft seal cuffed sterile polyvinyl chloride tracheal tube (Portex Limited CT 21, 6JL, UK) of 7 mm inner diameter in female and 8 mm in male patients. The tracheal tube cuff was inflated with air.

The cuff pressure was checked just after intubation using hand held endotracheal cuff pressure monitor (Portex Cuff Inflator/Pressure Gauge, SIMS Portex, Hythe, Kent, UK) and then every half hourly till end of surgery and maintained at 20 cm of H2O.

Ventilation was controlled, and no nasogastric tube was inserted. Anesthesia was maintained with 66% nitrous oxide in oxygen with 1% of isoflurane and intermittent doses of atracurium and fentanyl as required. The last dose of atracurium was given 20 min prior to extubation. At the end of surgery, the muscle relaxation was reversed with a combination

of neostigmine 0.05 mg/kg and glycopyrrolate 0.01 mg/kg. The patients were extubated after meeting regular extubation criteria (like return of consciousness, adequate muscle power, sustained head lift for 5 seconds, sustained hand grip for 5 seconds, spontaneous ventilation, and the ability to follow verbal commands with eye opening), and the patients were shifted to post anaesthesia care unit. Presence of sore throat was noted at rest (Figure 1) and on swallowing (Figure 2) immediately after extubation, and 2 h, 4 h, and 24 h postoperatively. In the postoperative ward, patients were also monitored for any drug-related side effects.

Statistical Analysis

Data was expressed as mean and 95% confidence interval of mean and tests of normality (Kolmogorov-smirnov, shapiro-wilk) for continuous variables (height, weight, age) were used. Categorical data (gender) was expressed as frequency of occurrence. Comparison of continuous data between groups was done using ANOVA of means. P value of <0.05 was considered statistically significant. Comparison of categorical data between groups was done using pearson chi- square, continuity correction, likelihood ratio, fishers exact test, P value of <0.05 was considered statistically significant. IBMSPSS_21 was used for statistical analysis.

Results

There were hundred patients were enrolled into 4 groups of the present study. There were no significant differences between four groups in terms of age, sex, and weight.

1. No significant differences between the groups were observed by one way ANOVA for continuous variable, age and weight and chi-square test for categorical variable, gender. P<0.05 was considered statistically significant. Demographic data was presented as either, mean with 95% confidence interval for mean or as numbers (Table 1).
2. There was no significant difference in POST at rest (Figure 1) at 0 hr (Table 2), 4 hr (Table 4) and 24hrs (Table 5) among the four groups. Incidence of POST at rest at 2hr (Table 3) was significantly lower in ketamine group.
3. Incidence of POST at swallowing (Figure 2) at 0hrs (Table 6) and 24hrs (Table 9) was not significantly different among the groups.

   Significant difference in POST at swallowing was seen at 2hrs (Table 7) with ketamine, tramadol and 1.5% saline as compared to normal saline. But based on relative risk assessment ketamine

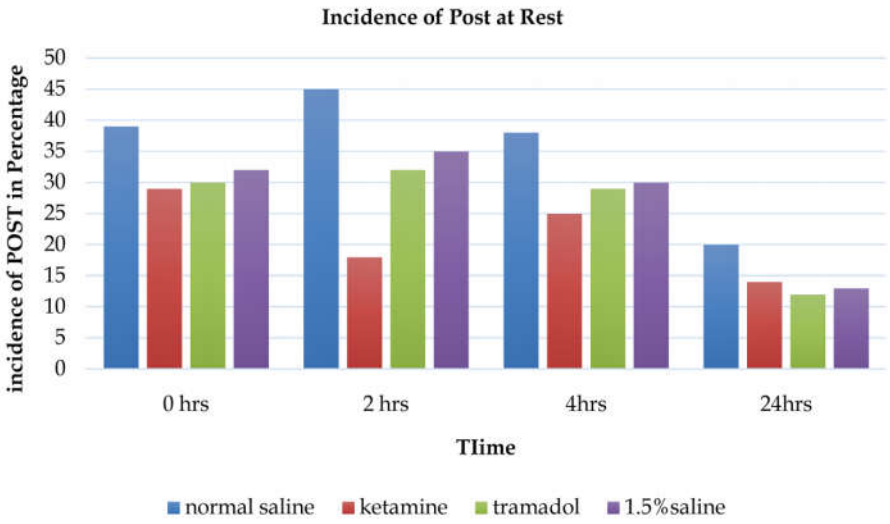

Fig. 1: Incidence of POST at rest

Table 1: Demographic data

Variables	Group A (normal saline)	Group B (ketamine)	Group C (tramadol)	Group D (1.5% saline)	P Value
Age(years)	50.8±11.9	51.5±12.7	52.3±12.4	52.48±10.18	0.325
Sex(male/female)	14/11	13/12	15/10	12/13	0.46
Weight (Kgs)	68±9.08	61±9.06	60±9.45	63±9.1	0.09

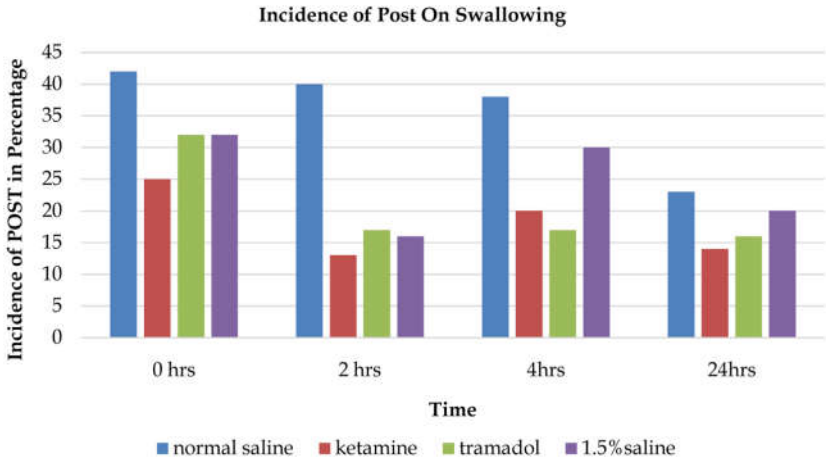

Fig. 2: Incidence of POST on swallowing

Table 2: Incidence of POST at rest at 0 hour

Drug	Post	Pearson Chi square P Value	Fishers Exact Test	R.R. When N.S is Used
N.S (n=25)	36%			
Ketamine (n=25)	28%	0.135	0.261	1.64
Tramadol (n=25)	28%	0.614	0.315	1.23
1.5% SALINE (n=25)	32%	0.025	0.013	1.12

Table 3: Incidence of POST at rest at 2hrs

Drug	POST	Pearson Chi square P Value	Fishers Exact Test	R.R. when N.S IS Used
N.S (n=25)	44%			
Ketamine (n=25)	16%	0.04	0.03	3.61
Tramadol (n=25)	32%	0.08	0.12	1.57
1.5% Saline (n=25)	36%	0.23	0.32	1.32

Table 4: Incidence of POST at rest at 4hrs

Drug	Post	Pearson Chi square P Value	Fishers Exact Test	R.R. when N.S IS used
N.S (n=25)	36%	-	-	-
Ketamine (n=25)	24%	0.13	0.24	1.67
Tramadol (n=25)	28%	0.45	0.32	1.43
1.5% Saline (n=25)	32%	0.23	0.26	1.32

Table 5: Incidence of POST at rest at 24hrs

Drug	Post	Pearson Chi Square p value	Fishers Exact Test	R.R. when N.S IS Used
N.S (n=25)	20%			
Ketamine (n=25)	16%	0.09	0.12	1.22
Tramadol (n=25)	12%	0.34	0.46	1.54
1.5% saline (n=25)	12%	0.21	0.25	1.46

Table 6: Incidence of POST on swallowing at 0hr

Drug	Post	Pearson Chi square P Value	Fishers Exact Test	R.R. when N.S IS used
N.S (n=25)	44%			
Ketamine (n=25)	24%	0.13	0.09	1.89
Tramadol (n=25)	32%	0.37	0.32	1.41
1.5% saline (n=25)	32%	0.26	0.30	1.32

Table 7: Incidence of POST on swallowing at 2hrs

Drug	Post	Pearson Chi square P Value	Fishers Exact Test	R.R. when N.S is used
N.S (n=25)	40%			
Ketamine (n=25)	12%	0.02	0.03	3.34
Tramadol (n=25)	16%	O.03	0.03	2.56
1.5% saline (n=25)	16%	0.03	0.04	2.64

Table 8: Incidence of POST on swallowing at 4hrs

Drug	Post	Pearson Chi square P Value	Fishers Exact Test	R.R. when N.S IS used
N.S (n=25)	36%			
Ketamine (n=25)	20%	0.04	0.04	4.3
Tramadol (n=25)	16%	0.03	0.04	2.6
1.5% saline (n=25)	28%	o.14	0.09	1.8

Table 9: Incidence of POST on swallowing at 24hrs

Drug	Post	Pearson Chi square P Value	Fishers Exact Test	R.R. when N.S Is Used
N.S (n=25)	24%	-	-	-
Ketamine (n=25)	12%	0.24	0.13	2.3
Tramadol (n=25)	16%	0.47	0.35	1.9
1.5% Saline (n=25)	20%	0.51	0.62	1.2

caused more decrease in incidence of POST at swallowing at 2hrs compared to tramadol and 1.5% saline. At 4 hrs (Table 8) only ketamine caused significant difference. The other variations observed are due to chance error.

4. With respect to age and gender, there was no significant difference in POST "at rest" and "on swallowing" between the four groups.

Discussion

General anesthesia with endotracheal intubation can result in sore throat and hoarseness which may be considered to be minor by some and troublesome by others. Therefore, identification of risk factors and prevention of these symptoms would add to patient satisfaction. Present study compared the efficiency of preoperative gargle with ketamine, tramadol, 1.5% saline and normal saline in reducing the incidence of post-operative sore throat following general anaesthesia with endotracheal tube for elective surgeries in ASA 1 or 2 cases aged between 18-60 years.

In our study we did not find any significant difference between groups in terms of age, gender and weight. Patient sex, age, gynaecological surgery, use of succinylcholine, larger tracheal tubes, cuff design and intracuff pressures have all been shown to contribute to POST [4,14,15]. Increased incidence of POST in females was reported by Biro et al [1] but in our study we did not find such association of POST with gender.

Similar to the results of study by Canbay et. al., no correlation was observed between incidence of POST, age, weight and duration of intubation [6]. Application of lignocaine jelly was avoided in our study as Maruyama et. al., Kori K et. al. found increased incidence of POST on application of 2% lignocaine jelly to the endotracheal tube [16,17].

Succinylcholine was found to increase incidence of POST by Higgins et. al. [14] Therefore to avoid any bias succinylcholine was not used in our study. Suzuki et al suggested that keeping the cuff pressure under 15mmHg (20.55cm of water) prevented postoperative hoarseness or sore throat at 24hrs. McHardy et al and Suzuki et al found that monitoring and adjustment of intracuff pressure reduces the incidence of POST [18,19]. Therefore in all our cases cuff pressure was maintained at 20mm of water and monitored every 30 min to reduce the effect of this confounding factor.

The incidence of POST in normal saline group was lower in our study as compared to incidence reported by Canbay et al and Agarwal et al respectively in their studies [3,6].

This could be because we standardized the cuff pressure to 20 cm of water, lignocaine jelly on endotracheal tube was avoided and succinylcholine was not used, all of which have been shown to

increase incidence of POST.

In study by canbay et. al. there was increase in incidence of POST at 24hrs. This could be because all patients had undergone septorhinoplasty which causes dryness and inflammation of oral cavity due to mouth breathing in the postoperative period, increasing the incidence of late onset POST [6].

In our study the incidence of POST at rest for Ketamine group was 29%, 18%, 25% and 14% at 0hr, 2hrs, 4hrs and 24hrs respectively.

Our results are comparable to the results of study by Rudra et al who also observed statistically significant reduction in the incidence of POST in ketamine group compared to control group [20].

The incidence of POST on swallowing for tramadol group was 32%, 17%, 17% and 16% at at 0hr, 2hrs, 4hrs and 24hrs respectively. The results are similar to study by Rashwan et al who showed reduction in incidence and severity of POST by tramadol gargle at 2hrs, 6hrs and 12hrs [21].

There are no studies to compare the effect of 1.5% saline on incidence of POST. It was hypothesized that similar to its role for providing symptomatic relief in acute bronchiolitis and sore throat due to upper respiratory tract infections it may be beneficial in POST too [13].

According to risk estimate tables the incidence of POST was significantly more frequent in normal saline group compared to the other three groups with the reduction being maximum in ketamine group. Sore throat after endotracheal intubation might be because of local trauma leading to aseptic inflammation of the pharyngeal mucosa leading to oedema congestion and pain.

NMDA receptors have a role in nociception and inflammation. Ketamine and Tramadol by antagonizing NMDA receptors reduce the inflammation [12].

This may be the reason for reduction of incidence of POST with preoperative ketamine and tramadol gargle in our study. The drawback of our study was absence of measurement of serum ketamine and tramadol levels to know the systemic effects of these drugs. But the doses were low and drugs were given as gargles. No adverse effects were observed.

Conclusion

The incidence of POST in the patients undergoing GA with endotracheal intubation for routine cases is quiet common and remains for next 24 hrs. There was no significant difference between the groups for age, weight and gender. Among all the groups ketamine was found to be most effective in prevention of POST followed by tramadol. Based on the risk estimate analysis even 1.5 % saline reduces incidence of POST. Therefore due to the cost effectiveness and efficacy of the treatment 1.5 % saline may be considered in practice for reducing POST.

Key Message

Due to cost effectiveness and efficacy of the treatment 1.5% saline may be considered in clinical practice for reducing POST.

References

1. Biro P, Seifert B, Pasch T. Complaints of sore throat after tracheal intubation: a prospective evaluation. Eur J Anaesthesiol 2005;22:307–11.
2. Macario A, Weinger M, Carney S, Kim A. Which clinical anesthesia outcomes are important to avoid? The perspective of patients. AnesthAnalg 1999;89: 652–8.
3. Agarwal A, Nath SS, Goswami D, Gupta D, Dhiraaj S, Singh PK. An evaluation of the efficacy of aspirin and benzydamine hydrochloride gargle for attenuating postoperative sore throat: A prospective, randomized, single-blind study. Anesth Analg. 2006;103:1001–3.
4. Ratnaraj J, Todorov A, McHugh T, Cheng MA, Lauryssen C. Effects of decreasing endotracheal tube cuff pressures during neck retraction for anterior cervical spine surgery. J Neurosurg. 2002;97:176–9.
5. Ogata J, Minami K, Horishita T, et. al. Gargling with sodium azulene sulfonate reduces the postoperative sore throat after intubation of the trachea. Anesth Analg. 2005 Jul;101(1):290-3.
6. Canbay O, Celebi N, Sahin A, Celiker V, Ozgen S, Aypar U. Ketamine gargle for attenuating postoperative sore throat. Br J Anaesth. 2008;100:490–3.
7. Agarwal A, Gupta D, Yadav G, Goyal P, Singh PK, Singh U. An evaluation of the efficacy of licorice gargle for attenuating postoperative sore throat: a prospective, randomized, single-blind study. . Anesth Analg. 2009 Jul;109(1):77-81.
8. Lin CY, Tsai PS, Hung YC, Huang CJ. L-type calcium channels are involved in mediating the anti-inflammatory effects of magnesium sulphate. Br J Anaesth. 2010;104:44–51.
9. Zhu MM, Zhou QH, Zhu MH, Rong HB, Xu YM, Qian YN, et al. Effects of nebulized ketamine on allergen-induced airway hyperresponsiveness and inflammation in actively sensitized Brown-Norway rats. J Inflamm (Lond) 2007;4:10.
10. Tan PH, Yang LC, Chiang PT, Jang JS, Chung HC, Kuo CH. Inflammation-induced up-regulation of ionotropic glutamate receptor expression in human

skin. Br J Anaesth. 2008;100:380–4.

11. Carlton SM. Encyclopedia of Pain. Berlin, Heidelberg: Springer; Inflammation, role of peripheral glutamate receptors; 2007.pp.984–7.
12. Chan L, Lee ML, Lo YL. Postoperative sore throat and ketamine gargle. . Br J Anaesth. 2010 Jul;105(1):97.
13. Yen-Ju Chen,Wen-Li Lee, Chuang-Ming Wang,Hsin-Hsu Chou.Nebulized Hypertonic Saline Treatment Reduces Both Rate and Duration of Hospitalization for Acute Bronchiolitis in Infants: An Updated Meta-analysis. Pediatr Neonatol 2014 Dec;55(6):431-8.
14. Higgins PP, Chung F, Mezei G. Postoperative sore throat after ambulatory surgery. Br J Anaesth. 2002;88:582–4.
15. Hu B, Bao R, Wang X, Liu S, Tao T, Xie Q, et. al. The size of endotracheal tube and sore throat after surgery: A systematic review and meta-analysis. PLoS One. 2013; 8:e74467.
16. Maruyama K, Sakai H, Miyazawa H, Iijima K, Toda N, Kawahara S, et al. Laryngotracheal application of lidocaine spray increases the incidence of postoperative sore throat after total intravenous anesthesia. J Anesth. 2004;18:237–40.
17. Kori K, Muratani T, Tatsumi S, Minami T. Influence of endotracheal tube cuff lubrication on postoperative sore throat and hoarseness. Masui. 2009;58:342–5.
18. McHardy FE, Chung F. Postoperative sore throat: cause, prevention and treatment . Anaesthesia. 1999;54 (5):444-53.
19. Suzuki N, Kooguchi K, Mizobe T et al. Postoperative hoarseness and sore throat after tracheal intubation: Effect of a low intracuff pressure of endotracheal tube and the usefulness of cuff pressure indicator. Masui 1999;48(10):1091-95.
20. Rudra A, Ray S, Chatterjee S, Ahmed A, Ghosh S. Gargling with ketamine attenuates the postoperative sore throat. Indian J Anaesth. 2009 Feb;53(1):40-3.
21. Rashwan S, Elmawgoud A A and Badawy AA. Effect of tramadol gargle on postoperative sore throat: A double blinded randomized placebo controlled study. Egyptian Journal of Anaesthesia. 2014;(30):235- 9.

Original Research Article

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A Comparative Study of Efficacy of Intrathecal Fentanyl and Nalbuphine as an Adjuvant to Bupivacaine 0.5% Heavy for Lower Limb and Lower Abdominal Surgeries

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Abstract

Introduction: Opioids have been extensively used as an adjuvant because of excellent results in neuraxial blocks. Fentanyl is widely used but is found to have higher incidence of pruritus for which Nalbuphine was considered as an adjuvant.

Aim: To compare the efficacy of Fentanyl and Nalbuphine as an adjuvant to bupivacaine 0.5% heavy.

Methods and Material: Randomised control trial was carried out on 60 patients between 18-60 years of age and ASA grade I and II with groups having 30 patients each: GROUP A - Bupivacaine (2.5 ml) + Fentanyl 25µg (0.5 ml), GROUP B - Bupivacaine (2.5 ml) + Nalbuphine 400ug (0.5 ml). The observation and results were compared and statistical analysis was done. Statistical analysis was performed by the SPSS program for Windows. For comparing the two main groups Paired t test was applied. In this study p value < 0.05 is considered as statistically significant.

Results: Onset of sensory block was significantly rapid with nalbuphine (2.05±0.887 mins) as compared to fentanyl group (4.67±0.816mins) ($p<0.001$). The duration of analgesia was statistically prolonged with fentanyl (244.27±5.457mins), compared with the nalbuphine (243.25±8.091 mins). ($p< 0.05$) but it was clinically not significant.

Conclusion: 400 mcg intrathecal nalbuphine is superior to 25mcg intrathecal fentanyl regarding the duration of analgesia and reduced the analgesic requirement in the early postoperative period.

Keywords: Analgesia; Anesthesia; Bupivacaine; Nalbuphine; Fentanyl; Spinal.

Introduction

Spinal anesthesia, defined as regional anesthesia obtained by blocking nerves in the subarachnoid space, was introduced in clinical practice by Karl August Bier in 1898 [1].

Spinal anesthesia using local anesthetics like cocaine, procaine, lignocaine, bupivacaine, ropivacaine is one of the most popular techniques for both elective and emergency surgical procedures.

Adding adjuvant drugs to intrathecal local anesthetics improve or prolong analgesia, decrease the adverse effects associated with high doses of single local anesthetic, increase speed of onset of neural blockade(reduce latency) and increases analgesic gap [2,3].

A number of adjuvants have been used along with local anesthetics which include Opioids (Morphine, Fentanyl, Nalbuphine, Nalbuphine, Pentazocine, etc.), Alpha-2 Agonists(clonidine, dexmedetomidine) GABA Agonists (Midazolam), NMDA Receptor Antagonists (Ketamine), Neostigmine, NSAIDS, Neuromuscular Blocking Drugs, Dextrans, Adenosine [3,4].

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Opioids have been extensively used as an adjuvant because of excellent results in neuraxial blocks. Fentanyl is widely used and has become standard adjuvant drug via intrathecal and extrathecal approaches for various lower surgeries for postoperative pain relief [5].

But Fentanyl was found to have higher incidence of pruritus for which Nalbuphine was considered as an adjuvant.

In the present study we intend to compare the effects of fentanyl a pure agonist opioid agent with Nalbuphine an agonist antagonist opioid agent when used intrathecally in patients undergoing lower limb surgery.

Aim and Objectives

Aim

- To compare the efficacy of Fentanyl and Nalbuphine as an adjuvant to bupivacaine 0.5% heavy for lower limb and lower abdominal surgeries.

Objectives

To study and compare Fentanyl and Nalbuphine as an adjuvant to bupivacaine 0.5% heavy with respect to:

1. Onset and duration of sensory block.
2. Onset and duration of motor block.
3. Duration of post-operative analgesia
4. Adverse effects – hypotension, bradycardia, nausea vomiting, respiratory depression, shivering and pruritus.

Material and Methods

Study Design

Randomised Control Trial On "A Comparative Study of Efficacy of Intrathecal Fentanyl and Nalbuphine as an Adjuvant to Bupivacaine 0.5% Heavy for Lower Limb and Lower Abdominal Surgeries"was carried out on 60 patients between 18-60 years of age and ASA grade I and II physical status.

Inclusion Criteria

1. ASA grade I and II of either sex
2. Age between 18 to 60 years
3. Patient with written valid consent
4. Patient undergoing elective lower limb surgery.

Exclusion Criteria

1. Patient refusal
2. Allergy to any anesthetic drug
3. Infection at the site of injection
4. Patient on anticoagulants or bleeding disorder
5. ASA III and IV
6. Patients on tranquilizers, hypnotics, sedatives, and other psychotropic drugs.
7. Duration of surgery > 2 hours

Sample Size Estimation

30 per group making total of 60

Methodology

Pre anesthetic check-up was done on the previous day and on morning of surgery. Routine and specific investigations were noted.

Patients were randomly allocated into 2 groups each having 30 patients.

Group A: Intrathecal bupivacaine 0.5% heavy (2.5 ml) + Fentanyl 25µg (0.5 ml)

Group B: Intrathecal bupivacaine 0.5% heavy (2.5 ml) + Nalbuphine 25ug (0.5 ml)

All the patients were kept fasting overnight prior to the scheduled day of operation. Sedatives and hypnotics, inclusive of Opioids were avoided in pre medication as well as intra operatively. Patients received Inj. Ranitidine 50mg IV as premedication after entering the operation theatre. All standard monitors (ECG, NIBP, SpO2) were applied. Baseline BP, PR, RR were recorded. All patients were preloaded through 18 G cannula with 10 ml/kg of RL solution over 15-20 min. Under all aseptic precautions, lumbar puncture was performed in the $L_{3-4.}$ Intervertebral space using 25 G Quincke's spinal needle in sitting position. The patient received either one of the drug solution. Patient were turned supine and position of table was kept horizontal. Recording of HR, SBP, DBP, MAP, SpO2 and RR was done every 3 mins for 15 min, every 5 mins for 30 mins, and every 15 mins till 3 hours. In the intra operative period, crystalloid solutions (Ringer Lactate) 4ml/kg/hr was infused. The onset of sensory block was tested by pin-prick method using a 24G hypodermic needle every 2 minutes until the level had stabilized for 4 consecutive tests. Motor block was assessed by modified Bromage

scale. VAS was noted when the patient first complains of pain. VAS > 3 was treated with inj. Diclofenac 75mg IV.

The following parameters were noted:

1. Time to onset of sensory block (i.e. time from intrathecal injection of drug to complete loss of sensation to pin prick at T10).
2. Time taken to achieve the highest level of sensory block (time from intrathecal injection to highest level of sensory block).
3. The time for two dermatomal segments regression of sensory level.
4. Time taken to achieve complete motor block by Modified Bromage Score (time from intrathecal injection to achievement of Bromage 3).
5. Duration of motor block was noted (time from Bromage 3 to Bromage 2).

Modified Bromage Scale (for grading of motor block)

1. Grade 0 - No motor block
2. Grade 1 - inability to raise extended leg, able to move knees and feet
3. Grade 2 - inability to raise extended leg and move knees, able to move feet
4. Grade 3 – complete motor block of lower limbs.

6. Duration of analgesia (time from onset of sensory block to first complaint of pain by patient).
7. Peri-operative pain was assessed using 10 point Visual Analogue Scoring method (0-no pain, 10-worst pain)

   Pain score '0' to '3' - Mild pain, Pain score '3' to '7' - Moderate pain, Pain score > 7 - Severe pain
8. Adverse effects

A. If Hypotension occurred (MAP fall below 20% of base line) – was treated as follows in that order, till blood pressure normalized.

- Bolus of 100 – 200 ml of crystalloid solution
- Sympathomimetics

Inj. Mephenteramine IV 6mg to begin with and repeated if necessary, not to exceed the maximum of 30mg.

Inj.dopamine 3-10 mcg / kg / min I.V. infusion if no response to mephenteramine.

- Colloid/Blood transfusion in case hypovolemia ensued due to bleeding.

B. If Bradycardia(HR<50) was encountered,

- Inj. Atropine 0.5mg IV was given

C. If Respiratory depression RR<10/min.

- Oxygenation and IPPV if required.

D. If Nausea and vomiting

- Inj. Ondansetron 4 mg i.v.

E. Shivering

- Use of patient warming system-baer hugger.

F. Pruritus

- Inj hydrocortisone 100mg iv.

Results

The observation and results of the study were compared and statistical analysis was done. Data was managed in an excel spreadsheet. Statistical analysis was performed by the SPSS program for Windows, version 17.0. Continuous variables are presented as mean±SD, and categorical variables are presented as absolute numbers and percentage. For

Table 1: Comparison of age, height, weight and sex in study groups

	Group F	Group N	P Value
Age in years	35.10 ± 12.17	33.53 ± 11.39	0.880
Height in cm	162 ± 4.63	163.23 ± 4.23	0.357
Weight in Kg	65.93 ± 4.97	64.43 ± 6.66	0.239
Sex			
F	4 (13.3%)	8 (26.7%)	0.186
M	26 (86.7%)	22 (73.3%)	

Table 2: Comparison of ASA physical status in study groups

ASA	Group F Frequency (%)	Group N Frequency (%)	P Value
I	19 (63.3%)	16 (53.3%)	0.659
II	11 (36.7%)	14 (46.7%)	
Total	30 (100%)	30 (100%)	

comparing the two main groups Paired t test was applied.

In this study p value < 0.05 have been considered as statically significant.

Data is presented as Mean ± SD

The two groups were comparable with regards to age, height, weight. There were no difference in the demographical profile i.e. age, sex, height, weight and ASA grade between two groups and the two groups were comparable and statistically not significant.

On intra group comparision after SAB, there was no statistically difference in the intraoperative PR, SBP, DBP, RR and SpO_2 between the groups.

Onset of sensory was earlier in Nalbuphine group with a p- value of less than 0.001 and the result was statistically significant.

The onset of motor block was comparable in both the groups.

Duration of sensory and motor block were comparable in both groups

Table 3: Comparison of preoperative vitals in study groups

	Group F Mean ± SD	Group N Mean ± SD	P Value
SBP	125.6 ± 12.76	124.07 ± 10.73	0.366
DBP	78.33 ± 8.17	75.63 ± 7.78	0.446
PR(bpm)	79.43 ± 9.94	80.83 ± 10.76	0.812
SPO2	100.00 ± 0.00	100.00 ± 0.00	–
RR(cpm)	14.23 ± 1.72	14.23 ± 1.72	0.539

Table 4: Onset of Sensory and Motor Blocks

	Group F	Group N	P-value
Time of onset of sensory block (T10)	4.67±0.816	2.05±0.887	<0.001
Time to highest sensory	4.6±0.91	4.55±1.276	0.18
Time to motor bromage 3	4.8±1.146	4.85±1.089	0.985

Table 5: Duration of Sensory and Motor blocks

	Group F	Group N	P value
Duration of motor block	148.33±7.108	148.6±7.308	0.854
Time of 2 dermatomal regression	145.07±5.788	144.85±5.204	0.52

Table 6: Duration of Analgesia

	Group F	Group N	P value
Duration of analgesia (VAS>3)	244.27±5.457	243.25±8.091	0.047

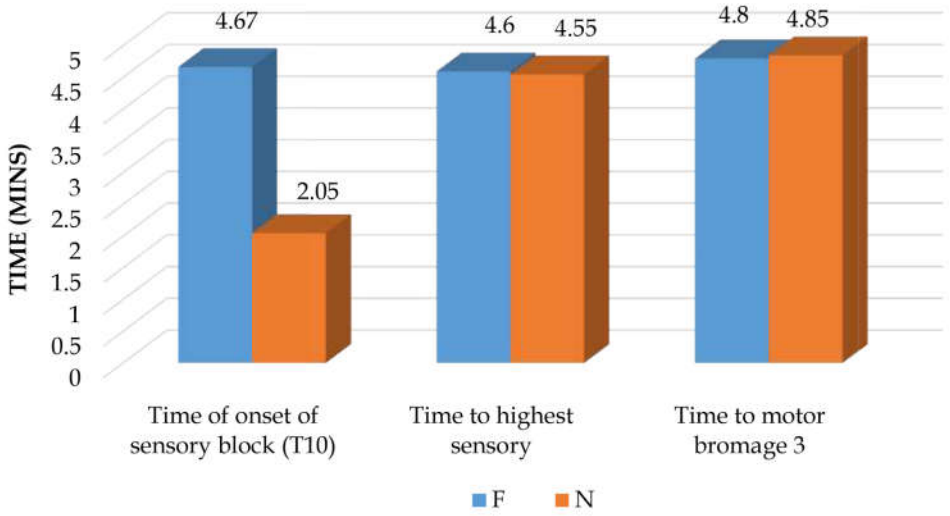

Fig. 1: Onset of Sensory and Motor Blocks

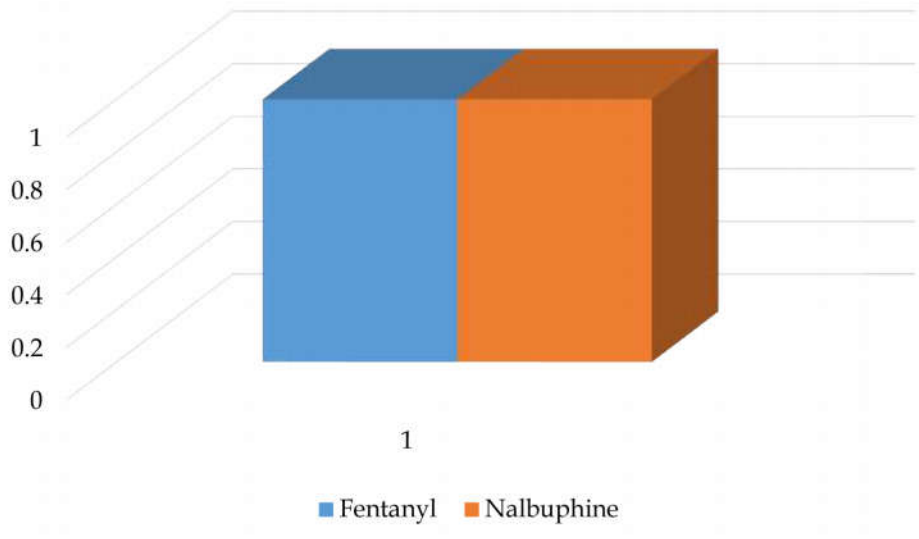

Fig. 2: Duration of Sensory and Motor blocks

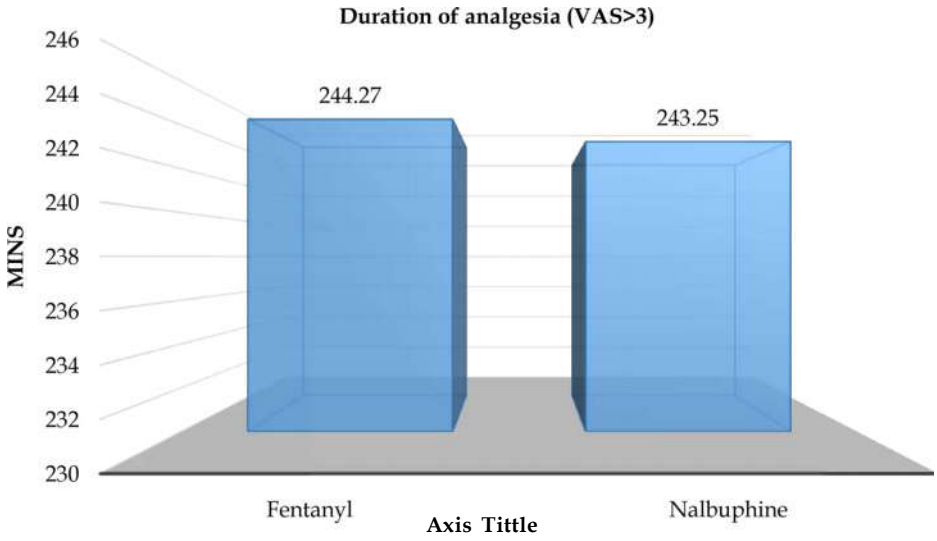

Fig. 3: Duration of Analgesia

The duration of analgesia was more for fentanyl but it was statistically not significant.

Discussion

Regional anaesthesia as an alternative to general anaesthesia or to supplement general anaesthesia has become a popular procedure in clinical anaesthesiology. The development of different local anaesthetics and various techniques in regional anaesthesia have been boosted by the growing interest in regional anaesthesia due to its effective pain relief without compromising the patient's consciousness and improved patient comfort. Furthermore, it has been influenced by the implementation of perioperative anaesthesia standards and the increasing awareness among healthcare professionals that postoperative analgesia plays an important part in the convalescence of patients

In this study we have used Bupivacaine along with nalbuphine or fentanyl for postoperative pain relief. Here we have compared analgesia and side effects of nalbuphine (400mcg in 0.5 ml) and fentanyl (25 mcg in 0.5 ml) with bupivacaine when administered by intrathecal route.

In our study, the onset of sensory block was delayed in Group F (4.67±0.816 mins) when compared to Group N (2.05±0.887 mins) by about 2.5 mins. It was both statistically and clinically significant.

The onset of complete motor block was comparable in fentanyl than Nalbuphine group.

The duration of sensory block and the duration of analgesia were comparable in nalbuphine and fentanyl group with no statistically significant difference.

Also in the present study, no statistically significant difference was found between both groups as regards the duration of motor block, hemodynamics and oxygen saturation. Neither bradycardia nor oxygen desaturation was recorded.

Hala Mostafa Gomaa et. al. [6], in their study compared intrathecal Nalbuphine 800mcg with fentanyl 25 mcg after cesarean section, concluded that- The onset of complete motor block was significantly more rapid in fentanyl group than in nalbuphine group. The duration of post-operative analgesia was more prolonged in nalbuphine group but the difference was insignificant. No significant difference was found between both groups as regards the duration of sensory block, motor block, duration of analgesia.

Culebras et. al. [7] compared intrathecal morphine (0.2 mg) added to hyperbaric bupivacaine with different doses of intrathecal nalbuphine (0.2 mg), (0.8 mg) and (1.6 mg) and their study concluded that intrathecal nalbuphine 0.8 mg provides good intra-operative and early post-operative analgesia without side effects (no PONV or pruritus).

Mukherjee et. al. [8] had studied 100 patients undergoing lower limb orthopedic surgery using subarachnoid block. They used different doses of nalbuphine intrathecally (200, 400 and 800) mcg added to 0.5% hyperbaric bupivacaine. They concluded that the duration of sensory block and the duration of effective analgesia were prolonged with the doses 400 mcg and 800 mcg but the side effects were higher with the dose 800 mcg.

Fournier et. al. [9] compared between intrathecal nalbuphine 400 mcg and intrathecal morphine 160 mcg in old patients undergoing total hip replacement using continuous spinal anesthesia. They concluded that intrathecal nalbuphine produces faster onset of pain relief but the duration of analgesia is shorter than intrathecal morphine.

Tiwari et. al. [10] had compared intrathecal nalbuphine 200 mcg and 400 mcg added to hyperbaric bupivacaine with bupivacaine alone. They concluded that the duration of sensory block and duration of analgesia was maximally prolonged with nalbuphine 400 mcg without complications.

Conclusion

Both fentanyl and nalbuphine in a dose of 25mcg and 400mcg were comparable in all aspects of intrathecal block except for onset of sensory block which was significantly faster in Nalbuphine group.

References

1. Barasch PG, Collen BF. Clinical anaesthesia, 6th edition, Lippincott, Williams and Wilkins; 2006. pp.700-706.
2. Brunton LL, Lazon JS, Parker LL, Goodman and Gilman's. The pharmacological basis of therapeutics. 11th edition, McGraw Hill Medical Publication; pp.571-582.
3. Saxena AK, Arava AK. Current concepts in neuraxial administration of opioids and non opioids: an overview and future perspectives. Indian J. Anaesth. 2004;48(1):13-24.
4. HindleA.Intrathecal opioids in the management of acute postoperative pain. Continuing Education in Anaesthesia. Critical Care & Pain J; 2008;8(3):81-85.
5. Kaur M, Katyal S, Kathuria S, Singh P. A comparative evaluation of intrathecal bupivacaine alone, sufentanil or butorphanol in combination with bupivacaine for endoscopic urological surgery. Saudi Journal of Anaesthesia. 2011;5(2):202-207.
6. Gomaa HM, Mohamed NN, Zoheir HA, Ali MS. A comparison between postoperative analgesia after intrathecal nalbuphine with bupivacaine and intrathecal fentanyl with bupivacaine after cesarean section. Egypt J Anaesth. 2014;03:8-14.
7. Culebras X, Giovanni G, Jiri Z, Christian K, and Rene AM. Advantages of Intrathecal Nalbuphine Compared with Intrathecal Morphine, After Cesarean Delivery: An Evaluation of Postoperative Analgesia and Adverse Effects. AnesthAnalg. 2000;91:601–5.
8. Mukherjee A, Pal A, Agrawal J, Mehrotra A, Dawar N. Intrathecal nalbuphine as an adjuvant to subarachnoid block: what is the most effective dose? Anesth Essays Research. 2011;5:171-5.
9. Fournier R, Van GE, Macksay M, Gamulin Z. Onset and offset of intrathecal morphine versus nalbuphine for postoperative pain relief after total hip replacement. ActaAnaesthesiol Scand. 2000;44:940-5.
10. Tiwari AK, Tomar GS, Agrawal J. Intrathecal bupivacaine in comparison with a combination of nalbuphine and bupivacaine for subarachnoid block: A randomized prospective double-blind clinical study. Am J Ther 2013;20:592-5.

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A Comparison of Ultrasound Guided Versus Ultrasound with Nerve Stimulation Technique for Obturator Nerve Block in Transurethral Resection of Bladder Tumour

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Abstract

Introduction: The aim of the study was to compare the effectiveness of two different techniques in blocking obturator nerve (ON) and adductor spasm during transurethral resection of bladder tumor (TURBT).

Methodology: We designed a prospective, randomized, double-blind study, in which fifty patients with American Society of Anesthesiologists Status II and III were scheduled to undergo TURBT for lateral and posterolateral bladder wall tumor were. Group I (ultrasound only group, n = 25) patients received 4 ml of bupivacaine 0.5% each at anterior, and posterior division of ON under real-time US visualization and Group II (ultrasound-nerve stimulation group, n = 25) received the same amount of bupivacaine 0.5% for each division using US-guidance with nerve stimulation-assisted technique. Block success and performance time and complications were measured along with patient and surgeon satisfaction into two groups. We did two sample independent t-test and Pearson's Chi-square/Fisher's exact test.

Results: A success rate of 88% was achieved in Group II as compared to 70% in Group I with increased block performance time in Group II (5min) versus (3 min) in Group I. A better patient and surgeon satisfaction were seen in Group II with combination of US and nerve stimulation technique. No complications were encountered.

Conclusion: We conclude that both techniques are safe and easy to perform; however, nerve stimulation along with US results in a higher success rate.

Keywords: Nerve Stimulation; Obturator Nerve Block; Obturator Reflex; Ultrasound.

Introduction

Peripheral nerve blocks are not only widely-used for surgical anesthesia but for both postoperative and nonsurgical analgesia as well. Nerve blocks are often used as an alternatives to avoid the adverse effects of other anesthetics or analgesics. The most common indication being their use to avoid complications of general anesthesia, particularly respiratory-related effects. In certain clinical situations nerve blocks have shown distinct benefits over general or neuraxialanesthesia [1]. With the advent of ultrasound imaging direct visualization of needle relative to target nerves, blood vessels, and related structures has been made possible and easily available. Ultrasound guided nerve blocks have shown to be more succesful [2], have decreased placement [3] and onset times [4] and lower requirement of anesthetic dose [5].

On the other hand, nerve stimulator guided technique utilizes a less expensive equipment and requires less extensive training than the ultrasound guided technique. However, there are concerns of a higher incidence of nerve trauma than ultrasound

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guidance, because it is a "blind" technique. Combining the two techniques may bring the best of the two techniques.

During transurethral resection of lateral bladder wall lesions the obturator nerve may be stimulated resulting in spasm of the adductor muscles of the hip, which may lead to complications. Therefore, obturator nerve block (ONB) is commonly employed while performing transurethral surgeries. In this study, we compared ultrasound with nerve stimulation technique and ultrasound only technique in giving ONB to patients undergoing transurethral resection of bladder tumor (TURBT).

Methodology

Study Design and Setting

We designed a prospective randomized, double-blind study in the Department of Anaesthesiology, Mahatma Gandhi Mission Institute of Health Sciences, Navi Mumbaifrom May 2015 till April 2016. The medical college and hospital is located in Maharashtra, about an hour drive from Mumbai, Maharashtra. The study was approved by the institutional ethics committee and was done according to the Bioethical guidelines as prescribed by the Indian Council of Medical Research, New Delhi.

Sample Population and Randomization

Using previously published data, we calculated the sample size of our study [6] to be 50, to show a significant difference of atleast 5% in the successful motor block rate, keeping probability of Type 1 error at 0.05 and power of the study at 80%. During the study period, we enrolled patients aged 18 to 80 years, of either gender, belonging to the American Society of Anesthesiologists (ASA) Status II and III category who were undergoing TURBT of the lateral and postero-lateral bladder wall tumor at Mahatma Gandhi Mission Institute of Health Sciences, Navi Mumbai from May 2015 till April 2016. The diagnosis of bladder wall tumor was made after extensive investigations which included ultrasonography. The decision to perform TURBT on these patients was made by the treating surgeon. The patients were explained the purpose of the study and informed written consent was taken from them. We excluded patients who had a diagnosis of inguinal lymphadenopathy, any coagulation disorder, infection of the injection site, known hypersensitivity to local anesthetics or any pre-exisiting ON injury. Two patient groups were formed, one receiving the block under ultrasound guidance (US) and the other one receiving nerve block under ultrasound guidance with nerve stimulation (US-NS). Using random number generator software, the patients were allocated either of the two groups in 1:1 allocation ratio. The person generating the random number was not involved in the coordination of the trial.

Study Procedure

After randomization, the principal investigator evaluated all patientsand explained the procedure to them. Without giving any sedation or premedication, all patients were anesthetised to T10 level using 25 gauge spinal block with 3 ml of 0.5% hyperbaric bupivacain at the L3-L4 or L4-L5 level. Later the patients were in supine position with leg externally roatated and abducted at 30°. Under sterile conditions, the inguinal region was prepared for ultrasound probe with a linear (vascular) transducer, with a frequency range of 7–12 MHz and the anterior and posterior divisions of the ON were visualized between the muscle layers of adductor longus, adductor brevis, and adductor magnus.

Ultrasound Only Group (Group I)

To reach the anterior division of ON located between adductor longus and brevis a 22-gauge, 10 cm long locoplexneedle was advanced under US-guidance, laterally to medially and 5 ml of bupivacaine 0.5% was injected. After withdrawing the needle slightly, we redirected it towards the posterior division of the nerve, which is between adductor brevis and magnus and another volume of 5 ml of bupivacaine was injected. We monitored the spread of the anesthetic solution under real-time visualization of ultrasound.

Ultrasound with Nerve Stimulation Group (Group II)

Patients in this group received the nerve block under ultrasound guidance assisted with nerve stimulation technique. The nerve stimulator that we used in our study was Microcontroller-based nerve stimulator (LCD-GEMI-Model: DSL-007). After directing theneedle tip (22-gauge, 10 cm) towards the anterior division of ON, nerve stimulator was turned on to deliver stimulation current at 1–2 mA (2 Hz) and muscle contraction was elicited as a result.

The stimulation current was then gradually reduced to 0.5 mA. The needle was redirected toward the posterior division of ON after the current was reduced to zero. Using the same procedure as before another 5 ml of 0.5% bupivacaine was injected.

Outcome Measures

Primary outcomes of the study were to measure and compare the rate of succesful motor blockade and block performance time achieved by the two methods. Secondary outcomes were to compare the satisfaction rates of the surgeon and the patients, the onset time for both the methods, number of needle passes required during the procedure and any complications observed. The surgeon, who was masked to the group allocation of the patients, entered the operating room to start TURBT 10 minutes after the nerve blockage procedure. Before starting the surgery, the surgeon assessed the motor blockade. Motor bloackade as evaluated by the surgeon was scored as 0 = Adductor spasm, 1 = Reduced adductor spasm and 2 = No adductor spasm, which was measured at 10, 15, 20 minutes after injection, and only a score of 2 was considered as a successful block. The block was noted as failure when the spasm persisted after 20 minutes.

We calculated the success rate of motor blockade as the number of patients who had a succesful block as defined above within 20 min after block placement. We also noted the block performance time intraoperatively, which was the time between the start of sonography and needle removal at the end of block. Block onset time was defined as the time from the end of anestheticinjection until a motor block score of 2 was reached. This time was not noted for failed blocks.

Additionally, we noted the number of needle redirections which were needed to complete the nerve block. Any redirections needed to complete the bloackage were recordedas additional needle passes. Postoperatively we asked the patient and surgeon about their satisfaction with the procedure. Finally, complications like vascular injury, hematoma formation, nerve injury, phlebitis and thrombosis, visceral or organ injury and any other were noted.

Statistical Analysis

The collected data was entered in microsoft excel sheet to prepare a masterchart. Normality of the data was checked using the Kolmogorov-Smirnov test. Between group comparisons were made for quantitative variables using two-sample t-test, and the categorical variables by using Pearson's Chi-square/Fisher's exact test. Quantitative data was represented using means and standard deviations. P value less than 0.05 was considered to be statistically significant. Statistical Package for Social Sciences (SPSS) version 23 was used for data analysis and presentation.

Results

In the present study, 50 patients were randomly assigned either to the ultrasound only group (Group I) or the ultrasound-nerve stimulation group (Group II). There was no significant difference in the demographic characteristics of the two study groups as shown in Table 1. Using t-test for equality of means, the two groups were comparable in terms of age weight, and ASA status (p more than 0.05). When camparison was made with respect to the primary outcomes of the study, success rate of motor blockade

Table 1: Baseline characteristics of the patients included in the study

Variable	Group I	Group II	p value
Number of patients	25	25	
Age (years)	48.23±11.42*	47.6±9.33	0.451
Weight (kilograms)	64.88±8.43	63.44±11.72	0.0924
Males/Females	18/7	19/6	0.972
American Society of Anesthesiologists Status	2.42±0.44	2.74±0.68	0.543

*mean±standard deviation

Table 2: Comparison of both intervention and control group

Outcome variables	Group I (n=25)	Group II (n=25)	p value
Primary outcomes			
Success rate of motor blockade	18 (70%)	22 (88%)	<0.01
Block performance time (minutes)	3	5	<0.05
Secondary outcomes			
Block onset time (minutes)	13.42±4.33*	5.58±1.89	<0.001
Number of needle passes	2.28±1.48	2.93±1.16	0.487
Surgeon satisfaction	18 (70%)	23 (90%)	<0.01
Patient satisfaction	17 (68%)	24 (96%)	<0.05

*mean±standard deviation

was found to be higher in US-NS group (p value less than 0.01, Table 2). Similarly, the block performance time was higher in the intervention group (p value less than 0.05). Block onset time was found to be 5.58±1.89 minutes in the US-NS group which was statistically significantly lower than in the US group (p vlaue less thab 0.001). Surgeon and patient satisfaction was found to be statistically higher in the intervention group as comapred to the control group. No difference in the number of needle passes required to achieve motor blaockage was noted in this study sample (Table 2).

Discussion

This prospective randomized study demonstrates that US-NS enabled a more succesful, higher block performance time, less onset times and higher satisfaction of patients and surgeons as compared to US only. Previosuly, adductor muscle contraction has been reported in 20 to 55% of patients during the resection of lateral and inferolateral bladder tumors [7]. Blocking the obturator nerve, which runs close to the lateral bladder wall, can prevent this effectively. Patel et. al. showed that ONB prevented the development of obturator reflex in 28 of the 30 patients, with the two patients presenting with the accessory the obturator nerve [8]. Different approaches to ONB have been suggested since Labat's description in 1928 [9]. Since then efforts were made to improve upon the technique of nerve blocks. With the advances in imaging and wider availability, ultrasound imaging is increasingly used to guide peripheral nerve blocks. This allows real-time visualization of nerves, nearby structures, and the needle-tip to optimize block success. Mechanical nerve stimulation and electric stimulation were further steps in improving outcomes in patients undergoing peripheral nerve blocks.

Baseline data in our patients was comparable. This has helped us to remove confounders like age, gender, weight or ASA status of our study patients. Statistically insignificant differences in the mean weights of both the study groups helps to remove the confounding effect of weight because variations in weight affect metabolism of anethetic agents.The success rate of OBN using nerve stimulation technique has been reported to be 84% to 96% [10]. Bolat et al and Min et al reported a success rate of 88.6% [11] and 95% [12] for ONB using the nerve stimulator. Many factors influence this, presence of an acccesory obturator nerve being one of them. It is present in 10-30% of the cases [13] and runs parallel to the main obturator nerve along the medial side of the psoas muscle. Conflicting data about the superiority of any particular ONB technique makes the decision for an anesthetistdifficult. Recent studies have reported higher success rates of 93% to 97% in ultrasound-guided ONB procedures [14]. Some studies have reported similar outcomes with the use of either NS or US-NS techniques for peripheral nerve block [15].

Randomization and sampling has enabled us to remove some of the bias and balance out the confounfers in our study. However, small sample size is one of the limitations of our study. Due to the inherent subjective nature of the involved surgical experience in the succesful surgical outcome, the results of our study might not be applicable to other geographical locations.

Conclusion

Our results demonstrate that ultrasound-nerve stimulation technique has better objective and subjective clinical outcomes. We need studies with larger sample and at multiple sites to support our results.

References

1. Lin E, Choi J, Hadzic A. Peripheral nerve blocks for outpatient surgery: evidence-based indications. CurrOpinAnaesthesiol 2013;26:467.
2. Walker KJ, McGrattan K, Aas-Eng K, Smith AF. Ultrasound guidance for peripheral nerve blockade. Cochrane Database Syst Rev 2009;CD006459.
3. Lewis SR, Price A, Walker KJ, et al. Ultrasound guidance for upper and lower limb blocks. Cochrane Database Syst Rev 2015;CD006459.
4. Gelfand HJ, Ouanes JP, Lesley MR, et al. Analgesic efficacy of ultrasound-guided regional anesthesia: a meta-analysis. J ClinAnesth 2011;23:90.
5. McNaught A, Shastri U, Carmichael N, et. al. Ultrasound reduces the minimum effective local anaesthetic volume compared with peripheral nerve stimulation for interscalene block. Br J Anaesth 2011; 106:124.
6. Choquet O, Capdevila X, Bennourine K, Feugeas JL, Bringuier-Branchereau S, Manelli JC. A New Inguinal Approach for the Obturator Nerve BlockAnatomical and Randomized Clinical Studies. The Journal of the American Society of Anesthesiologists. 2005;103(6): 1238-45.
7. Tatlisen A, Sofikerim M. Obturator nerve block and transure- thral surgery for bladder cancer. Minerva UrolNefrol 2007;59:137e41.

8. Patel D, Shah B, Patel BM. Contribution of obturator nerve block in the transurethral resection of bladder tumors. Indian J Anaesth 2004;48:47e9.
9. Labat G. Regional anesthesia; its technique and clinical application. WB Saunders: Philadelphia, PA; 1928.pp.286–287.
10. Jo YY, Choi E, Kil HK. Comparison of the success rate of inguinal approach with classical pubic approach for obturator nerve block in patients undergoing TURB. Korean journal of anesthesiology. 2011;61(2):143-7.
11. Bolat D, Aydogdu O, Tekgul ZT, Polat S, Yonguc T, Bozkurt IH, et. al. Impact of nerve stimulator-guided obturator nerve block on the short-term outcomes and complications of transurethral resection of bladder tumour: A prospective randomized controlled study. Can UrolAssoc J 2015;9:E780-4.
12. Min HG, Cheon MY, Choi KT. Use of nerve stimulator for the obturator nerve block. Korean J Anesthesiol 2006;50:650-4.
13. Woodburne RT. The accesory obturator nerve and the innervation of the pectineus muscle. Anat Rec. 1960;136:367-9.
14. Lee SH, Jeong CW, Lee HJ, Yoon MH, Kim WM. Ultrasound guided obturator nerve block: a single interfascial injection technique. Journal of anesthesia. 2011;25(6):923-6.
15. Duncan M, Shetti AN, Tripathy DK, Roshansingh D, Krishnaveni N. A comparative study of nerve stimulator versus ultrasound-guided supraclavicular brachial plexus block. Anesthesia, essays and researches. 2013;7(3):359.

Original Research Article

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To Evaluate Efficacies of Dexmedetomidine and Clonidine as an Adjuvants in Epidural Anaesthesia with Ropivacaine

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Abstract

Aim: To evaluate efficacies of dexmedetomidine and clonidine as adjuvants to ropivacaine in Epidural Anaesthesia in patients undergoing lower limb orthopaedic surgeries.

Materials and Methods: A randomized prospective study to compare the efficacies of dexmedetomidine and clonidine as adjuvants to ropivacaine in epidural anaesthesia (60 patients in each group.) Patients who were ASA physical status class I and II, Age 18-60 years , either sex, Height 150-170 cms and Elective lower limb orthopaedic surgeries are included in study.

Results: Present study was undertaken to compare the efficacy of epidural Clonidine or Dexmedetomidine with ropivacaine in patients undergoing elective lower limb orthopaedic surgeries. 120 ASA I and II patients of either sex,posted for elective lower limb orthopaedic surgeries were chosen for the study and the patients were divided into two groups of 60 each. Group RC received 17ml of 0.75% of ropivacaine with clonidine 30mcg. Group RD received 17ml of 0.75% of ropivacaine with dexmedetomidine 50mcg. The time of onset of sensory block was tested with bilateral pin prick method and motor block was assessed by onset of Bromage scale 3, and it was found that the onset of sensory block with Dexmedetomidine was earlier compared to Clonidine. During the procedure we observed bradycardia was more in Dexmedtomedine and hypotension was more in Clonidine Group. Bradycardia was treated successfully with vagolytic agents. Hypotension was successfully treated with vasopressors. Also few patients developed nausea and dry mouth, which were negligible. Intraoperatively sedation score was assessed using Ramsay Sedation Scale and there was higher incidence of sedation with Dexmedetomidine group. Regression of motor block to Bromage 1 was observed and the time to regression was significantly prolonged to 450.6±29.37 in the Dexmedetomidine group while it was 343.2±30.99 in the Clonidine group. Post operative analgesic requirement was low in Dexmedetomidine group compared to Clonidine group.

Conclusion: In conclusion, Dexmedetomidine (50mcg) is a better adjuvant when administered epidurally with ropivacaine 0.75% than clonidine (30mcg), as there is significantly longer duration of sensory and motor block, additional benefits of intraoperative sedation and prolonged post-operative analgesia.

Keywords: Dexmedetomidine; Clonidine; Epidural Anaesthesia; Ropivacaine.

Introduction

The task of medicine is to preserve,restore health and to relieve pain [1]. Relief of pain is the main challenge faced by anaesthesiologist and this is the reason why various techniques of pain relief have been developed over ages [2]. Epidural anaesthesia is the most commonly used technique for providing not only peri-operative anaesthesia but post-operative analgesia in lower abdominal and limb surgeries as it has the benefit of providing anaesthesia

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for prolonged duration with repeated doses. New amide local anaesthetic Ropivacaine has minimal cardio-vascular and central nervous system toxicity as well as lesser propensity of motor block during post-operative epidural analgesia [3,4,5]. Opioids like fentanyl have been used traditionally as an adjuvant for epidural administration in combination with lower dose of local anaesthetics to achieve the desired anaesthetic effect as it provides dose-sparing effect of local anaesthetic and superior analgesia [6]. Efforts to find a better adjuvant in regional anesthesia are underway long. Many techniques and drug regimens with partial or greater success have been tried from time to time to calm the patients and to eliminate the anxiety component during regional anaesthesia. The intense motor block,continuous supine position for a prolonged duration and the inability to move the body during regional anaesthesia brings a feeling of discomfort and phobia in many patients [7]. Alpha 2 adrenergic agonists have both analgesic and sedative property when used as adjunct in regional anaesthesia. Dexmedetomidine is a highly selective alpha2 adrenergic agonist with an affinity of eight times greater than clonidine. The stable haemodynamics and the decreased oxygen demand due to enhanced sympathoadrenal stability make them very useful pharmacologic agents [8]. Prolongation of lumbar epidural analgesia using a single-shot technique has been achieved by various adjuvants like epinephrine, opioids, ketamine and alpha 2 agonists. The rationale to combine these drugs is that the component drugs may produce analgesia by additive or even synergistic mechanisms and that the combination may allow reduced doses of each drug and correspondingly fewer dose-related side effects. With this background information after receiving instituitional ethics committee approval we planned a double-blind prospective randomized clinical study at our institute with an aim to compare the analgesic and sedative effects of both these drugs when used epidurally as adjuvants to ropivacaine in patients undergoing lower limb orthopaedic surgeries.

Materials and Methods

A randomized prospective study to compare the efficacies of dexmedetomidine and clonidine as adjuvants to ropivacaine in epidural anaesthesia (60 patients in each group).

Inclusion Criteria

Patients who were ASA physical status class I and II, Age 18-60 years, either sex, Height 150-170 cms and Elective lower limb orthopaedic surgeries.

Exclusion Criteria

Patients who were ASA grade 3 and above, Height <150cm and >170cm, Opioid dependant, History of drug allergy to clonidine, dexmedeto-midine, amide-local anaesthetic, Patients with skeletal abnormalities, Neurological involvement/disease, Psychiatric diseases and Contraindications of central neuraxial blockade. 60 patients were allocated in each group, posted for elective lower limb (orthopaedic) surgery.

Thorough pre Anaesthetic check up was done one day prior to the surgery and laboratory investigations were noted. The procedure of Epidural anaesthesia was explained to the patients in local language and patients were put NPO 6hours for solids and 3hours for liquids. Patients were premedicated with tab.ranitidine 150mg and tab.alprazolam 0.5mg the night prior surgery. Keeping the operating room ready with necessary drugs and equipment and securing intravenous access in the pre-anaesthesia holding area baseline vitals were noted.A balanced salt solution (ringer lactate) 500ml was given over a period of 20-30minutes after shifting the patients into the operating room. Patients were administered epidural block in either sitting position or lateral position in L3-4 or L4-5 space with 18G touhy needle and epidural catheter was secured 5cms into epidural space and test dose of 3ml of 2% lignocaine hydrochloride solution containing adrenaline 1:2,00,000 was injected. Group RC: Receives 17ml of 0.75% of ropivicaine with 30mcg clonidine. Total volume = 17.2ml+0.8ml NS = 18cc. Group RD: Receives 17ml of 0.75% of ropivicaine with 50mcg dexmedetomidine. Total volume = 18cc.The bilateral pin-prick method to evaluate and check the sensory level & modified bromage scale for motor block. Modified bromage scale, 0 – No block, 1 – Inability to raise extended legs, 2 – Inability to flex knee and 3– Inability to flex ankle & foot. Time of onset of sensory block level at T10, peak sensory block level, motor block level, intensity of motor block and duration of analgesia was recorded. Ramsey sedation scale for sedation score was used. Patient is anxious and agitated or restless or both. Patient is cooperative, oriented and tranquil. Patient responds to commands only. Patient has a brisk response to a light glabellar tap or loud auditory stimulus. Patient asleep, sluggish response to light glabellar tap or loud auditory stimulus. Patient doesn't respond to painful stimulus. Heart rate(HR), blood pressure (NIBP), O_2 saturation (SpO_2) were monitored continuously and recordings were made every for every 5 minutes during the first 30 minutes, every 10 minutes till the end of surgery and every 30 minutes post operatively. Comparision of post operative block characteristics, Mean time to 2 segment regression, Mean time for regression to

bromage 0, Time to first epidural top-up and Any side effects like hypotension (defined as systolic arterial pressure falling more than 20% mmHg) was noted and treated with inj. Mephentermine 6mg in bolus doses and bradycardia (heart rate <50 bpm) was noted and treated with inj. Atropine 0.6mg. A Comparative two group randomized clinical study with 120 patients with 60 patients in Group RC (Clonidine) and 60 patients in Group RD (Dexmedetomidine) is undertaken to study the changes in haemodynamics and side effect. Statistical analysis was done by applying Chi-square test, Anova test and students t test to analyse the data, p value was determined. P > 0.05 is not significant. P < 0.05 is significant. P < 0.001 is highly significant.

Results

One Hundred Twenty patients were allocated in two groups; 60 patients were administered dexmedetomidine and remaining 60 patients were administered clonidine as adjuvant.

Table 1 shows There is a slight difference in the age in between both the groups. In group dexmedetomidine the mean age was 42.00±7.46 and in clonidine group it was 37.80±6.19 and it is statistically significant (P value < 0.05). There is no statistically significant difference in the male and female population in both the groups (P value >0.05). The average height is also similar in both the study groups and does not hold any statistical significance (P value>0.05). In dexmedetomidine group 28 patients out of 60 attained the highest dermatomal level of sensory analgesia (T4). In clonidine group 15 out of 60 patients attained the same level. In dexmedetomidine group 29 individuals attained highest dematomal level of T6 whereas, 30 patients in clonidine group attained the same level. In clonidine group 2 individuals out of 60 attained a maximum sensory level of T10. There is a statistically significant difference between dexmedetomidine and clonidine regarding highest dermatomal level of sensory analgesia. The P value being 0.001. The average time taken to attain sensory anaesthesia in dexmedetomidine group is 10minutes whereas, in clonidine it is 18minutes. The average time taken to attain a motor blockade to modified bromage scale 3 in dexmedetomidine group is 12minutes but in clonidine group it is 17minutes. There is a statistically significant difference between dexmedetomidine and clonidine with regards to the time taken for establishment of highest sensory and motor blockade to bromage 3 respectively. The P value being <0.001. The mean level of sedation in dexmedetomidine group is 3 and that in clonidine group is 2 which is statistically significant. The P value being <0.001.

Table 2 shows that the time taken for 2-segment regression in dexmedetomidine is 229 +minutes as and in clonidine group it is 160 minutes on an

Table 1: Shows demographic parameters in two study groups (n=120), highest dermatomal level of sensory analgesia in two study groups treatment groups (n=120), Onset of anaesthesia in two groups (n=120) and sedation level in both the study groups

Parameter	Dexmed (N=60)	Clonidine (N=60)	P value
Age (Mean ± SD)	42.00±7.46	37.80±6.19	.002
Gender			
Male Frequency (%)	44(73.3)	45(75.0)	1.00
Female Frequency (%)	16(26.7)	15(25.0)	
Height (Mean ± SD)	160.65±5.43	159.87±6.08	.386
Highest dermatomal level of sensory analgesia	**Dexmed (N=60)**	**Clonidine (N=60)**	**P value**
T4	29 (48.3%)	15 (25.0)	0.001
T6	29 (48.3%)	30 (50.0)	
T8	2 (3.3%)	13 (21.7%)	
T10	0 (0.0%)	2 (3.3%)	

Parameter	Groups of treatment	Mean	Mean difference	P value	95% CL Lower	95% CL Upper
Time to achieve highest sensory level	Clonidine	18.10	7.667	<0.001	6.372	8.96
	Dexmed	10.43				
Time for establishment of motor blockade to modified bromage scale 3	Clonidine	17.77	6.050	<0.001	4.681	7.41
	Dexmed	12.80				
Sedation	Dexmed	3.30	0.467	<0.001	0.207	0.726
	Clonidine	2.83				

average and is statistically significant with a P value of 0.001. The average time for rescue top-up is 156 minutes in dexmedetomidine group and in clonidine group it is 123 minutes.The mean difference between the two groups is 33 minutes and does not hold any statistical significance as the P value is 0.162. The average time taken for motor regression to modified bromage scale 0 is 379 minutes in dexmedetomidine group but the in clonidine group it was 283 minutes and it holds high statistical significance as the P value is 0.0001.

Table 3 shows the baseline mean arterial blood pressure in dexmedetomidine group is 96mm Hg and that in clonidine group is 99mmHg with a P value of 0.154 which is statistically insignificant. The mean difference of mean arterial blood pressure in the baseline and pre-op 2 is -2 respectively and does not hold any statistical significance. The pre operative systolic blood pressure in both the study groups was satistically insignificant as the P value is >0.05.

The pre operative diastolic blood pressure in both study groups is insignificant as the P value is >0.05. The pre operative mean arterial blood pressure in both study groups is also insignificant as the P value is >0.05. The intra operative mean arterial pressure in dexmedetomidine group is 97mm Hg and whereas in clonidine is 88mm Hg with a P value of 0.287 which is statistically insignificant. The intra operative systolic blood pressure in both the study groups in the first 30mins after administering the drugs does not hold any statistical significance as the P values at each time interval are >0.05. The intra operative diastolic blood pressure in both the study groups in the first 30mins after administering the drugs does not hold any statistical significance as the P values at each time interval are >0.05.

The intra operative mean arterial blood pressure in both the study groups in the first 30mins after administering the drugs does not hold any statistical significance as the P values at each time interval are >0.05. The intra operative mean arterial blood pressure in both the study groups in the first 30mins after administering the drugs does not hold any statistical significance as the P values at each time interval are >0.05. Initially after the administration of both the study drugs the fall in diastolic blood pressure was more in clonidine group when compared to dexmedetomidine,but the fluctuations in both the groups were minimal. The fall and fluctuations in mean arterial blood pressure was more with clonidine when compared to dexmedetomidine and the MAP was constantly lower in clonidine group.

Table 4 shows the average post operative mean arterial pressure in dexmedetomidine is 87mm Hg and in clonidine is 83mm Hg with a P value of 0.02 which is statistically significant. The P value of post operative systolic blood pressure, diastolic blood pressure and mean arterial blood pressure is statistically significant as it is less than <0.05.

The post operative systolic blood pressure, diastolic blood pressure and mean arterial blood pressure is constantly lower in clonidine group when compared to dexmedetomidine group. The baseline heart rate in dexmedetomidine group is 82/min and

Table 2: Shows two segment regression time, time for rescue top up, time for motor regression, in both the groups

Parameter	Groups of treatment	Mean	Mean difference	P value	95% CL Lower	Upper
2 segment regression Time	Dexmed Clonidine	229.58 160.80	68.783	0.001	55.963	1.604
Time for rescue top up	Dexmed Clonidine	156.67 123.67	33.000	0.162	16.922	82.922
Time for motor regression	Dexmed Clonidine	379.55 283.17	96.383	0.0001	79.102	113.665

Table 3: Shows pre-operative BP, intra-operative BP

Parameter	Groups of treatment	SBP	DBP	MAP	Mean Diff	95% CL Lower	Upper
Pre-op 1 (Baseline)	Dexmed Clonidine	132.85 136.38	81.73 81.72	96.72 99.48	-2.767	6.588	1.054
Pre-op 2 (after fluid bolus)	Dexmed Clonidine	136.10 123.67	83.83 83.53	98.98 101.18	-2.200	5.956	1.556
Intra-op	Dexmed Clonidine	119.11 118.35	76.25 73.87	97.71 88.18	9.52870	8.130	27.19

Table 4: Shows post-operative BP in two study groups, pre-operative heart rate

Parameter	Groups of treatment	SBP	DBP	MAP	Mean Diff	95% CL Lower	95% CL Upper
Post-op (Arterial BP)	Dexmed	116.44	75.50	7.94	4.26250	1.66	6.86
	Clonidine	111.39	71.01	3.68			
Pre-op heart rate (Baseline)	Dexmed		Mean-82.78		-0.450	-4.564	3.664
	Clonidine		Mean-83.23				
Pre-op 2(after fluid bolus)	Dexmed		Mean-85.93		-0.833	-4.572	2.905
	Clonidine		Mean-86.77				

Table 5: Shows descriptive analysis of various anaesthesia related parameters in two study groups (n=120)

Parameter	Dexmed (N=60)	Clonidine (N=60)
Time taken to achieve highest sensory level (Mean ± SD)	10.43±2.35	18.10±4.49
Time taken for establishment of motor blockade to modified broma (Mean ± SD	12.80±2.92	18.85±4.49
Level of Sedation (Mean ± SD)	3.30±0.696	2.83±0.74
2 segment regression time (Mean ± SD)	229.58±42.85	160.80±26.06
Time for rescue top up (Mean ± SD)	156.67±20.82	123.67±32.78
Time for motor regression to modified bromage scale (Mean ± SD)	379.55±56.16	283.17±37.62

in clonidine group is 83/min and holds no statistical significance as the P value is >0.05. The heart rate after administration of a crystalloid bolus in dexmedetomidine is 85/min and in clonidine group it was 86/min. There is no statistical significance as the P value >0.05. The intra operative heart rate in dexmedetomidine is 76/min and in clonidine group is 74/min and does not hold any statistical significance as the P value >0.05.

The post operative heart rate in dexmedetomidine is 73/min and in clonidine group is 74/min and does not hold any statistical significance as the P value >0.05. After administering the study drugs, initially there is a fall in the blood pressure in both the groups, but in dexmedetomidine group the fall is realatively less than that in clonidine group at al time intervals. The post operative heart rate is low in both the study groups, but in dexmedetomidine the fluctutaions are relatively low when compared to clonidine.

Discussion

The present study was performed to compare clonidine and dexmedetomidine in their efficacy as adjuvants in epidural anaesthesia. Various studies have stated that the dose of clonidine is 1.5 – 2 times higher than that of dexmedetomidine when used in epidural route.

In our study design Group RC received 17ml of 0.75% of ropivacaine with clonidine 30mcg and Group RD received 17ml of 0.75% of ropivacaine with dexmedetomidine 50mcg, injected epidurally in patients undergoing elective lower limb orthopaedic surgeries.

The following parameters were observed namely highest dermatomal level of sensory analgesia, time to achieve highest sensory level, time taken for establishment of motor blockade to modified bromage scale 3, time to two-segment regression, time of rescue top-up and changes in haemodynamic parameters. In our study the demographic profile of patients in both groups were comparable with regards to age, height and gender.

Bajwa SJ, et. al. [9], compared the efficacy and clinical profile of two α2 agonists, dexmedetomidine and clonidine in a 50 adult female patients who underwent vaginal hysterectomies under epidural anaesthesia. In their studies the demographic profile, was comparable and statistically non significant in both groups.

In the study done by MS Saravana Babu et. al. [10], the demographic profile of patients in both groups was comparable with regards to age, weight and height and was statistically insignificant.

In our study, on comparing the highest level of sensory anaesthesia in between both the groups, patients who received dexmedetomidine as an adjuvant attained a sensory level of T4 whereas those in clonidine attained a level of T6. The time taken to achieve T4 level was 10 mins in dexmedetomidine and 18 mins in clonidine group. Motor blockade to modified bromage scale 3 was achieved earlier in dexmedetomidine group (12 mins) when compared to clonidine group (17 mins).

Bajwa SJ [9] et. al. 24 found that addition of dexmedetomidine to ropivacaine as adjuvant resulted in early onset of analgesia as well as prolonged analgesia. Dexmedetomidine not only provided higher

dermatomal spread but also helped in achieving the maximum sensory anaesthetic level in shorter period (10.43±2.35) compared to clonidine (18.10±4.49). Modified bromage scale 3 was achieved earlier (12.80±2.92) in dexmedetomidine group when compared to clonidine group (18.85±4.49). All these initial block characteristics turned out to be statistically significant values on comparison ($p< 0.001$).

MS Saravana Babu et. al. [10] found that addition of dexmedetomidine to ropivacaine as an adjuvant resulted in an earlier onset (7.33±1.76 min) of analgesia as compared to addition of clonidine (8.40±1.61). Dexmedetomidine not only provided early onset but also helped in achieving the peak analgesic level (VAS – 0) in a shorter period (11.66±2.05 min) compared with clonidine (13.20±2.90 min). The sedation score was more and better in dexmedetomidine group than in clonidine group in our study ($P <0.001$).

Anand et al concluded that sedation was more in patients who received dexmedetomidine as adjuvant in caudal block ($P <0.001$).

Bajwa SJ et. al. [9] reported that sedation score was better in dexmedetomidine group when compared with clonidine group which was statistically significant ($P < 0.005$). The average time for 2-segment regression was more in dexmedeto-midine group (229 mins) when compared to clonidine group (160 mins) and the time for motor regression to modified bromage scale 0 was more in dexmedetomidine group (379 mins) whereas in clonidine group, it was less (283mins) in our study.

Vijay et al reported that in dexmedetomidine group the duration of post operative analgesia was upto 15hours, which resulted in a better quality of sleep and a prolonged duration of arousable sedation.

Bajwa SJ, et. al. [9] found that there was decreasing trend in heart rate as well as mean arterial blood pressure in both groups and decrease was statistically significant in clonidine group ($p< 0.005$) when compared with dexmedetomidine group.

Swami SS, Keniya VM, Ladi SD, Rao R [11], compared efficacy of dexmedetomidine and clonidine as adjuvant to local anaesthetics in supraclavicular brachial plexus block in their studies they also found that there was decreasing trend in heart rate as well as MAP in dexmedetomidine group as compared to clonidine group.

Bajwa SJ, Bajwa SK, Kaur J, Singh G, Arora V, Gupta S, et. al. [9] observed that dexmedetomidine provided smooth and prolonged post operative analgesia compared to clonidine.

In our study there was prolonged time to two segmental dermatomal regression (229.58±42.85) in dexmedetomidine group as compared to clonidine group (160.80±26.06) as well as return of motor power to bromage 0 (397.55±56.16) in dexmedetomidine group as compared to clonidine group (283.17±37.62), therefore the time to rescue analgesia was comparatively shorter in clonidine group (123.67±32.78) as compared to dexmedeto-midine group (156.67±20.82).

In our study the side effect profile was also comparable with incidence of nausea in clonidine group (10%) compared to dexemedetomedine group (5%) and dry mouth in dexemedetomedine group (20%) compare to clonidine group (10%) which was non statistically significant.

Shobhana Gupta, Virendra Pratap (2014) conducted a study among 60 paediatric patients of ASA status I and II between the age of 1 and 6 years undergoing lower abdominal surgeries. The caudal block was administered with inj. ropivacaine 0.2% with clonidine 2 mcg/kg (group A) and inj. ropivacaine 0.2% with dexmedetomidine 2mcg/kg (group B) after induction with general anesthesia. Hemodynamic parameters were observed before, during, and after the surgical procedure. Postoperative analgesic duration, total dose of rescue analgesia, pain scores, and any side effects were looked for and recorded.

They concluded that addition of dexmedetomidine or clonidine to caudal ropivacaine significantly promoted analgesia in children undergoing lower abdominal surgeries with significant advantage of dexmedetomidine over clonidine and without an increase in incidence of side-effects [12].

Nasr DA et. al., (2013) studied the efficacy of caudal dexmedetomidine on stress response and post-operative pain in paediatric cardiac surgeries. They concluded that caudal dexmedetomidine attenuated stress response to surgical trauma and provided better post-operative analgesia [13].

Xiang Q et. al., (2013) studied effect of caudal dexmedetomidine combined with bupivacaine in children undergoing inguinal hernia repair. They found that addition of dexmedetomidine to caudal bupivacaine could reduce the response to hernia sac traction and prolong the duration of post-operative analgesia in children undergoing inguinal hernia [14].

Conclusion

In conclusion, Dexmedetomidine (50mcg) is a better adjuvant when administered epidurally with ropivacaine 0.75% than clonidine (30mcg), as there

is significantly longer duration of sensory and motor block, additional benefits of intraoperative sedation and prolonged post-operative analgesia.

References

1. Howard l Fields, Joseph B Martin. Pain-pathophysiology and management in Harrison's principles of internal medicine, 15th edition, McGrawhill, 2001.
2. Parameshwara G. Spinal , epidural compared to spinal epidural analgesia, the history of central neuraxial block.Indian j Anaesth 2001;45(6):406-412.
3. McClellan KJ, Faulds D. Ropivacaine: An update of its use in regional anesthesia. Drugs 2000;60:1065-93.
4. McNamee DA, Parks L, McClelland AM, Scotts, Milligan KR, Ahlen K, et. al. Intrathecal ropivacaine for total hip arthroplasty: Double-blind comparative study with isobaric 7.5mg/ml and 10mg/ml solutions.Br J Anaesth 2001;87:743-7.
5. Benzon HT, Wong HY, Belavic AM Jr, Goodman I, Mitchell D, Lefheit T, et. al. A randomized double blind comparison of epidural fentanyl infusion versus patient controlled analgesia with morphine for post-thoracotomy pain. Anaeth Analg 1993;76:316-22.
6. Cousins MJ. Neural blockade in clinical anaesthesia and pain medicine. 4th ed. Philadelphia: Lippincott Williams and Wilkins; 2009.
7. Kamibayashi T, Maze M. Clinical uses of alpha-2 adrenergic agonists.Anaesthesiology 2000;93:1345-9.
8. Hall JE, Uhrich TD, Barney JA, Arain SR, Ebert TJ. Sedative, amnestic and analgesic properties of small-dose dexmedetomidine infusions Anesth Analg. 2000;90:699–705.
9. Bajwa SJ, Bajwa SK, Kaur J. Comparison of epidural ropivacaine and ropivacaine clonidine combination for elective caesarean sections. Saudi J Anaesth. 2010; May;4(2):47-54.
10. Sarvana Babu MS, Verma AK, Agarwal A, Tyagi CM, Upadhaya M, Tripathi S.A. Comparative study in the post-operative spine surgeries: Epidural ropivacaine with dexmedetomidine and ropivacaine with clonidine for post –operative analgesia. Indian J Anaesth 2013;57:371-6.
11. Swami SS, Keniya VM, Ladi SD, Rao R. Comparison of dexmedetomidine and clonidine (α2 agonist drugs) as an adjuvant to local anaesthia in supraclavicular brachial plexus block: A randomised double blind prospective study. Indian J Anaesth 2012;56:243-9.
12. Shobhana Gupta, Pratap V. Addition of Clonidine or Dexmedetomidine to Ropivacaine prolongs caudal analgesia in children. . Indian J Pain 2014;28:36-41.
13. Nasr DA, Abdelhamid HM. The efficacy of caudal dexmedetomidine on stress response and postoperative pain in pediatric cardiac surgery. Ann Card Anaesth. 2013;16(2):109-14.
14. Xiang Q, Huang DY, Zhao YL, Wang GH, Liu YX, Zhong L, Luo T. Caudal dexmedetomidine combined with bupivacaine inhibit the response to hernia sac traction in children undergoing inguinal hernia repair. Br J Anaesth 2013;110(3):420-4.

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An Observational Study to Compare Dexmedetomidine and Clonidine as Adjuvant to Local Anaesthetic Ropivacaine (0.5%) in Supraclavicular Brachial Plexus Block for Upper Limb Surgery

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Abstract

Context: Various adjuvants have been used with Ropivacaine in supraclavicular blocks to enhance sensory and motor block along with prolongation of postoperative analgesia.

Aim: To compare the effect of dexmedetomidine and clonidine as adjuvant to 0.5% ropivacaine in supraclavicular brachial plexus block with respect to onset and duration of sensory and motor block and duration of analgesia.

Methods and Material: After ethical committee's approval, a prospective randomised study of 60 patients aged18-60 years were randomly divided into two groups (Group C and Group D) of 30 each. Group C received 50mcg clonidine with ropivacaine (29ml), Group D received 50mcg dexmedetomidine with ropivacaine (29ml), via supraclavicular approach. Onset and duration of sensory and motor block and duration of analgesia in both groups were evaluated. Intraoperative hemodynamics and adverse effects were observed.

Statistical Analysis: Numerical-variables were presented as mean & standard-deviation while categorical-variables were presented as frequency and percent. For analysis, unpaired student t-test and chi-square test were used.

Results: Early onset and prolonged duration of sensory and motor block and prolonged duration of analgesia was seen in group D, as compared to group C.

Conclusion: Dexmedetomidine produces rapid onset and prolonged duration of sensory and motor block and also prolonged duration of analgesia with good hemodynamic stability with no side effects as compared to clonidine.

Keywords: Dexmedetomidine; Clonidine; Ropivacaine; Brachial Plexus Block.

Introduction

Upper limb surgeries are mostly performed under peripheral nerve blocks such as the brachial plexus block which provide very good anaesthesia and analgesia intraoperatively along with reduced incidences of complications like delayed recovery from anaesthesia, unwanted effect of anaesthetic drugs used during general anaesthesia, hypotension, bradycardia stress of laryngoscopy and tracheal intubations and also provide very good postoperative analgesia. The brachial plexus block, via supraclavicular approach, provide safe, effective, low-cost complete anaesthesia/analgesia of the upper limb. It is done at the level of distal trunks where it is in its tightest formation which allows rapid analgesia/anaesthesia of the upper limb. Numerous methods were used by Schoenmakers et. al. (2012) and Scott DB et al (1989) to extend the duration of analgesia like using higher volume of local anaesthetics [8] but that increased the risk of LA systemic toxicity [9]. Continuous catheter-based nerve blocks, as studied by Ilefelid BM et al(2011) and

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Salinas FV et al(2006), provide very good postoperative analgesia [6] but it's time consuming and is costly and needs skills [7]. There have always been a search for an ideal adjuvant. Many adjuvants like tramadol, fentanyl, sodabicar-bonate, dexamethasone & various alpha 2 agonists like clonidine and dexmedetomidine have been used in 2012 with varying degrees of success [13].

This study is designed to compare the effect of dexmedetomidine and clonidine with ropivacaine. We have used 0.5% ropivacaine for supraclavicular brachial plexus block instead of bupivacaine owing to its more cardiostable and less lipophilic properties.

Methods

Study Type

Observational study

Duration of Study: One year and 6 months

Sample Size: 60 patients selected using randomised sampling allocated into two equal groups using chit-method.

Setting: Dhiraj hospital, piparia.

Patients belonging to ASA I and II of age group 18-60 years, normotensive posted for upper limb surgeries and those giving written and informed consent were included in the study whereas patients not giving consent, hypertensive, heart rate less than 50 beats per minute, systolic blood pressure less than 100mmHg, patients with heart block, hyperthyroid patients and patients on adrenoceptor agonist/ antagonist therapy were excluded from the study.

After approval of institutional ethical committee, 60 consenting patients fulfilling the inclusion criteria were considered for the study. A pre-anesthetic checkup was done for all patients, which included a detailed history, general physical and systemic examination.

Basic investigations in the form of complete haemogram, bleeding profile, random blood sugar, blood urea, serum creatinine and chest x ray were carried out.

Patients were kept nil per oral for 6 hours. On arrival of the patient in the operating room, an 18-gauge intravenous line was secured in the unaffected limb and Ringer's lactate was started. The patients were connected to multichannel monitor which records Heart rate (HR), non-invasive measurements of systolic and diastolic blood pressure and mean arterial pressure (SBP, DBP, MAP), continuous electrocardiography (ECG) monitoring and oxygen saturation. The total volume of the solution used was same in both the groups by adding saline when ever needed. The study drug was prepared by a senior anaesthesiologist who was not involved in the study. Under aseptic precautions, perivascular supraclavicular brachial plexus block was performed using paraesthesia technique. A negative aspiration for blood was performed before each incremental injection of 5ml to a total volume of 30ml of drug solution was given. A brief massage for one minute was performed to facilitate an even drug distribution.

Onset of sensory block was assessed by the pin prick response on the areas of all four nerves of the upper limb.

Assessment of motor block was carried out using the Bromage three point score [0= normal motor function with full flexion and extension of elbow, wrist and fingers, 1= decrease motor strength with ability to move fingers and/or wrist only, 2= complete motor blockade with inability to move fingers] by the same observer at each minute till complete motor blockade after drug injection. Onset Time of Motor Block (OTMB) was taken as the time interval in minutes from time-0 till motor block started appearing i.e BS score $\geq$ 2. Time for Complete Motor Block (TCMB) was taken as the duration of time in minutes from time-0 till complete motor block was achieved i.e. BS score=3. Thereafter effect of block was tested every 30 minutes. Total Duration of Motor Block (TDMB) was taken as the duration of time in minutes from the TCMB till the time when BS score < 3 in the postoperative period. Adequacy of block was evaluated by Allis clamp test before handing over the patient to surgeon. The test was done by asking the patient whether they felt any discomfort when pressure was applied with the Allis clamp at the area of the surgical field. The readings were recorded as follows:

a. Complete (Total comfort to patient)

b. Inadequate (Discomfort: Requiring supplementation)

The block was considered to be incomplete when any of the segments supplied by the median, ulnar, radial and musculocutaneous nerve did not have analgesia after 30 minutes of drug injection. Block was considered as a failure if complete sensory and motor block was not achieved even after 45 minutes. Failed blocks were converted to GA and recorded.

Sedation of patient was assessed by the Ramsay Sedation Score. Level of sedation was assessed at an interval of every 20 min from Time-0 till the end of surgery using the 5 point sedation scale. Blood loss assessment was done and fluid administered as per the loss was done. Duration of surgery was noted.

Ramsay Sedation Score

Score Response

1 Anxious or restless or both
2 Cooperative, orientated and tranquil
3 Responding to commands
4 Brisk response to stimulus
5 Sluggish response to stimulus
6 No response to stimulus

Postoperative Management

With stable haemodynamics, all the patients were shifted to the recovery room and were constantly monitored for pain as well as any associated complaints.

Postoperatively, sensory block, motor block and post-operative pain (by Visual Analogue Scale) were assessed. VAS was recorded at an interval of every 1 hour till the score ≥ 4. HR, SBP, DBP, MAP and RR were recorded at an interval of every 30 minutes.

Results

The demographic profile in terms of age, sex, weight, height and ASA physical status were comparable among the two groups of patients (Table 1). Duration of surgery was also comparable in two groups (Table 1). Group D produced statistically significant earlier onset with prolonged duration of sensory blockade as compared to group C ($p<0.0001$) (Table 2). Group D produced statistically significantly earlier onset and prolonged duration of motor blockade as compared to group C ($p<0.0001$) (Table 3). Group D produced significantly prolonged duration of analgesia as compared to group C ($p<0.0001$) (Table 4).

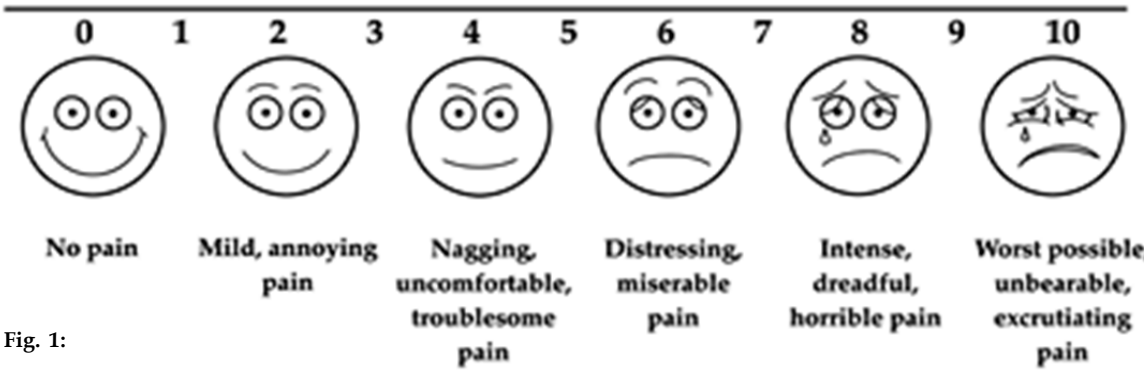

Fig. 1:

Table 1: Patient Characteristics

Patient Characteristics	Group C (N = 30) (Mean ± SD)	Group D (N = 30) (Mean ± SD)	P value
Age (Years)	38.56±7.77	40.1±14.14	0.6031
Gender (M/F)	18/12	17/13	N.A.
Weight (Kg)	60.4±7.77	61.56±16.26	0.7257
ASA Physical Status (I/II)	14/16	17/13	N.A.
Duration of Surgery (min)	87±21.21	97±7.07	0.0173

Abbreviations: [ASA= American society of Anaesthesiologists; M/F=Male/Female; Kg=kilogram; min=minutes; N=number of patients; SD= standard deviation; N.A.= not applicable]

Table 2: Sensory Characteristics of Brachial Plexus Blockade

Sensory Characteristics (Minutes)	Group C (N = 30) (Mean ±SD)	Group D (N = 30) (Mean ±SD)	P value
Onset	14.9±0.7	8.1±1.4	<0.0001
Duration	435.63±3.53	729.53±17.67	<0.0001

Abbreviations: [N=number of patients; SD= standard deviation]

Table 3: Motor Characteristics of Brachial Plexus Blockade

Motor Characteristics (Minutes)	Group C (N = 30) (Mean ± SD)	Group D (N = 30) (Mean ± SD)	P value
Onset	24.16±0.70	11.63±0.70	<0.0001
Duration	473.46±14.84	692.53±28.99	<0.0001

Abbreviations: [N=number of patients; SD= standard deviation]

Table 4: Duration of Effective Analgesia

Variable	Group C (N = 30) (Mean ±SD)	Group D (N = 30) (Mean ±SD)	P value
Effective Analgesia (minutes)	475.06±9.89	811.66±21.21	<0.0001

Abbreviations: [N=number of patients; SD= standard deviation]

Table 5: Comparison of VAS In Both Groups

VAS>3	Group C (N=30) Mean ± SD	Group D (N=30) Mean ± SD	P value
Time (in min)	505±0.0	847±42.42	<0.0001

Abbreviations: [N=number of patients; SD= standard deviation; min=minutes]

Group D produced statistically significant reduction in the pulse rate intraoperatively at 15, 45, 90 and 120 minutes and postoperatively at 8 hours as compared to group C ($p<0.0001$). The changes in systolic blood pressure during both the intraoperative and postoperative period in both the groups was comparable with no statistically significant changes ($p>0.05$).

The changes in diastolic blood pressure during the intraoperative period in both the groups was comparable with no statistically significant changes ($p>0.05$). The changes in diastolic blood pressure during the postoperative period in both the groups was comparable with only statistically significant change occurring at 1, 10 & 12 hours ($p<0.0001$).

The changes in respiratory rate during the intraoperative period in both the groups was comparable with no statistically significant changes ($p>0.05$). The changes in respiratory rate during the postoperative period in both the groups was comparable with only statistically significant change occurring at 1& 6 hours ($p<0.0001$). There was a statistically significant difference in VAS score on comparing both the groups (Table 5). No complications were observed in any of the two groups throughout our study period.

Discussion

Brachial plexus block is one of the most commonly performed peripheral nerve blocks in routine practice. It can be used as the sole anaesthetic technique or in combination with general anaesthesia for intraoperative and postoperative anaesthesia & analgesia. Brachial plexus roots, present between the scalenus anterior and medius muscle, combines to form the trunks which carry the entire sensory, motor and sympathetic innervations of the upper extremity in a very small surface area. It is at this level supraclavicular blocks are performed. As a result, the block is rapid in onset, predictable and dense anaesthesia is achieved with high successful rate. Search for longer acting local anesthetic is great and wide spread.

Supremacy of lignocaine remains unchallenged despite the introduction of various local anesthetics. The only drawbacks of it are shorter duration of action and increased risk of overdose and toxicity. The limiting factor in the more widespread use of this agent for block is the duration of action of the local anesthetics available which means either use of perineural catheters for longer surgeries or addition of adjuvants which prolong the duration of motor and sensory block and analgesia. A few groups, in 2014, had compared the effects of the alpha 2 agonists clonidine and dexmedetomidine with bupivacaine and with 0.75% Ropivacaine [4].

In our study, the drugs selected for supraclavicular block were ropivacaine (0.5%), and dexmedetomidine and clonidine as adjuvants. Simpson D et. al. (2005) found that ropivacaine had structural similarity to bupivacaine but with low lipid solubility and without cardiotoxic effects of bupivacaine [12].

Dexmedetomidine and clonidine has been previously studied by various authors as an adjuvant to local anaesthetic in supraclavicular block. Dexmedetomidine and clonidine are both α_2 selective agonists. There is a possibility that they work in a similar manner and may indicate a class effect. Very few studies have compared ropivacaine with dexmedetomidine and clonidine as adjuvants for supraclavicular block in India. Hence, ropivacaine (0.5%) with dexmedetomidine and clonidine combination was selected for our study.

The rationale for choosing this concentration of ropivacaine (0.5%) is supported by the study done by Klein et. al. in 1998, who found that for interscalene brachial plexus block, increasing the concentration of ropivacaine from 0.5% to 0.75% failed to improve onset or duration of block, suggesting that the risk of increased total dose of local anesthetic may be avoided. Hickey and co-workers, in 1992, had shown that 0.25% ropivacaine when used for subclavian perivascular brachial plexus block for upper limb surgery required frequent analgesia supplementation due to the low concentration of local anesthetic used [5].

We have used Dexmedetomidine 1µg/kg and clonidine 1µg/kg in our study, but in 2010 Shivinder Singh et al used various doses of Dexmedetomidine and clonidine 0.5µg/kg for brachial plexus block [11].

But Singelyn et. al. in 1996 had found that a minimum dose of clonidine (0.5µg/kg) added to mepivacaine prolonged the duration of analgesia & anaesthesia after brachial plexus block and no added benefit of exceeding the dose of clonidine more than 1.5µg/kg [10]. Dexmedetomidine has α_2/ α_1 selectivity ratio eight time higher than clonidine but, an equipotent dose of both was unknown so dose selection was done according to previous studies by Gandhi R et. al. (2012) where dexmedeto-midine and clonidine were used in 1µg/kg [3].

Karthik G et. al., in 2015, had compared dexmedetomidine and clonidine with levobupivacaine and Don Sebastian et. al. [1] in 2015 had used dexmedetomidine and clonidine with ropivacaine in brachial plexus block. Erlacher W et. al. in 2000 found that ropivacaine did not provide higher level of motor block and the clinical advantage of levobupivacaine was not substantial [2].

The demographic profile between the two groups was quite similar and provided us the uniform platform to evenly compare the results obtained.

The onset of sensory and motor block in both group C and group D and the difference between two groups is statistically significant ($p<0.0001$) . Both sensory and motor onset is early with dexmedetomidine compare to clonidine. Sensory onset in group C was 14.9±0.7 mins whereas in group D it was 8.1±1.4 mins, whereas motor onset in group C was 24.16±0.7 mins and in group D it was 11.63±0.7 mins. Karthik G et. al. (2015) and Don Sebastian et al (2015) [1] also found significantly faster sensory and motor onset with dexmedeto-midine than clonidine.

Sarita Swami et. al. (2012) also found faster sensory block with dexmedetomidine compare to clonidine but motor onset in their study was more rapid in clonidine group.

The total duration of sensory and motor block in group D were 729.53±17.67 mins and 692.53±28.99 mins whereas, in group C, duration of sensory and motor blocks were 435.63±3.53 mins and 473.46±14.84 mins respectively. The difference between two groups were statistically significant ($p<0.0001$).

Similar to our study, Karthik G et. al. (2015), Don Sebastian et. al. (2015) [1] and Sarita Swami et. al. (2012) found longer sensory and motor block with dexmedetomidine compare to clonidine when they were combined, as an adjuvant, with local anaesthetic in brachial plexus block. Many studied have shown the addition of clonidine extending the duration of brachial plexus block but Erlacher et. al. (2000) did not find much advantage of clonidine as an adjuvant.

Average total duration of analgesia in group D was 811.66±21.21 min whereas in group C it was 475.06±9.89 min which was significantly longer in dexmedetomidine group and difference between two was statistically significant ($p<0.0001$). In Don Sebastian et. al. (2015) [1] study duration of analgesia with 50µg of clonidine and 50µg dexmedetomidine was 510min and 720 min respectively which were similar to our result. Karthik G et. al. (2015) and Sarita Swami et al (2012) also reported significantly longer duration of analgesia with dexmedetomidine than clonidine.

None of the patients from any of the two groups required any sedation during intraoperative period. Dexmedetomidine also produce better arousable sedation than clonidine. Similar to our study, Karthik G et. al. (2015), Sarita Swami et. al. (2012) and Don Sebastian et. al. (2015) also recorded better sedation with dexmedetomidine than clonidine.

On comparison of haemodynamic parameters between the two groups, the baseline pulse and blood pressure between group D and group C were comparable ($P>0.05$). But, 15, 45, 90 & 120 mins after the block, pulse rate in group D was significantly lower than group C ($p<0.05$). The difference in mean SBP, DBP & RR between the two groups was

statistically insignificant (p>0.05). No significant side effects of clonidine or dexmedetomidine were noted in our study.

Singelyn et. al. in 1996 reported that a minimum dose of clonidine (0.5 μg/kg) added to mepivacaine prolonged the duration of anaesthesia and analgesia after brachial plexus block. No added benefits were found with the doses exceeding 1.5 μg/kg. The enhancing effect of a small dose of clonidine on lignocaine was because of the evoked inhibition of C-fiber action potential. Similar effects were found in our study too.

Anjan Das et. al. (2014) concluded that the addition of 100 mcg of dexmedetomidine to ropivacaine 0.50% solution for supraclavicular brachial plexus block prolonged the duration of sensory and motor blockade thus reducing the requirement of rescue analgesia in the post-operative period, but had no appreciable effect on the time of onset of sensory & motor blockade.

Conclusion

From our study, with the use of α-2 agonists, Dexmedetomidine (50mcg) and Clonidine (50mcg) as adjuvants to local anaesthetic solution (0.5% ropivacaine) in supraclavicular brachial plexus block for upper limb surgeries, we conclude that there was faster onset and prolonged duration of sensory and motor block with prolonged duration of postoperative analgesia with dexmedetomidine as compared to clonidine. Haemodynamic parameters, side effects and sedation scores were comparable between the two drugs.

Key Message

Dexmedetomidine, when added to Ropivacaine, in supraclavicular brachial plexus-block, produced faster onset longer duration of sensory and motor block and longer analgesia duration with reduced complications and stable hemodynamics compared to Clonidine.

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Nil

Conflict of Interest

Nil

Source of Support

Nil

References

1. Don Sebastian, Ravi M, Comaprision of dexmedetomidine and clonidine as adjuvant to Ropivacaine in supraclavicular brachial plexus blocks. IOSR-JDMS, 2015 March;14(3):91-97.
2. Erlacher W, Schuschnig C, Orlicek F, Marhofer P, Koinig H, Kapral S. The effects of clonidine on ropivacaine 0.75% in axillary perivascular brachial plexus block. Acta Anesth Scand, 2000;44:53-7.
3. Gandhi R, Shah A, Patel I. Use of dexmedetomidine along with bupivacaine for brachial plexus block. Natl J Med Res. 2012;2(1):67-69.
4. Harshvardhan HS. Efficacy of Dexmedetomidine Compared to Clonidine added to Ropivacaine in Supraclavicular Nerve Blocks: A Prospective, Randomized, Double Blind Study. Int J Med Health Sci. 2014;3(2):127-32.
5. Hickey R, Rowley CL, Candido KD, Hoffman J, Ramamurthy S, Winnie AP. A comparative study of 0.25% ropivacaine and 0.25% bupivacaine for brachial plexus block. Anesth Analg. 1992;75:602–6. [PubMed].
6. Ilfeld BM. Continuous peripheral nerve blocks: a review of the published evidence. Anesth Analg 2011;113:904–25.
7. Salinas FV. The effect of single-injection femoral nerve block versus continuous femoral nerve block after total knee arthroplasty on hospital length of stay and long-term functional recovery within an established clinical pathway. Anesth Analg 2006;102:1234–9.
8. Schoenmakers KP, Wegener JT, Stienstra R. Effect of local anesthetic volume (15 vs 40 mL) on the duration of ultrasound-guided single shot axillary brachial plexus block: a prospective randomized, observer-blinded trial. Reg Anesth Pain Med 2012;37:242–75.
9. Scott DB. Acute toxicity of ropivacaine compared with that of bupivacaine. Anesth Analg 1989;69:563-96.
10. Singelyn FJ, Gouveineur J, Robert A. A minimum dose of clonidine added to mepivacaine prolongs duration analgesia after brachial plexus block. Anesth Analg 1996;83:1046-50.
11. Shivinder Singh, Amitabh Aggarwal. A randomised controlled double-blinded prospective study of the efficacy of clonidine added to bupivacaine as compared with bupivacaine alone used in supraclavicular brachial plexus block for upper limb surgeries. Indian Journal of Anesthesia. 2010;54:552-556.
12. Simpson D, Curran MP, Oldfield V, Keating GM. Ropivacaine A review of its use in regional anaesthesia and acute pain management. Drugs 2005;65(18): 2675-717.
13. Yaksh TL, Ilfeld BM, Wiese AJ. Perineural local anesthetic and adjuvant action: the meaning of an ex vivo data set for efficacy and safety. Reg Anesth Pain Med 2012;37:366–8.

Original Research Article

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Effect of Oral Clonidine Premedication on Perioperative Haemodynamic Response and Post Operative Analgesic Requirements for Patients Undergoing Laparoscopic Surgeries

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Abstract

Background: The first focus on haemodynamic response to laryngoscopy and tracheal intubation was done in 1950 by Burstein. King et al in (1951) described the abnormal circulatory reaction to laryngoscopy. Its association with a rise in blood pressure, tachycardia and increased level of catecholamines was highlighted by Prys-Roberts in (1971) and by Siedlecki in 1975. Recognizing the hazardous effect of such reflex reactions, many techniques were studied and clinically tried to obtund these reactions. At the same time, The first publication on diagnostic laparoscopy by Raoul Palmer appeared in the early 1950s, followed by the publication of Frangenheim and Semm. Hans Lindermann and Kurt Semmpractised CO_2 hysteroscopy during the mid-1970s. However this procedure is not risk free, In fact it produces significant changes in haemodynamically compromised patients.The hallmark of laparoscopy is creation of carbon dioxide pneumoperitonium and change in the patients position from trendelenburg to reverse trendelenburg. It also results in stress hormone responses (cortisol, epinephrine and non–epinephrine) especially when CO_2 pneumoperitonium is used concomitantly. Laryngoscopy with or without tracheal intubation amounts to a highly noxious stimulus to the homeostasis of the patient.

Aims: Designed to assess the effect of oral Clonidine premedication on hemodynamic response to endotracheal intubation and to compare intra-operative haemodynamic parameters, pain and sedation scores, time of first post-operative analgesia and dverse effects

Material and Method: Total 60 patients ASA grade I and II in the age group 20 to 55 years were included in this study and they were randomly divided into two groups:

Group 1 (n=30), patient received oral clonidine 150 mcg orally 90 min before induction

Group 2 (n=30), patients received oral vitamin C 100 mg orally 90 min before induction

All patients were posted for elective surgeries and were randomly selected.

Conclusion: The basal and perioperative arterial blood pressure and heart rate after giving premedication was lower in clonidine group as compared to placebo group. Time for 1st post-operative analgesia requirement in clonidine group was significantly prolonged in comparison with the ranitidine group.

Keywords: Clonidine; Laparoscopic Surgeries; Hemodynamic Response and Analgesia.

Introduction

Reid and Bruce in 1940, Burstein in 1950 and King, Harris in 1951described the haemodynamic response to laryngoscopy and intubation of the trachea [1]. It is characterized by hypertension, tachycardia and increased concentration of circulating catecholamines (Prys-Roberts 1971) [2]. Though transitory, they may be deleterious to the patient because of the increased cardiac work involved. They may also be associated with arrhythmias.

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Oral Clonidine, an alpha-2 agonist, which acts on the central nervous system to reduce the sympathetic outflow, has been used in this study in a dose of 150mcg to assess its usefulness in attenuating the haemodynamic response [3]. After oral intake, onset of action starts within 30-60 minutes and peak plasma concentration is reached within 90 minutes which is comparable to intravenous clonidine. Keeping in mind the cost-effectiveness and the ease of administration, oral clonidine has been used in this study. Premedication with clonidine blunts the stress response to tracheal intubation, surgical stimuli and the narcotic and anaesthetic doses are also reduced. In addition clonidine increases cardiac baroreceptor reflex sensitivity to increase in systolic blood pressure, and thus stabilizes blood pressure [4,5].

Accordingly, this study was designed to evaluate the effects of oral clonidine premedication on heamodynamic response and modulation of post-operative pain in patients undergoing laparoscopic surgeries.

Aims and Objectives

This prospective randomized, single blind, comparative study was conducted on adult patients undergoing laparoscopic surgeries with the following objectives;

- Designed to assess the effect of oral Clonidine premedication on hemodynamic response to endotracheal intubation
- To compare intra-operative haemodynamic parameters.
- To compare pain and sedation scores
- To compare time of first post-operative analgesia
- To compare both adverse effect

Material and Methods

Preanaesthetic evaluation was done a day before the proposed surgery. Relevant history was taken, physical examination carried out and cardiovascular and respiratory systems were assessed for any abnormalities. Basic routine investigations were carried out in all cases. Other investigations like blood urea, serum creatinine and chest X ray were done whenever necessary.

Patients of ASA grade I and grade II, of either sex, older than 20years but younger than 55years and scheduled for laparoscopic surgeries were included in study.

Patients not fulfilling eligibility criteria such as lack of patient consent, drug dependence, history of bronchial asthma, allergy to clonidine, hypertensive and diabetic patients, patients with severe coronary insufficiency, recent myocardial infarction, concomitant use of monoamine oxidase inhibitors, tricyclic antidepressants, or opioids and regnant patients were excluded from this study.

Study Method

All patients were advised to take tablet Alprazolam 0.5 mg before bedtime and be nil orally after 10p.m. on the preoperative day. After arrival in the pre-op room vitals were checked,peripheral venous access and standard monitoring were secured and inj. ondansetron 4mg/iv and ranitidine 50mg/iv, oral clonidine given 150mcg/90 min prior to surgery. After shifting the patient to operation theatre, base line pulse rate, systolic blood pressure, diastolic blood pressure, respiratory rate, ECG, SpO_2 and intraoperatively end tidal carbon dioxide ($ETCO_2$) were recorded.

Patients were premedicated with intravenous injection glycopyrolate 0.2mg, and inj Midazolam-1mg, and sedated with pentazocine 0.6mg/kg IV, on operating table 5 min before induction of anaesthesia. Induction of anaesthesia was carried out with inj. propofol 2mg/kg with 2% lidocaine and muscle relaxant vecuronium 0.1 mg/kg given IV. After intubating the patient, maintained with propofol 100mcg/kg/min, isoflurane, N_2O/40% O_2 mixture. Controlled mechanical ventilation was applied to maintain endtidal CO_2 between 30-40 mmHg. The mean arterial blood pressure was maintained (MAP) was maintained at 20% above or below the pre – operative value by adjusting the rate of propofol.

Haemodynamics was recorded, prior to induction, 1 min after endotracheal intubation, 5 min after endotracheal intubation and every 30mins intraoperatively. At the end of surgery, patient was given neostigmine 0.05 mg/kg and glycopyrrolate 0.01mg/kg intravenously to reverse the neuromuscular blockade. The patient was extubated after a satisfactory reversal and throat suction and transferred to recovery room. Intraoperatively, all patients were infused with Ringer lactate and Dextrose normal saline in a dose of 6 ml/kg/hour in the first 30-minute and 4 ml/kg/hour subsequently till the end of surgery. Patients were followed up postoperatively at hourly intervals till 9 hours after administration of clonidine, keeping in mind the elimination half time of clonidine and VAS, sedation score and adverse events was recorded at 30min, 60min, 90min, and 120min postoperatively.

Rescue analgesia was given with Inj.Diclofenac sodium 75mg/iv over 30 min 12hrly. The following parameters were observed and noted :

1. Vital signs including pulse, systolic Blood pressure, diastolic blood pressure, SpO_2, respiratory rate, were monitored at
   1. base line
   2. pre induction
   3. 1 min after intubation
   4. 5min after intubation
   5. Start of pneumoperitoneum
   6. 30 min after intubation
   7. 15min after Release
   8. After extubation
2. Emergence times from the discontinuation of anesthesia to the removal of endotracheal tube were noted.
3. Side effects like hypotension, bradycardia, sedation, post-operative nausea and vomiting, cough shivering etc.
4. Times to requirement of first analgesic were noted. Rescue analgesia as given in the form of inj diclofenac sodium 75 mg iv.
5. Pain intensity was assessed using a 10 cm visual analog scale (VAS) 0-no pain 10-intolerable pain.

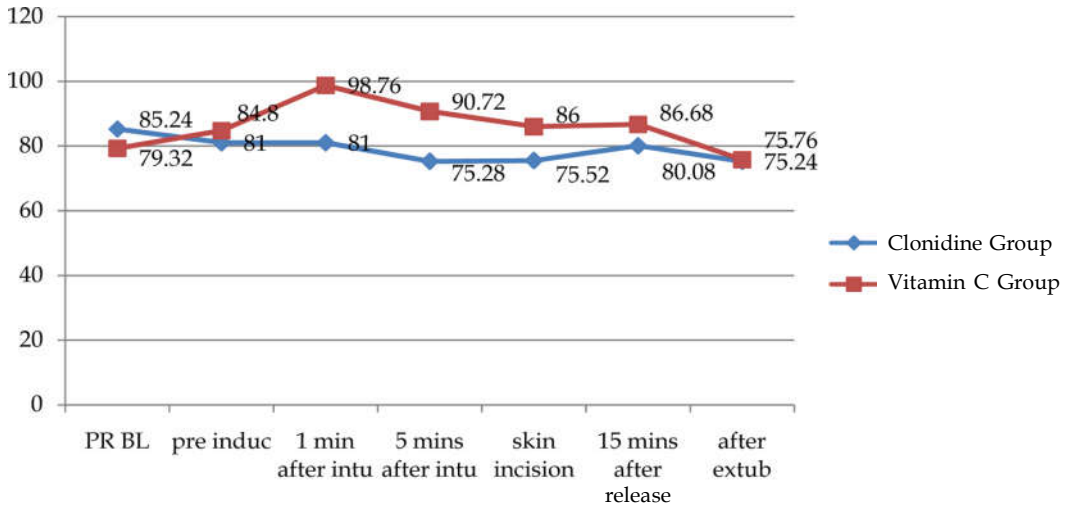
The degree of sedation was graded as

0 point - patient awake and talkative

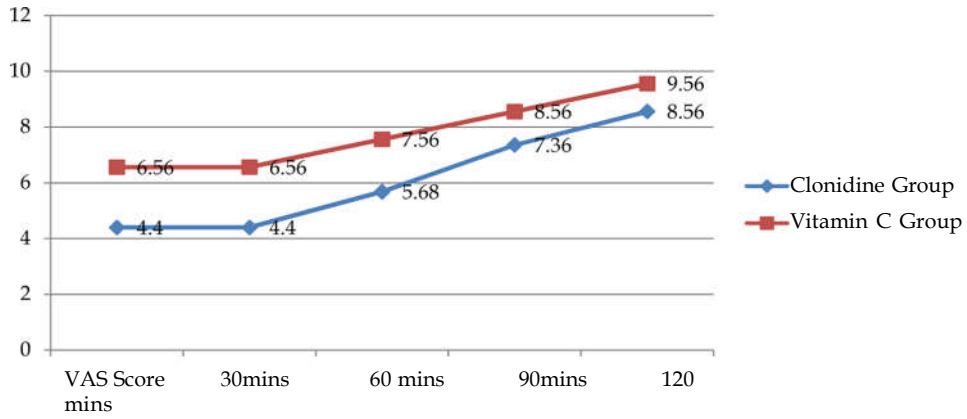
1 point - patient awake but uncommunicative

2 point – patient drowsy, quiet and easily arousable

3 point – patient asleep.



Graph 1: Mean Pulse rate for Clonidine group is significantly lower than for Vitamin C group at 1 mins, 5 mins after intubation, skin incision and 15 mins after release. (P value <0.05/0.01). However there is no significant difference in Mean Pulse Rate between Clonidine Group and Vitamin C group, pre induction and after extubation. (P value >0.05)

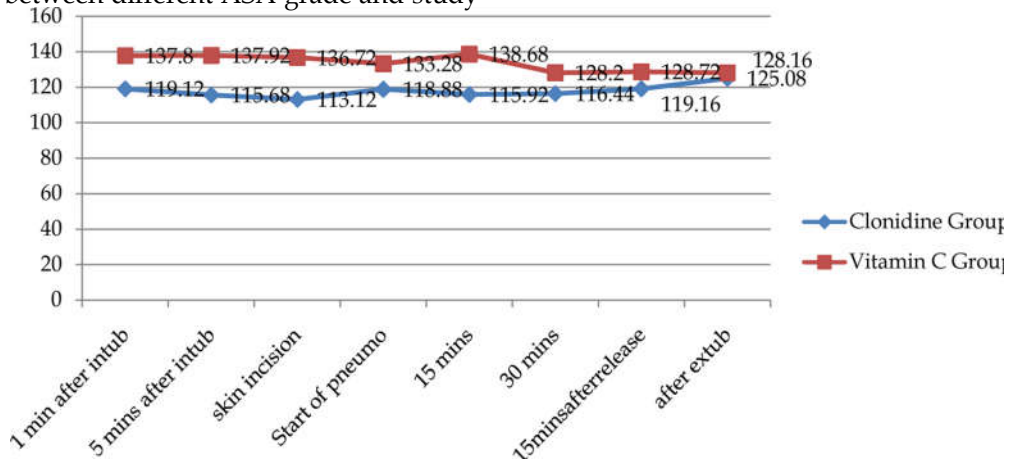


Graph 2: Mean VAS-Score for Clonidine group is significantly lower than for Vitamin C group at baseline, 30 mins, 60 mins, 90 mins and 120 mins

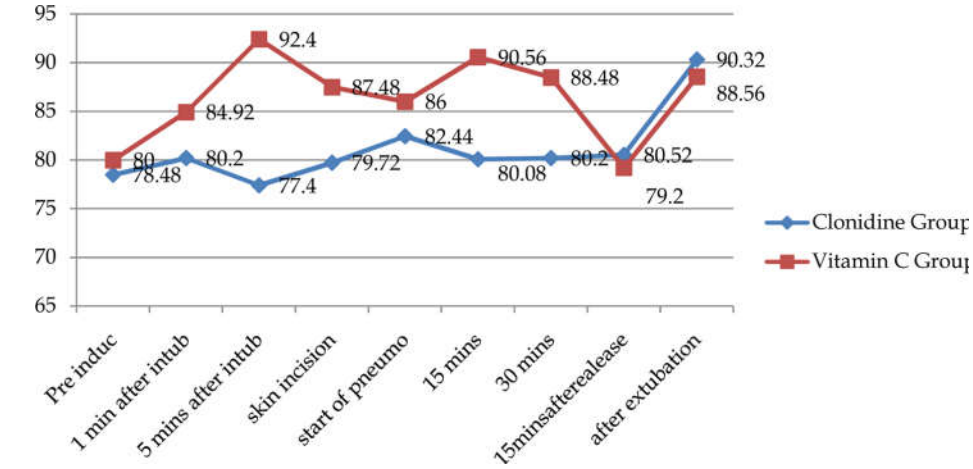
Results

There was no statistically significant difference between different age, weight and gender of study population. There was no statistically significant difference between different ASA grade and study population. The mean hemoglobin was higher in clonidine group as compared to vitamin C group though statistically not significant.

Respiratory Rate between Clonidine group and Vitamin C group are not significantly different across all observations. (P value >0.05)



Graph 3: Mean Systolic Blood Pressure for Clonidine group is significantly lower than for Vitamin C group at 1 mins, 5 mins after intubation, skin incision, start of pneumo peritoneum, 15 mins and 30 mins (P value <0.01). However there is no siginificant difference in Mean Systolic Blood Pressure between Clonidine Group and Vitamin C group after extubation. (P value >0.05)



Graph 4: Mean Diastolic Blood Pressure for Clonidine group is significantly lower than for Vitamin C group at 1 mins, 5 mins after intubation, skin incision, start of pneumo peritoneum, 15 mins and 30 mins (P value <0.05/ 0.01). However there is no significant difference in Mean Diastolic Blood Pressure between Clonidine Group and Vitamin C group pre induction, 15 mins after release and after extubation (P value >0.05)

Table 1: Trend of VAS over a period of time amongst different study group

	Group	Mean	Std. Deviation	Std. Error Mean	T value	P value
VAS-score (baseline)	Clonidine Group	4.40	0.500	0.100	-15.173	<0.01 (Highly Significant)
	Vitamin C Group	6.56	0.507	0.101		
30 min	Clonidine Group	4.40	0.500	0.100	-15.173	<0.01 (Highly Significant)
	Vitamin C Group	6.56	0.507	0.101		
60 min	Clonidine Group	5.68	0.476	0.095	-13.512	<0.01 (Highly Significant)
	Vitamin C Group	7.56	0.507	0.101		
90 min	Clonidine Group	7.36	0.490	0.098	-8.514	<0.01 (Highly Significant)
	Vitamin C Group	8.56	0.507	0.101		
120 min	Clonidine Group	8.56	0.507	0.101	-6.973	<0.01 (Highly Significant)
	Vitamin C Group	9.56	0.507	0.101		

Table 2: Emergence time in minutes amongst different study group

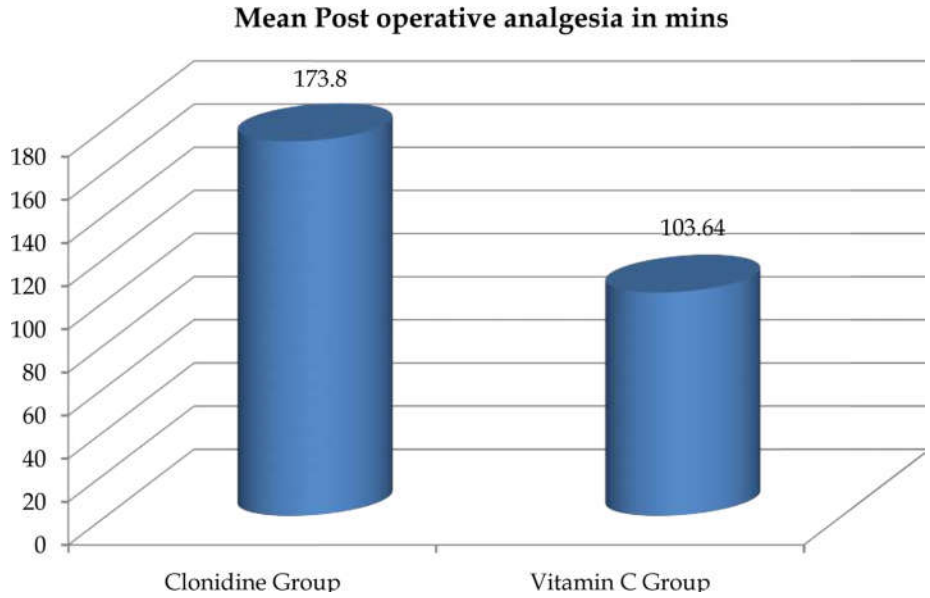
	Group	Mean	Std. Deviation	Std. Error Mean	T value	P value
Emergence time (min)	Clonidine Group	4.40	0.645	0.129	0.864	> 0.05 (Not Significant)
	Vitamin C Group	4.24	0.663	0.133		

Independent sample t test applied. T value is 0.864, P value >0.05

Table 3: Post-operative analgesia in minutes amongst different study group

	Group	Mean	Std. Deviation	Std. Error Mean	T value	P value
1st post op analgesia (min.)	Clonidine Group	173.80	17.443	3.489	15.815	< 0.01 (Highly Significant)
	Vitamin C Group	103.64	13.702	2.740		

Independent sample t test applied. T value is 15.815, P value <0.01.



Graph 5: Post-operative analgesia was significantly higher in clonidine group as compared to vitamin C group

As seen in the Table 1, SpO_2 readings between Clonidine group and Vitamin C group are not significantly different across all observations (P value >0.05).

As seen in the Table 2, Emergence time was higher in clonidine group as compared to vitamin C group though statistically not significant $ETCO_2$ readings between Clonidine group and Vitamin C group are not significantly different across all observations. (P value >0.05), except at 1 min after intubation.

Discussion

Laparoscopic surgeries have revolutionized the world of surgeries. But it also results in stress hormone responses (cortisol, epinephrine and nor epinephrine) due to pneumoperitonium and changes in position from trendelenburg to reverse trendelenburg. Clonidine is an alpha -2 adrenoceptor agonist. It shows central sympatholytic effect. Clonidine has been shown to reduce perioperative hemodynamic instability, and augments the effectsof anaesthesia.

Pneumoperitonium during laparoscopic surgery produces significant haemodynamic changes, which can be detrimental especially in elderly and haemodynamically compromised patients. Various techniques and pharmacological agents have been used to counteract these detrimental effects of pneumoperitonium.

During laparoscopic surgery procedural changesin the patient's position and surgical stress, especially following pneumoperitonium cause labile haemodynamics. The choice of anesthetic technique for upper abdominal laparoscopic surgery is mostly limited to general anesthesia with muscle paralysis, tracheal intubation and IPPV.

This study was carried out in 25 ASA grade I and II patients, to evaluate the effect of clonidine premedication on haemodynamic response and the post-operative pain associated with laparoscopic surgeries. Clonidine is rapidly and completely absorbed after oral administration and reaches peak plasma concentrations within 60-90min.

In my study tablet clonidine was given 90min before scheduled laparoscopic surgeries Clonidine, an imidazoline derivative is a selective alpha 2 adrenergic agonist. It is a potent anti-hypertensive drug. It produce dose related fall in the heart rate and blood pressure associated with decreased systemic venous resistance and cardiac output. Clonidine was administered 150MCG orally 90min before surgery in our study.

Dose of clonidine varied from 2 to 5 mcg/kg in different studies, higher dose of clonidine that is 5mcg/kg is usually required for potentiation of postoperative analgesia by intra thecal morphine. A small oral dose of clonidine decreased the incidence of perioperative myocardial ischemic episodes without affecting haemodynamic stability.

Aho et al used 3mcg /kg and 4.5mcg/kgclonidine for suppression of haemodynamicresponse to pneumoperitonium.rise in blood pressure and heart rate was less in both the groups but 4.5mcg/kg clonidine produced greater fall in the mean arterial pressure before induction [6].

Joris et al used very high dose of clonidine, 8mcg / kg for reducing the level of catecholamine and vasopressin following pneumoperitonium [7].

Malek et. al. used 150mcg of clonidine as i.v infusion and intramuscularly while Sung et al used 150mcg of oral clonidine as premedication for maintenance of haemodynamic stability during pneumoperitonium [8].

In my study, tablet clonidine 150mcg orally was given 90min. before scheduled surgery. Hypertension and tachycardia were noticeable during the application of CO_2 pneumoperitonium in the placebo group. Clonidine premedication effectively blunted the cardiovascular response to surgical stress, especially pneumoperitonium. Compared with the base line values there was significantly less increase in heart rate and SBP, DBP in the clonidine group compared to the placebo group.

Following pneumoperitonium with CO_2, patients were hyperventilated to maintain normocapnia. Every effort was made to maintain intra-abdominal pressure. Haemodynamic changes associated with pneumoperitonium were first recognized in 1947.

Diamant et al reported 35% decrease in cardiac output In a dogwith raised intraabdominal pressure of 40mmHg [9].

Ishizaki et. al. tried to evaluate the safe intra-abdominal pressure during laparoscopic surgery. They observed significant fall in cardiac output at 16 mm of Hg of intra-abdominal pressure. Haemodynamic alterations were not observed at 12 mm of Hg of intra-abdominalpressure. Based on all these observations the current recommendation is to monitor intra-abdominal pressure and to keep it as low as possible [10].

Cunningham et. al. [11] and Dorsaty et. al. (12) assessed the ejection fraction of left ventricle by trans esophageal echocardiography during pneumo-peritonium. No significant change in ejection fraction was reported up to 15mmHg of intra-abdominal pressure. Considering all these facts intra-abdominal pressure was kept below 14 mmHg.

Despite of maintaining normocapnia and keeping intra-abdominal pressure below 14mmHg significant rise in heart rate, SBP, DBP was noticed in placebo group. Rise in SBP, DBP was statistically significant. Slight fall in SBP, DBP, was noticed following premedication with clonidine. Following intubation and pneumoperitonium, increase in arterial pressure was noticed but it never crossed the base line value. Hence clonidine premedication was able to achieve haemodynamic stability during pneumoperitonium.

Similar findings were reported by Aho et. al., joris et. al., Malek et. al., Sung et. al., Yu et. al. and laisalmi et. al. [6-8,13-15]. Aho et. al. observed that 4.5mcg/kg of clonidine significantly decreased the mean arterial pressure before induction of anesthesia, so they recommended 3mcg/kg of clonidine for perioperative haemodynamic stability [6].

Joris et. al. used higher dose of clonidine for reduction of catecholamine and vasopressin associated with pneumoperitonium. Clonidine significantly reduced the concentration of catecholamine but not vasopressin and cortisol concentration [7].

Similarly Sung et. al. observed haemodynamic stability during pneumoperitonium with 150mcg clonidine. Requirement of sevoflurane was also less in clonidine group [13].

Finally Yu et. al. recommended the routine use of clonidine premedication in laparoscopic patients [14].

The adverse effects in the post op period were less in the patients who had clonidine premedication in comparison to the placebo group. Side effects were observed less in clonidine group with nausea occurring in only 10% cases as compared to placebo

group 13.3% though not significant (p>0.05). No case of Shivering and vomiting was found in clonidine group [15]. This finding corroborates with the findings of Nicholaou et. al., where they concluded that the clonidine inhibits cold thermoregulatory response due to an effect on central integration control and output from the thermoregulatory centers.

Thus he opined that clonidine can be used as an effective agent for inhibition of perioperative shivering which can adversely increase metabolic rate and cardiac work and may also disrupt surgical repair or result in wound dehiscence [16].

Clonidine increases gastrointestinal motility by decreasing sympathetic outflow and increasing parasympathetic outflow from central nervous system.Although many workers have reported the antiemetic property of clonidine, the mechanism by which it acts warrants further investigation.

In our study time of requirement for 1st dose of analgesic was prolonged in patients of clonidine in comparison with the placebo group. Most of the patients in the clonidine group required only 1 dose of during the post-operative 24hrs period while most patients in the placebo group required 2 or more than 2 doses of paracetamol 1gm i.v.

Similarly more patients in the clonidine group required no diclofenac sodium or only one dose of diclofenac sodium during the post-operative period of 24hrs, while 2 or more than 2 doses were requiredin most of the placebo group patients. The median time for 1stpost-operative analgesia in clonidine group is 172.5min. In ranitidine group is 101.5. Time for 1stpost-operative analgesia requirement in clonidine group was significantly prolonged in comparison with the ranitidine group with p value <0.05.

Conclusion

After discussing and reasoning the observations and results, study can be summarized as follows

- The basal and perioperative arterial blood pressure and heart rate after giving premedication was lower in clonidine group as compared to placebo group.
- Time for 1stpost-operative analgesia requirement in clonidine group was significantly prolonged in comparison with the ranitidine group.

References

1. King B D, Harris L C, et. al. Reflex circulatory responses to direct laryngoscope and tracheal intubation performed during general anaesthesia, 1951;12: 556-566.
2. Prys-Roberts C, Greene LT, Meloche R, FOEX P. Studies of anaesthesia in relation to hypertension. II: Haemodynamic consequences on induction and endotracheal intubation. Br.J.Anaesth 1971;43:531-46.
3. Hayashi Y, Maze M. Alpha 2 adrenoceptor agonists and anaesthesia. Br J Anaesth. 1993;71:108–18.
4. Harron DW, Riddell JG, Shanks RG. Effects of azepexole and clonidine on baroreceptor mediated reflex bradycardia and physiological tremor in man. Br J ClinPharmacol. 1985;20:431–6.
5. Patel HSP, Kashi NA. Effect of intravenous clonidine premedication on perioperative hemodynamic response in patients undergoing laparoscopic cholecystectomy: a case control study. Int J Med Sci Public Health 2016;5:1213-1219.
6. Aho M, Scheinin M, Lehtinen AM, et. al. Intra muscularly administreddexmeditomidine attenuated haemodynamic and stress responses to gynaecologic laparoscopy. A nesthAnalg 1992;932-9.
7. Joris J. Chiche JD, LamyM, clonidine reduced haemodynamuic changes induced by pneumo-peritonium during laparoscopic cholecystectomy. Br J Anesth 1995;74:A 124.
8. Malek KJ, Knor J, Kurzova A, Lopourova M. Adverse haemodynamic changes during laparoscopic cholecystectomy and their possible suppression with clonidine premedication. comparision with intravenous and intramuscular premedication. Rozhl Chir 1999;78:286-91.
9. Diamant M, Benumot JL, Saidman LJ. Haemodynamics of creased intra abdominal pressure: interaction with hypovolemia and halothane anesthesia. Anesthesiology 1978;48:23-7.
10. Ishizaki Y, Bandae Y, Shimomura K, Abe H, Ohtomo Y, Idez Y. safe intra abdominal pressure of carbon dioxide pneumoperitonium during laparoscopic surgery. Surgery 1993;114:54.
11. Cunningham AJ, Turner J, Rosenbaum S et. al. Transesophageal echocardiographic assessment of haemodynamic function during laparoscopic cholecystectomy. Br J Anesthes 1993;9:128.
12. Dorsay GA, Greene FL ,Baysinger CL. Haemodnamic changes during laparoscopic cholecystectomy monitored with transoesophageal echocardiography.
13. Sung CS,Lin SH, Chan KH, Chang WK, Chow LH, Lee T. effect of oral clonidine premedication on perioperative haemodynamic response and postoperative analgesic requirement for patients undergoing laparoscopic cholecystectomy. Acta Anaesthesiol Scand, 2000;38:23-9
14. Yu HP, Hseu SS, Yien HW, Teng YH, Chan KH. Oral clonidine premedication preserves heart rate variability for patients undergoing laparoscopic cholecystectomy. ActaAnaesthesiolSca, 2003;47:185-90.

15. Laisalmi M, Koivusalo AM, valta P, tikkanen I, lindgrer. clonidine provides opioid sparing effect, stable haemodynamic and renal integrity during laparoscopic cholecystectomy. Endosc 2001;15: 1331-5.
16. Nicolaou G, Jonston CE, Bristow GK. Clonidine decrease vaso-constriction and shivering threshold, without affecting the sweat-ing threashold. Can J Anaesth 1997;44(Suppl).:636-44.

Original Research Article

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A Randomized Clinical Trail to Compare Palonosetron and Ondansetron for Prevention of Post Operative Nausea and Vomiting

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Abstract

Abstract: Nausea and vomiting is known to be associated with the use of anaesthetic technique for many years. Ondansetron a gold standard drug used for treatment of post operative nausea and vomiting (PONV) is short acting and multiple doses are needed. Objective of the present study is to compare the efficacy of palonosetron and ondansetron for prevention of PONV in patients undergoing abdominal surgery under general anaesthesia.

Methods: 140 patients undergoing abdominal surgery under general anesthesia were randomised and allocated into two groups after taking into consideration inclusion and exclusion criteria. Group I received ondansetron 8mg intravenously and Group II received palonosetron 0.075mg intravenously 5 min before the induction of anesthesia. In all patients general anaesthesia given using thiopentone as inducing agent. Occurrence of PONV was noted and was scored for 24 hrs.

Results: The incidence of PONV was significantly lower in the palonosetron group compared with the ondansetron group (24.3% vs 78.6%, respectively). Emetic episodes were observed in 5.71% of patients in palonosetron group compared to 61.4% of patients in ondansetron group (P value <0.001). The results were clinically and statistically significant.

Conclusion: Incidence of PONV and emetic episodes is less in patients who had received palonosetron in comparison to those who had received ondansetron. From the study we conclude that palonosetron is more efficacious than ondansetron for prevention of PONV in patients undergoing abdominal surgery under general anesthesia.

Keywords: Post Operative Nausea and Vomiting; Palonosetron; Ondansetron; General Anaesthesia.

Introduction

Post operative nausea and vomiting (PONV) remains a significant problem even in the modern day anaesthesia practice and continues to be a significant. During the past decade, anaesthesiologists have been modifying their anaesthetic techniques to ensure a more rapid and smooth recovery. However in-spite of these advances, nausea and vomiting still occurs with unacceptable frequency in association with surgery and anaesthesia and description of it as "the big little problem" [2] encapsulates much of the general perception. Post operative nausea and vomiting in addition to being distressing and unpleasant to the patients, has a potential to adversely affect the patient in the form of delayed recovery, unexpected hospital stay and can also cause post surgical morbidities like wound dehiscence, pulmonary aspiration, surgical site bleeding and dehydration [3].

Various drugs have been used to prevent PONV namely antihistamines, phenothiazine derivatives, anticholinergic and dopamine receptor antagonists. Use of these drugs is associated with unwanted side effects like sedation, dysphoria, extrapyramidal symptoms, dry mouth, restlessness and tachycardia

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[4,5,6]. The management of nausea and vomiting has improved greatly in recent years, with the introduction of 5 Hydroxytyptamine (5-HT_3) receptor antagonists. The commonly used drug of this group is Ondansetron [7]. Ondansetron is being considered as a gold standard drug for treatment of PONV. 2nd generation drug Palonosetron has been recently introduced and has higher receptor affinity and longer half life which confers it prolonged duration of action [5]. Studies evaluating efficacy and safety of palonosetron for PONV revealed that a single dose of palonosetron 0.075mg significantly decreased the emetic episodes, nausea severity and use of rescue medication in patients undergoing abdominal surgeries under general anesthesia for first 24 hours. Further studies were done to demonstrate the continued effect of palonosetron for 24 to 72 hrs. Palonosetron was also reported to be as effective as ondansetron for prevention of chemotherapy induced nausea and vomiting (CINV) following use of highly emetogenic chemotherapeutic agents. The incidence of PONV is relatively high in patients undergoing abdominal surgeries under general anesthesia. Still no studies were found which evaluated the relative efficacy of palonosetron and ondansetron in preventing PONV.

Hence the present study was done to compare the efficacy of palonosetron and ondansetron for prevention of PONV in patients undergoing abdominal surgeries under general anaesthesia.

Methodology

Institutional ethical committee approval was taken and consent was taken from enrolled 140 patients. Patients aged between 18 to 60 years, with ASA status 1 and 2 were scheduled to undergo elective abdominal surgeries under general anesthesia were randomly allocated into two groups. All patients had one of the PONV risk factors like female gender, history of PONV, motion sickness, nonsmoking status. Patients who have already received antiemetics or had nausea and vomiting 24 hrs preceding the surgery were excluded from the study.

After thorough pre-anaesthetic evaluation and clinical examination patients were randomized to receive either ondansetron 8mg (Group I) or palonosetron 0.075mg (group II) intravenously using computer generated randomization table. A trained nurse who was not involved in the study prepared the drug and numbered them. Normal saline was added to palonosetron to make total volume of 4 ml. Patients did not receive any premedication. Patients received either palonosetron 0.075 mg or ondansetron 8 mg intravenously 5 min prior to induction of anesthesia. Standard anesthesia regime was used for all the patients. Patients were premeditated with glycopyrrolate 0.004mg/kg, midazolam 0.05mg/kg fentanyl 2μ/kg. Following pre oxygenation anaesthesia was induced with thiopentone sodium 5mg/kg and intubation facilitated with injection Suxamethonium 2mg/kg. Endotracheal intubation was done with appropriate size endotracheal tube. Anaesthesia was maintained with N_2O 50% and oxygen 50% and vecuronium 0.1 mg/kg. Neuromuscular blocked was reversed with injection glycopyrrolate 0.04mg/kg and neostigmine 0.05mg/kg. Pulse rate, blood pressure, SpO_2 and $ETCO_2$ were monitored throughout perioperative period. Post operative analgesia was provided by diclofenac sodium 75 mg IM or with paracetamol infusion of 10 mg/ kg four times daily in patients who donot tolerate diclofenac. Post operatively patients were monitored for Nausea and vomiting every hourly for first 24 hours. Incidence of the ponv was compared according to nausea and vomiting score. 0 = No emetic symptoms,1 = Nausea (defined as unpleasant sensation associated with awareness of urge to vomit) 2 = Retching (labored, spasmodic and rhythmic contraction of respiratory muscles without expulsion of gastric contents,) 3 = Vomiting. (Forceful expulsion of gastric contents from mouth). Patients received intravenous Dexamethasone 0.1mg/kg as rescue antiemetic and were administered when PONV score was ≥ 2. A complete response was defined as absence of ponv and no use of rescue antiemetic Occurrence of side effects like headache, dizziness, constipation were recorded.

Statistical Analysis Sample size was calculated by power analysis with α error of 0.05, β error of 0.2 and power of study being 80%. Minimum of 70 patients were included in each group. All data was expressed as mean +/- standard deviation. Demographic data was analyzed using unpaired 't' test. Efficacy of drugs was compared using chi square test with P value of < 0.05 being considered significant.

Results

140 patients undergoing abdominal surgery under general anaesthesia were enrolled in the study and all of them completed the study. Demographic profiles in both the groups were comparable with regards to the patient characteristics, duration of the procedure and ponv risk factors. (P value > 0.05) (Table 1) It was observed that the incidence of post operative nausea

and vomiting in group I is 78.57% (55) as compared to 24.29% (17) in group II with p value < 0.001 (Table 2). It was observed that the incidence of vomiting in group I is 61.43% (43) as compared to 5.71% (04) in group II (P value of <0.001) which is statistically significant. (Table 3).

Discussion

Post operative nausea and vomiting (PONV) is very common sequelae of general anaesthesia and is very unpleasant and distressing for the patient. It is leading cause of delayed discharge andunanticipated hospital admission after ambulatory surgical procedure [8]. Incidence of postoperative nausea and vomiting in an untreated adult surgical population receiving general anaesthesia is around 20-30%, but it increases up to 80% in patients with risk factors for PONV. PONV is very frequent in abdominal surgeries leading to the recommendation of routine prophylactic administration of antiemetics [9]. The etiology of nausea and vomiting after abdominal surgeries under GA are multifactorial in origin. Age, type of surgery, anaesthetic procedure and duration of surgery may influence PONV.

Numerous interventional methods have been studied for the prevention of nausea and vomiting. Non pharmacological methods include acupuncture, electropuncture, transcutaneous electrical nerve stimulation, acupoint stimulation and acupressure. Pharmacological methods include Dopamine receptor antagonists (phenothiazines, buterophenones and benzamides), Histamine receptor antagonists (dimenhydrinate), Muscarinic receptor antagonists (scopolamine), and serotonin receptor antagonists (ondansetron). Miscellaneous drugs like propofol, clonidine, dexamethasone and ephedrine are also tried for prevention of nausea and vomiting. Above drugs are effective in reducing PONV with varying efficacy and are associated with unwanted side effects.

Hence introduction of 5-HT_3 receptor antagonists in 1990s was heralded as the major advance in prophylaxis of PONV as they lack the major adverse effects which were observed commonly with traditionally used antiemetic drugs [10,11]. These 5-HT_3 receptor antagonists produced no sedation, extrapyramidal reactions, adverse effects on vital signs or laboratory tests or drug interactions [12]. Half life of Palonosetron is 40 hrs [5], this confers Palonosetron prolonged duration of action and less frequent dosing as compared to Ondansetron. Studies were done to find out for the optimal dose of Palonosetron. White PF et al did a placebo controlled randomized study to evaluate palonosetron across a range of doses for prophylaxis against PONV. 1µg/Kg and 30µg/Kg doses produced a significantly better complete response in the first 24 hours (44% p=0.004) and 45%(p=0.002) vs 19%) and a lower incidence of nausea during the same period.[5]Second study to optimise the dose of Palonosetron was done in 2008

Table 1: Demographic data of the patients

	Group I (N= 70)	Group II (N= 70)	P value
Age	41.1±15.16 yrs	43±13.86 yrs	0.444
Sex			
Males	34 (48.6%)	31 (44.3%)	
Females	36 (51.4%)	39 (55.7%)	0.611
Body weight	57.5±8.57 Kg	58.7±8.11 Kg	0.13
ASA status I,II	32, 38	32, 38	1.0
Duration	2.66±0.83 hrs	2.93±0.82 hrs	0.055

Table 2: Incidence of post operative nausea and vomiting

Nausea & Vomiting	Group I		Group II	
	Number	%	Number	%
Yes	55	78.57	17	24.29
No	15	21.43	53	75.71

Table 3: Incidence of Emetic episodes

Emetic episodes	Group I		Group II	
	Number	%	Number	%
Vomiting	43	61.43	04	5.71
No Vomiting	27	38.57	66	94.29

by Kovac AL et al. In the study palonosetron in dose of 0.025 mg, 0.05 mg and 0.075 mg was used and were compared in 546 patients undergoing laparoscopic surgery. The palonosetron 0.075mg dose was statistically superior to placebo for all end points during the first 24 hrs, including CR (complete remission), emesis, nausea rates and reduction in nausea severity. Based on these two studies minimum effective dose of palonosetron in the setting of PONV is 0.075mg [13]. Present study was done to compare the efficacy of palonosetron 0.075mg and ondansetron 8mg administered 5 min prior to the induction of anaesthesia in the patients undergoing abdominal surgeries under general anaesthesia. The study was designed in such a way as to control all the factors that can interfere with the interpretation of the results of the study with a standardized anaesthesia regimen like (avoiding use of propofol for induction, avoiding use of tramadol and opoids for post operative analgesia). The duration of anaesthesia, surgery and the anaesthetic used were similar in both the groups. Therefore it is likely that the difference in the incidence of emetic episodes in both the groups were attributable to Ondansetron and Palonosetron. In the study both the groups were comparable with respect to age, sex, body weight, ASA grading and duration of the surgery (Table 1). The duration of anaesthesia and surgery has a bearing on post operative nausea and vomiting as prolonged duration of surgery with frequent bowel handling will increase the incidence of post operative nausea and vomiting, hence increasing the requirement of antiemetic. In the study it was found that the incidence of PONV was 79% in Ondansetron group and 24% in Palonosetron group (P value = <0.001). The results were both clinically and statistically significant (Table 2). The study confirms the finding that Palonosetron at a dose of 0.075 mg improves the control of nausea and vomiting. Control over nausea and vomiting is even seen to extend over second and third day, an effect that may be most marked after major operations requiring inpatient stay. From the study we can also say that Palonosetron 0.075mg reduces the severity of delayed nausea, which is particularly relevant in day surgery population, in whom it is difficult to identify those at risk of post discharge PONV and for whom early return to normal activities is important. From the study it was also found that the incidence of emetic episodes were 6% in Paolnosetron group and 61% in Ondansetron group (p value = <0.001), in 24 hrs post operative period in the patients undergoing abdominal surgeries under general anaesthesia (Table 3). The results were both clinically and statistically significant. In the study it was noticed that incidence of vomiting was high in the Ondansetron group mainly between 3-6 hours. This is mainly due to its relative short life of 3.5 to 5 hrs. In the patients who received Palonosetron, the incidence of vomiting was less because it has longer duration of action of 40 hrs. Both Palonosetron and Ondansetron has non serious adverse effects like short duration head ache, constipation, dizziness and prolongation of QTc interval. But no side effects were observed in patients of both the groups in our study.

Limitation in the present study are; 1. We did not include in the study the phase of the menstrual cycle of the female patients. All antiemetic have effect on the incidence of vomiting on different phases of the menstrual cycle, with the studies showing the incidence of vomiting less in women in postovulatory phase. 2. We did not include in our study the patients undergoing ear surgeries and strabismus surgeries who are also at high risk of having PONV.

Scope of the study: Seeing the results, study can be done on patients undergoing day care surgeries where single dose of palonosetron is highly effective for PONV. On the basis of promising results for combination therapy with Palonosetron in CINV, similar combination studies can be done for prevention of PONV in surgical patients. Combination of Palonosetron with Dexamethasone is very effective in prevention of nausea, and when neurokinin–1 antagonists such as Aprepitant is added to the above combination, incidence of vomiting is still further reduced to low levels even in high risk patients. So from the results of the present study and from the results of other cited studies, it can be concluded that Palonosetron is more effective than Ondansetron to prevent post operative nausea and vomiting in patients undergoing abdominal surgeries under general anaesthesia.

References

1. Barash PG. Textbook of clinical anaesthesia; 6th South Asian edn. Wolters Kluwer publishers New Delhi; 2010.
2. Kappor PA. The big Little problem; Anaesth. Analag 1991;73:243-5.
3. Muchatuta NA, Paech MJ. Management of postoperative nausea & vomiting; focus on palonosetron; Therapeutics and Clinical Risk Management 2009:5 21-34.
4. Wang JJ, Ho TS, Liu SH, Ho MC. Prophylactic antiemetic effect of dexamethasone in women undergoing ambulatory laproscopic surgery Br. J. Anaesth.; 2000;84(4):459-62.

5. Jimenez, Jimenz FJ, Garcia-Ruiz PJ, Molina JA. Drug induced movement disorders; Drug Safety 1997;16: 180-204.
6. Watch MF, White PF. Post operative nausea and vomiting; Its etiology treatment and prevention; Anaesthesilogy 1992;77:162-84.
7. Mckenzie R, Kovoc A, O'Connor T. Comparison of Ondansetron versus placebo to prevent postoperative nausea and vomiting in women undergoing gynaecological surgery;Anaesthesiology1993;78:21-8.
8. Gold BS, Kitz Ds, Lecky JA, Neuhans JH. Unanticipated admission to the hospital following ambulatory surgery. JAMA 1989;262; 3008-10.
9. Lerman J. Surgical and patient factors involved in post operative nausea and vomiting. British Journal of Anaesthesia 1992;69:245-325.
10. Paxton DL, Mckay CA, Mirakin KR. Prevention of nausea and vomiting after day care gynaecological laproscopy. Anaesthesia 1995;50:403-06.
11. Craft TM, Upton PM. Anaesthesia clinical aspects. 3rd Edition 2001;279-81.
12. Yoshitaka F, Hiroyoshi T, Hideori T. Optimal antiemetic dose of granisetron for prevention of post operative nausea and vomiting. Can J Anaesthesia 1994;41(9):794-7
13. Kovac AL, Eberhart L, Kotarski J. A Randomized, double blind study to evaluate the efficacy and safety of three different doses of palonosetron versus placebo in preventing postoperative nausea and vomiting over a 72 hrs period; Anesth Analg. 2008 Aug;107(2):439-44
14. Aapro MS, Genolier CD. Palonosetron as an anti-emetic and anti-nausea agent in oncology; Therapeutics & clinical risk management 2007;3(6): 1009-1020.

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An Observational Study to Compare Recovery of Elderly Patients from General Anaesthesia with Sevoflurane or Desflurane

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Abstract

Background: The clinical study was undertaken to compare the recovery of elderly patients from general anaesthesia with sevoflurane or desflurane with reference to spontaneous eye opening, obeying verbal commands, recall of name, squeezing fingers, time to extubation and orientation and Modified Aldrette Score.

Material and Method: Study was conducted on 60 patients of either sex, belonging to ASA I, II and III posted for elective surgeries. Age of the patients were above 60 years and were divided into groups of 30 each (group D and group S).All patients were pre medicated with inj. glycopyrrolate 0.004 mg/kg i.v, inj. fentanyl 1microgram/kg i.v., inj ondansetron 0.1 mg/kg i.v., inj.ranitidine 50mg i.v. After preoxygenation with 100% for 5 minutes, patients were induced with injection propofol 1-2 mg/kg i.v. and intubation facilitated with injection succinyl choline 1.5mg/kg i.v. Anaesthesia was maintained with either desflurane (group D) or sevoflurane (group S) in combination with N_2O 50% in O_2 50% . All patients were mechanically ventilated. Both group received Fresh gas Flow of 4 lit/min for first 10 mins. After 10 mins FGF was reduced to 2 lit/min. with desflurane and sevoflurane adjusted so as to maintain hemodynamic parameter within 20% of baseline values or according to clinical parameters. Muscle relaxation was maintained by using injection atracurium i.v (loading dose) and top up doses were guided by PNS. Desflurane/Sevoflurane and N_2O were turned off after the last skin suture. Neuromuscular blockade was reversed by inj. neostigmine 0.05 mg/kg and inj. glycopyrrolate 0.008 mg/kg and patients were extubated . Time to extubation was recorded as time from discontinuation of inhalation to extubation. Pulse rate (P.R), systolic blood pressure (SBP), Diastolic blood pressure (D.B.P), oxygen saturation (SpO_2), electrocardiography (ECG) were observed throughout the surgery at every 10 mins. Recovery was assessed in the PACU by using the Modified Alderete Score every 5 minutes for intial 10 minutes and then every 10 minutes till 60 minutes.

Result: The recovery parameters of spontaneous eye opening, obeying verbal commands, recall of name, squeezing of fingers, time to extubation and place of stay were significantly shorter in patients of Desflurane group as compared to patients of Sevoflurane group ($p<0.05$). Patients given desflurane achieved Modified Aldrete Score of 9 significantly faster than patients given sevoflurane.

Conclusion: We concluded that although sevoflurane and desflurane provided similar intra-operative conditions, desflurane provided more rapid recovery and the return of cognitive functions in the early post operative period.

Keywords: Desflurane; Sevoflurane; Elderly.

Introduction

With the development of society to the aging, more and more elderly people face Surgery and anaesthesia related problems. In elderly patients, due to organ degeneration; heart, lung, brain and reduced reserve function of important organs; have poor tolerance to anaesthetics.

At the same time elderly patients with declined liver and kidney function, drug clearance cycle is extended accordingly. Therefore, the choice of anaesthesia maintaining drugs in elderly patients has the top priority [1].

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Geriatric patients are those who are above 65 years of age and account for a large Proportion of population. Due to the development in medical treatment, the life expectancy of the people is continuously on the rise, resulting in the rise of elderly population [2]. But, age related diseases, like age-related degeneration in respiratory and cardiovascular function and other associated systemic diseases are still prominent.

Therefore, such patients are at risk of having complications due to anaesthesia [3].

Postoperative cognitive dysfunction (POCD) is defined as postoperative psychomotor disorder [4]. Anaesthetic agents and physiological changes resulting from it are associated with psychomotor function disorder [5,6]. This POCD was seen in 25.8% of the elderly within 1 week of surgery and after 3 months of surgery in 99% of the cases.Postoperative cognition function are affected by anaesthetic drug and their residual effects can alter the central nervous system [7,8,9]. The knowledge of the factors that cause the cognitive deterioration and analysis of the methods of evaluation and treatment will help if effective measures are taken to reduce the frequency and severity of this condition [10].

More rapid recovery from prolonged anaesthesia may be an advantage in the elderly in whom cognitive impairment (e.g. delirium, confusion) is a problem during recovery [11].

Eger and colleague speculated that the lower partition coefficients of desflurane favour sits more rapid elimination from the body and additional factors such as effects of degradation products of sevoflurane might delay recovery from sevoflurane after longer anaesthesia [12].

Chen and colleagues1 found that compared with sevoflurane, desflurane gave a faster emergence from anaesthesia and less time in the PACU in elderly patients undergoing total knee or hip replacement. However, recovery of cognitive function, measured by the Mini Mental State test, was no different between desflurane and sevoflurane [13].

Discharging patients from Post Anaesthesia Care Unit (PACU) depends upon Modified Aldrete Score [14]. It consists of 6 factors taken into account by the clinician that checks whether the patient can be released or not. There are 6 questions, each with 3 choices that are given different scores. The score values range from 0 to 12, 0 being the patient is closest to the anesthesia state, 9 being the guideline to discharge and the closer the score gets to 12, the closest to all anesthetic being worn off from the system.

Hence, we decided to carry out the present observational and interventional study to compare the recovery profile of sevoflurane and desflurane in elderly patients undergoing surgery under general anaesthesia using Modified Aldrete score monitoring scale.

Methods

After approval from institutional ethical committee, this observational and interventional study was conducted at S.B.K.S. Medical institute and research centre over a period of one year and six months. Primary aim of our study was to observe recovery profile in elderly patients undergoing general anaesthesia with desflurane and sevoflurane using modified aldrete score.

We selected patients who were ready to give informed written consent, aged 60 years and above of both genders, belonging to ASA Grade I, II and III, posted for planned surgeries under general anaesthesia expected to last more than1 hour. Patients with severely compromised respiratory diseases/ cardiac disease/renal and hepatic dysfunction, Morbid obesity, Family history of Malignant Hyperthermia, history of exposure to general anaesthesia within last one week were excluded from the study.

After obtaining informed and written consent from patients, patients were randomly allocated by "chit method" into 2 groups of 30 each. All the patients in group D received desflurane and group S received sevoflurane as an inhalational agent. Pre-anaesthetic checkup comprising of detailed history and systemic examination, thorough airway examination and investigations (Complete blood count , Random blood sugar, Serum electrolytes, Coagulation profile, Liver and renal function tests, Chest x-ray, Electro-cardiography, 2-D echo if indicated) was carried out. All the Patients were kept nil by mouth foratleast 6 hours prior to surgery and were given tablet Alprazolam 0.25mg orally on the night before surgery. After taking patient inside operation theatre baseline vital parameters (Heart rate, NIBP, SpO_2, ECG were recorded. After securing 20 G intravenous catheter, injection (inj.) Ringer Lactate was started. Patients were Premedicated with inj. glycopyrrolate 0.004 mg/kg, inj. fentanyl 1microgram/kg, inj. Ondansetron 0.1 mg/kg and inj.ranitidine 50mg intravenously (i.v). After preoxygenation with 100% for 5 minutes, patients were induced with inj. propofol 1-2 mg/kg i.v (till loss of eye-lash reflex) and intubation was facilitated with inj. succinyl choline 1.5mg/kg i.v. After intubation, Anaesthesia was maintained with either desflurane (group D) or sevoflurane (group S)

in combination with N_2O 50% in O_2 50%. All patients were mechanically ventilated.

Both the groups received Fresh gas Flow (FGF) of 4 litre/minute for first 10 mins, with desflurane dial concentration 3-6% in group D and sevoflurane dial concentration 1-3% in group S. After 10 minutes, FGF was reduced to 2 litre/minute with desflurane and sevoflurane adjusted so as to maintain hemodynamic parameter within 20% of baseline values or according to clinical parameters. Muscle relaxation was maintained by using inj. Atracurium 0.5 mg/kg i.v (loading dose) and 0.1 mg/kg incremental dose as guided by Peripheral nerve stimulator. All patients were mechanically ventilated by anaesthesia work-station. N_2O and inhalational agent were turned off after the last skin suture. Neuromuscular blockade was reversed with inj. Neostigmine 0.05 mg/kg and inj. Glycopyrrolate 0.008 mg/kg i.v., once spontaneous respiration recovered and patients were extubated after fulfilment of extubation criteria. After the discontinuation of inhalation anaesthetics, recovery was assessed with Spontaneous eye opening, obeying verbal commands, recall of name, squeezing fingers, time to extubation and orientation. Time to extubation was recorded as time from discontinuation of inhalational agent to extubation. Intermediate recovery was assessed in PACU (post anaesthesia care unit) by using the modified alderete score every 5 minutes for initial 10 minutes and then every 10 minutes till 60 minutes. Heart rate, NIBP, SpO_2, ECG were observed throughout the surgery. Patients were observed for side effects like nausea, vomiting, headache and treated accordingly.

Statistical Analysis

Keeping the power of study as 80% and confidence limit at 95%, the minimum sample size calculated by using the formula ($n= (Z\alpha/2+Z\beta)2 * (p1(1-p1)+p2(1-p2)) / (p1-p2)2$) came around 30 in each group. Hence, we studied total 60 patients randomly allocated into two groups of 30 each. Quantitative data was presented with the help of Mean and Standard deviation. Qualitative data was presented with the help of frequency and percentage table.

Association among the study groups is assessed with the help of Chi-Square test. 'p' value less than 0.05 is taken as significant. Appropriate statistical software; MS Excel, SPSS ver. 20 was used for statistical analysis. Graphical representation was prepared in MSExcel 2010.

Observation and Results

In our study, demographic data (age, gender, ASA status) were statistically comparable to each other in both groups (Table 1). Duration of surgery and anaesthesia were also comparable between both the groups (Table 2). Immediate recovery parameters including spontaneous eye opening, obeying verbal commands, recall of name, squeezing of fingers, time to extubation and orientation to place of stay were significantly shorter in patients of Group D compared to Group S (p value <0.05) (Table 3).

Intermediate recovery was assessed using modified aldrete score at 5, 10, 20, 30, 40, 50 and 60 minutes after arrival to PACU. Patients in group D achieved modified aldrete score of 9 or more at 5minutes after reaching PACU while in group S score of 9 or more was achieved at 20 minutes after reaching PACU. Modified aldrete score was significantly higher in group D at 5, 10 and 20 minutes. (p value <0.05) (Table 4). After 20 minutes modified aldrete score was comparable between two groups. Hemodynamic parameters (heart rate, SBP, DBP and MAP and SpO_2

Table 1: Demographic data

	Group D	Group S	p value
Age (Y)	70.33 ± 7.56	71.96 ± 6.85	>0.05
Gender (M/F)	16/14	18/12	>0.05
ASA grade (I/II/III)	14/9/7	12/10/8	>0.05

Y-Years M-Male F- Female, Age presented as mean±SD
Gender and ASA grade presented as number of patients

Table 2: Duration of surgery and anaesthesia

	Group D	Group S	p value
Duration of surgery (m)	62.32±11.78	64.98±12.26	0.4
Duration of Anesthesia (m)	81.14±12.24	82.34±13.47	0.71

m - minutes

were comparable between both groups throughout the study (graph 1 and 2). Total 3 patients in group D had drowsiness in comparison with 6 patients in group S. Nausea/vomiting was not seen in both groups. Headache was seen in 1 and 2 patients in group D and group S respectively. Although the incidence of side effects was more in Group S, statistically there was no significant difference between the two groups (Table 5).

Table 3: Comparison of Recovery Parameters

Parameters	Group D	Group S	p value
Spontaneous Eye Opening	4.9±1.5	7.1±2.6	0.0002*
Obeying verbal commands	6.3±2.6	8.2±3.1	0.0127*
Recall of name	5.4±1.6	7.8±2.5	0.0001*
Squeezing Fingers	6.8±2.1	9.3±2.2	0.0001*
Time to Extubation	5.2±3.1	8.3±3.4	0.0005*
Place of Stay	5.8±1.9	8.2±2.2	0.0001*

All parameters presented in minutes as mean±SD, *p value <0.05 :statistically significant

Table 4: Comparison of Modified Aldrete Score among study groups

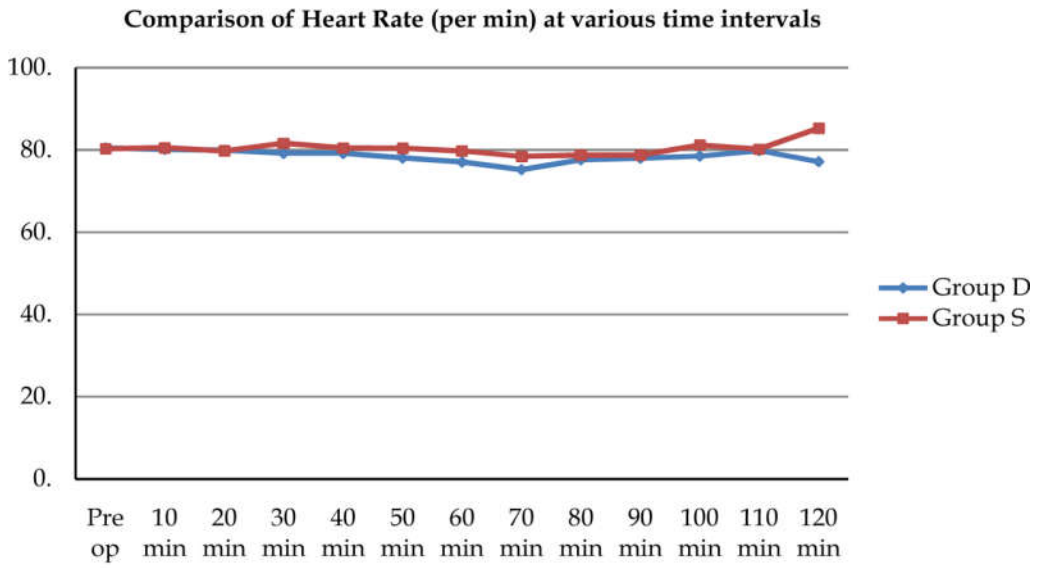
Modified Aldrete Score	Group D	Group S	p value
Arrival	8.5±0.4	8.1±0.6	0.0036*
After 5 mins	9.1±0.4	8.7±0.4	0.0003*
After 10 mins	9.3±0.2	8.9±0.4	0.0001*
After 20 mins	9.5±0.2	9.4±0.2	0.0577
After 30 mins	9.6±0.2	9.5±0.1	0.173
After 40 mins	9.6±0.2	9.5±0.1	0.173
After 50 mins	9.8±0.1	9.7±0.4	0.1892
After 60 mins	9.9±0.5	9.8±0.1	0.0359

All parameters presented as mean±SD, * p value <0.05 :statistically significant

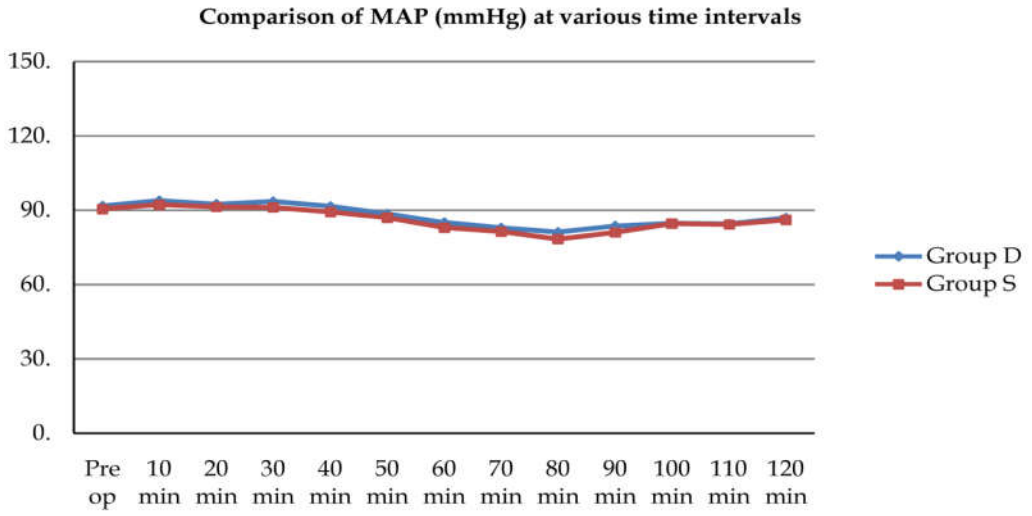
Table 5: Comparison of Side Effects among study groups

Side Effects	Group D N (%)	Group S N (%)	p value
Drowsiness	3 (10%)	6 (20%)	>0.05
Nausea/Vomiting	0 (0%)	0 (0%)	>0.05
Headache	1 (3.3%)	2 (6.7%)	>0.05

N: number of patients



Graph 1: Comparison of Heart Rate (per min) at various time intervals



Graph 2: Comparison of Mean Arterial Pressure MAP (mmHg) at various

Discussion

Due to the development in medical treatment, the life expectancy of the people is continuously on the rise, resulting in the rise of elderly population. But, age related diseases, like age-related degeneration in respiratory and cardiovascular function and other associated systemic diseases are still prominent. Therefore, such patients are at risk of having complications due to anaesthesia [3].

The solubility of desflurane compared with sevoflurane suggests more rapid recovery from desflurane anaesthesia. This could be important after prolonged anaesthesia and fast recovery may be advantageous in the elderly where slow recovery of mental function is a concern. We compared emergence from desflurane vs sevoflurane in elderly patients undergoing two or more hours of anaesthesia [15].

The present observational study was undertaken to compare the recovery profile of sevoflurane and desflurane in elderly patients undergoing surgery under general anaesthesia. The recovery parameters of spontaneous eye opening, obeying verbal commands, recall of name, squeezing of fingers, time to extubation and orientation to place of stay were significantly shorter in patients of Desflurane group as compared to patients of Sevoflurane group. Patients given desflurane achieved Modified Aldrete Score of 9 significantly faster than patients given sevoflurane.

Sevoflurane, a halogenated ether is a highly volatile anesthetic which hasfaster induction due to low blood: gas partition coefficient (blood: gas partition coefficient of 0.65 and fat: blood solubility 48 at 37°C). Desflurane is also halogenated ether, with a low solubility in blood and body tissues (blood: gas partition coefficient of 0.42 and fat: blood solubility 27 at 37°C) leads to rapid induction and recovery. Both of them have a shorter emergence times compared to the other anesthetics [16,17,18].

Jadhav PK in a study, compared postoperative cognitive function and the time to specific recovery events in elderly patients anaesthetized with sevoflurane or desflurane. Though they used MMSE for assessment of recovery profile, this study concluded that Desflurane was marginally better anesthetic agent in terms or recovery to sevoflurane [19].

Deepak TS et. al. also found similar result in their prospective study. They compared post-Operative Cognitive Functions after General Anesthesia with Sevoflurane and Desflurane in South Asian Elderly patients. The recovery parameters of spontaneous eye opening, obeying verbal commands, recall of name, squeezing of fingers, time to extubation and orientation to place of stay were significantly shorter in patients of Desflurane group as compared to patients of Sevoflurane group. Also that, patients given desflurane achieved Modified Aldrete Score of 9 significantly faster than patients given sevoflurane.

They also assessed cognitive function at 6 hour postoperatively which was comparable in both the groups. They concluded that faster early recovery was associated with desflurane in elderly patients. However, postoperative recovery of cognitive function was similar with both volatile anaesthetics [20].

Chen X et. al. found that compared with sevoflurane, desflurane gave a faster emergence from anaesthesia and less time in the PACU in elderly

patients undergoing total knee or hip replacement. However, recovery of cognitive function, measured by the Mini Mental State test, was no different between desflurane and sevoflurane in their study [13].

Ergonenc J et. al. found higher MAS with desflurane initially and concluded that desflurane provide better quality and more rapid recovery than sevoflurane [21].

Xuefeng et al compared sevoflurane and desflurane in recovery of older patients undergoing thoracoscopic lobectomy and found that desflurane can shorten extubation and recovery time and thus improve the time of recovery [1].

Heavner JE et. al. compared desflurane with sevoflurane and suggested more rapid early recovery from desflurane anaesthesia. This finding is similar to our study but in contrast to our study, intermediate recovery profile was similar with both inhalational agents in their study [15].

The pharmacokinetic properties (lower blood gas partition co-efficients 0.45 and 0.65 respectively) of desflurane and sevofluranefavours better intra-operative hemodynamics and rapid post-operative recovery.

The haemodynamic variables (pulse rate, systolic blood pressure, diastolic blood pressure, mean arterial pressure, SpO_2) were comparable in both the groups and there was no statistically significant difference. This correlates to the studies of Kaur A et. al. [22], Nathanson MH et. al. [23] and Jindal R et. al. [16].

In contrast to previous volunteer studies [24,25] in our study desflurane did not produce an increase in HR above baseline levels, nor the tachycardia which has been reported after a sudden increase in the inspired concentration of desflurane. It was observed that although the incidence of side effects was more in Sevoflurane group as compared to Desflurane group there was no significant difference between the two groups. The limitation of our study was that we did not observe for recovery of cognitive function at the time of discharge from the hospital. So, we cannot comment about the effect of desflurane and sevoflurane on cognitive function. Also that, our study patients had surgery of 1or 2 hour duration. It might get different result for longer duration of exposure to inhalational agents.

Conclusion

From our study we can conclude that desflurane has better early and intermediate recovery profile in elderely patients with stable hemodynamic parameters. This property of desfurane can help in reducing the incidence of postoperative cognitive dysfunction in elderely patients after general anaesthesia.

Conflict of Interest

There is no conflict of interest.

References

1. Xuefeng Li, Guifeng Liu, Yunpengfei Li, Huiying Li and Feng Liang. A comparative study of sevoflurane and desflurane in the recovery of older patients undergoing thoracoscopiclobectomy. BIO Web Conf. 2017 Jan 11;8:01046. International Conference on Medicine Sciences and Bioengineering 2016 (ICMSB 2016).
2. Monk TG, Price CC. Postoperative cognitive disorders. CurrOpinCrit Care. 2011;17:376-81.
3. Moller JT, Cluitmans P, Rasmussen LS, Houx P, Rasmussen H, Canet J, et al. Long-term postoperative cognitive dysfunction in the elderly ISPOCD1 study. ISPOCD investigators. International Study of Post-Operative Cognitive Dysfunction. Lancet. 1998;351: 857-61.
4. Öðün CÖ, Topal A, Duman A, Erol A, Ökesli S. Remifentanil-sevofluran-azot protoksit anestezisinde propofol ve tiyopental' un orta ve ileri Ya°taki Kadýnlardaderlenme yeve Erken Kognitif Fonksiyonlara Etkisi. J Turk Anaesth Int Care. 2002;30:209-17.
5. Hoke JF, Cunningham F, James MK, Muir KT, Hoffman WE. Comparative pharmacokinetics and pharmacodynamics of remifentanil, its principle metabolite (GR 90291) and alfentanil in dogs. J PharmacolExpTher. 1997;281(1):226-32.
6. Ucuzal M, Akyolcu N. Postoperative cognitive changes in elderly. Turk J Geriatr. 2008;11(3):119-27.
7. Wang W, Wang Y, Wu H, Lei L, Xu S, Shen X, et al. Postoperative cognitive dysfunction: current developments in mechanism and prevention. Med SciMonit. 2014;20:1908-12.
8. Davison LA, Steinhelber JC, Eger EI 2nd, Stevens WC. Psychological effects of halothane and isoflurane anesthesia. Anesthesiology. 1975;43:313-24.
9. Drummond GB. The assessment of postoperative mental function. Br J Anaesth. 1975;47:130-42.
10. Sebel PS, Hoke JF, Westmoreland C, Hug CC Jr, Muir KT, Szlam F. Histamine concentrations and hemodynamic responses after remifentanil. Anaest Analg. 1995;80(5):990-3.
11. Parikh SS, Chung F. Postoperative delirium in the elderly. Anesthesia & Analgesia; 1995;80:1223-32.
12. Eger El,II, Bowland T, Ioneuscu P, et. al. Recovery and kinetic characteristics of desflurane and

sevoflurane in volunteers after 8 h exposure, including kinetics of degradation products. Anesthesiology 1997;87:517–26.

13. Chen X, Zhao M, White PF, Li S, Tang J, Wender RH, et. al. The recovery of cognitive function after general anesthesia in elderly patients: a comparison of desflurane and sevoflurane. Anesthesia & Analgesia; 2001;93:1489-94.
14. Aldrete JA. (1995) The post-anesthesia recovery score revisited. J ClinAnesth; 7(1):89-91.
15. Heavner JE, Kaye AD, Lin BK and King T. Recovery of elderly patients from two or more hours of desflurane or sevoflurane anaesthesia.Br J Anaesth 2003;91(4):502-6.
16. Jindal R, Kumra VP, Narani KK, Sood J. Comparison of maintenance and emergence characteristics after desflurane or sevoflurane in outpatient anaesthesia. Indian J Anaesth. 2011;55(1):36-42.
17. Eberts TJ, Schmid PG. Inhaled anesthetics. In: Barash PG, Cullen BF, StoeltingRK, Cahalan MK, Stock MC, eds. Clinical Anesthesia. 6th ed. Philadelphia: Lippincott Williams and Wilkins; 2009.pp.413-443.
18. Morgan GE Jr, Mikhail MS, Murray MJ. Inhalational anesthetics. In: MorganGE Jr, Mikhail MS, Murray MJ, eds. Clinical Anesthesiology. 4th ed. NewYork: McGraw-Hill; 2006.pp.155-178.
19. Jadhav PK. A comparison of desflurane and sevoflurane in the recovery of cognitive function after general anesthesia in elderly patients. Int J Res Med Sci 2015;3(11):3278-82.
20. Deepak TS, Vadlamani S, Kumar KS, Kempegowda P. Post-Operative Cognitive Functions after General Anesthesia with Sevoflurane and Desflurane in South Asian Elderly. M.E.J. ANESTH. 2013;22(2):143-148.
21. Ergonenc J, Ergonenc T, Idin K, Uzun U, Dirik A, Gedikli G, Bican G. The recovery time of sevoflurane and desflurane and the effects of anesthesia on mental and psychomotor functions and pain. Anesth Essays Res. 2014 Sep-Dec;8:367-371.
22. Kaur A, Jain AK, Sehgal R, Sood J. Hemodynamics and early recovery characteristics of desflurane vssevoflurane in bariatric surgery. J Anaesthesiology Clin.Pharmacology. 2013;29:36-40.
23. Nathanson MH, Fredman B, Smith I, White PF. Sevoflurane versus desflurane for outpatient anesthesia: a comparison of maintenance and recovery profiles. AnesthAnalg 1995;81:1186–90.
24. Ebert TJ, Muzi M. Sympathetic hyperactivity during desflurane anesthesia in healthy volunteers. A comparison with isoflurane. Anesthesiology 1993;79:444-53.
25. Weiskopf RB, Moore MA, Eger El II, et. al. Rapid increase in desflurane concentration is associated with greater transient cardiovascular stimulation than with rapid increase in isoflurane concentration in humans. Anesthesiology 1994;80:1035-45.

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Comparitive Study of I-Gel Vs Supreme LMA in Anaesthetised Patients on Spontaneous Ventilation

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Abstract

The aim of this study is to study and compare two supraglottic airway devices I-gel and supreme laryngeal mask airway, in anaesthetised adult patients with spontaneous ventilation, with respect to Ease of insertion, Number of insertion attempts and Haemodynamic changes like heart rate, mean arterial pressure, Systolic and diastolic blood pressure.

Keywords: I-Gel; Supreme LMA; Haemodynamics; Heart Rate; Blood Pressure.

Aim of the Study

To study and compare two supraglottic airway devices I-gel and supreme laryngeal mask airway, in anaesthetised adult patients with spontaneous ventilation, with respect to

- Ease of insertion .
- Number of insertion attempts .
- Haemodynamic changes like heart rate, mean arterial pressure, Systolic and diastolic blood pressure.

Materials and Methods

The study was conducted on 60 adult patients who were scheduled for elective surgery under general anaesthesia, requiring endotracheal intubation. The approval for the study was obtained from the Institutional Ethics Committee and informed consent was obtained from all patients.

Inclusion Criteria

Patient selected for the study were:

- Patients aged between 15 -60 years
- American Society of Anaesthesiologists (ASA) grade I-II
- Mallampatti (MP) grade 1 and 2
- Body Mass Index (BMI) between 20 -25kg/m^2
- Scheduled for elective surgeries

Exclusion Criteria

- Age <15 years and > 60 years
- ASA III and IV
- MP 3 and 4
- Patients having any abnormality of the neck, anticipated difficult airway
- Mouth opening ≤ 2 cm
- Upper respiratory tract infections

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- History of obstructive sleep apnea
- Obese patients with BMI >28kg/m^2
- Patients with increased risk of aspiration
- Duration of surgery >1hr.

They were randomly allocated into 2 groups. i-gel and supreme LMA group with 30 patients.

Methodology

Procedure

The patients will be divided into 2 groups, of 30 each, in a random, single blinded manner. A detailed medical history, complete physical examination and routine investigations will be done for all the patients. IV line will be secured, the patients will be premedicated with Inj Metaclopramide 10 mg. i .v., Inj Glycopyrolate 0.2 mg, Inj Fentanyl 2mcg/kg and Inj. Midazolam 0.05mg/kg i.v just before induction. Monitoring of pulse, NIBP, ECG will be done. Baseline values of HR and MAP will be recorded. After preoxygenation for 3 minutes, anaesthesia will be induced with Propofol 2 mg/kg i.v. Induction of anaesthesia will be confirmed by loss of verbal contact with the patient, loss of eyelash reflex and relaxation of the jaw. If coughing, gagging or body movement occurred during insertion, a further dose of Propofol 0.5 mg/kg will be given to achieve an adequate depth of anaesthesia.

The size of the device is decided by anaesthetist based on patient's body weight and manufacturer's recommendation, size 3 for patients weighing between 30-50 kgs, size 4 for patients between 50 -90 kgs. For Supreme-LMA, size 3 for patients 30 to 50 kg, size 4 for patients 50 to 70 kg will be used as per manufacturer's recommendation.

The following parameters will be measured.

- Heart rate, mean arterial pressure, Systolic and diastolic blood pressure. at baseline, after insertion of device, during surgery and at the end of surgery after removal of device.
- Number of insertion attempts

At the end of the operation, anaesthetic agents will be discontinued, allowing smooth recovery of consciousness. The device will be removed after the patient regains consciousness spontaneously and responds to verbal command to open the eyes.

If it is not possible to insert the device or ventilate through it, two more attempts of insertion will be allowed. If placements had failed after three attempts, the case will be excluded from the study and the patient will be intubated and this case will be considered as a failed attempt.

After securing the device, spontaneous ventilation will be maintained using O_2 (33%)+N_2O (66%)+ intermittent Inj. Propofol. Ventilation will be judged to be optimal if there is adequate chest expansion and stable oxygenation, SpO_2 not less than 95%.

Results

Among the total cases, 56% of the cases were males and 44% were females in i Gel group. In the supreme LMA group, 53% of the cases were males and 47% were females (Table 1).

It is evident that both the groups had a majority of males. With the P Value being > 0.05, both the groups are statistically insignificant with regard to gender.

Among the total cases, In i Gel group 23% belong to the age group 1 5-30 years, 43% belong to 31-45

Table 1: Gender

Gender	I Gel	%	Supreme LMA	%	P value
Male	17	56	16	53	
Female	13	44	14	47	0.801
Total	30	100	30	100	

Table 2: Age

Age (in years)	I Gel	%	Supreme LMA	%	P value
15 – 30	7	23	6	20	
31 – 45	13	43	14	47	
46 – 60	10	33	10	33	
Total	30	100	30	100	0.541
Mean	37.90	-	38.47	-	-
SD	12.32	-	11.60	-	-

Table 3: BMI

BMI (kg/m²)	I Gel	%	Supreme LMA	%	P Value
< 20	13	43	14	47	
20 - 25	17	57	16	53	
Total	30	100	30	100	0.359
Mean	22.47		23.12		
SD	6.49		6.12		

Table 4: ASA Classification

	I Gel	%	Supreme LMA	%	P Value
ASA I	22	73	15	50	
ASA II	8	27	15	50	
Total	30	100	30	1 00	0.539

Table 5: MPC Classification

MPC	I Gel	%	Supreme LMA	%	P Value
MPC I	15	50	14	47	
MPC II	15	50	16	53	0.145
Total	30	100	30	1 00	

Table 6: Type of Surgeries

Type of Surgeries	I Gel	%	Supreme LMA	%	P value
Kwire	7	23	6	20	
Incision and drainage	10	33	12	40	
Fibroadenoma breast	5	17	5	17	
Puerperal sterilization	8	27	7	23	0.09
Total	30	100	30	100	

Table 7: No of Attempts

No of Attempts	I Gel	%	Supreme	%	P Value
1st attempt	21	70	LMA	77	
2nd attempt	9	30	23	23	0.601
Total	30	100	7	100	P Value

Table 8: Heart Rate–Post Intub Ation

Heart Rate	I G el	%	Supreme	%	P Value
70 – 80	8	27	LMA	23	
81 – 90	1 4	46	7	50	
91 - 100	8	27	15	27	
Total	3 0	100	8	10 0	0.021
Mean	86. 27	-	30	-	
S.D.	3 .4 7	-	84.15	-	

years and 33% belongg to 46–60 years. In Supreme L MA group, 20% belong to the age group 15–30 years, 40% belong to 31–45 years and 40% belong to 46–60 years.

It is evident from the table that i n both the groups the majo rity of the age group who under went minor surgeries lies between 31–45years .

With the P Value being > 0.05, both the groups are statistically insi gnificant with regard to age.

In the present study, patients in which iGel was used the BMI lesser than 20 kg/m² was seen in 43% and percentage of patients with BMI between 20 – 25 kg/m² was 57%. In the supreme LMA cases, the BMI lesser than 20 kg/m² was seen in 47% and 53% of the patients had BMI between 20–25 kg/m².

Patients with BMI greater than 25 kg/m² have been excluded from the study.

With the P Value being > 0.05, both the groups are statistically insignificant with regard to BMI.

The percen tage of patients who were asse ssed under ASA I in the i Gel group were 73% and 27% were assessed under ASA II classification. Wher eas in the Supreme LMA group, the patients assessed ac cording to ASA classificati on I and II were equally distribu ted.

With the P Va lue being > 0.05, both the groups are statistically insi gnificant with regard to ASA Classification.

With regar d to the MPC Classification, the percentage of patients asses sed under MPC I and MPC II w as equal in the i Gel group. In the Supreme LMA group, 4 7% of the patients were as sessed under MPC I and 53% were assessed under MPC II.

With the P Value being >0.05, both the groups are statistically insignificant with regard to MPC classification.

Incision and dr ainage (I & D), Fibroadenoma breast and Puerperal sterili zation .

It is signif icant from the above table that i ncision and drainage was do ne in majority of the patients. 33% in the I Gel group and 40% in Supreme LMA group.

With the P Value being > 0.05, both the groups are statistically ins ignificant with regard to th e type of surgeries.

In the present study, iGel was placed in the first attempt 70% (n - 21) and 30% (n -9) in the second attempt. In the Supreme LMA group, the instrument was placed in the first attempt in 77% (n -23) and placed in the second attempt in 23% of the cases.

With the P Value being > 0.05, both the groups are statistically insignificant with regard to the number of attempts in inserting the instrument for securing the airway.

In the present study, 27% of the patient s had heart rate between 70 – 80 beats per min(bpm), 46% of the cases were between 81–90 bpm and 27% of the cases were between 91–100 bpm among the i Gel cases.

With regard to the cases used with Suprem e LMA, 23% of the patient s had the heart rate between 70–80 bpm, 50% of the cas es were between 81–90 bpm a nd 27% of the cases were between 91–100 bpm.

With the P Value being < 0.05, there was a statistical significance wit h regard to heart rate post intu bation with iGel and suprem e LMA. Also it is evident that i Gel group is better compar ed to the supreme LMA group .

In this study, 27% of the patients had the systolic blood pressure between 110–120, 40% of the patients had between 121-130 and 33% of the patients had between 131–140 among the i Gel group.

With regard to the patients used with Supreme LMA, 22% of the patients had the systolic blood pressure between 110 – 120, 42% of the patients had between 121-130 and 36% of the patients had between 131–140.

It is evident that majority of the patients included in this study had systolic blood pressure ranging between 121-130.

In this stu dy, 23% of the patients had t he systolic blood pressure pre intubation between 110 – 120, 33% of the patients had between 121-130 and 44% of the patients had between 131–140 among the i Gel group.

With regard to the patients used with Sup reme LMA, 30% of the patients had the systolic bloo d pressure between 110–120, 37% of the patients haad between 121-130 and 33% of the patients had between 131–140.

Table 9: Systolic Blood Pressure

SBP (mm/Hg)	I Gel	%	Supreme LMA	%
110 – 120	8	27	7	22
121 – 130	12	40	13	42
131 – 140	10	33	10	36
Total	30	100	30	100
Mean	124.41		123.52	
SD	4.25		4.62	

Table 10: Systolic blood press URE – pre intubation

SBP	I Gel	%	Supreme	%	P Value
(mm/Hg)	7	23	LMA	30	
110 – 120	10	33	9	37	
121 – 130	13	44	11	33	0.584
131 – 140	30	100	10	100	
Total	125.41	-	30	-	
Mean	3.14	-	123.52	-	

It is evide nt that majority of the patients included in this study had systolic blood pressure – pre intubation ranging between 121–130.

With the P Value being > 0.05, there is n o statistical significance wit h regard to systolic blood pres sure – pre intubation.

In this study, 23% of the patients had the systolic blood pressure Post intubation between 110–120, 33% of the patients had between 121-130 and 44% of the patients had between 131–140 among the i Gel group.

With regard to the patients used with Supreme LMA, 30% of the patients had the systolic blood pressure between 110–120, 37% of the patients had between 121-130 and 33% of the patients had between 131–140.

It is evide nt that majority of the patients included in this study had systolic blood pressure–post intubation ranging between 121–130.

With the P Value being < 0.05, there is a statistical significance wit h regard to systolic blood pres sure – post intubation.

In this study, 40% of the cases had the Diastolic blood pressure between 71-80, 40% of the cases hadbetween 81-90 and 20% of the cases had between 91–100 among the i Gel group. With regard to the patients used with Supreme LMA, 37% of the cases had the diastolic blood pressure between 71-80, 40% of the patients had between 81-90 and 23% of the patients had between 91-100. It is significant that majority of the patients included in the study had diastolic blood pressure 81-90.

In this stu dy, 43% of the cases had the Diastolic blood pressure p re intubation between 71-80, 37% of the cases had betw een 81-90 and 20% of the cases had between 91–10 0 among the i Gel group. With re gard to the patients used wi th Supreme LMA, 40% of the ca ses had the diastolic blood pressure between 71-80, 37% of the patients had bet ween 81-90 and 23% of the patients had between 91-100.

It is significant that majority of the patients included in the study ha d diastolic blood Pressure pre intubation 71-80.

With the P value being > 0.05, there was a statistical significance wit h regard to diastolic blood p ressure pre intubation. Also it is evident that i Gel group is better compared to thee supreme LMA group based on the mean calculations.

In this study, 37% of the cases had the Diastolic blood pressure post intubation between 71 - 80, 40% of the cases had between 81 - 90 and 20% of the cases had between 91–100 among the i Gel group. With regard to the patients used with Supreme LMA, 33%

Table 11: Systolic blood pressure – post intubation

SBP (mm/Hg)	I Gel	%	Supreme LMA	%	P Value
110 – 120	8	23	9	30	
121 –130	11	33	1 2	37	
131 – 140	13	44	8	33	
Total	30	100	30	100	0.022
Mean	126.51		127 .25		
SD	3.46		3.62		

Table 12: Diastolic blood pressure

DBP	I Gel	%	Supreme LMA	%
71 – 80	12	40	11	37
81 – 90	12	40	12	40
91 - 100	6	20	7	23
Total	30	100	30	100
Mean	83.41	-	85.52	-
SD	4.25	-	4.62	-

Table 13: Diastolic blood press ure – pre intubation

DBP	I Gel	%	Supreme	%	P Value
71 – 80	13	43	LMA	40	
81 – 90	11	37	12	37	
91 – 100	6	20	11	23	0.321
Total	30	100	7	100	
Mean	83 .41	-	30	-	
SD	4.25	-	85.52	-	

Table 14: Diastolic blood pressure–post intubation

DBP	I Gel	%	Supreme LMA	%	P Value
71 – 80	11	3 7	1 0	33	
81 – 90	12	40	12	40	
91 - 100	7	23	8	27	0.026
Total	30	100	30	100	
Mean	83.41	-	85.52	-	
SD	4.25	-	4.62	-	

Table 15: Mean arterial pressure

MAP	I Gel	%	Supreme LMA	%	P Value
71 – 80	11	37	10	33	
81 - 90	12	40	12	40	
91 - 100	7	23	8	27	0.014
Total	30	100	30	100	
Mean	84.12	-	82.52	-	
SD	10.25	-	09.67	-	

Table 16: Complications

Complications	I Gel	%	Supreme	%	P Value
Sore throat	8	27	LMA	23	
Blood stain	7	23	7	30	
Laryngospasm	6	20	9	17	
Pharyngealspasm	3	10	5	10	0.699
Mucosal injury	6	20	3	20	
Total	30	100	6	100	

of the cases had the diastolic blood pressure between 71-80, 40% of the patients had between 81-90 and 27% of the patients had between 91-100.

It is significant that majority of the patien ts included in the study had diastolic blood Pressure post intubation 81-90.

With the P Value being < 0.05, there wa s statistical significance wit h regard to diastolic blood pr essure post intubation. Also it is evident that i Gel group is better compared to thee supreme LMA group based o n the mean calculations.

In this study, 37% of the patients had the Mean arterial pressure between 71- 80, 40% of the patients were between 81-90 and 23% of the patients were between 91–100 in the i Gel group.

With regard to the patients used with Supreme LMA, 33% of the patients had the Mean Arterial Pressure between 71-80, 40% of the patients were between 81-90 and 27% of the patients were between 91-100. It is evident that majority of the patients had MAP between 81-90 in both the groups.

With the P Value being < 0.05, both the groups are statistically sig nificant with regard to me an arterial pressure. Also it is evident that i Gel grou p is better compared to thee supreme LMA group based o n the mean calculations.

Among the total cases, 23% had sore throa t, 30% had blood stain, 17% had laryngospasm, 10% had pharyngealspasm, and 20% had mucosal injury i n the i Gel group. In the Su preme LMA group, 27% had sor e throat, 30% had blood stain, 23% had laryngospasm, 20% had pharyngealspasm , and 10% had mucosal injury.

There is no statistical significance with regard to complications encountered in the placement of iGel and supreme LMA.

Discussion

The study was conducted in Sree Balaji Medical college and hospital with 60 patients. Out of which 30 patients were intubated with iGel and Supreme LMA was used in 30 patients. These supraglottic devices were used in minor procedures. The majority of the patients included in this study were in the age group of 31 to 45 years.

In our study, we found that i -Gel may be more useful than the supreme LMA for controlled ventilation and this was both statistically significant and clinically rel evant. We found that the i -Gel was slightly easier to insert compared to Supreme LMA but the clinical relevance of the difference is not

known. Moreover, time to achieve an effective airway was similar between the two devices.

The first attempt and overall insertion success rates were similar between groups. Richez et. al. [13] carried out one of the earliest studies to evaluate the I -gel. They found that insertion success rate was 97%. Insertion was easy and was performed at the first attempt in every patient. I -gel is easily and rapidly inserted, providing a reliable airway in over 90% of cases. This disagrees with other studies that have shown a high success rate with both devices. No complete failure occurred in the I -Gel group. Acott [22], assessed the use of I-gel as an airway device during general anesthesia. In accordance with our results, they reported that a single insertion attempt was required in the majority of patients and all the insertion times recorded were less than 10 seconds. Similar results were obtained in study done by Gatward et. al. [23], who evaluated size 4 I -gel airway in 100 non -paralyzed patients and found that first insertion attempt was successful in 86% of patients, the second attempt in 11% of patients and the third attempt in 3% of patients Our study has a number of limitations. First, our study was conducted in non -paralysed patients, hence our findings may be less applicable to paralysed pati ents. However, there is indirect evidence from mucosal pressure studies that pharyngeal muscle tone is similar in paralysed and non-paralysed patients. Second, both devices were inserted by anaesthesiologist. Therefore, our results may not be applicable to inexperienced users.

Jindal et. al. [21] reported hemodynamic stability with both LMA and I-gel devices, with no statistically significant difference between both devices, whi ch is inconsistent with our findings. In our study, there is change in heart rate, systolic and diastolic blood pressure and mean arterial pressure while inserting the supreme LMA as compared to i-gel. One of the most important parameters to be compared between both supraglottic devices was postoperative complications. It was estimated that difference between S-LMA and I-gel regarding postoperative complications was not statistically significant except nausea and vomiting which was significantly higher in S-LMA due to high incidence of gastric insufflation. Consistent with our results, no major complications associated with I -gel have been described to date. Protection against aspiration is probably comparable with LMA family. Minor complications like sore throat, sor tongue were reported.

During maintenance of anaesthesia the airway was clear throughout the operation for most of the cases . One patient developed mild laryngospasm and the other patient had sore throat. No conclusions can be drawn about the incidence of these complications due to the small numbers involved. There was minimal blood-staining with both the devices. Postoperative sore throat was also similar to both supraglottic airway devices. There are some limitations of the present study. Firstly, we studied only low risk patients assessed under ASA I and II who had normal airways, secondly not obese.

Conclusion

In conclusion, both LMA and I -Gel cause significant alteration in the hemodynamic status of the patients, and SpO_2. The postoperative complications are significantly different among both LMA and I -Gel patients. Insertion of I-Gel is significantly easier and more rapid than insertion of LMA. Leak pressure is significantly higher with I -gel than with LMA and thus incidence of gastric insufflation is significantly lower with I -gel.

References

1 . Peppard SB, Dickens JH. Laryngeal injury following short term. Ann Otol Rhinol Laryngol, 1983.pp.327-30. [PubMed: 688183].

2. Jayashree S. Laryngeal mask airway and its variants. Indian J Anaesth, 2005;49:275-80.

3. Asai T, Murao K, Shingu K. Efficacy of the laryngeal tube during intermittent positive pressure. Anaesthesia, 2000.pp.1099-102. [PubMed: 11069337].

4. Levitan RM, Kinkle WC. Initial anatomic investigations of the IgeL airway. A novel supraglottic airway without inflatable cuff. Initial anatomic investigations of the Igel. Anaesthesia, 2005.pp.1022-6. [PubMed: 16179048].

5. Practice guidelines for management of the difficult airway. An updated report by the American Society of Anesthesiologists Task Force on Management of the Difficult Airway. Anesthesiology. 2003. pp.1269-1277.

6. Shorten GD, Opie NJ, Graziotti P, et al. Assessment of upper airway anatomy in awake, sedated, and anesthetised patients using magnetic resonance imaging. Anaesth Intensive Care. 1994.p.165-169.

7. Williams PJ, Bailey PM. Comparison of reinforced laryngeal mask airway and tracheal intubation for adenotonsillectomy. Br J Anaesth, 1993.pp.30-33.

8. McClune S, Regain M, Moore. Laryngeal mask airway for caesarean section. Anaesthesia. 1990.pp.227-228.

9. Nanji GM, Maltby JR. Vomiting and aspiration pneumonitis with the laryngeal mask airway. Can J Anaesth, 1992;39:446-447.

10. Wharton NM, Gibbison B, Gabbott D, Haslam GM, Cook TM. I-gel insertion by novices in manikins and patients. Anaesthesia, 2008;63:991-5.

11. Gatward JJ, Cook TM, Seller C, Simpson T, Vanek V, Handel J, Kelly F. Evaluation of the i-gel airway in 100 patients. Anaesthesia, 2008;63:1124-30.

12. Gibbison B, Cook TM, Seller C. Case series: protection from aspiration and failure of protection from aspiration with the i -gel airway. Br J Anaest, 2008;100: 415 -17.

13. Schmidbauer W, Bercker S, Volk T, Bogusch G, Mager G, Kerner T. Oesophageal seal of the novel supralaryngeal airway device I-Gel in comparison with the laryngeal mask airways Classic and ProSeal using a cadaver model. Br J Anaesth, 2009;102: 135-9.

14. Verghese C, Ramaswamy B. LMA-Supreme-a new single-use LMA. With gastric access: a report on its clinical efficacy. Br J. 2008;101:405-10.

15. O'Connor CJ Jr, Stix MS. Bubble Solution Diagnoses Proseal™ Insertion into the Glottis. Anesth Analg 2002;94:1671-2.

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Comparative Study between Esmolol and Xylocard for Attenuation of Pressor Responses during Laryngoscopy and Intubation

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Abstract

Background: Cardiovascular complications are one of the most common causes of anesthesia-related morbidity and mortality.The present work was undertaken to compare the effect of lignocaine (Xylocard) with esmolol on blunting the hemodynamic responses to endotracheal intubation.

Methods: Laryngoscopy and intubation was done within 15 to 20 seconds.In group I: Inj. Lignocaine (Xylocard) i.v. was administered 3 minutes before laryngoscopy and intubation.In group II: Inj. Esmolol i.v. was administered 3 minutes before laryngoscopy and intubation. Changes in heart rate (HR), systolic blood pressure (SBP), diastolic blood pressure (DBP) and mean arterial blood pressure (MAP) were measured before induction of general anesthesia (baseline), 1, 3, and 5 min after tracheal intubation.

Results: The heart rate response between lignocaine (Xylocard) and esmolol was very significant at all times starting from 1 to 10 minutes ($p \leq 0.05$) with esmolol showing a favorable response towards attenuation of heart rate. In systolic blood pressure, Esmolol group showed a better attenuation compared to lignocaine group (Xylocard) until 3 minutes post-laryngoscopy. Attenuation of diastolic blood pressure was significant with esmolol than with lignocaine (Xylocard) group until 3 minutes ($p<0.05$). In mean arterial pressure, Esmolol caused significant attenuation of pressor response ($p<0.05$) at 1 minute and 3 minute post-laryngoscopy.

Conclusion: Esmolol is more efficient than lignocaine (Xylocard) in attenuating the sympathetic responses to laryngoscopy and intubation.Esmolol at a bolus dose of 1.5 mg/kg i.v. administered 3 minutes before laryngoscopy appears to be very effective and should be viewed as potential treatment strategy for attenuating hemodynamic changes during induction of anesthesia.

Keywords: Esmolol; Xylocard; Laryngoscopy; Intubation; Hemodynamic; Bangalore.

Introduction

Cardiovascular complications are one of the most common causes of anesthesia-related morbidity and mortality. Pressor response during laryngoscopy and endotracheal intubation has been known from years. These responses though transient, will be tolerated by normal individuals, but can be potentially harmful in those individuals with cardiovascular compromise. In patients with IHD, HTN or cerebrovascular insufficiency there is increased risk of subarachnoid haemorrhage, arrhythmias and cardiac failure in response to intubation. Laryngoscopy and tracheal intubation induces changes in circulating catecholamine levels. Norepinephrine, epinephrine and dopamine levels rise, but the rise in norepinephrine levels is consistently associated with elevation of blood pressure and heart rate [1-5].

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Perioperative myocardial infarction is a leading cause of postoperative morbidity and mortality due to hypertension and tachycardia. Such anesthesia-related deaths could be reduced by controlling the hemodynamic changes that occur due to myocardial ischemia. There is increasing evidence that the control of the heart rate and blood pressure response to endotracheal intubation is essential in preventing adverse cardiovascular outcomes, as rate pressure product (RPP) acts as an indicator of oxygen demand by the heart at the onset of ischemia, there is therefore a need for assessment in this direction as there are currently no available studies in the Indian population on the efficacy of lidocaine and esmolol in attenuating hemodynamic responses during intubation.

Many strategies have been advocated to minimize these haemodynamic adverse responses to laryngoscopy and tracheal intubation at different levels of the reflex are [6] Block of the peripheral sensory receptors and afferent input – topical application and infiltration of local anaesthetic to superior laryngeal nerve; Block of central mechanisms of integration and sensory input – Fentanyl and morphine. The present work was undertaken to compare the effect of lignocaine (Xylocard) withesmolol on blunting the hemodynamic responses to endotracheal intubation.

Material and Methods

A clinical comparative study of attenuation of sympathetic response to laryngoscopy and intubation was done in 50 patients posted for elective surgeries. Study was conducted in St. Martha's Hospital, Bangalore from 2015 to 2016. Institutional committee approved our study protocol. Informed consent was taken from enrolled patients. Patients undergoing various orthopedic, ENT, gynecological, general surgical and laparoscopic procedures were selected. The study criterion includes: Patients scheduled for elective surgeries; Age between 18 to 60 years of both the sexes; Patients with ASA grade I and II; Mallampati airway assessment of grade I and excludes: Emergency surgeries; Patients of anticipated difficult intubation; Patients with ASA grade III or higher; Patients with cardiovascular compromise; Patients on beta blockers or calcium blockers.

Presurgical Protocol

Patients were selected after thorough preanaesthetic assessment and investigations. 50 patients were randomly allocated into one of the two study groups containing 25 each.

Group I: patients received 1.5 mg/kg lignocaine intravenously 3 minutes before laryngoscopy and intubation.

Group II: patients received 1.5 mg/kg esmolol intravenously 3 minutes before laryngoscopy and intubation.

The following routine investigations done in enrolled patients: complete blood count, ESR, Random Blood Sugar, Blood urea, serum creatinine, Bleeding time and Clotting time, Urine, albumin, sugar and microscopy, X-ray chest and PA view, ECG. All the patients were visited the day before surgery and preanaesthetic counseling was done. All patients received tab Alprazolam 0.5 mg orally at night the previous day and the morning of surgery. On entering the operation theatre, pulse oximeter, non-invasive blood pressure and ECG monitor were connected. A preinduction heart rate, systolic and diastolic blood pressures were recorded, i.v. infusion of ringer lactate solution was started.

Surgical Protocol

All patients were preoxygenated with 100% oxygen for 3 minutes before induction. Induction was achieved with Inj. Thiopentone sodium 5 mg/kg i.v. given in 2.5% solution. Inj. Glycopyrrolate 0.2 mg i.v. was given along with Thiopentone.After induction of anaesthesia (loss of eyelash reflex), heart rate, systolic and diastolic blood pressures were recorded. Inj. Succinylcholine was administered at a dose of 1.5 mg/kg i.v. Laryngoscopy was done using rigid laryngoscope with Standard Macintosh blade.

Intubation was done with appropriate sized, disposable, high volume, low pressure cuffed endotracheal tube. Oral intubation was done for all surgical procedures. Laryngoscopy and intubation was done within 15 to 20 seconds. Heart rate, systolic and diastolic blood pressures were recorded at 1, 3, 5, and 10 minutes interval from the onset of laryngoscopy. In group I: Inj. Lignocaine (Xylocard) i.v. was administered 3 minutes before laryngoscopy and intubation. In group II: Inj. Esmolol i.v. was administered 3 minutes before laryngoscopy and intubation. Patients were connected to Bain's circuit and anaesthesia was maintained with oxygen (33%), nitrous oxide (67%), halothane (0.5%) and non-depolarizing muscle relaxant vecuronium bromide at a dose of 0.05 mg/kg i.v. and IPPV. Adequacy of ventilation was monitored with $ETCO_2$ and SpO_2 maintained at 99-100%. Positioning, epinephrine infiltration and surgery were withheld till the completion of recording. At the end of the surgery, reversal was done with Inj. Neostigmine 0.05 mg/kg

and Inj. Glycopyrrolate 0.01 mg/kg i.v.An observation was made related to adverse effects of drugs and anaesthesia related problems were attended to appropriately.

Statistical Analysis

All the collected data was tabulated. Statistical analysis was done by student *t*-test and *P* values were calculated. Hemodynamic variables were represented by mean±SD. The comparison between the lignocaine (Xylocard) and esmolol groups are compared using Student's Independent sample (unpaired) "t" test. The difference is considered statistically significant, whenever $p \leq 0.05$ at all-time points measured. The statistical software used for analysis was SPSS. V. 15.0.

Results

Demographic profile related to age, sex and weight was comparable in the two groups statistically ($p>0.05$). Analysis by student unpaired "t" test showed that there was no significant difference in heart rate at pre and post-induction levels between lignocaine and esmolol groups ($p=0.844$, $p=0.319$). The heart rate response between lignocaine (Xylocard) and esmolol was very significant at all times starting from 1 to 10 minutes ($p \leq 0.05$) with esmolol showing a favorable response towards attenuation of heart rate. In systolic blood pressure, Esmolol group showed a better attenuation compared to lignocaine group (Xylocard) until 3 minutes post-laryngoscopy.

At 5, 7 and 10 minutes there was no significant difference between the two groups statistically. Attenuation of diastolic blood pressure was significant with esmolol than with lignocaine (Xylocard) group until 3 minutes ($p<0.05$). In mean arterial pressure, Esmolol caused significant attenuation of pressor response ($p<0.05$) at 1 minute and 3 minute post-laryngoscopy.

Discussion

Laryngoscopy and intubation is associated with rise in heart rate, blood pressure and incidence of cardiac arrhythmias. Variations of heart rate changes decrease with increasing age. Young patients show more extreme changes [7]. Marked fluctuations in haemodynamic responses are often seen in geriatric patients [8,9]. In our study, we selected the age range of 18 to 60 years. There was no significant difference between lignocaine (Xylocard) and esmolol groups ($p>0.05$). There was no significant difference observed in sexwise distribution of the cases between lignocaine (Xylocard) and esmolol group. The most significant laryngoscopic factor influencing cardiovascular responses is found to be the duration of laryngoscopy [7]. A linear increase in heart rate and mean arterial pressure during the first 45 seconds has been observed. Further prolongation has little effect. In our study, the duration of laryngoscopy and intubation was limited to 20 seconds.Adequate care was taken to achieve the required depth of anaesthesia avoiding hypoxia and hypercarbia which can influence the haemodynamic variations.

Analysis of Heart Rate

Lignocaine (Xylocard) group, the mean heart rate and standard duration at preinduction were 79.16±5.47. After induction, there was an increase of 3.2% with the mean of 81.76±5.95. At 1 minute from the onset of laryngoscopy, the heart rate increasedto 104.64±6.93 with an increase of 32% from preinduction values. At 3 minutes, heart rate was observed to be 101.64±10.05. Subsequently, the mean heart rate decreased is 91.12±7.21 (15%) and 86.36±5.92 (9%) at 5 and 7 minutes respectively. At the end of 10 minutes, hear t rate was 81.60±4.42 which was 3% above the baseline at preinduction [Table 2].

In esmolol group, the mean preinduction heart rate in this group was 79±5.66. Post-induction heart rate increased by 4.5% to 82.6±5.9. There was a further increase by 22.8% at 1 minute post laryngoscopy with a mean value of 96.96±9.96. A small fall in heart rate was observed at 3 minutes with a mean of 95.48±10.14. Heart rate further declined from the 5^{th} minute with a mean of 89.02±6.22 and further to 83.7±5.6 and 80.32±3.96 at 7^{th} and 10^{th} minutes respectively. Analysis by student unpaired "t" test showed that there was no significant difference in heart rate at pre and post-induction levels between lignocaine and esmolol groups ($p=0.844$, $p=0.319$). The heart rate response between lignocaine (Xylocard) and esmolol was very significant at all times starting from 1 to 10 minutes ($p\leq 0.05$) with esmolol showing a favorable response towards attenuation of heart rate. Intravenous lignocaine failed to attenuate the cardiovascular responses to laryngoscopy and intubation in a study by Miller CS and Warren SJ, its efficacy was noted by others [10-3]. It is recommended to use at a dose of 1.5 to 2 mg/kg i.v. optimal time for administration is 3 minutes before laryngoscopy and intubation [12].

Analysis of Systolic Blood Pressure

Lignocaine (Xylocard) group, preinduction systolic blood pressure was 131.2±12.76. At post-induction there was only 1% fall in systolic blood pressure with a mean of 129.8±12.26. There was 15% increase in systolic blood pressure following 1 minute after laryngoscopy with a mean value of 151.84±13.75 [Table 2]. The systolic blood pressure started to decrease at 3 minutes with the mean of 149.8±15.03. It further decreased till the end of 10 minutes to 2% below the baseline systolic blood pressure with a mean value of 128.44±12.02. Esmolol group, preinduction systolic blood pressure was 129.88±11.65. At post-induction, there was a fall in systolic blood pressure by 2.3%. There was 9.5% increase in systolic blood pressure following 1 minute after laryngoscopy with a mean value of 133.8±11.3. Systolic blood pressure increased slightly with a mean of 134.32±10.02 at 3 minutes post-laryngoscopy. From there on the systolic blood pressure started to

Table 1: Type of Surgery involved

Type of Surgery	Lignocaine	Esmolol	Total
Diagnostic lap	1	2	3
Exostosis excision	-	1	1
FESS	1	2	3
Fibroadenoma excision	-	1	1
Fibroadenoma excision	1	-	1
GJ pyloroplasty	-	1	1
Hemithyroidectomy	1	1	2
Hernia repair	-	1	1
Hysterectomy	1	1	2
I and D cold abscess	-	1	1
Ileocaecal mass excision	-	1	1
Laminectomy	2	1	3
Lap appendicectomy	1	-	1
Lap cholecystectomy	1	1	2
Lap cystectomy	1	1	2
Lap mesh repair	1	-	1
Laparotomy	2	-	2
Lymph node excision	1	-	1
Mastoidectomy	3	3	6
Myringoplasty	-	1	1
ORIF & DCP	1	-	1
ORIF & plating	1	-	1
ORIF internal fixation	-	1	1
Plating & bone graft	1	-	1
Septoplasty	1	-	1
Split skin graft	-	1	1
SSG	1	-	1
Submandibular gl. Exc.	1	-	1
Tension band wiring	-	1	1
Thyroidectomy	-	1	1
TO mass excision	1	-	1
Tonsillectomy	1	1	2
Vagotomy & GJ	-	1	1
Total	25	25	50

Table 2: Comparison between Lignocaine and Esmolol group of heart rate

HR	Lignocaine			Esmolol			t value	p value
	Mean	SD	% difference	Mean	SD	% difference		
Pre-induction	79.16	5.47	-	79.00	5.66	-	0.198	0.844
Post-induction	81.76	5.95	3.2	82.60	5.90	4.5	1.007	0.319
1 minute	104.64	6.93	32	96.96	9.96	22.8	8.598	0.000
3 minutes	101.64	10.05	28	95.48	10.14	20.7	5.388	0.000
5 minutes	91.12	7.21	15	89.02	6.22	12.7	2.513	0.015
7 minutes	86.36	5.92	9	83.70	5.60	6	3.789	0.000
10 minutes	81.60	4.42	3	80.32	3.96	1.67	2.392	0.021

Table 3: Comparison between lignocaine and Esmolol group of SBP

SBP	Lignocaine			Esmolol			t value	p value
	Mean	SD	% difference	Mean	SD	% difference		
Pre-induction	131.20	12.76	-	129.88	11.65	-	0.382	0.704
Post-induction	129.80	12.26	1	125.28	11.13	-2.3	1.365	0.179
1 minute	151.84	13.75	15	133.80	11.30	9.5	5.068	0.000
3 minutes	149.80	15.03	14	134.32	10.02	8.9	4.284	0.000
5 minutes	135.68	11.40	3	132.72	9.77	2.8	0.986	0.329
7 minutes	130.72	11.76	-0.3	130.44	9.69	-0.3	0.092	0.927
10 minutes	128.44	12.02	-2	129.80	10.02	-1.1	0.435	0.666

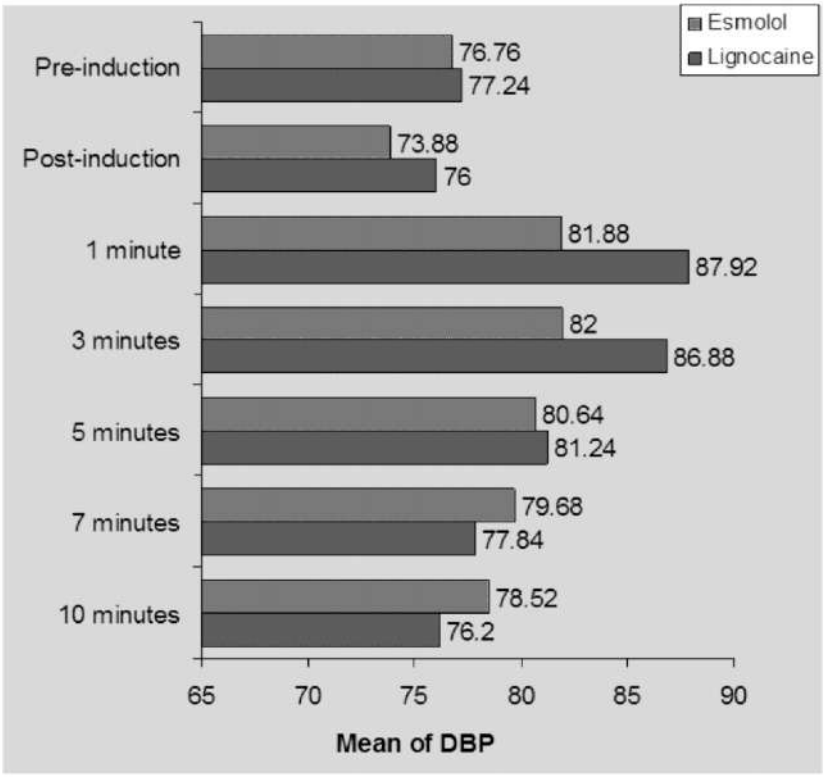

Fig. 1: Comparison between lignocaine and Esmolol group of DBP

fall with a mean of 132.72±9.77 at 5 minutes and 130.44±9.69 at 7 minutes. At 10 minutes post-laryngoscopy the systolic blood pressure almost returned to baseline with a mean value of 129.8±10.02. Esmolol group showed a better attenuation compared to lignocaine group (Xylocard) until 3 minutes post-laryngoscopy. At 5, 7 and 10 minutes there was no significant difference between the two groups statistically. Previous studies have shown that the unique pharmacokinetic behavior of esmolol makes it well suited for controlling the cardiovascular responses to tracheal intubation when used as continuous infusion technique [14-16].

A single alternative is using a bolus doses of esmolol and many studies have investigated this and concluded it to be efficacious [17-20].

Analysis of Diastolic Blood Pressure

Lignocaine (Xylocard) group, Mean preinduction diastolic blood pressure in this group was found to be 77.24±5.83. A decrease by 1.6% to 76±5.74 was noted after induction. It increased by 13% to 87.92±4.53 at 1 minute after laryngoscopy. It came down to 86.88±4.53 at 3 minutes and continued to fall at 5 and 7 minutes to 81.24±3.53 and 77.84±3.82 respectively [Figure 1]. By the end of 10 minutes the diastolic blood pressure was 76.20±4.82, a 1.3% below the baseline.

In Esmolol group,Diastolic blood pressure in this group before induction was 76.76±5.86. After induction 2.77% fall to 73.88±4.7 was noted. An increase by 9% to 8.2±4.65 at 1 minute post laryngoscopy was noted. Diastolic blood pressure started to decrease at 5 minutes to 80.64±4.88 and at 7 minutes to 79.68±4.55. At the end of 10 minutes, it was 0.5% above the baseline with a mean of

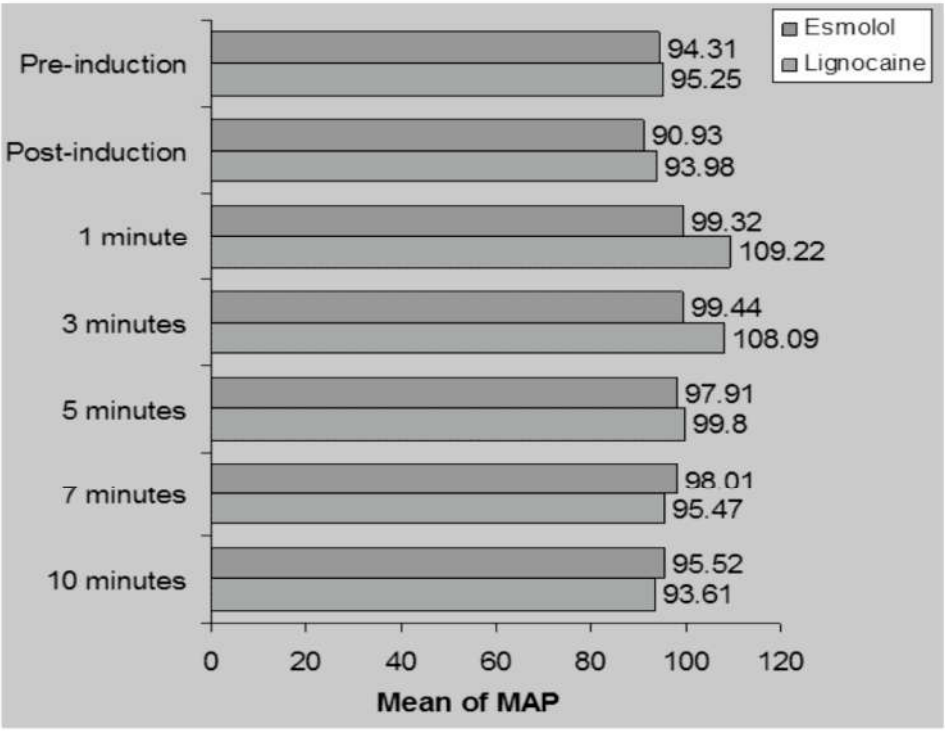

Fig. 2: Comparison between lignocaine and Esmolol group of MAP

78.52±3.99.Among the two study groups esmolol showed a better attenuation of diastolic blood pressure compared to lignocaine (Xylocard) till 3 minutes post-laryngoscopy.

Analysis of Mean Arterial Pressure

In Lignocaine (Xylocard) group, Preinduction mean value in this group was 95.25±7.08. Post-induction fall was 1.3% to 93.98±6.64. There was an increase by 14.6% to 109.22±6.26 at 1 minute and marginal fall is 108.09±7.92 at 3 minutes.

It decreased further over 5, 7 and 10 minutes [Figure 2]. At 10 minutes post-laryngoscopy, it showed a decrease of 1.7% below the baseline to 93.61±6.11. In Esmolol group, Preinduction mean arterial blood pressure was 94.31±6.24 in this group. There was an increase by 10.4% to 99.32±5.72 at 1 minute post-laryngoscopy. It started to decrease at 3 minutes to 99.44±5.28 and 5 and 7 minutes being 97.91±5.25 and 98.01±9.99 respectively. At 10 minutes, post-laryngoscopy it was 0.2% below the baseline to 95.52±4.89.

Esmolol caused significant attenuation of pressor response ($p<0.05$) at 1 minute and 3 minute post-laryngoscopy. Efficacy of intravenous lignocaine 1.5 mg/kg and two doses of esmolol 1mg/kg and 2 mg/kg for attenuating the cardiovascular responses to laryngoscopy and intubation was evaluated by Kindler et al. They found that esmolol 1 to 2 mg/kg was reliably effective in attenuating the hemodynamics response [18]. In our study, we have used 1.5 mg/kg i.v. bolus of esmolol.

Conclusion

Intravenous Lignocaine (Xylocard) and esmolol are effective agents significantly attenuates the sympathetic responses to laryngoscopy and tracheal intubation without any deleterious effect. Esmolol is more efficient than lignocaine (Xylocard) in attenuating the sympathetic responses to laryngoscopy and intubation. Esmolol at a bolus dose of 1.5 mg/kg i.v. administered 3 minutes before laryngoscopy appears to be very effective and should be viewed as potential treatment strategy for attenuating hemodynamic changes during induction of anesthesia.

References

1. Derbyshire DR, Smith G. Sympathoadrenal responses to anaesthesia and surgery. Br J Anaesth 1984;56: 725-737.

2. Shribman AJ, Smith G, Achola KJ. Cardiovascular and catecholamine responses to laryngoscopy with or without tracheal intubation. Br. J Anaesth 1987;59: 295-299.
3. Derbyshire DR, Chmielewski A, Fell D, Vater M, Achola K, Smith G. Plasma catecholamine responses to tracheal intubation. Br J Anaesth 1983;55:855-860.
4. Russell WJ, Morris RJ, Frewin DB, Drew SE. Changes in plasma catecholamine concentrations during endotracheal intubation. Br J Anaesth 1981;53:837.
5. Vincent J. Collins. Principles of Anaesthesiology, General and Regional Anaesthesia, 3rded, Vol. I and II: Philadelphia, Lea and Febiger 1993.
6. Prys Roberts C, Greene LT, Meloche R and Foex P. Studies of anaesthesia in relation to hypertension II: Haemodynamic consequences of induction and endotracheal intubation. Br J Anaesth 1971;43:531.
7. Buex MJL, Van Creel RTM, Scheck PAE, Stijnen T. Cardiovascular effects of forces applied during laryngoscopy. Anaesthesia 1995;50:17-22.
8. Splinter WM, Cervenko F. Haemodynamic responses to laryngoscopy and tracheal intubation in geriatric patients: Effects of fentanyl, lidocaine and Thiopentone. Can J Anaesth 1989;36(4):370-376.
9. Ismail S, Azam SI, Khan FA. Effect of age on haemodynamic response to tracheal intubation: A comparison of young, middle aged and elderly patients. Anaesth Intens Care 2002;30(5):608-614.
10. Robert Bedford F, John Persing A, Louis Poberskin, Albert Butler. Lidocaine or thiopental for rapid control of intracranial hypertension? Anaesth Analg 1989;59:435-447.
11. James F. Hamill, Robert Bedford F, David CW, Austin RC. Lidocaine before endotracheal intubation: Intravenous or laryngotracheal? Anaesthesiology 1981;55:578-581.
12. Stanley Tam, Frances Chung, Michael Campbell. Intravenous lignocaine: Optimal time for injection before tracheal intubation. Anaesth Analg 1987;66: 1036-1038.
13. Splinter WM, Cervenko F. Haemodynamic responses to laryngoscopy and tracheal intubation in geriatric patients: Effects of fentanyl, lidocaine and Thiopentone. Can J Anaesth 1989;36(4):370-376.
14. Menigaux C, Guignard B, Adam F, Sessler DI, Joley V, Chauvin M. Esmolol prevents movement and attenuates the BIS response to orotracheal intubation. Br J Anaesth 2002;89:857-862.
15. Orko R, Pouttu J, Ghignone M, Rosenberg PH. Effect of clonidine on haemodynamic responses to endotracheal intubation and on gastric acidity. Acta Anaesthesiol Scand 1987;31(4):325-329.
16. Menkhaus Paul G, Reeves JG, Kissin I, Michael Alvis J, Govier Ann V, Samuelson Paul N. Cardiovascular effects of esmolol in anaesthetized humans. Anaesth Analg 1985;64:327-334.
17. Singh H, Viehitvejpaisal P, Gaines GY, White PF. Comparative effects of lidocaine, esmolol and nitroglycerin in modifying the haemodynamic response to laryngoscopy and intubation. J Clin Anaesth 1995 Feb;791:5-8.
18. Feng CK, Chan KH, Liu KN, Or CH, Lee TY. A comparison of lidocaine, fentanyl and esmolol for attenuation of cardiovascular response to laryngoscopy and tracheal intubation. Acta Anaesthesiol Sin 1996 Jun;34(2):61-67.
19. Kindler CH, Schumacher DG, Schneider MC, Urwyler A. Effects of intravenous lidocaine and/or esmolol on haemodynamic responses to laryngoscopy and intubation: A double-blind controlled clinical trial. J Clin Anaesth 1996 Sept;8(6):491-496.
20. Helfman SM, Gold MI, Delisser EA, Everard A. Herrington CA. which drug prevents tachycardia and hypertension associated with tracheal intubation: Lidocaine, fentanyl or esmolol? Anaesth Analg 1991 Apr;72(4):482-486.

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Minimum Alveolar Concentration (MAC) of Desflurane for Effective Tracheal Intubation (MAC-EI)

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Abstract

Introduction: The minimum alveolar concentration (MAC) which prevents movement in response to surgical incision in 50% of patients for halothane and enflurane is less than that which prevents movement in response to laryngoscopy and tracheal intubation . Desflurane may differ from older anaesthetics in its capacity to prevent movement in response to laryngoscopy and tracheal intubation. *Aim:* To calculate the minimum alveolar concentration of desflurane for effective endo tracheal intubation.

Materials and Method: It was a prospective study conducted at Nizam's Institute of Medical Sciences, between July 2015 and September 2015. The study recruited seventy patients scheduled for general anaesthesia for an elective surgery with age ranging between 18 to 60 years of either gender with ASA physical status I and II. After giving the induction drugs, nitrous oxide in oxygen (50:50), each at 4 litres/minute with desflurane was commenced. Desflurane was started at 2% and increased by 2% every 30 sec, until patient lost consciousness, with entropy less than 60 and permitted manual ventilation. Then the dial setting was changed to achieve predetermined end-tidal desflurane concentration within the first 5 min, to start with 6% in the first patient (best guess for MAC-EI). After establishing and maintaining the target end-tidal concentration for 5 more minutes, tracheal intubation was attempted at 11th minute without neuromuscular relaxants and ±0.5% difference in the predetermined/target end-tidal desflurane concentration was allowed. Each concentration at which tracheal intubation was attempted was predetermined according to the up-and-down method (with 1% as step size). Outcome measure of success/failure (unresponsive/responsive) for intubation was based on a score formulated on parameters like, ease of intubation, vocal cords position & movement , reaction to intubation (in terms of movements)- score of 3-6 being regarded as success and ≥7 as failure. The Dixon's methodological principles were applied to determine MAC-EI in the present study. Values for MAC-EI were obtained by calculating the midpoint concentration of all independent pairs of patients involving a crossover, *i.e.,* responsive (failure) to unresponsive (success). We also calculated the eighteen crossover pairs, success to failure. Minimum alveolar concentration was defined as the average of the crossover midpoints in each crossover subgroup. Blood pressure (SBP & DBP), heart rate, saturation, response entropy, state entropy and train of four count (neuro muscular junction monitor) were noted at baseline. Along with these, desflurane dial setting, inspired concentration, endtidal concentration, FIO_2 and ET N_2O were also noted at 5minutes, 10minutes (pre-intubation) and 1 min, 3 min & 6 min post-intubation.

Results: The state entropy similar to the response entropy decreased across the time periods with least value noted just before intubation. The post hoc analysis showed significant decrease in all periods when compared to base line. There were no significant changes in oxygen saturation. Post hoc analysis of the heart rate data showed that there was a significant increase in heart rate when compared to base line at the time of intubation and one and 3 minute after intubation but this returned to normal at 6 min after intubation. There was significant decrease in Systolic and diastolic blood pressure across all periods when compared with the base line and was significant. The difference in desflurane dial concentration and inspired desflurane across the time periods was clinically not significant. The end tidal desflurane rose to the level of set concentration at the end of 5min, and was maintained at this level till intubation. The krushkal wallis test of the desflurane dial concentration, inspired concentration and end tidal concentration compared at different time periods revealed significant changes only in time period 1 (5 minutes after starting Desflurane). Although the desflurane decreases the entropy very fast,

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there is still a difference between failure and success groups and there is a difference also in the end tidal desflurane concentration between the success and failure groups, successful cases had a greater concentration of end tidal desflurane which corresponded to lower entropy values and successful intubation The MAC-EI for desflurane in 50% N_2O was calculated to be 6.37%.

Conclusion: The minimum alveolar concentration of desflurane for effective endo tracheal intubation is 6.37 using 50% N_2O. Desflurane is a safe and effective option to intubate patient, but it cannot be used as a sole agent because of risk of bronchospasm.

Keywords: Minimum Alveolar Concentration; End-tidal Desflurane Concentration; Effective Tracheal Intubation; Entropy.

Introduction

Tracheal intubation was usually performed under deep inhalational anaesthesia with ether. The continuing use of this technique to facilitate tracheal intubation with halothane and subsequently sevoflurane is still established, especially in paediatric practice. The technique has gained a small but popular niche in the armoury of the anaesthetist, when use of a neuromuscular blocking drug is undesirable. It may be used when there is a contraindication to a neuromuscular blocking drug, or in cases where tracheal intubation is necessary but prolonged muscle relaxation is not, such as in short ENT or gynaecological procedures. One avoids the potential serious and unwanted side-effects of succinylcholine, as well as the less common ones of non-depolarizing drugs, such as anaphylaxis.

The pharmacodynamic effects of inhaled anaesthetics must be based on a dose, and this dose is the minimum alveolar concentration or MAC , the alveolar concentration of anaesthetic at one atmosphere that prevents movement in response to a surgical stimulus in 50% of patients. It is analogous to the ED50 expressed for intravenous drugs. The MAC_{EI} is the minimum alveolar concentration for endotracheal intubation. MAC_{EI} of sevoflurane is 2.69% (endtidal concentration) in paediatric patients [1] and 4.52% (endtidal concentration) in adults [2]. The ED95 for tracheal intubation in adults is 8.07% (end tidal concentration) [2]. The minimum alveolar concentration (MAC) of desflurane in oxygen is 7.25% in the 18-30-yr age group, and 6.0% in the 31-65-yr age group [3].

Anaesthetics produce dose dependent effects on the Electro encephalogram (EEG) causing an increase in power combined with a decrease in the average EEG frequency. Various EEG derived parameters are used to describe the anaesthetic related effects. A novel EEG derived parameter for measuring the depth of anaesthesia is entropy. In adults, entropy values have been shown to correlate to the patient's anaesthetic state. High values of entropy indicate high irregularity of the signal, signifying that the patient is awake. A more regular signal produces low entropy values which can be associated with low probability of consciousness.

There are two Entropy parameters the fast reacting Response Entropy (RE) and the more steady and robust State Entropy (SE). State Entropy consists of the entropy of the EEG signal calculated up to 32 Hz. Response Entropy includes additional high frequencies up to 47Hz. Consequently the fast frontalis EMG (FEMG) signals enable a fast response time for RE [4].

The main purpose of the study was to calculate the minimum alveolar concentration of desflurane for effective endo tracheal intubation .

Materials and Method

This was a prospective study conducted, after institutional ethics committee approval , at Nizam's Institute of Medical Sciences, Hyderabad. This study was conducted between July 2015 and September 2015. The study recruited 70 patients scheduled for general anaesthesia for an elective surgery.

Inclusion Criteria

Age ranging between 18 to 60 years of either gender with ASA physical status I and II.

Exclusion Criteria

Patients with airway malformation, clinical evidence of a difficult airway, asthma or any signs of upper respiratory tract infection on preoperative examination. Patients who were taking sedatives, anti histaminics, CNS depressants or anti-seizure medication, or who had CNS disorders.

General Procedure

All the patients were premedicated with oral ranitidine 150mg the night before surgery and on the

morning of surgery. In the operating room intravenous access was secured. The patients were monitored with pulse oximetry, electrocardiogram (lead II and V5), noninvasive blood pressure (with a cycle time of 5min), end tidal carbon dioxide ($ETCO_2$), expired concentration of nitrous oxide, concentration fraction of inspired oxygen (FIO2), inspired and expired concentration of desflurane and MAC using Datex Ohmeda Aestiva 5 anaesthesia work station monitor, neuromuscular junction monitor (train of four count), and entropy for depth of anaesthesia. Accuracy of end tidal measurements was maximized by confirming the return of the $ETCO_2$ trace to zero and a plateau of the exhaled concentration values.

Premedication with inj fentanyl 1 mcg/kg IV prior to induction was done. Anaesthesia induction with propofol 1mg/kg and midazolam 1mg was done following which nitrous oxide in oxygen (50:50), each at 4 litres/minute with desflurane was commenced. Desflurane was started with 2% and increased by 2% every 30 seconds until patient lost consciousness, with entropy less than 60 and permitted manual ventilation. Then the dial setting was changed to achieve predetermined end-tidal desflurane concentration , to start with 6% in the first patient (best guess for MAC-EI) . The $ETCO_2$ during mask ventilation was maintained at 35±5 mmHg by adjusting the the TV and Respiratory rate given by the performer. Oral airway was inserted, when necessary during mask ventilation. After establishing and maintaining the target end-tidal concentration for 5 more minutes, tracheal intubation was attempted at 11th minute without neuromuscular relaxant and ± 0.5% difference in the predetermined/target end-tidal desflurane concentration was allowed. Each concentration at which tracheal intubation was attempted was predetermined according to the up-and-down method (with 1% as step size).

Baseline readings (Time period - 1) of blood pressure (SBP & DBP), heart rate, saturation, response entropy, state entropy and TOF count (neuro muscular junction monitor) were noted.

After giving the induction drugs , desflurane was started at 2% and increased by 2% every 30 sec, and reached the target end tidal concentration within the first 5 min . At this time second readings (Time period - 2) were noted along with desflurane dial setting, inspired concentration, endtidal concentration, FIO_2 and ET N_2O (Time period - 1 for these parameters as they weren't noted priorly at baseline). All these readings were repeated at 10 min (just before intubation) (Time period - 3 for those parameters whose readings were noted from baseline and Time period - 2 for those parameters whose readings were noted first at 5 minutes), 1 min after intubation, 3 min after intubation and 6 min after intubation (Time periods - 4 to 6 for those parameters whose readings were noted from baseline and Time periods- 3 to 5 for those parameters whose readings were noted first at 5 minutes) .

Intubation was attempted after waiting for a period of 10 min (Intubation was done at the 11th minute) ie, after a period of 5 min since the desflurane achieved the target end tidal concentration. The ETN2O was roughly uniform (50%) across all the patients at intubation. The TOF count of the neuromuscular junction monitor exhibited all the 4 twitches till intubation. Post Intubation, patients were mechanically ventilated by volume control mode with tidal volume of 8-11ml/kg and inspiratory and expiratory ratio of 1:2 and respiratory rate was adjusted to maintain the end tidal carbondioxide within 35± 5 mmHg.

The dial conc of desflurane was left unchanged as was at intubation till 6 minutes post intubation and the flows of N_2O and O_2(1:1) were also left unchanged at 4l/min each till 6 minutes post intubation for uniformity of the procedure in recording/noting various variables. Post 6 minutes of intubation, anaesthesia was maintained with 50% nitrous oxide in oxygen at 1l/min each and isoflurane 0.4-0.6%. Also, appropiate dosage of neuromuscular blocking drug was administered at this juncture for apt muscle relaxation and conduct of surgery.

Response to intubation was graded as follows depending on scoring given to parameters like, Ease of intubation, Vocal cords position & movement, Reaction to Intubation (in terms of movements):

Score	Ease of Intubation	Vocal cords	Reaction to Intubation (Movements)
1	Good	Open full	None
2	Fair	Open midway	Diaphragmatic movements
3	Difficult	Movements	Moderate coughing
4	Poor	Close	Severe coughing & bucking

Intubating conditions based on summation of scoring points for the three parameters-

Total Score: 3-Excellent, 4 to 6-good; 7 to 9-Poor; 10 to 12 –inadequate. The outcome measure of success (unresponsive) was if the score was 3-6 and if a score of 7 and above was recorded it was regarded as failure (responsive) of successful intubation.

Dixon's (Up And Down) method: The 'Dixon's (Up And Down) method' is standard method to determine MAC of inhalational agents. The end-tidal concentration of the agent midway between highest concentration allowing and lowest concentration preventing a response would be taken as MAC value [5]. The Dixon's methodological principles [6] were applied to determine MAC-EI in the present study (with 1% as step size). The first patient received an initial target end-tidal desflurane concentration of 6%. If the outcome was "success", then the next patient received a target end-tidal desflurane concentration of 5%, otherwise the patient received a target end-tidal desflurane concentration of 7%. In other words, the target end-tidal desflurane concentration to be administered depended upon the response of the previous patient and outcome measure of intubation as success (score: 3-6) or failure (score: 7 -12).

Statistical Analysis

Data analysis: Average of pairs of concentration between success (unresponsive) and failure (responsive) outcomes over the total of 70 patients was the estimated MAC-EI . Descriptive statistics were estimated using non-parametric methods. The "up-and-down method of Dixon" uses a limited data set (pair of crossovers) and does not allow for display of continuous relationship between end-tidal concentration and outcome. There are currently no formal methods of sample size estimation for Dixon's Up-And-Down method as the technique involves continual reassessment based on the patient's response to a particular dose. The critical issue in the methodology is the starting dose which should neither be high to cause adverse effects nor below to cause failure of drug-effect . Since the starting dose is 2 times the MAC of desflurane in 50% nitrous oxide and the fact that proposed study used pre-treatment with propofol and fentanyl, it is believed that a sample of 70 patients would suffice considering the previous studies on MAC and MAC-EI [1-3,7,8].

Comparision of variables: Non-parametric statistical methods were used in the present study. Comparison of independent variables was done by Mann-Whitney U test (for continuous variables) for 2 groups and by Kruskal-Wallis test for multi-groups. Chi-squared test was used for comparison of categorical variables. Comparison of variables at different time periods was made by Friedman's Test (Repeated measures Analysis of Variance-ANOVA).

Post-hoc analysis was done by non-parametric methods as applicable. Data analysis was facilitated by Minitab statistical software (Version 14, 2010). Descriptive data for continuous variables were presented as median inter quartile range (IQR).

Results

The mean age was 42 years in failure group and 41 years in successful intubation group. There was no difference in the age, gender, body mass index between the failure and success groups, they were comparable and yielded no statistical significance.

Values for MAC-EI were obtained by calculating the midpoint concentration of all independent pairs of patients involving a crossover, *i.e.,* responsive (failure) to unresponsive (success). We also calculated the eighteen crossover pairs, success to failure . Minimum alveolar concentration was defined as the average of the crossover midpoints in each crossover subgroup. The MAC of desflurane for effective endo tracheal intubation in this study was 6.37%.

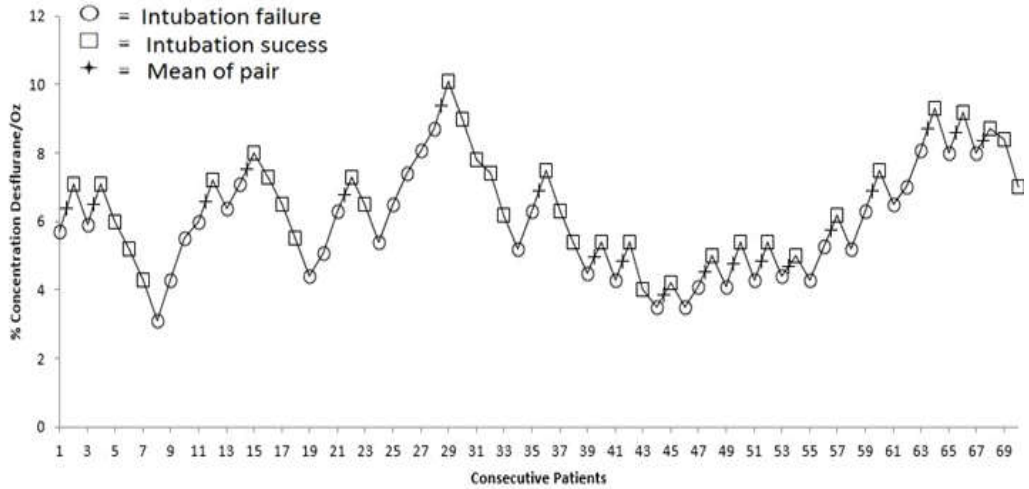

Fig. 1: The MACEI of desflurane for effective endotracheal intubation

Table 1: Response entropy and State entropy in different time periods

Variable	Time Periods	Median (IQR)	Significance in Comparision with base line
Response Entropy	Base line	97(94 - 98.25)	-
	5 min	35(29 - 49.25)	<0.01*
	Intubation	27.5(20 - 41.25)	<0.01*
	1 min after intubation	39(24 - 61.50)	<0.01*
	3 min after intubation	35(22.75 - 54.50)	<0.01*
	6 min after intubation	36(23 - 53.25)	<0.01*
State Entropy	Base line	87(87 - 89)	-
	5 min	33(27 - 45.75)	<0.01*
	Intubation	25(19 - 39)	<0.01*
	1 min after intubation	31.5(20 - 52.25)	<0.01*
	3 min after intubation	32(21.75 - 46.50)	<0.01*
	6 min after intubation	31(21.75 - 47.25)	<0.01*

*significance, P-value<0.05

Table 2: Vital parameters in different time periods

Vital parameter	Time Periods	Median (IQR)	Significance in Comparision with base line
Saturation (%)	Base line	100(99 - 100)	-
	5 min	100(99.75 - 100)	>0.05
	Intubation	100(99 - 100)	>0.05
	1 min after intubation	99(98 - 100)	>0.05
	3 min after intubation	99(97 - 100)	>0.05
	6 min after intubation	99(98 - 100)	>0.05
Heart rate (Beats/mt)	Base line	88.5(78 - 100)	-
	5 min	85(74.5 - 95)	>0.05
	Intubation	85(67.75 - 94)	<0.01*
	1 min after intubation	106(93 - 119)	<0.01*
	3 min after intubation	98(86 - 111)	<0.05*
	6 min after intubation	87(75.75 - 102)	>0.05
Systolic BP (mmHg)	Base line	122.5(117.5 to 140.25)	<0.01*
	5 min	111.5(100 to 131.25)	<0.01*
	Intubation	98(87 to 108.50)	<0.01*
	1 min after intubation	111.5(95.75 to 121)	<0.01*
	3 min after intubation	106(92.75 to 118.50)	<0.01*
	6 min after intubation	100(91 to 110.25)	<0.01*
Diastolic BP (mmHg)	Base line	77(71.75 - 83.50)	-
	5 min	72.5(66 - 85)	<0.01*
	Intubation	62(54 - 68.25)	<0.01*
	1 min after intubation	70.5(60 - 83.25)	<0.01*
	3 min after intubation	64.5(57.75 - 75)	<0.01*
	6 min after intubation	62(56.75 - 70)	<0.01*

*significance, P-value<0.05

The state entropy, similar to the response entropy decreased across the time periods with least value noted just before intubation. The post hoc analysis showed significant decrease in all periods when compared to base line.

There were no significant changes in saturation.

The heart rate decreased up to the time to intubation and then it increased. As opposed to what was expected, we did not find any increase in the heart rate when desflurane was started , this can probably be explained by the fact that the desflurane concentration was increased slowly. Post hoc analysis of the heart rate data showed that there was a significant increase in heart rate when compared to base line at the time of intubation and one and 3 minute after intubation but this returned to normal at 6 min after intubation.

There was significant decrease in Systolic and diastolic blood pressure across all periods when compared with the base line and was significant. The least systolic blood pressure was noted at 10 min or just before intubation.

Table 3: Concentration of Desflurane (%) in different time periods

Variable	Time Periods	Median (IQR)	Significance in comparision with base line (5 min)
Dial concentration of Desflurane	5 min	7(6 - 8)	-
	Intubation	7(6 - 8)	>0.05
	1 min after intubation	7(5.87 - 8)	>0.05
	3 min after intubation	6.75(5.87 - 8)	>0.05
	6 min after intubation	6.75(5.87 - 8)	>0.05
Inspired Desflurane concentration	5 min	6.4(5.5 - 7.5)	-
	Intubation	6.5(5.3 - 7.55)	>0.05
	1 min after intubation	6.5(5.3 - 7.7)	>0.05
	3 min after intubation	6.4(5.45 - 7.72)	>0.05
	6 min after intubation	6.4(5.3 - 7.7)	>0.05
End tidal Desflurane concentration.	5 min	6.0(4.97 - 7.10)	-
	Intubation	6.2(5.07 - 7.32)	<0.01*
	1 min after intubation	6.05(5.17 - 7.20)	<0.01*
	3 min after intubation	6.05(5.17 - 7.20)	<0.05*
	6 min after intubation	6.15(5.0 - 7.1)	<0.05*

*significance, P-value<0.05

Table 4: Comparison of Dial, Insp and ET Desflurane of different time periods by Kruskal- Wallis Test

Dial, Insp and ET des at time period	Median (IQR)	Significance
5 min	7.0(6.0 - 8.0) 6.4(5.5 - 7.5) 6.0(4.97 - 7.10)	<0.01*
Intubation	7(6 - 8) 6.5(5.3 - 7.55) 6.2(5.07 - 7.32)	0.065
1 min after intubation	7(6 - 8) 6.5(5.3 - 7.55) 6.05(5.07 - 7.32)	0.058
3 min after intubation	6.75(5.87 - 8.0) 6.40(5.45 - 7.72) 6.05(5.17 - 7.20)	0.061
6 min after intubation	6.75(5.87 - 8.0) 6.45(5.30 - 7.7) 6.15(5.0 - 7.10)	0.063

*significance, P-value<0.05

The desflurane variables were noted from 5 min onwards, so, that forms the base line value for this variable.

The difference in desflurane dial concentration and inspired desflurane concentration across the time periods was not significant.

The end tidal desflurane rose to the level of set concentration at the end of 5min, and was maintained at this level till intubation. The difference between the different time periods was not significant, though there was statistically significant difference when ETDes at different time periods was compared to that at base line (5 min) .

The Kruskal-wallis test of the desflurane dial concentration, inspired concentration and end tidal concentration compared at different time periods revealed significant changes only in time period 1 (at 5 mins), this shows that, desflurane because of its low blood gas solubility, equilibrates quickly in the body.

Although desflurane decreases entropy rapidly, there is still a difference in entropy between failure and success groups (with entropy being lower in success group) and there is a difference also in the end tidal desflurane concentration between the success and failure groups, cases in success group had a greater concentration of end tidal desflurane which corresponded to lower entropy values and successful intubation.

Table 5: Response, State Entropy and End tidal desflurane in Success and Failure groups

	Outcome	Median (IQR)	Significance
Response entropy			
at 5min	Failure	50(37 - 76)	0.2020
	Success	45(34 - 70)	
at intubation	Failure	59(34 to 90)	0.0165*
	Success	35(25 to 67)	
at 1 min after intubation	Failure	79(59 to 98)	0.00 *
	Success	39(30 to 66)	
State entropy			
at 5 min.	Failure	48(35 - 74)	0.2020
	Success	42(32 - 64)	
at intubation	Failure	49(31 - 78)	0.0447 *
	Success	34(23 - 59)	
at 1 min after intubation	Failure	67(50 - 91)	0.002*
	Success	34(27 – 56)	
End tidal desflurane			
at 5 min	Failure	6.5(5.4 - 8.7)	0.0209*
	Success	7.3(6.5 - 9.8)	
at intubation	Failure	6.5(5.5 - 8.7)	0.0147*
	Success	7.5(6.5 - 10.1)	
at 1 min after intubation	Failure	6.4(5.4 - 9.1)	0.0202*
	Success	7.4(6.3 - 10.2)	

*significance, P-value<0.05

Discussion

Desflurane because of its properties like low blood gas solubility is a rapidly acting inhalational agent and also, it is rapidly washed out of the body, without undergoing much metabolism which makes it the ideal agent for day care surgeries (where it is advantageous to avoid neuromuscular blocking drugs) and other small procedures. It may be used when there is a contraindication to a neuromuscular blocking drug or in cases where tracheal intubation is necessary but prolonged muscle relaxation is not, such as in short ENT or gynaecological procedures. One avoids the potential serious and unwanted side-effects of succinylcholine, as well as the less common ones of non-depolarizing drugs, such as anaphylaxis.

Minimum alveolar concentration (MAC) is a standard measure of potency of inhalational agents. It is defined as the minimum alveolar concentration of anaesthetic at one atmosphere which produces immobility in 50% of subjects exposed to a noxious stimulus, usually a skin incision. Variants of MAC have been described. For example, MAC that blocks the adrenergic responses is called as MAC-BAR, similarly MAC that is used for endo tracheal intubation is called as MAC-EI. There are no prior studies which calculate MAC-EI for desflurane, Kimura et al. [2], described MAC-EI for sevoflurane to produce "*effective intubation*". Unlike sevoflurane, desflurane is not suitable for sole inhalational induction because of it's pungent smell. Hence to enhance smooth induction, desflurane is usually pretreated with propofol.

In this study we calculated the minimum alveolar concentration of desflurane required for effective endo tracheal intubation. The '*Dixon's (Up And Down) method*' is standard method to determine MAC of inhalational agents. The end-tidal concentration of the agent midway between highest concentration allowing and lowest concentration preventing a response is taken as MAC value. Values for MAC were obtained by calculating the midpoint concentration of all independent pairs of patients involving a crossover, i.e., failure (responsive) to success (unresponsive). Minimum alveolar concentration was defined as the average of the crossover midpoints in each crossover subgroup. The MAC of desflurane for effective endo tracheal intubation in this study was 6.37%. As noted in the previous study, the minimum alveolar concentration (MAC) of desflurane/oxygen was 7.25±0.0% (mean±SD) in the 18-30-yr age group, and 6.0±0.29% in the 31-65-yr age group, the addition of 60% N_2O reduced the MAC to 4.0±0.29% & 2.83±0.58% respectively [3].

In a similar study , in patients older than 65 yrs MAC was 5.17±0.6% (mean±SD) in the desflurane/ oxygen group and 1.67±0.4% in the desflurane/ nitrous oxide/oxygen group [7]. Both these studies did not calculate the MACEI. There are no previous studies which calculated this value for desflurane

but similar studies were conducted on sevoflurane which revealed the MACEI for sevoflurane which was as high as 2 to 3 times its normal value. At this high dose of sevoflurane there were significant hemodynamic alterations which are detrimental to the patients [2]. The calculation of MACEI of desflurane is complicated because it cannot be used as a sole induction agent, and cannot be used in children because of its upper airway irritating property.

Yakaitis and colleagues were the first to evaluate the optimum end-tidal concentration for intubation. The concept of MAC-EI (EI=endotracheal intubation) was described - the minimum alveolar concentration of halothane needed by 50% of the population to prevent all movement both during and immediately after tracheal intubation. They studied 37 children, aged 2–6 yr, and found the MACEI value of halothane to be 1.4%, and found by extrapolation that the MACEI value for 95% of this population was 1.9% [9].

The same group then applied these study techniques to enflurane in a similar age group of patients and found the corrected MACEI value to be 2.9% [10]. For both halothane and enflurane, the MACEI appears to be about 30% greater than the MAC value.

Halothane was largely superseded by sevoflurane in the mid to late 1990's. Inomata and colleagues determined MAC-EI and MAC of sevoflurane in paediatric patients [1]. They studied 36 children aged 1-9 yrs . After establishing and maintaining the end-tidal concentration for 15 min, tracheal intubation was attempted with an uncuffed tracheal tube without neuromuscular relaxants or other adjuvants. Each concentration at which tracheal intubation was attempted was predetermined according to the up-and-down method (with 0.5% as a step size). MAC-EI & MAC of sevoflurane were 2.69% & 2.03% respectively .

Kimura and colleagues determined MAC-EI and MAC of sevoflurane in adult patients [2]. They studied 86 adult patients aged 16-59 yr . After establishing and maintaining the predetermined end-tidal concentration for 20 min, tracheal intubation was attempted using a cuffed tracheal tube without muscle relaxant or other adjuvants. The MAC-EI & MAC of sevoflurane for 50% of the population were 4.52% & 1.58% respectively . The authors accounted for this difference of MAC-EI in adults when compared to children, by the irritation & subsequent coughing caused by the cuff of adult tracheal tube & the fact that children have a relatively greater brain perfusion & quicker uptake. They suggested that anaesthesia induction followed by tracheal intubation can be accomplished in adults when sevoflurane is administered as a sole anesthetic, but in excess of 8% end-tidal concentration .

Swan et. al., studied the interaction between nitrous oxide and sevoflurane during tracheal intubation in 72 children aged 1-7yrs. The addition of N_2O 33 & 66% has been shown to decrease the MAC-EI value by 18 & 40%, from 2.66% with sevoflurane alone, to 2.16% & 1.57% respectively [8].

Katoh et. al., studied sevoflurane requirements for tracheal intubation with or without fentanyl [11]. They pretreated a group of 80 adults with fentanyl - 1, 2 & 4 μg/kg, 4min before intubation. MACEI of sevoflurane was 2.07, 1.45 & 1.37% respectively in the pretreated groups, compared with 3.55% in the group without fentanyl pretreatment .

In healthy volunteers, in the absence of concomitant N_2O and/or opioid administration, sudden steep increases in the inspired concentration of desflurane may cause transient increases in sympathetic activity with associated increases in heart rate and blood pressure. The haemodynamic changes are more common at concentrations >6% and more severe with large (>1%), sudden increments. Without treatment, and without further increases in desflurane concentration, these increases in heart rate and blood pressure resolve in approximately 4 minutes [12]. Administration of sympatholytic drugs (fentanyl, alfentanil, esmolol, and clonidine) prior to a sudden steep increase of desflurane blunts or blocks the increase in heart rate and blood pressure.

In the present study we included 70 patients, & though the sample size estimation could not be done as there were no previous studies determining MAC-EI for desflurane, it was based upon previous studies determining MAC-EI & MAC of sevoflurane [1,2,8] or MAC of desflurane [3,7]. We started off with a desflurane concentration of 6% (best guess for MAC-EI). After premedicating the patient with fentanyl, propofol and midazolam we increased the dial setting of the desflurane by 2% every 30 sec until the target (predetermined) dial setting was achieved. Then this concentration was maintained for 5 more min and the patient was intubated in the 11^{th} minute.This was done to equilibrate the desflurane dial , inspired and endtidal concentrations with each other, and also to wait for the effect of propofol to fade away. As the concentration of desflurane increased there was subjective difficulty in doing bag mask ventilation but there were no complications.

Previous studies which calculated the MAC value for inhalational agents used different time periods after achieving the target end tidal concentration.

Gold et. al. [7], while calculating the MAC value of desflurane (with and without 60% N_2O) in elderly patients, waited for 10 min & Fisher et. al. [13], when calculating the MAC value of desflurane in children with 60% N_2O, also waited for 10 min after the target end tidal concentration was achieved. In the studies by Inomata et. al. [1], in children and Kimura et. al. [2], in adults for calculating MAC-EI & MAC of sevoflurane and in the study by Swan et. al. [8], in children for calculating MAC-EI of sevoflurane in different concentrations of N_2O , they waited for 15, 20 and 10 minutes respectively after the target end tidal concentration was achieved. We considered pretreatment with drugs like fentanyl in our study based upon the findings in prior studies which indicated their role in decreasing the MAC-EI [11].

We intended to calculate MAC EI of desflurane in 50% N_2O , based upon the studies substantiating the reduction of MAC EI for sevoflurane [8] and MAC for Desflurane [3,7] with the addition of N_2O. Some studies also supported the addition of N_2O, which resulted in faster loss of consciousness and reduced excitement in rapid induction technique with sevoflurane [14].

Dixon's methodology which was used in our study to determine the MAC-EI of desflurane ,was priorly used in other studies also which determined MAC-EI and MAC for sevoflurane [1] and MAC for desflurane [3,7,13].

The scoring system used in our study for assessing success / failure of intubation was roughly based upon the same criteria (presence or absence of - purposeful muscular movements, vocal cord movements, coughing , bucking) used to regard an intubation attempt as successful (unresponsive) ,or as a failure (responsive), as in other studies which calculated MAC EI of sevoflurane [1,2,8].

The sympathetic stimulation which is associated with desflurane which causes increase in the heart rate and blood pressure was not seen probably because of the slow increase in the desflurane dial setting by 2% for every 30 sec, co-administration with N_2O and pretreatment with fentanyl. There was actually increase in the heart rate and blood pressure immediately after intubation showing that the concentration required for immobility is still insufficient to wipe out the autonomic responses (MAC-BAR). This raise in heart rate and blood pressure returned to pre-intubation levels within 6 min post-intubation.

The results of the study show that the MACEI for desflurane is 6.37, which is close to its MAC of 6 but this is calculated using 100% O_2 and in the present study we used 50% N_2O. We used N_2O in this study to make it cost effective, without the use of N_2O the MAC EI would be much higher. Entropy was also recorded in our study, which substantiated a greater depth of anaesthesia in those with a successful outcome of intubation, who also supposedly had a greater concentration of end tidal desflurane concentration.

Conclusion

The minimum alveolar concentration of desflurane for effective endo tracheal intubation is 6.37 using 50% N_2O. Desflurane is a safe and effective option to intubate patient, but it cannot be used as a sole agent because of risk of bronchospasm. Slow elevation of the desflurane concentration will decrease the hemodynamic alterations.

References

1. Inomata S, Watanabe S, Taguchi M, Okada M. End-tidal sevoflurane concentration for tracheal intubation and minimum alveolar concentration in pediatric patients. Anesthesiology 1994;80(1):93-6.
2. Kimura T, Watanabe S, Asakura N, Inomata S, Okada M, Taguchi M. Determination of end-tidal sevoflurane concentration for tracheal intubation and minimum alveolar anesthetic concentration in adults. Anesth Analg 1994;79(2):378-81.
3. Rampil IJ, Lockhart SH, Zwass MS, Peterson N, Yasuda N, EgerII EI, Weiskopf RB, Damask MC. Clnical characteristics of desflurane in surgical patients: Minimum alveolar concentration. Anesthesiology 1991;74:429-33.
4. Bein B. Entropy. Best Pract Res Clin Anaesthesiol 2006; 20(1):101-9.
5. Eger EI. Age, minimum alveolar anesthetic concentration, and minimum alveolar anesthetic concentration-awake. Anesth Analg 2001;93(4): 947-53.
6. Dixon WJ. Quantal response variable experimentation: The up-and-down method, Statistics in Endocrinology. Edited by McArthur JW, Colton T. Cambridge, MIT Press, 1967.pp.251-264.
7. Gold MI, Abello D, Herrington C. Minimum alveolar concentration of desflurane in patients older than 65 yr. Anesthesiology 1993;79(4):710-4.
8. Swan HD, Crawford MW, Pua HL, Stephens D, Lerman J. Additive contribution of nitrous oxide to sevoflurane minimum alveolar concentration for tracheal intubation in children. Anesthesiology 1999; 91:667-71.

9. Yakaitis RW, Blitt CD, Angiulo JP. End-tidal halothane concentration for endotracheal intubation. Anesthesiology 1977;47(4):386-8.

10. Yakaitis RW, Blitt CD, Angiulo JP. End-tidal enflurane concentration for endotracheal intubation. Anesthesiology 1979;50:59-61.

11. Katoh T, Nakajima Y, Moriwaki G, Kobayashi S, Suzuki A, Iwamoto T, Bito H, Ikeda K. Sevoflurane requirements for tracheal intubation with and without fentanyl. Br J Anaesth 1999;82(4):561-5.

12. Jakobsson J. Desflurane: A clinical update of a third-generation inhaled anaesthetic. Acta Anaesthesiologica Scandinavica 2012;56(4):420-32.

13. Fisher DM, Zwass MS. MAC of desflurane in 60% nitrous oxide in infants and children. Anesthesiology 1992;76(3):354-6.

14. Dubois MC, Piat V, Constant I, Lamblin O, Murat I. Comparison of three techniques for induction of anaesthesia with sevoflurane in children. Paediatr Anaesth 1999;9(1):19-23.

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Effects of Rocuronium Bromide and Suzxamethonium on Intubating Conditions: A Comparative Study

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Abstract

Background: In general anaesthesia rapid and safe endotracheal intubation is critical. Aspiration of gastric content, during induction and intubation is a major risk factor which determines the outcome of anaesthesia. The ideal muscle relaxant is the one who produces faster onset of action; resultant in to reduction in the incidence of side effects. With this background present study was done to compare the effects of rocuronium and suxamethonium on intubating conditions.

Material and Methods: Total 90 ASA grade I and II patients who were scheduled to laparoscopic appendectomy under general anesthesia selected. These patients were randomly divided in to 3 groups consisting 30 patients in each. Group I (S60) patients received suxamethonium 2mg/kg with intubation attempted at 60 seconds and patients of groups II (R60) and III (R90) received rocuronium0.6 mg.kg, with intubation attempted at 60 seconds and rocuronium 0.6 mg.kg, with intubation attempted at 90 seconds respectively.

Results: The intubating conditions were acceptable in all the patients belonging to group I (S60) and group III (R90), while 04 patients in group II (R60) had unacceptable intubating conditions. Rocuronium found haemodynamically stable as suxamethonium.

Conclusion: Rocuronium provides acceptable intubating conditions as comparable with suxamethonium with no incidence of side effects or complications.

Keywords: Rocuronium; Suxamethonium; Intubating Conditions; Appendectomy.

Introduction

Tracheal intubation is a routine procedure to ensure a safe protected airway through which one can provide intermittent positive pressure ventilation during all procedures carried out under general anesthesia.

Aspiration of gastric content, during induction and intubation is a major risk factor which determines the outcome of anesthesia. The ease with which endotracheal intubation is performed depends upon degree of muscle relaxation, depth of anesthesia and skill of anaesthesiologist [1]. The ideal muscle relaxant is the one who produces faster onset of action; resultant in to reduction in the risk of side effects.

Traditionally, suxamethonium is being used to facilitate rapid sequence induction and endotracheal intubation. Although suxamethonium has rapid time of onset and brief duration of action, it also produced many adverse systemic effects including cardiac dysrhythmias, muscle fasciculations, hyperkalemia, elevated intracranial, intra-gastric and intra-ocular pressure. Different techniques have been tried, including 'priming' [2] to decrease the effective onset time of nondepolarizing muscle relaxants like vecuronium, pancuronium or atracurium.

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Rocuronium is a non depolarizing muscle relaxant and whose formula is based on vecuronium bromide. Some studies suggested that; unlike suxamethonium, rocuronium has little or no cardiovascular effects. In contrast to conventional anesthetic neither priming nor marked increased doses are required to achieve a rapid onset. Therefore, rocuronium could be potentially ideal for fast intubation, with no or minimum side effects, in all patients receiving general anesthesia. With this background the present study was conducted with following objectives; 1) To assess the intubating conditions achieved with rocuronium bromide and suxamethonium 2) To compare the changes in hemodynamic parameters due to both drugs.

Material and Methods

The present comparative study was conducted after institutional ethical committee's (IEC) approval. Patients were enrolled, after explaining the purpose and procedure of the study and written informed consent was obtained. Total 90 ASA grades' I and II patients scheduled to undergo laparoscopic appendectomy, under general anesthesia were selected. An increased risk of pulmonary aspiration, neuromuscular disease, medications known to influence neuromuscular function, anticipated difficulty with airway management was excluded from study. Selected patients were randomly divided in to 3 groups consisting 30 patients in each. Group I patients received suxamethonium and patients of groups II and III received rocuronium as follows.

Group I (S60): Suxamethonium 1.5 mg/kg with intubation attempted at 60 seconds;

Group II (R60): Rocuronium 0.6 mg.kg with intubation attempted at 60 seconds;

Group III (R90): Rocuronium 0.6 mg.kg with intubation attempted at 90 seconds.

All minimum necessary investigations were performed before commencing study. All the patients received tablet famotidine 40 mg orally at 10 pm. on the night before surgery and fasted overnight. On the day of surgery baseline pulse rate, blood pressure, body weigh were recorded. Intramuscular premedication in the form of injection glycopyrrolate 0.2 mg was given 30 minutes prior to induction of anesthesia. Inj. Midazolam 1.5 mg and inj.Butorphanol 1 mg given as intravenous premedication. Pre-oxygenation was carried out with 100% O_2 for 5 minutes. Anesthesia was induced with injection propofol2 mg/kg/IV. Abolition of eyelid and eyelash confirmed induction in all cases. Immediately after induction muscle relaxants were administered intravenously according to their dose in specified groups and time onset of apnoea noted. Laryngoscopy and intubation was attempted as specified for the groups i.e. at 60 seconds after the injection of suxamethonium of 2mg/kg in group I (S60) and at 60 and 90 seconds after injection of rocuronium of 0.6 mg/kg in group II (R60) and group III (R90) respectively.

Intubation conditions were assessed according to three point scales (0-2) and if the scores were in between 5 to 8 and 0 to 4, then it labeled as acceptable and unacceptable intubating conditions respectively (Table 1). If the patients having difficult intubating

Table 1: Assessment of intubation conditions

Sr. No	Variables	Conditions		
1	Jaw relaxation	Good	Incomplete	Poor
2	Vocal cord position	Full abducted	Moderately abducted	Slightly abducted
3	Reaction to intubation	None	Bucking	Gross movement
	Score	2	1	0
	Interpretations			
	Excellent (7 to 8)	Acceptable	Fair (2 to 4)	Unacceptable
	Good (5 to 6)		Poor (0 to 1)	

Table 2A: Age wise distribution of patients

Sr. No	Age groups (yrs)	No of patients		
		Group I (S60)	Group II (R60)	Group III (R90)
1.	20-25	23	19	18
2.	26-30	06	10	09
3.	31-35	01	01	03
	Total	30	30	30
	Mean ± Sd.	23.86±2.94	24.46±3.81	25.73±4.09

One way ANOVA F=2.057, P=0.13 Non significant

Table 2B: Weight wise distribution of patients

Sr. No	Weight groups (Kg)	No of patients		
		Group I (S60)	Group II (R60)	Group III (R90)
1.	40-55	17	17	18
2.	56-70	11	10	11
3.	≥ 71	02	03	01
	Total	30	30	30
	Mean ± Sd.	54±9.04	57.26±9.46	54.7±7.89

One way ANOVA F=1.135, p=0.32 Non significant

Table 3: Distribution according to mean apnoea onset time

Study groups	Mean apnoea time (Mean ± SD)
Group I (S60)	25.06 ± 6.89 *
Group II (R60)	32.83 ± 8.63 * #
Group III (R90)	29.76 ± 10.21 * #

* One way ANOVA: F=6.094 p=0.003 Significant
# Un paired t test: 1.258 d.f.=58, p=0.21 Non significant

Table 4: Intubating conditions and acceptability

Groups	Acceptable		Unacceptable		Total
	Excellent	Good	Fair	Poor	
Group I (S60)	30	00	00	00	30
Group II (R60)	15	11	03	01	30
Group III (R90)	30	00	00	00	30

Table 5: Intubating conditions

Study Groups	Intubating scores (Mean ± SD)
Group I (S60)	7.8 ± 0.4 * @ $
Group II (R60)	6.06 ± 1.55 * # $
Group III (R90)	7.5 ± 0.5 # @ $

*Tukey Kramer test: p=0.001 Significant, # Tukey Kramer test: p=0.00 1 Significant @ Tukey Kramer test: p=>0.05 Non significant $ One way ANOVA: F: 27.686 p=<0.0001 Significant

Table 6: Distribution according to mean pulse rate

Study groups	Pre-Op.	Just before induction	After induction	Just before laryngoscopy	Just after Intubation	1 Min later	5 Min. later	Post Op.
Group I (S60)	87.3±8.16*	91.22±9.54	95.2±9.20	96.83±8.82 *	109.03±111.20*	101.86±9.92	95.4±10.21	92.2 ±8.83
Group II(R60)	90.58±10.59$	94.7±10.93	103.46±11.14	108.00±11.14$	118.36±10.86 $	111.36±12.41	111.36±12.41	99.96±11.35
Group III(R90)	93.13±8.83@	89.87±16.91@	98.96±10.51	104.53±14.05@	110.23 ±14.30	105.36±13.92	100.53±11.33	98.96 ±9.96

*One way ANOVA: F=39.574, p<0.001 Significant, $One way ANOVA: F=50.080, p<0.001 Significant @One way ANOVA: F=14.218, p<0.001 Significant

Table 7: Distribution according to systolic blood pressure

Study Groups	Pre-Op.	Just before induction	After induction	Just before laryngoscopy	Just after Intubation	1 Min. later	5 Min. later	Post Op.
Group I (S60)	126.86 ±13.19@	125.33±15.86	114.6 ± 15.70	116.33±13.95	139.93±14.24@	122.13±11.23	114.13±11.28	125.6±11.73
Group II (R60)	121.33 ±10.87#	121.66±9.67	113.53±11.25	112.86± 8.44	135.2± 13.72#	118.4±11.72	113.06±11.35	119.66±8.68
Group III (R90)	120.93 ±11.09 *	115.12±21.81	111.46±12.09	114.26±13.88	132.53 ±12.39*	119.6±14.58	112.8±8.89	123.26±11.99

@ Unpaired 't' test: t=3.668 d.f=58, p=0.0005 Significant
# Unpaired 't' test: t=4.340 d.f=58, p=0.0001 Significant
* Unpaired 't' test: t=3.821 d.f=58, p=0.0002 Significant

Table 8: Mean duration of action of intubating dose of relaxant

	Group I (S60)	Group II (R60)	Group III (R90)
Mean ± SD	7.8 ± 0.4 $ #	24.83 ± 3.62 $ #	25.86 ± 6.87 #
Statistical test	$ Unpaired 't' test: t=0.72 d.f:58, P 0.47 Non-significant # One way ANOVA: F=153.13, P=0.0001 Significant		

condition were managed according to difficult airway management protocol.

At the end of surgery residual neuromuscular blockage was reversed with injection neostigmine 0.05 mg/kg and atropine 0.02 mg/kg or glycopyrrolate 10µg/kg. Vitals were recorded before and after induction, 1 and 5 minutes after intubation and thereafter every 10 minutes throughout the surgical procedure in all the groups. Side effects and complication noted if any.

Data Analysis

Data coding and entry was done in Microsoft Excel spread sheets and descriptive and inferential statistical analysis was done by using SPSS version 21 (Statistical Package for Social Sciences) software. One way ANOVA, Tukey Kramer multiple comparison test, Un-paired 't' test, mean, standard deviation used and differences wereconsidered to be significant if p value was < 0.05.

Results

In present study total 90 patients aged 20-50 years of ASA Grade I and II, scheduled for laparoscopic appendectomy under general anesthesia were selected and divided in equally in three groups.

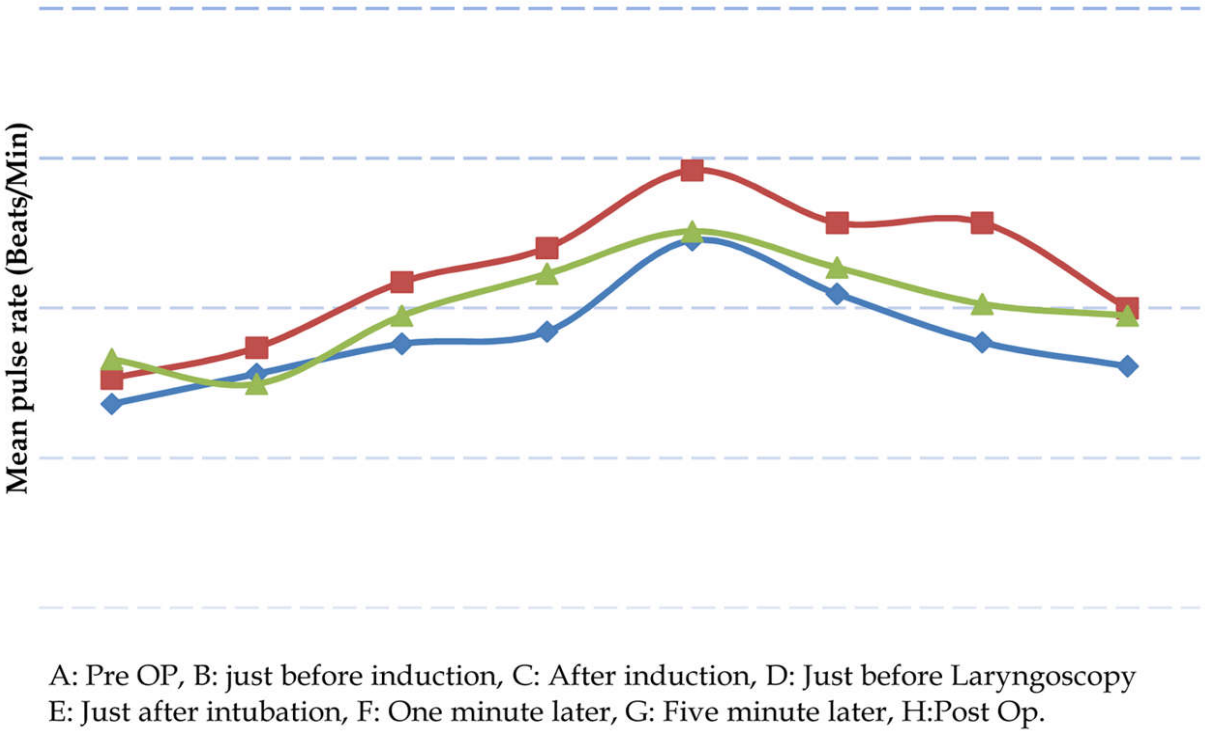
No statistical significance was observed in between mean age of three study groups and also similar result showed with mean weight of the participants (Table 2).

The mean time of apnoea onset of suxamethonium group I (S60) was 25.06±6.89, for group II (R60) and group III (R90) it was32.83±8.63 and 29.76±10.21 respectively. Statistically significant difference was observed in between mean apnoea onset time of all three groups (S60, R60 and R90) but non-significant difference was seen in between two rocuronium groups. i.e. R60 and R90 (Table 3).

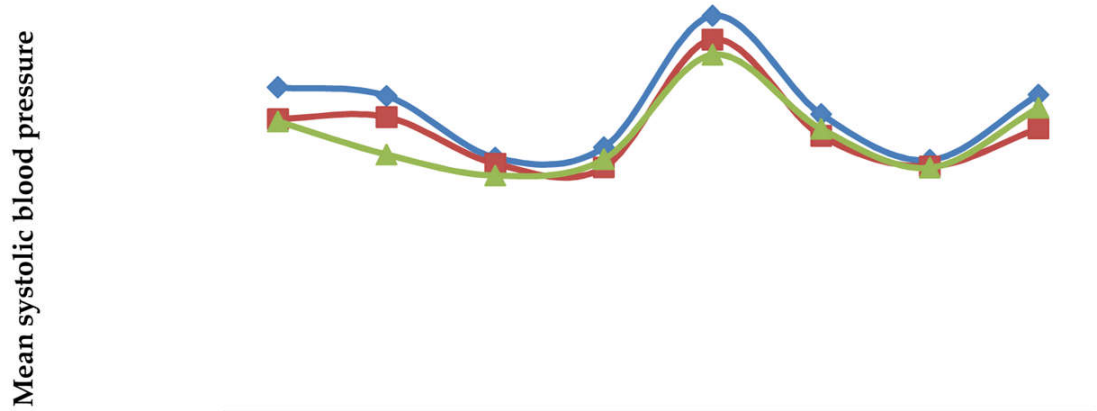
The intubating conditions were acceptable in all the patients belonging to group I (S60) and group III (R90), while 26 patients in group II (R60) had acceptable conditions and remaining 4 patients had unacceptable intubating conditions (Table 4). On statistical analysis the significant difference was observed in the mean intubating score of group I and group II, group II and group III and All three groups except group I and group III (Table 5).

In all three groups mean pulse found to be increased after giving muscle relaxant i.e. just before laryngoscopy and just after induction as compared pre operative reading (Graph 1). The difference found to be significant groups in all (Table 6).

The mean systolic blood pressure rose just after intubation as compared to basal reading. The difference between basal mean systolic blood pressure and mean blood pressure just after the intubation found to be statistical significant in all three study groups (Table 7). The mean systolic blood pressure started decreasing immediately after intubation and



Graph 1: Mean pulse pressure at various stages



	A	B	C	D	E	F	G	H
Group I (S60)	126.86	125.33	114.6	116.33	139.33	122.13	114.13	125.6
Group II (R60)	121.33	121.66	113.53	112.86	135.2	118.4	113.06	119.66
Group III (R90)	120.93	115.12	111.46	114.26	132.53	119.6	112.8	123.26

Graph 2: Systolic blood pressure at various stages

it felt below basal level at one minute after intubation (Graph 2).

The mean clinical duration of action of intubating dose of group I (S60), group II (R60) and group III (R90) were 7.8±0.4, 24.83±3.62 and 25.86±6.87 respectively. The duration of action of both rocuronium groups was more than that ofsuxamethonium and in these three group's difference was found statistically significant ($P < 0.0001$) but was not significant in group II (R60) and group III (R90). (P 0.47) (Table 8). No side effects or complications were encountered in present study also there was no incidence of regurgitation or aspiration of gastric content.

Discussion

Muscle relaxation is used to serve two purposes: one to secure the patients airway quickly and smoothly with minimum chances of hypoxia, regurgitation and aspiration of gastric contents and other to provide surgical relaxation [2]. The ideal neuromuscular blocking agent is one which has brief duration of action, provides profound relaxation and is free from hemodynamic changes.

In present study total 90 patients included randomly who were scheduled for laparoscopic appendectomy under general anesthesia. The mean age of patients was 23.86±2.94 years in group I (S60), 24.46±3.81 years in group II (R60) and 25.73±4.09 in group III (R90). On other hand the mean body weight in group I (S60), group II (R60) and group III (R90) were 54±9.04, 57.26±9.46 and 54.7±7.89 kg respectively. The mean age and weight in all age groups were comparable i.e. no statistical significant difference was observed.

Apnoea onset time is defined as the time interval between injection of muscle relaxant and complete cessation of spontaneous respiration. In this study apnoea time was clinically evaluated. Huizinga et.al [3] used relaxograph to measured apnoea time. In present study mean apnoea onset time was less in suxamethonium group than in both rocuronium groups and the difference were statistical significant; while mean apnoea onset time showed no statistical difference in between two rocuronium groups.

Intubating conditions were acceptable in all patients of group I (S60) and group III (R90) while out of 30 patients of group II (R60), 26 and 4 patients had acceptable and unacceptable conditions respectively. In a study conducted by Wierdaet al [4] found that intubating conditions were excellent at 1 minute and they also found that the mean time to 75% block was faster in rocuronium group compared to vencuronium. Similarly comparable results were obtained in other studies like Cooper et. al [5], Huizinga et. al [3] and Sehgal et. al. [6].

Stability of vital parameters like pulse and blood pressure are highly desirable during anesthetic management. In present study pulse rate and systolic blood pressure were recorded at various stages. In this study mean pulse rate was found to be increased after giving relaxant as compared to pre operative values. The difference between basal mean systolic blood pressure and mean blood pressure just after the intubation found to be statistical significant in all three study groups ($P < 0.001$). Even after decreased in pulse rate 1 minute after intubation it remains high to basal values comparatively. Booth et. al. [7] showed transient to moderate increased heart rate at a dose of 0.6 mg/kg of rocuronium. In a study conducted by Cooper R et. al. [5] no significant change in heart rate was found with rocuronium 0.6 mg/kg.

The current study showed raised in mean systolic blood pressure just after intubation in all three groups and it was statistically significant as compared to basal values. The mean systolic blood pressure decreased at 1 minute after intubation and remained nearly same as basal level in all three groups. Cooper R et. al. [5] reported no significant change in blood pressure.

The clinical duration of action of muscle relaxant was defined as the time interval between injection of muscle relaxant and initiation of spontaneous diaphragmatic activity with increased resistance felt during ventilation. In present study mean clinical duration of action was more in both rocuronium groups as compared to suxamethonium group and difference was found statistically significant ($P < 0.0001$) similar results were observed by Cooper et. al. [5], Huizinga et. al. [3], Magorian et. al .[8]etc.

Conclusion

Rocuronium provides produces comparable results as suxamethonium with no incidence of side effects or complication.

References

1. Comparison of intubating conditions of rocuronium bromide and vecuronium bromide with succinylcholine using "Timing Principle". J AnaesthClinPharmacol. 2010;26(4):493-97.
2. Chatrath V, Singh I, Chatrath R, Arora N. Comparison of Intubating Conditions of Rocuronium Bromide and VecuroniumBromide with Succinylcholine Using "Timing Principle"JAnaesthClinPharmacol 2010; 26(4):493-497.
3. Huizinga CT, Vandenbrom RH, Wierds JM, Hommes FD, Hennis PJ. Intubating conditions and onset of neuromuscular block of rocuronium; a comparison with suxamethonium. ActaAnaesthesiolScand 1992; 36:463-468.
4. Wierda JMKH, Hommes FDM, Nap HJA, Broek L. Time course of action and intubating conditions following vecurorium, rocuronium and mivacurium. Anaesthesia 1995;50:393-96.
5. Cooper R, Mirakhur RK, Clarke RS, Boules Z. Comparison of intubating conditions after administration

of Org 9426 and suxamethonium. British Jr. Anaes. 1192;69:269-73.

6. Sehgal A, Bhatia PK, Tulsiani KL. Comparison of onset time, duration of action and intubating conditions achieved with suxamethonium and rocuronium. Indian Journal of Anaesthesia 2004:48:129-33.
7. Booth MG, Marsh B, Bryden FM, Robertson EN, Baird WLM. A comparison of pharmacodynamics of rocuronium and vecuronium during halothane anaesthesia. Anaesthesia 1992;47:832-34.
8. Magorian T, Flannery KB, Miller RD. Comparison of rocuronium, scucinylcholine and vencuronium for rapid sequence induction of anaesthesia in adult patients, Anesthesiology 1993:79:913-18.

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A Comparative Evaluation of the Efficacy of Dexmedetomidine versus Fentanyl as Anesthetic Adjuvant in Attenuating the Neuroendocrine Stress Response, as Assessed Indirectly, during Laparoscopic Cholecystectomy

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Abstract

Background and Aims: Hyperglycemia and hemodynamic perturbations are the main features of neuroendocrine stress response to surgical trauma and anesthesia. We conducted a study to evaluate and compare dexmedetomidine and fentanyl as anesthetic adjuvants in attenuating neuroendocrine stress response by measuring the changes in the perioperative serial blood glucose levels and monitoring hemodynamic variations during laparoscopic cholecystectomy.

Methodology: Sixty healthy adult patients scheduled for elective laparoscopic cholecystectomy were randomly assigned into two groups (Group D and Group F) of 30 each. Group D patients received dexmedetomidine 1µg/kg/15min whereas group F patients received fentanyl 2µg/kg/15min as loading dose and then the patients were infused with 0.2-0.7µg/kg/h of the respective drug till the end of surgery. Blood glucose levels were measured preoperatively before administration of premedication (baseline) (T_0), at 30 minutes after beginning of surgery (T_1) and 5 minutes postextubation (T_2). Heart rate (HR), oxygen saturation (SpO_2), systolic (SBP), diastolic (DBP) and mean arterial pressures (MAP) were assessed at specific time intervals.

Result: Blood glucose concentration increased in both groups, though group F showed a more obvious increment than group D. T_1 and T_2 mean values in group D (115.57 and 118.80mg/dl respectively) were significantly ($p=0.020$ and $p< 0.001$ respectively) lower than that in group F (122.37 and 128.90mg/dl respectively). HR, SBP, DBP and MAP were also significantly lower in group D than group F at various time points.

Conclusion: Dexmedetomidine is a better anesthetic adjuvant than fentanyl in attenuating the neuroendocrine stress response during laparoscopic cholecystectomy.

Keywords: Anesthetic Adjuvant; Dexmedetomidine; Fentanyl; Laparoscopic Cholecystectomy; Neuroendocrine Stress Response.

Introduction

The stress response to surgery and anesthesia is mediated by complex interactions between the neuroendocrine, immunological and hematopoietic systems [1]. Hyperglycemia and hemodynamic variations (hypertension, tachycardia) are the predominant aspects of this neuroendocrine stress response and correlate well with the increased plasma concentrations of cortisol, glucagon and catecholamines. They vary with the extent of surgical trauma and are associated with adverse clinical outcomes especially in patients with compromised organ function; and can be remarkably modulated by appropriate anesthetic technique [2].

Laparoscopic cholecystectomy is associated with multiple postoperative advantages such as minimal degrees of surgical trauma, pain and pulmonary dysfunction, thus permitting faster recovery, early ambulation and shorter hospital stay [3]. Inspite of these benefits, the peritoneal carbondioxide (CO_2) insufflation resulting in increased intraabdominal

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pressure and increased CO_2 absorption; along with reverse Trendelenberg position required in laparoscopic cholecystectomy, induce pathophysiological changes characterized by decrease in cardiac output, increased arterial pressures and increased systemic and pulmonary vascular resistances [4].These hemodynamic changes are mediated by mechanical and neurohumoral factors like increased plasma concentrations of cortisol, adrenaline , noradrenaline and vasopressin; and can be profoundly influenced by various agents like opiods, β-blockers, α_2-agonists, propofol and vasodilators like nitroglycerine, thereby diminishing negative consequences and improving the clinical outcome of laparoscopic cholecystectomy, particularly in patients with diabetes mellitus and cardiovascular compromise [5].

Dexmedetomidine is a highly selective α_2-agonist (α_2:α_1 activity=1620:1). By its action on locus coeruleus in brainstem, it exhibits sedative, anxiolytic, analgesic and thus anesthetic sparing properties without causing respiratory depression. It also produces sympatholysis by diminishing the central sympathetic outflow and the plasma concentrations of noradrenaline and adrenaline [6]. Thus, when used as an anesthetic adjuvant, it provides hemodynamic stability during laryngoscopy, tracheal intubation, pneumoperi-toneum and emergence from anesthesia by obtunding the neuroendocrine stress response [7,8].

Thus, we designed a study to compare the efficacy of dexmedetomidine (drug with multidimentional properties) and fentanyl (commonly used opioid) as anesthetic adjuvants in attenuating the neuroendocrine stress response during laparoscopic cholecystectomy by measuring the changes in perioperative serial blood glucose levels and hemodynamic variables. A similar study has been done by Gupta et. al. [9] in which dexmedetomidine and fentanyl are used as premedicants only.

Materials and Methods

Patient Selection

A prospective randomized double blind study was conducted after obtaining approval from the Institutional Ethical Committee and written informed consent was taken from all the patients. Sixty adult nonobese (body mass index <30) patients aged 20-65 years, with physical status of ASA I or II of either sex, posted for elective laparoscopic cholecystectomy under general anesthesia were selected for the study. Patients not willing to give consent, with known allergic reaction especially to the study drugs, with anticipated difficult airways, on chronic medications like opioids, β-blockers, methyl-dopa, steroids, etc. i.e the drugs which affect sympathetic activity or hormonal secretions, with history of cardiorespiratory, hepatic, renal, metabolic or any significant psychiatric or neurological disorders were excluded from the study.

Study Design and Randomization

Thorough preanesthetic evaluation and routine investigations were carried out in all patients on the previous day of surgery. On the day of surgery, after confirming the preanesthetic check-up and fasting status, a multipara monitor was attached to each patient in operation theatre and baseline value of heart rate (HR), oxygen saturation (SpO_2), systolic (SBP), diastolic (DBP) and mean arterial pressures (MAP) was recorded. Baseline blood glucose value was estimated using glucometer before the administration of premedication. Premedications given were tablet alprazolam 0.25 mg and tablet ranitidine 150 mg on the night before surgery, and injection glycopyrrolate 0.2 mg intramuscularly 1h before surgery. An intravenous infusion of ringer lactate was started and then intravenous injections of ondensetron 4mg, metoclopramide 10 mg and midazolam 1 mg were given.

The patients were randomly allocated by envelope method into one of the two groups (group D and group F) of 30 patients each. Group D patients received intravenous dexmedetomidine 1μg/kg over 15 minutes and group F patients received intravenous fentanyl 2μg/kg over 15 minutes before induction of anesthesia and then the patients received continuous infusions of the respective drug @ 0.2-0.7 μg/kg/h till the end of surgery.

The study drug was prepared and the loading dose administered by the resident anesthesiologist who was not a part of data collection and patient management, in a 50 ml syringe with normal saline as a diluent, such that the concentration of dexmedetomidine and fentanyl was 8μg/ml. The patients, attending anesthesiologist and the primary investigators were all blinded to group allocation and the study drug being given to the patient.

Anesthetic Management

Patients were preoxygenated for 3 minutes and then induced with injection propofol 2mg/kg till the loss of response to verbal commands and then tracheal intubation was facilitated by injection vecuronium 0.1mg/kg. Anesthesia was maintained with

isoflurane 1-1.5%, 60% nitrous oxide in oxygen and injection vecuronium bromide as a muscle relaxant. The lung mechanics was adjusted to maintain an $ETCO_2$ value of 35-45 mm of Hg and intraabdominal pressure was maintained between 12 and 15 mm of Hg throughout the laparoscopic procedure.

Blood glucose level was estimated using glucometer preoperatively (T_0) before the administration of premedication (baseline), 30 minutes after beginning of surgery (T_1) and 5 minutes post-extubation (T_2).

All the patients were monitored and the changes in hemodynamic parameters of HR, SPO_2, SBP, DBP and MAP were recorded at various time points of baseline/prior to premedication, after loading dose administration, after induction, after intubation, soon after pneumoperitoneum creation, 5, 10, 20, 40, 60, 80, 100 and 120 minutes after pneumoperitoneum and after extubation. Intraoperatively, patients were monitored for any bradycardia or tachycardia, hypotension or hypertension and managed accordingly.

All the patients received intravenous infusion of diclofenac sodium 75mg; and then the study drug infusion and isoflurane were stopped at the end of procedure. The residual neuromuscular blockade was antagonized with injection neostigmine 0.05 mg/kg and injection glycopyrrolate 0.01mg/kg and the endotracheal tube was removed when spontaneous respiration was adequate and regular and the patients obeyed simple verbal commands. The patients were then shifted to postanesthesia care unit for observation and managed accordingly.

Statistical Analysis

Sample size was calculated to detect the difference of atleast 20% in HR and MAP with a power of 0.80 and α error of 0.05. The Statistical Software namely SPSS 18.0, and R environment ver 3.2.2 were used for the analysis of the data and Microsoft word and Excel have been used to generate graphs, tables, etc.

Descriptive and inferential statistical analysis has been carried out in the present study. Results on continuous measurements are presented as mean ± standard deviation and results on categorical measurements are presented in number (%). Significance is assessed at 5% level of significance.

To find the significance of study parameters on continuous scale between two groups (intergroup analysis) student unpaired t test has been used, for those within each group (intragroup analysis) student paired t test and for those on categorical scale between the two groups, Chi Square/Fisher Exact test has been used.

Results

Demographic profile such as age, sex and weight of the patients in both groups (D and F) was comparable. The duration of surgery was also comparable in the two groups (Table 1).

Serial Blood Glucose Level

Baseline (T_0) mean blood glucose value in group D (90.93±6.58) was comparable (p=0.276) to that in group F (92.87±7.04).We observed that, T_1 and T_2 mean values in both groups showed statistically significant ($p< 0.001$) increase from the basal value. However, this increase was more striking in group F than group D. This observation is in accordance with that of Gupta et. al. [9]. The increment of T_1 value from the basal value was 27% (group D) and 32% (group F) and that of T_2 was 31% and 39% in group D and group F respectively, and all of them were statistically significant ($p< 0.001$).

In our study, both T_1 and T_2 mean values in group D (115.57 and 118.80 mg/dl respectively) were statistically and significantly (p=0.020 for T_1 and $p < 0.001$ for T_2) lower than that in group F (122.37 and 128.90 mg/dl respectively) (Table II). In comparison, Gupta et. al. [9] found that the mean blood glucose value at 2.5 hours after surgery in dexmedetomidine group was significantly (p=0.043) lower than that of fentanyl group and that at 30 minutes after beginning of surgery did not show significant difference (p=0.53).This difference may be due to the fact that they have used dexmedetomidine and fentanyl as premedicants, whereas we have given the drugs to our patients in the form of loading dose as well as continuous infusions.

Hemodynamic Parameters

The mean basal values of HR, SpO_2, SBP, DBP and MAP were comparable in both groups. In our study, HR, SBP, DBP and MAP in group D were significantly lower than that in group F, but within hemodynamically stable limits.

In group D, the decrease in HR values from baseline was clinically and statistically significant ($p<0.001$) from the time of loading dose administration till 120 minutes after pneumoperitoneum creation, whereas that after extubation was not significant (p=0.051). On the other hand, HR in group F showed significant decrease from baseline after loading dose administration ($p<0.001$), after induction ($p<0.001$) and at 120 minutes after pneumoperitoneum (p= 0.016), whereas that after extubation showed

significant increase ($p < 0.001$) and at all other times there was no significant change from baseline.In intergroup comparison, HR in group D decreased significantly than in group F after induction ($p= 0.0430$), after intubation ($P= 0.005$), throughout the pneumoperitoneum ($P< 0.001$) and after extubation ($P= 0.001$).(Graph 1).

Significant bradycardia (HR < 50 bpm) was seen in two patients in group D that responded instantly to injection atropine 0.6 mg. This effect of dexmedetomidine is due to decreased central sympathetic outflow, which was also seen in other studies [10,11]. No patients in group F developed bradycardia. There was not much variation in SPO_2 in both the groups throughout the procedure.

In group D, SBP, DBP and MAP mean values showed significant ($p< 0.001$) decrease from baseline from the time of loading dose administration till after extubation and that in group F, decreased significantly ($p<0.001$) from baseline after loading dose administration, after induction and after intubation, whereas, that after extubation showed significant increase ($p < 0.001$), and that throughout the pneumoperitoneum showed no significant change from baseline. MAP values in group D were significantly lower than that in group F after loading dose administration ($p=0.001$), after induction ($p= 0.001$), throughout the pneumoperitoneum ($p < 0.001$) and after extubation ($p< 0.001$) (Graph 2).

Three patients (10%) in group D developed hypotension (MAP < 20% from baseline) which was treated with faster infusions of intravenous fluids and two patients out of them required vasopressors.

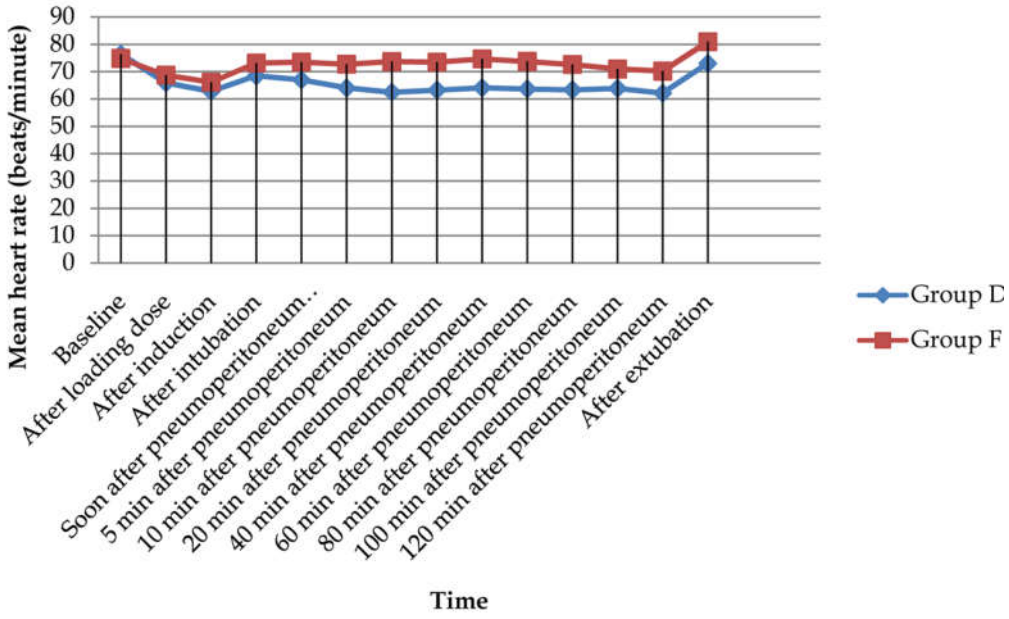
Discussion

Hyperglycemia and hemodynamic perturbations are the main aspects of the neuroendocrine stress response to surgery and anesthesia. Perioperative hyperglycemia is the result of increased hepatic glycogenolysis and gluconeogenesis, due to increased

Table 1: Demographic profile and duration of surgery of patients in group D and F

Parameters	Group D	Group F	P value
Age(years)	43.57±7.97	43.53±7.75	0.987
Gender (M/F)	13/17	14/16	1.000
Weight (Kg)	60.60± 7.70	61.47± 7.68	0.664
Duration of surgery(min)	98.47±12.29	99.47± 11.69	0.748

Values are in mean ± standard deviation.*$p<0.05$ is considered as significant. Both groups D and F were comparable in age, gender, weight and duration of surgery.

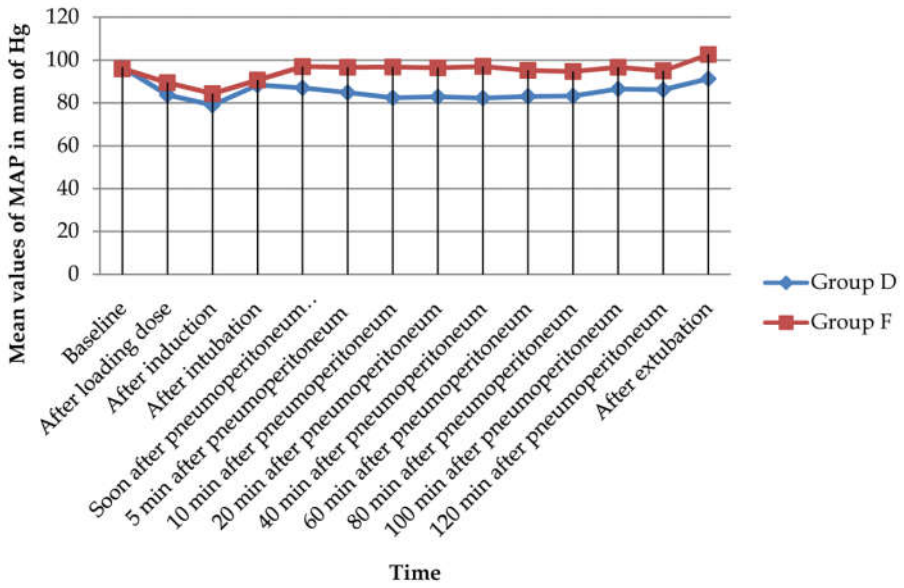


Graph 1: Perioperative variations in heart rate (beats/minute) in both groups

Table 2: Perioperative serial mean blood glucose values in mg/dl in group D and group F.

Time	Group D	Group F	P value
Preoperative/baseline(T_0)	90.93±6.58	92.87± 7.04	0.276
At 30 min after beginning of surgery (T_1)	115.57±11.29	122.37± 10.67	0.020*
At 5 min postextubation (T_2)	118.80± 9.70	128.90± 8.05	< 0.001*

Values are in mean ± Standard deviation. *p value < 0.05 is statistically significant. Baseline mean blood glucose level was comparable in both groups whereas that at 30 minutes after beginning of surgery and at 5 minutes postextubation were significantly lower in group D than that in group F.



Graph 2: Perioperative variations in MAP in mm of Hg in both groups. MAP – mean arterial pressure.

secretion of catabolic hormones like ACTH, cortisol, catecholamines and glucagon; in addition to the relative deficiency of insulin and peripheral insulin resistance [12]; and is linked with potential clinical hazards like increased susceptibility to infection, endothelial dysfunction and impaired wound healing and can be remarkably modulated by appropriate anesthetic technique as shown in several studies [13-16].

In our study, there was statistically significant ($p< 0.001$) increase in the perioperative blood glucose level from the basal value in both groups, reflecting the neuroendocrine stress response to surgery. Though, the increase was more marked in fentanyl group than in dexmedetomidine group.

In theory, α_2- adrenoreceptor agonists by their action on postsynaptic α_2- adrenergic receptors on pancreatic β-cells can cause hyperglycemia by inhibiting insulin release [6]. But interestingly, in their study, Ahmed et. al. [17] and Yacout et. al. [18] observed that intravenous infusion of dexmedetomidine reduced the hemodynamic and neuroendocrine stress response to cardiopulmonary bypass and major surgeries respectively, as indicated by clinically and statistically significant reduction in heart rate, mean arterial pressure, blood glucose level and plasma levels of cortisol, adrenaline and noradrenaline. Also, Harsoor et. al. [11] found that when dexmedetomidine was given at loading dose of 1µg/kg/10 min followed by continuous infusion of 0.5µg/kg/h till the end of surgery, it was effective in attenuating metabolic stress response to major surgeries as suggested by stable blood glucose levels without affecting intraoperative cardiovascular stability.

Even, Uyar et. al. [19] have shown that a single bolus dose of 1µg/kg/10 min given before induction of anesthesia was effective in blunting the hemodynamic and neuroendocrinal responses to skull-pin insertion in patients undergoing craniotomy, as evidenced by significant lower levels of HR, arterial blood pressures and blood glucose levels as well as that of plasma cortisol and prolactin in dexmedetomidine group as compared to the placebo group. In contrast to our study, Bulow et. al. [20] observed that hyperglycemia was higher in

dexmedetomidine group when they compared it with remifentanil in TIVA in patients undergoing gynecologic videolaparoscopic surgery.

Dexmedetomidine, a highly selective α_2-adrenergic agonist possesses sedative, anxiolytic, analgesic, anesthetic sparing and sympatholytic properties without causing respiratory depression; which have enabled it to be used as a highly effective anesthetic adjuvant. Its biphasic cardiovascular response can be overcome by infusing loading dose slowly over 10 or more minutes [6].

Thus, when administered as a continuous infusion, dexmedetomidine exhibits an expected and stable hemodynamic response, even during stressful conditions of laryngoscopy, intubation, pneumoperitoneum and extubation as seen in our study and many other recent studies [8,10,12].

In our study, the mean values of HR and MAP were significantly lower in group D than that in group F at various time points but within hemody-namically stable limits. Also, the rise in HR and MAP in response to creation of pneumo-peritoneum and extubation was more effectively suppressed by dexmedetomidine than fentanyl [9,22,23].

Similarly, Bilgi et. al. [24] observed that dexmedetomidine in comparison to fentanyl diminished the sympathetic response to laryngoscopy and intubation in hypertensive patients, maintained stable hemodynamics intraoperatively as well as during extubation. Also Goyal et. al. [25] found that dexmedetomidine is superior to fentanyl in attenuating pressor responses to laryngoscopy, intubation and extubation and provides better hemodynamic stability in breast cancer surgeries.

Conclusion

We conclude that, dexmedetomidine as an anesthetic adjuvant is more effective than fentanyl in attenuating the neuroendocrine stress response to laryngoscopy, intubation, pnemoperitoneum and extubation; though we suggest that dexmedetomidine be used cautiously, as it can cause bradycardia and hypotension. Further studies involving the use of dexmedetomidine in patients with diabetes mellitus and cardiovascular compromise will enable them to achieve better clinical outcome from laparoscopic surgeries.

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Nil

Conflicts of Interest

There are no conflicts of interest.

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References

1. Weissman C. The metabolic response to stress: an overview and update. Anesthesiology. 1990 Aug;73(2):308-27.
2. Schricker T, Lattermann R, Schreiber M, Geisser W,Georgieff M, Radermacher P. The hyperglycaemic response to surgery: pathophysiology, clinical implications and modification by the anaesthetic technique.Clinical Intensive Care. 1998;9(3):118-128.
3. Jean L Joris. Anesthesia for Laparoscopic Surgery. In: Miller R D, editor. Miller's Anesthesia 7th ed. Philadelphia: Elsevier, Churchill Livingstone; 2010.pp.2185-202.
4. Myre K, Rostrup M, Buanes T, Stokland O. Plasma catecholamines and haemodynamic changes during pneumoperitoneum. Acta Anaesthesiologica Scandinavica. 1998 March;42(3):343- 347.
5. Joris J L, Chiche J D, Canivet J L, Jacquet N J, Legros J J, Lamy M L.Hemodynamic changes induced by laparoscopy and their endocrine correlates: effects of clonidine. J Am Coll Cardiol. 1998 Nov;32(5): 1389-96.
6. Ralph Gertler, H Cleighton Brown, Donald H Mitchell and Erin L Silvius. Dexmedetomidine: a novel sedative- analgesic agent. Proc (Bayl Univ Med Cent). 2001 Jan;14(1):13-21.
7. Manne G R, Upadhyay M R, Swadia V N. Effects of low dose dexmedetomidine infusion on haemodynaminc stress response, sedation and post-operative analgesia requirement in patients undergoing laparoscopic cholecystectomy. Indian J Anaesth.2014 Nov-Dec;58(6):726-31.
8. Chavan SG, Shinde GP, Adivarekar SP, Gujar SH and Mandhyan S. Effects of dexmedetomidine on perioperative monitoring parameters and recovery in patients undergoing laparoscopic cholecystectomy. Anesth Essays Res. 2016 May-Aug;10(2):278-283.
9. Gupta K, Maggo A, Jain M, Gupta PK, Rastogi B and Singhal A B. Blood glucose estimation as an indirect assessment of modulation of neuroendocrine stress response by dexmedetomidine versus fentanyl premedication during laparoscopic cholecystectomy:

A clinical study. Anesth Essays Res. 2013 Jan-Apr;7(1): 34-38.

10. Vora KS, Baranda U, Shah VR, Modi M, Parikh GP and Butala BP. The effects of dexmedetomidine on attenuation of hemodynamic changes and there effects as adjuvant in anesthesia during laparoscopic surgeries. Saudi J Anaesth. 2015 Oct-Dec;9(4):386-392.
11. Harsoor SS, Rani DD, Lathashree S, Nethra SS, Sudheesh K. Effect of intraoperative Dexmedetomidine infusion on Sevoflurane requirement and blood glucose levels during entropy-guided general anesthesia. J Anaesthesiol Clin Pharmacol. 2014 Jan; 30(1):25-30.
12. JP Desborough. The stress response to trauma and surgery. Br J Anaesth. 2000;85:109-17.
13. Zlata Mujagiæ, Elsada Èièko, Vesna Vegar- Brozoviæ, Mirsada Prašo. Serum levels of glucose and lactate in patients treated under total intravenous anesthesia with propofol- fentanyl and under balanced anesthesia with isoflurane- fentanyl. Biochemia Medica 2007;17(1):71-8.
14. Schricker T, Galeone M, Wykes L, Carli F. Effect of desflurane/ remifentanil anesthesia on glucose metabolism during surgery: a comparison with desflurane/ epidural anesthesia. Acta Anaesthesiol Scand. 2004 Feb; 8(2):169-73.
15. Walsh ES, Paterson JL, O' Riordan J B, Hall GM. Effect of high-dose fentanyl anaesthesia on the metabolic and endocrine response to cardiac surgery. Br J Anaesth. 1981 Nov;53(11):1155-65.
16. Hall G M. The anaesthetic modification of the endocrine and metabolic response to surgery. Ann R Coll Surg Engl. 1985 Jan;67(1):25-29.
17. Ahmed M Mukhtar, Eman M Obayah and Amira M Hassona. The use of dexmedetomidine in pediatric cardiac surgery. Anesth Analg. 2006 July;103(1:52-56.
18. Yacout AG, Osman HA, Abdel- Daem MH, Hammouda SA, Elsawy MM. Effect of intravenous dexmedetomidine infusion on some proinflammatory cytokines, stress hormones and recovery profile in major abdominal surgery. Alexandria Journal of Medicine 2012;48:3-8.
19. Uyar AS, Yagmurdur H, Fidan Y, Topkaya C, Basar H. Dexmedetomidine attenuates the hemodynamic and neuroendocrinal responses to skull-pin head holder application during craniotomy. J Neurosurg Anesthesiol. 2008 July;20(3):174-9.
20. Bulow NM, Barbosa NV, Rocha JB. Opioid consumption in total intravenous anesthesia is reduced with dexmedetomidine : a comparative study with remifentanil in gynecologic videolaparoscopic surgery. J Clin Anesth 2007 Jun;19(4):280-5.
21. Acharya G, Gokharu S, Arora KK et al. Effect of Two Different Doses of Dexmedetomidine on Hemodynamics in Patients undergoing Laparoscopic Surgeries under General Anesthesia- A Comparative Study. Int J Healthcare Edu and Med Inform 2016; 3(1):12-18.
22. Aksu R, Akin A, Biçer C, Esmaoðlu A, Tosun Z, Boyaci A. Comparison of the effects of dexmedeto-midine versus fentanyl on airway reflexes and hemodynamic responses to tracheal extubation during rhinoplasty: A double-blind, randomized, controlled study. Curr Ther Res Clin Exp. 2009 Jun;70(3):209-20.
23. Kataria AP, Attri JP, Kashyap R and Mahajan L. Efficacy of dexmedetomidine and fentanyl on pressor response and pneumoperitoneum in laparoscopic cholecystectomy. Anesth Essays Res. 2016 Sep-Dec; 10(3): 446-450.
24. Bilgi KV, Vasudevan A, Bidkar PU. Comparison of dexmedetomidine with fentanyl for maintenance of intraoperative hemodynamics in hypertensive patients undergoing major surgery: A randomized controlled trial. Anesth Essays Res. 2016 May-Aug;10(2):332-7.
25. 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 Jul-sep;11(3):611-616.

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An Observational Study on Effects of Rocuronium Bromide during Tracheal Intubation among Elective Caesarean Section Patients

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Abstract

Background: Aspiration of gastric content, during induction and intubation is a major risk factor which determines the outcome of anaesthesia. As all the patients undergoing caesarean section are considered full of stomach due to delayed gastric emptying, rapid intubation is mandatory in them. The ideal muscle relaxant is the one who produces faster onset of action; resultant in to reduction in the incidence of side effects. The aim of this study was to determine the effects of rocuronium during tracheal intubation on patients who were scheduled for elective caesarean section.

Material and Methods: Total 90 ASA grade I and II near term patients who were to undergo elective caesarean section were included. Selected patients were randomly divided in to 3 groups consisting 30 patients in each. Group I (S60) patients received suxamethonium 1.5 mg/kg with intubation attempted at 60 seconds and patients of groups II (R60) and III (R90) received rocuronium 0.6 mg.kg with intubation attempted at 60 seconds and rocuronium 0.6 mg.kg with intubation attempted at 90 seconds respectively.

Results: The intubating conditions were acceptable in all the patients belonging to group I (S60) and group III (R90), while 04 patients in group II (R60) had unacceptable intubating conditions. Rocuronium found haemodynamically stable as suxamethonium.

Conclusion: Rocuronium provides acceptable intubating conditions in patients undergoing elective caesarean section with no incidence of side effects or complications.

Keywords: Rocuronium; Suxamethonium; Caesarean Section; Intubating Conditions.

Introduction

The most important aspect of general anaesthesia is rapid and safe endotracheal intubation. Tracheal intubation is a routine procedure to ensure a safe protected airway through which one can provide intermittent positive pressure ventilation during all procedures carried out under general anaesthesia. Aspiration of gastric content, during induction and intubation is a major risk factor which determines the outcome of anaesthesia and endotracheal intubation is mandatory to avoid morbidity and mortality due to this. The ease with which endotracheal intubation is performed depends upon degree of muscle relaxation, depth of anaesthesia and skill of anaesthesiologist [1]. The ideal muscle relaxant is the one who produces faster onset of action; resultant in to reduction in risk of side effects.

As all the patients undergoing caesarean section are considered full of stomach due to delayed gastric emptying, rapid intubation is mandatory in them. Traditionally, suxamethonium is being used to facilitate rapid sequence induction and endotracheal intubation. Although suxamethonium has rapid onset of time and brief duration of action it also showed many adverse systemic effects including cardiac

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dysrhythmias, muscle fasciculation, hyperkalemia, elevated intracranial, intragastric and intraocular pressure. Different techniques have been tried including 'priming' [2] to decrease the effective onset time of nondepolarizing muscle relaxants like vecuronium, pancuronium or atracurium. Though priming accelerates the onset of block of most non depolarizing relaxant by 30-60 seconds, intubation time is still long and is considered unsafe.

Rocuronium is a non depolarizing muscle relaxant introduced in nineties and whose formula was based on vecuronium bromide [3]. Different studies suggested that unlike suxamethonium rocuronium has little or no cardiovascular effects, placental transfer is limited and it has no adverse effects towards neonate. In contrast to conventional anaesthetic neither priming nor marked increased doses are required to achieve a rapid onset. So rocuronium could be potentially ideal for fast intubation with no or minimum side effects in all patients receiving general anaesthesia including caesarean section. With this background in mind current study was conducted with following aim and objectives.

Aim

To study effect of rocuronium bromide during tracheal intubation in patients undergoing elective caesarean section.

Objectives

- To assess the intubating conditions with rocuronium bromide and suxamethonium.
- To study the changes in hemodynamic parameters.
- To assess the effect of rocuronium on neonates.

Material and Methods

The present study was conducted after institutional ethical committee's approval. Patients were enrolled after explaining the purpose and procedure of the study and written informed consent was obtained. Total 90 ASA grade I and II near term patients who were to undergo elective caesarean section were included. Patients of foetal distress, known case of intrauterine foetal death or congenital anomalies, multiple gestations, patients with difficult airway or obesity (weight > 100kg), ASA grade III or more and patients on drugs like anticonvulsant, polypeptide antibiotics etc were excluded from study. Selected patients were randomly divided in to 3 groups consisting 30 patients in each. Group I patients received suxamethonium and patients of groups II and III received rocuronium as follows.

Group I (S60): Suxamethonium 1.5 mg/kg with intubation attempted at 60 seconds;

Group II (R60): Rocuronium 0.6 mg.kg with intubation attempted at 60 seconds;

Group III (R90): Rocuronium 0.6 mg.kg with intubation attempted at 90 seconds.

All minimum necessary investigations were performed before commencing study. All the patients received tablet famotidine 40 mg orally at 10 pm. on the night before surgery and fasted overnight. On the day of surgery baseline pulse rate, blood pressure, body weigh were recorded.

Intramuscular premedication in the form of injection glycopyrrolate 0.2 mg was given 30 minutes prior to induction of anaesthesia. Pre-oxygenation was carried out with 100% O_2 for 3 minutes. Anaesthesia was induced with injection thiopentone 5 mg/kg/IV. Abolition of eyelid and eyelash confirmed induction in all cases. Immediately after induction muscle relaxants were administered intravenously according to their dose in specified groups and time onset of apnoea noted.

Laryngoscopy and intubation was attempted as specified for the groups i.e. at 60 seconds after the injection of suxamethonium of 1.5 mg/kg in group I (S60) and at 60 and 90 seconds after injection of rocuronium of 0.6 mg/kg in group II (R60) and group III (R90) respectively.

Intubation conditions were assessed according to three point scales (0-2) and if the score were in between 5 to 8 and 0 to 4 were labelled it as acceptable and unacceptable intubating conditions respectively (Table 1). If the patients having difficult intubating condition were managed according to difficult airway management protocol.

At the end of surgery residual neuromuscular blockage was reversed with injection neostigmine 0.05 mg/kg and atropine 0.02 mg/kg or glycopyrrolate 10µg/kg. Vitals were recorded before and after induction, 1and 5 minutes after intubation and thereafter every 10 minutes throughout the surgical procedure in all the groups. Side effects and complication noted if any. Every neonate was evaluated by paediatrician and Apgar scores at 1 and 5 minutes were noted.

Data Analysis

Data coding and entry was done in Microsoft Excel spread sheets and descriptive and inferential statistical analysis was done by using SPSS version

21 (Statistical Package for Social Sciences) software. One way ANOVA, Tukey Kramer multiple comparison test, Un-paired 't' test, mean, standard deviation used and differences were considered to be significant if p value was < 0.05.

Results

In present study total 90 full term parturients, scheduled to undergo elective caesarean section were divided in equally in three groups. On one way ANOVA the difference of the age groups and weight groups in between three groups found statistically non significant. (Table 2 A & B). The mean time of apnoea onset of suxamethonium group I (S60) was 25.06±6.89, for group II (R60) and group III (R90) it was 29.76±10.21 and 32.83±8.63 respectively. Statistically significant difference was observed in between mean apnoea onset time of all three groups (S60, R60 and R90) but non-significant difference was seen in between two rocuronium groups. i.e. R60 and R90 (Table 3).

Table 1: Assessment of intubation conditions

Sr. No	Variables	Conditions		
1	Jaw relaxation	Good	Incomplete	Poor
2	Vocal cord position	Full abducted	Slightly abducted	Moderately abducted
3	Reaction to intubation	None	Bucking	Gross movement
	Score	**2**	**1**	**0**
	Interpretations			
	Excellent (7 to 8)	Acceptable	Fair (2 to 4)	Unacceptable
	Good (5 to 6)		Poor (to 1)	

Table 2A: Age wise distribution of patients

Sr. No	Age groups (yrs)	No of patients		
		Group I (S60)	Group II (R60)	Group III (R90)
1.	20-25	23	19	18
2.	26-30	06	10	09
3.	31-35	01	01	03
	Total	30	30	30
	Mean ± Sd.	23.86±2.94	24.46±3.81	25.73±4.09

One way ANOVA F=2.057, p=0.13 Non significant

Table 2B: Weight wise distribution of patients

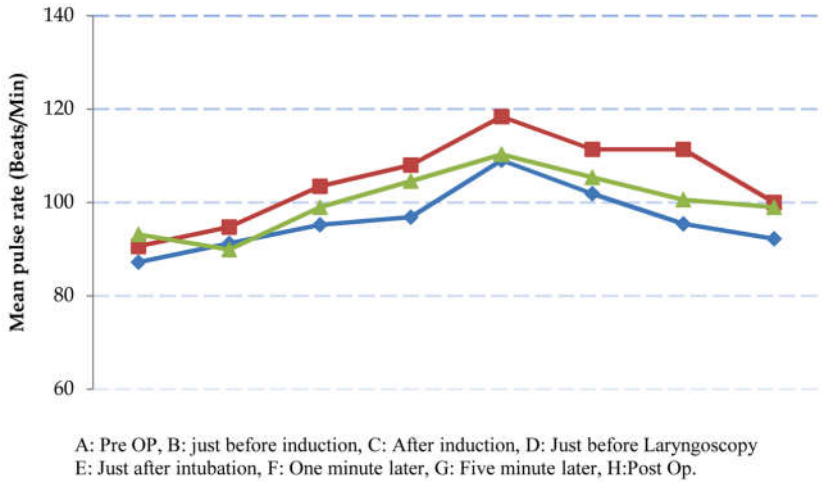
Sr. No	Weight groups (Kg)	No of patients		
		Group I (S60)	Group II (R60)	Group III (R90)
1.	40-55	17	17	18
2.	56-70	11	10	11
3.	≥ 71	02	03	01
	Total	30	30	30
	Mean ± Sd.	54±9.04	57.26±9.46	54.7±7.89

One way ANOVA F=1.135, p=0.32 Non significant

Table 3: Distribution according to mean apnoea onset time

	Mean apnoea time (Mean ± SD)
Group I (S60)	25.06 ± 6.89 *
Group II (R60)	29.76 ± 10.21 * #
Group III (R90)	32.83 ± 8.63 * #

* One way ANOVA: F=6.094 p=0.003 Significant
\# Un paired t test: 1.258 d.f.=58, p=0.21 Non significant



Graph 1: Mean pulse pressure at various stages

Table 4: Intubating conditions and acceptability

Groups	Acceptable		Unacceptable		Total
	Excellent	Good	Fair	Poor	
Group I (S60)	30	00	00	00	30
Group II (R60)	15	11	03	01	30
Group III (R90)	30	00	00	00	30

Table 5: Intubating conditions

Groups	Intubating scores (Mean ± SD)
Group I (S60)	7.8 ± 0.4 * @ $
Group II (R60)	6.06 ± 1.55 * # $
Group III (R90)	7.5 ± 0.5 # @ $

*Tukey Kramer test: p=0.001 Significant #Tukey Kramer test: p=0.00 1 Significant @Tukey Kramer test: p=>0.05 Non significant $One way ANOVA: F: 27.686 p= <0.0001 Significant

Table 6: Distribution according to mean pulse rate

Study group	Pre-Op.	Just before IND'N	After IND'N	Just before L'SCOPY	Just after Intubation	1 Min later	5 Min. later	Post Op.
Group I (S60)	87.3±8.16 *	91.22 ±9.54	95.2 ±9.20	96.83 ±8.82 *	109.03 ±111.20 *	101.86 ±9.92	95.4 ±10.21	92.2 ±8.83
Group II(R60)	90.58 ±10.59$	94.7 ±10.93	103.46 ±11.14	108.00 ±11.14 $	118.36 ±10.86 $	111.36 ±12.41	111.36 ±12.41	99.96 ±11.35
Group III(R90)	93.13 ±8.83 @	89.87 ±16.91@	98.96 ±10.51	104.53 ±14.05 @	110.23 ±14.30	105.36 ±13.92	100.53 11.33	98.96 ±9.96

*One way ANOVA: F=39.574, p<0.001 Significant, $One way ANOVA: F=50.080, p<0.001 Significant, @One way ANOVA: F=14.218, p<0.001 Significant

Table 7: Distribution according to systolic blood pressure

Study group	Pre-Op.	Just before IND'N	After IND'N	Just before L'SCOPY	Just after Intubation	1Min. later	5Min. later	Post Op.
Group I (S60)	126.86±13.19@	125.33±15.86	114.6± 15.70	116.33±13.95	139.93±14.24@	122.13±11.23	114.13±11.28	125.6 ±11.73
Group II(R60)	121.33±10.87#	121.66±9.67	113.53±11.25	112.86±8.44	135.2±13.72#	118.4±11.72	113.06± 11.35	119.66 ±8.68
Group III(R90)	120.93±11.09*	115.12±21.81	111.46±12.09	114.26±13.88	132.53±12.39*	119.6±14.58	112.8 ±8.89	123.26 ±11.99

@Unpaired 't' test: t=3.668 d.f=58, p=0.0005 Significant, #Unpaired 't' test: t=4.340 d.f=58, p=0.0001 Significant, *Unpaired 't' test: t=3.821 d.f=58, p=0.0002 Significant

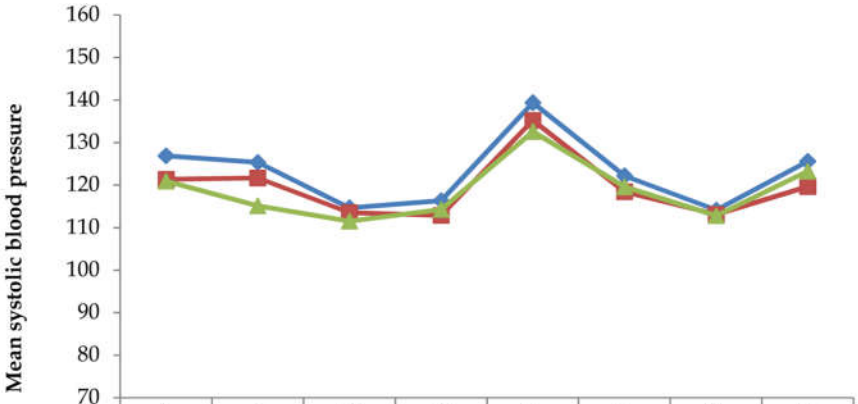
The intubating conditions were acceptable in all the patients belonging to group I (S60) and group III (R90), while 26 patients in group II (R60) had acceptable conditions and remaining 4 patients had unacceptable intubating conditions (Table 4). On statistical analysis the significant difference was observed in the mean intubating score of group I and group II, group II and group III and All three groups except group I and group III (Table 5).

In all three groups mean pulse found to be increased after giving muscle relaxant i.e. just before laryngoscopy and just after induction as compared pre operative reading (Graph 1). The difference found to be significant groups in all (Table 6).

The mean systolic blood pressure rose just after intubation as compared to basal reading. The difference between basal mean systolic blood pressure and mean blood pressure just after the intubation found to be statistical significant in all three study groups (Table 7). The mean systolic blood pressure started decreasing immediately after intubation and it felt below basal level at one minute after intubation (Graph 2).

The mean clinical duration of action of intubating dose of group I (S60), group II (R60) and group III (R90) were 7.8±0.4, 24.83±3.62 and 25.86±6.87 respectively. The duration of action of both rocuronium groups was more than that of suxamethonium and in these three group's difference was found statistically significant (P < 0.0001) but was not significant in group II (R60) and group III (R90). (P 0.47) (Table 8).

The mean Apgar score at 1 min was 6.96±0.78, 7.1 ±0.907 and 6.96±0.795 of group I (S60), group (R60) and group III (R90) respectively. Similarly the mean Apgar score at 5 min was 9.16±0.778, 9.1±1.04



	A	B	C	D	E	F	G	H
Group I (S60)	126.86	125.33	114.6	116.33	139.33	122.13	114.13	125.6
Group II (R60)	121.33	121.66	113.53	112.86	135.2	118.4	113.06	119.66
Group III (R90)	120.93	115.12	111.46	114.26	132.53	119.6	112.8	123.26

Graph 2: Systolic blood pressure at various stages

Table 8: Mean duration of action of intubating dose of relaxant

	Group I (S60)	Group II (R60)	Group III (R90)
Mean ± SD	7.8 ± 0.4 $ #	24.83 ± 3.62 $ #	25.86 ± 6.87 #
Statistical test	$ Unpaired 't' test: t=0.72 d.f:58, P 0.47 Non-significant # One way ANOVA: F=153.13, P=0.0001 Significant		

Table 9: Distribution according to Apgar score

	Apgar score at 1 Min Group I (S60)	Group II (R60)	Group III (R90)
Mean ± SD	6.96 ± 0.71	7.1 ±0.90	6.96 ±0.79
Statistical test	One way ANOVA: F=0.298, P=0.747 Non significant		

	Apgar score at 5 Min Group I (S60)	Group II (R60)	Group III (R90)
Mean ± SD	9.16 ±0.77	9.1 ±1.04	9.03 ±0.80
Statistical test	One way ANOVA: F=0.163, P=0.84 Non significant		

and 9.03±0.80 of group I (S60), group II (R60) and group III (R90) respectively.

No statistical difference was observed of Apgar score of 1 min and 5 min among three groups (Table 9). No side effects or complications were encountered in present study also there was no incidence of regurgitation or aspiration of gastric content.

Discussion

The goal of tracheal intubation is to secure the patients airway quickly and smoothly with minimum chances of hypoxia, regurgitation and aspiration of gastric contents. Pregnant patients have delayed gastric emptying, so they are more risk of gastric contents aspiration. Traditionally suxamethonium has long been choice of muscle relaxant however it falls short of the qualities of an ideal 'muscle' relaxant due to its side effects. Keeping this objective in mind the present study undertook to evaluate the properties of alternate muscle relaxant like rocuronium that has the same advantages of rapid onset and good to excellent intubating conditions as suxamethonium, but fewer side effects.

In present study total 90 pregnant women included randomly who were scheduled for elective caesarean section. The mean age of patients was 23.86±2.94 years in group I (S60), 24.46±3.81 years in group II (R60) and 25.73±4.09 in group III (R90). On other hand the mean body weight in group I (S60), group II (R60) and group III (R90) were 54±9.04, 57.26±9.46 and 54.7±7.89 kg respectively. The mean age and weight in all age groups were comparable i.e. no statistical significant difference was observed.

Apnoea onset time is defined as the time interval between injection of muscle relaxant and complete cessation of spontaneous respiration. In this study apnoea time was clinically evaluated. Huizinga et. al [4] used relaxograph to measured apnoea time. Abouleish et. al. [5] considered disappearance of T1 as tie of onset of action of rocuronium in the patients undergoing caesarean section. Baraka et. al. [6] measured the time from injection of rocuronium to maximum neuromuscular block by stimulating ulnar nerve at wrist and measuring TOF response at adductor pollicis; and considered it as onset time. In this study apnoea mean apnoea onset time was faster in suxamethonium group than in both rocuronium groups. The difference was statistical significant while mean apnoea onset time showed no statistical difference in between two rocuronium groups.

Intubating conditions were acceptable in all patients of group I (S60) and group III (R90) while out of 30 patients of group II (R60), 26 and 4 patients had acceptable and unacceptable conditions respectively. In a study conducted by Wierda et. al. [7] in adult found that intubating conditions were excellent at 1 minute and they also found that the mean time to 75% block was faster in rocuronium group compared to vencuronium. Abouleish et. al. [5] found that excellent intubating conditions could be achieved in 90% of caesarean section patients with patients with rocuronium 0.6 mg/kg when combined with 6 mg/kg of thiopentone and waiting time of 80 seconds after injection. Similarly comparable results were obtained in other studies like Cooper et. al.[8], Huizinga et. al. [4] and Sehgal et. al. [9].

Stability of vital parameters like pulse and blood pressure are highly desirable during anaesthetic management. In present study pulse rate and systolic blood pressure were recorded at various stages. In this study mean pulse rate was found to be increased after giving relaxant as compared to pre operative values. The difference between basal mean systolic blood pressure and mean blood pressure just after the intubation found to be statistical significant in all three study groups ($P < 0.001$). Even after decreased in pulse rate 1 minute after intubation it remains high to basal values comparatively. Booth et. al. [10] showed transient to moderate increased heart rate at a dose of 0.6 mg/kg of rocuronium. In a study conducted by Cooper R et. al. [8] no significant change in heart rate was found with rocuronium 0.6 mg/kg.

This study showed raised in mean systolic blood pressure just after intubation in all three groups and it was statistically significant as compared to basal values. The mean systolic blood pressure decreased at 1 minute after intubation and remained nearly same as basal level in all three groups. Cooper R et. al. [8] reported no significant change in blood pressure.

The clinical duration of action of muscle relaxant was defined as the time interval between injection of muscle relaxant and initiation of spontaneous diaphragmatic activity with increased resistance felt during ventilation. In present study mean clinical duration of action was more in both rocuronium groups as compared to suxamethonium group and difference was found statistically significant ($P < 0.0001$) similar results were observed by Cooper et. al. [8], Huizinga et. al. [4], Magorian et. al. [11] and Baraka et. al. [6] etc.

In present study regarding Apgar score, no statistically significant difference was observed at 1 minute and 5 minute among three study groups. No adverse neonatal outcome and side effects or

complications were reported during study. Abouleish et. al. [5] and Kelly MC et. al. [12] and Baraka et. al. [6] reported similar comparable results with the present study. McCourt et. al. [13] reported erythema in 6 and 17 patients given suxamethonium 1mg/kg and rocuronium 0.6 mg/kg respectively.

Conclusion

Rocuronium provides acceptable intubating conditions in patients undergoing elective caesarean section with no incidence of side effects or complication.

References

1. Shukla A, Dubey KP, Sharma MSN. Comparative evaluation of haemodynamic effects and intubating conditions after the administration of org 9426 (rocuronium) and succinylcholine. Ind J Anaesth. 2004;48(6):476-479.
2. Chatrath V, Singh I, Chatrath R, Arora N. Comparison of Intubating Conditions of Rocuronium Bromide and Vecuronium Bromide with Succinylcholine Using "Timing Principle" J Anaesth Clin Pharmacol 2010; 26(4):493-497.
3. Goodman Gilman A, Hardman JG, Limbird LE eds. The pharmacological basis of therapeutics. 10th ed. London: McGraw-Hill, 2001.
4. Huizinga CT, Vandenbrom RH, Wierds JM, Hommes FD, Hennis PJ. Intubating conditions and onset of neuromuscular block of rocuronium; a comparison with suxamethonium. Acta Anaesthesiol Scand 1992; 36:463-468.
5. Abouleish E, Abboud T, Lechevalier T, Zhu J, Chalian A, Alford K. Rocuronium for casesarean section. British Jr.Anaes. 1994;73:336-41.
6. Baraka AS, Sayyid SS, Assaf BA. Thiopental – rocuronium versus ketamine-rocuronium for rapid sequence intubation in patients undergoing caesarean section. Anesth Analg. 1997;84:1104-07.
7. Wierda JMKH, Hommes FDM, Nap HJA, Broek L. Time course of action and intubating conditions following vecurorium, rocuronium and mivacurium. Anaesthesia 1995;50:393-96.
8. Cooper R, Mirakhur RK, Clarke RS, Boules Z. Comparison of intubating conditions after administration of Org9426 and suxamethonium. British Jr. Anaes. 1192;69:269-73.
9. Sehgal A, Bhatia PK, Tulsiani KL. Comparison of onset time, duration of action and intubating conditions achieved with suxamethonium and rocuronium. Indian Journal of Anaesthesia 2004;48: 129-33.
10. Booth MG, Marsh B, Bryden FM, Robertson EN, Baird WLM. A comparison of pharmacodynamics of rocuronium and vecuronium during halothane anaesthesia. Anaesthesia 1992;47:832-34.
11. Magorian T, Flannery KB, Miller RD. Comparison of rocuronium, scucinylcholine and vencuronium for rapid sequence induction of anaesthesia in adult patients, Anesthesiology 1993:79:913-18.
12. Kelly MC, Mirakhur RK, Carabine CA, Kumar N, McGrath K, Loan PB et. al. Rocuronium placental transfer and neonatal effects. Anesthesiology 1996;85:A883.
13. McCourt KC, Salmela L, Mirakhur RK, Carroll M, Makinen MT, Kansanaho M et. al. Comparison of rocuronium and suxamethonium for use during rapid sequence induction of anaesthesia. Anaesthesia 1998;53:867-71.

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Comparitive Study of Bupivacaine with Fentanyl versus Bupivacaine for Epidural Labour Analgesia

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Abstract

Labour is an extremely painful process. Labour pain is of major concern since most parturients experience significant pain of extremely severe intensity. Labour pain can have deleterious effects on the mother, on the foetus and on the labour outcome. Among the current methods of obstetric analgesia, regional analgesia (the most widespread technique being epidural analgesia) offers the best effectiveness/safety ratio. We conducted this study to compare the efficacy of a mobile epidural using 0.0625% bupivacaine and 0.0002% fentanyl versus a conventional epidural using 0.125% bupivacaine for labour analgesia.

Keywords: Labour Analgesia; Bupivacaine; Fentanyl; Epidural.

Introduction

Labour is an extremely painful process. Labour pain is of major concern since most parturients experience significant pain of extremely severe intensity. Labour pain can have deleterious effects on the mother, on the foetus and on the labour outcome. Among the current methods of obstetric analgesia, regional analgesia (the most widespread technique being epidural analgesia) offers the best effectiveness/safety ratio [1]. The increased availability of epidural analgesia and the favorable experiences of women who have had painless labor with epidural block have reshaped the expectations of pregnant women entering labor [2]. Compared with other forms of pain relief, epidural analgesia is associated with the highest level of maternal satisfaction [3]. Adding an opioid to local anaesthetic solutions can provide effective analgesia with bupivacaine sparing and a reduction in motorblock [4,5]. The use of either an intermittent bolus or a continuous infusion of local anesthetic (with or without an opioid) is considered to provide similar analgesic efficacy and no measurable outcome differences [6,7]. The efficacy and duration of epidural opioid alone is considered inferior to epidural local anesthetic, but the benefits of an opioid should outweigh the side effects such as nausea, pruritus, and sedation [8,9]. An epidural opioid local anesthetic combination may enhance the duration and quality of pain relief at less intense motor blockade and contribute to the good progress of labor and vaginal delivery [3].

We conducted this study to compare the efficacy of a mobile epidural using 0.0625% bupivacaine and 0.0002% fentanyl versus a conventional epidural using 0.125% bupivacaine for labour analgesia.

Aim of the Study

To compare the efficacy of epidural analgesia using 0.0625% Bupivacaine and 0.0002% fentanyl versus an epidural using 0.125%

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Bupivacaine alone for labour analgesia.

The Following Parameters are Compared:

- Quality of analgesia (VAS)
- Duration of labour
- Motor block (Bromage score)
- Time from epidural to delivery
- Rate of operational delivery

Materials and Methods

This is a prospective randomised study conducted on Fifty parturients who were admitted to the antenatal ward and who requested pain relief during labor and who fulfilled the recruitment criteria were selected for the study. The procedure was explained to them in detail and written consent was obtained from them.

Ethical Requirement

The study was performed in accordance with the principles stated in the Declaration of Helsinki. Ethical approval of the study protocol was obtained from the Ethics Committee at the Institution before the study was undertaken.

Informed Consent

Written informed consent was obtained from each patient in the prescribed format prior to performance of any study related procedures: before physical examination, laboratory screening or any other investigational procedure and before administration of any study related medication. The patients were given full information about the nature, procedure and importance of the study.

Inclusion Criteria

- ASA Status I & II.
- Females in the age group from 18 to 30 years.
- Primigravida.
- Adequate gynaecoid pelvis.
- Cervical dilatation less than 4 cm.

Exclusion Criteria

- Patient refusal.
- Patients with pregnancy induced hypertension, heart disease, anaemia and other complications of pregnancy.
- Cervical dilatation greater than 4 cm
- Patients who received systemic opioids within 4 hours of epidural request
- Coagulopathy
- Patients with clinically significant renal, hepatic, cardiovascular, haematopoetic, pulmonary, gastrointestinal, nervous or endocrine disorders
- Patients unwilling or unable to comply with the study procedures

Study Procedures

IV access was secured but no IV fluid load was given. The patients were shifted to the operation theatre for insertion of the epidural catheter in aseptic manner. An epidural catheter was sited at the L3-L4 lumbar interspace using a standard midline technique with an 17-gauge Tuohy needle. The procedure was clearly explained to the patient. The visual analog scale was shown to them and interpretation of the scale explained in detail. Anaesthesia machine was checked and all emergency airway equipments like laryngoscopes, blades of different sizes, endotracheal tubes, LMAs, oropharyngeal airways were kept ready. An emergency drug tray containing all the emergency drugs was also kept ready.

Patient's vital parameters like heart rate, blood pressure, respiratory rate and fetal heart rate were continuously monitored during the procedure. The baseline values were recorded. The drugs to be administered epidurally were prepared and stored in a sterile container.

Procedure

With the patient in sitting position, under aseptic precaution L3-L4 interspace was identified and skin infiltration was done with 1.5 ml of 2% lignocaine. Using a 17G Tuohy needle and 'loss of resistance to air' technique the epidural space was identified. After confirmation by negative aspiration test 19G epidural catheter was inserted and 5 cms kept inside the epidural space. The catheter was tapped firmly to the back. The patient was turned to supine position. After negative aspiration of blood and CSF the initial dose of LA solution given in divided doses. A standard epidural test dose itself will result in augmentation of motor blockade. The bolus dose was given in divided doses with 5 mins interval checking for motor block after the first dose. Epidural top-ups were not given till patient complained of pain or discomfort. With the catheter in place patients were shifted to the

labour ward, where they were closely monitored till delivery.

For Group–A 0.0625% Bupivacaine with Fentanyl

15 ml of 0.0625% bupivacaine with fentanyl 30 micrograms and maintained on maternal request with bolus doses of 10ml of 0.0625% bupivacaine with fentanyl 2 micrograms/ml.

For group B – 0.125% plain Bupivacaine

15ml of 0.125% of plain bupivacaine and maintained with 10 ml bolus doses of 0.125% plain bupivacaine.

Parameters that were Compared

- Analgesia was measured using visual analogue scores (VAS) on a 100 mm line. Measurements were performed every 10 minutes until analgesia was established and at 30 min and 1 hr after the initial dose. Thereafter 2 hourly VAS were recorded until delivery.
- Motor Power was assessed using a modified Bromage score 30 mins after each top-up and at each request to get out of bed (score 0 = no weakness, able straight leg raise against resistance, 1 = not able to straight leg raise, able to flex knee, 2 = unable to flex knee, able to flex ankle, 3 = unable to move lower limb.
- Mode of delivery was recorded, as were time intervals between top-ups, duration of first and second stages of labour, and time from insertion of epidural until delivery.
- Tolerability was assessed by checking for complications like dural puncture,venous puncture, pruritus, nausea, vomiting, rigor, drowsiness, urinary retention, hypotension, respiratory depression.

Results

A total of 180 patients were screened for the study. 50 patients who fulfilled the inclusion criteria were enrolled for the study and were divided into two groups -

- *Group A*: 25 patients
- *Group B*: 25 patients

Patients were randomly allocated to groups A or B to receive either of the two study therapies–either epidural bolus administration of 0.0625% bupivacaine with 0.0002% fentanyl (Group A) or epidural bolus administration of 0.125% plain bupivacaine (Group B).

All patients in both the groups completed the study. There were no drop outs in the study. The following flow chart explains the progress of participants through the trial.

Physical Characteristics

Physical characteristics like age, height and weight were comparable in both the groups.

Age Distribution

The age distribution in both groups are shown in the Table 1 below.

Table 1: Age distribution

Age Distribution	Group - A	Group - B
< 20	9	10
20-30	16	15
Total	25	25
Mean ± SD	21.2000 ± 2.533	20.0800 ± 1.824
T-test value	1.79	
P value (Using Student T-test)	0.037	

Table 2: Weight distribution

Weight frequency	Group - A	Group - B
50-59	5	5
60-69	17	14
70-79	3	6
Mean ± SD	64.44 ± 5.58	64.68 ± 5.71
T-test value	0.15	
P value (Using Student T-test)	0.862 (Not Significant)	

Weight Distribution

The distribution of weight in both the groups are shown in Table 2. The values are similar in both groups and are statistically comparable. The Student T test done on the values revealed no statistical significance.

Height Distribution

The distribution of weight in both the groups are shown in Table 3. The values are similar in both groups and are statistically comparable. The Student T test done on the values revealed no statistical significance.

Mode of Delivery

One patient in Group A and two patients in Group B were delivered by Caesarean section. The indication for Caesarean section was failure to progress in labour. Two patients in Group B were delivered by outlet forceps delivery. The indication for forceps delivery was maternal exhaustion. All others were delivered by Labour Natural with episiotomy (Table 4).

Time from Epidural to Delivery

The time from epidural to delivery in both groups were comparable. The Student t test done on the values revealed no statistical significance (Table 5).

Duration of Labour

The total duration of labour in both groups were comparable. The duration of first and third stage of labour was comparable. Student T-test was done on duration on total and each stage of labour. The P-values were all >0.05 implying that differences were not statistically significant. Duration of the second stage of labour was significantly shorter in group A (P =0.009) (Table 6).

Table 3: Height distribution

Height frequency	Group - A	Group - B
50-59	1	3
60-69	17	16
70-79	7	6
Total	25	25
Mean ± SD	158.32 ± 4.63	156.84 ± 5.93
T-test value	0.98	
P value (Using Student T-test)	0.317 (Not Significant)	

Table 4: Mode of Delivery

Mode of Delivery	Group - A	Group - B
Labour Natural	24	21
Caesarean section	1	2
Outlet forceps	-	2
Chi-Square value	2.53333	
P value	0.28177 (Not Significant)	

Table 5: Time from epidural to delivery

Group	No. of cases	Mean time from epidural to delivery in mins	SD	Student t test P value
Group A	24	161.8750	13.578	0.900 (Not Significant)
Group B	23	166.9565	13.878	

Table 6: Duration of labour

Stage of Labour	Group - A		Group - B		T-test	P-value
	Mean (mins)	SD	Mean (mins)	SD		
First Stage	162.08	11.83	161.74	10.18	0.11	0.916
Second Stage	49.21	7.65	55.00	6.74	2.75	0.009**
Third Stage	16.67	4.08	16.96	3.91	0.25	0.805
Total	227.54	16.12	233.70	14.16	1.39	0.172

Number of Top-UPS Given

Number of top-ups given in both groups were comparable. The Chi-Square test done on the values revealed no statistical significance (Table 7).

Motor Blockade

This was assessed using the Modified Bromage Scale. The patients in group A had minimal motor blockade when compared to patients in group B. The Chi- Square test showed statistical significance with regard to motor blockade between the two groups (Table 8).

Vas Scale

The pain perceived by the patients was assessed by showing them a VAS scale which contained pictures of faces depicting pain on one end and smiling face on the other end. In between the two, there were pictures expressing intermediate emotions. The other side had a scale marked from 0 to 100. The scale had a slider which the patients move to point below the image which they felt expressed their perceived pain. The VAS score was assessed at 0, 5, 15, 30, 45, 60, 120 and 180 minutes. The initial VAS score ranged between 80 and 100 for all the patients. VAS score for pain was comparable in both groups throughout labour (Table 9).

Table 7: Number of top-ups

No. of top-ups	Group - A		Group - B	
	N	%	N	%
1	0	0	0	0
2	10	40	10	40
3	15	60	15	60
4	0	0	0	0
Chi-Square Value			0.00000	
P value			1.00000 (Not Significant)	

Table 8: Motor block- Bromage score

Bromage Scale	Group - A		Group - B	
	N	%	N	%
0	12	48	0	0
1	12	48	14	56
2	1	4	11	44
3	0	0	0	0
Chi-Square Value			20.48718	
P value			0.00004 (Significant)	

Table 9: VAS score

Time in Mins	Group - A		Group - B		Student t test
	Mean	Std Deviation	Mean	Std Deviation	P value
0	94.00	7.07	94.00	7.07	1.000
5	57.60	11.65	56.80	10.69	0.794
15	11.60	8.50	15.40	7.90	1.000
30	0.20	1.00	5.80	5.72	0.000
45	10.20	6.20	13.00	6.45	0.102
60	12.20	8.05	13.60	7.43	0.847
120	11.40	10.16	12.80	8.55	0.787
180	9.00	4.79	11.80	4.54	0.707

Table 10: Patient comfort level Comfort level

Comfort Level	Group - A		Group - B	
	N	%	N	%
1- Poor	0	0	0	0
2- Fair	0	0	15	60
3- Good	8	32	10	40
4- Excellent	0	0	0	0
Chi-Square Value			32.2222	
P value			< 0.001 (Significant)	

Patient Comfort Level

This was assessed by asking the patient how they felt at the end of the delivery. Majority of patients (68%) in group A had excellent pain relief. 32% of patients in group A had good pain relief. In group B, 60% of patients had fair pain relief and 40% of patients had good pain relief (Table 10).

Upper Sensory Level

Patients in both groups had a mean sensory level of T9. The maximum was only T11 and minimum level was T8 (Table 11).

Haemodynamic Variables

All haemodynamic variables were recorded at 0 mins (baseline), 5 mins, 15 mins, 30 mins, 45 mins, 60 mins and thereafter every 15 mins. For the purpose of statistical comparison after the first hour, only the hourly recording or that during every top-up was considered.

Maternal Pulse Rate

Pulse rate recordings were found to be comparable between the two groups. The two way ANOVA test done on the pulse rate recordings showed no statistical difference between the two groups.

Summary of ANOVA for 2X10 factorial experiment with repeated measures on the second factor (10 times) (Table 12).

Systolic Blood Pressure

Systolic blood pressure were normal (i.e.) > 100 mm of Hg in both the groups and was not statistically significant between the groups (Table 13).

The two way ANOVA test showed no significant statistical difference between the two groups and also with time.

Diastolic Blood Pressure

The two groups had no significant difference in the diastolic blood pressure as was seen in the systolic

Table 11: Upper sensory level

Comfort Level	Group - A		Group - B	
	N	%	N	%
T6	0	0	0	0
T7	0	0	0	0
T8	5	20	6	24
T9	8	32	8	32
T10	7	28	8	32
T11	5	20	3	12

Table 12: Maternal pulse rate

Time in mins	Group - A		Group - B	
	Mean	Std Deviation	Mean	Std Deviation
0	90.26	11.14	91.44	9.57
2	92.43	9.65	93.28	9.57
5	91.48	12.11	89.36	7.20
15	91.83	9.44	89.12	7.66
30	90.87	6.20	86.40	6.03
45	90.09	6.59	85.84	4.93
60	89.74	8.10	87.60	3.61
2 hours	88.35	6.23	89.52	6.12
3 hours	88.48	9.12	89.76	2.07

Sources of variation	Sum of square	DF	Mean square	F value	P value
Between drugs	174.68	1	174.68	0.39	0.53

blood pressure. The two way ANOVA test showed no statistical difference between the two groups (Table 14).

Foetal Heart Rate

There was not much variation between the two groups and the ANOVA test did not show any statistical significance between the two groups (Table 15).

Apgar Score

APGAR score estimated at one and five minutes are tabulated in Table 16.

Complications

Hypotension (SBP <90 mm Hg or < 30% of baseline) was present in one case each in both the groups. Both cases responded to 6 mg of Ephedrine IV. Pruritus was present in one case each in both thegroups. It was only mild and reassurance was all that was needed. One patient in group B had vomiting (Table 18).

Statistical Report

Data were analysed using SPSS 11.5. Descriptive analysis for nonparametric variables was expressed in proportion and parametric variables in mean and standard deviation. The treatment difference was

Table 13: Maternal systolic blood pressure

Time in Mins	Group - A		Group - B	
	Systolic blood pressure Mean	Std Deviation	Systolic blood Pressure Mean	Std Deviation
0	116	6.455	115.84	7.116
5	113.6	9.074	114.4	8.210
15	112.4	7.141	111.12	6.685
30	112.72	7.414	111.84	7.701
45	108.88	7.096	112.4	6.481
60	112.16	7.369	111.12	6.483
2 hours	112.56	9.028	107.24	7.674
3 hours	108.36	7.658	112.40	7.000

Summary of ANOVA for 2X 9 factorial experiment with repeated measures on the second factor (9 times)

Sources of variation	Sum of square	DF	Mean square	F value	P value
Between drugs	16245	2	8122.5	5.871	0.553
With time	8415.4	7	1202.2	0.8689	0.141

Table 14: Maternal diastolic blood pressure

Time in mins	Group - A		Group - B	
	Diastolic blood pressure Mean	Std Deviation	Diastolic blood pressure Mean	Std Deviation
0	75.52	4.665	76.16	4.394
5	75.62	4.605	75.28	4.468
15	75.44	5.116	75.68	5.558
30	74.80	4.619	76.0	4.761
45	75.12	4.438	74.56	5.523
60	75.12	4.868	73.56	4.142
2 hours	76.16	4.394	76.16	4.580
3 hours	75.28	4.686	76.40	4.435

Sources of variation	Sum of square	DF	Mean square	F value	P value
Between drugs	183.6	2	918.28	0.6980	0.5141
With time	9286.9	7	1326.7	1.008	0.4656

Summary of ANOVA for 2X 9 factorial experiment with repeated measures on the second factor (9 times)

assessed using t test for independent samples for parametric variables and by Chi square test for non-parametric variables. Statistical significance was assessed using p at 0.05 cut off or 95% confidence interval (95% CI).

Discussion

A number of methods exist to provide pain relief to the labouring parturient. Of the regional techniques, epidural analgesia is considered the gold standard

Table 15: Foetal heart rate

Time in mins	Group - A		Group - B	
	mean foetal heart rate	Std Deviation	mean foetal heart rate	Std Deviation
0	142.17	8.65	142.24	15.66
5	140.87	11.08	145.28	6.29
15	138.87	7.16	151.00	6.01
30	142.26	6.16	146.00	8.10
45	145.65	7.92	142.92	4.64
60	145.22	9.74	146.72	4.58
2 hours	149.22	10.25	145.68	12.56
3 hours	144.70	12.19	152.88	5.23

Summary of ANOVA for 2X 9 factorial experiment with repeated measures on the second factor (9 times)

Sources of variation	Sum of square	DF	Mean square	F value	P value
Between drugs	945.96	1	945.96	7.3	0.08

Table 16: One minute APGAR

Comfort Level	Group - A		Group - B	
	N	%	N	%
5	0	0	0	0
6	2	2	5	20
7	11	44	6	24
8	12	48	14	56
9	0	0	0	0
10	0	0	0	0

P value by Chi square test did not show statistical difference.

Table 17: Five minute APGAR

Comfort Level	Group - A		Group - B	
	N	%	N	%
5	0	0	0	0
6	0	0	0	0
7	0	0	2	8
8	18	72	15	60
9	5	20	8	32
10	2	8	0	0

P value by Chi square test did not show statistical difference.

Table 19: Complications

Complication	Group – A	Group - B
Hypotension	1	1
Pruritus	1	1
Vomiting	0	1
Respiratory depression	0	0
Urinary retention	0	0

among all other techniques and it is the only technique which can provide a complete and convincing pain relief making labour a pleasurable experience.

In our study, we have demonstrated that with an epidural top-up technique using 0.0625% bupivacaine with fentanyl 2 microgram / ml (group A) analgesia was similar to that using 0.125% plain bupivacaine (group B), but motor power was retained allowing women to mobilize. There also appear to be beneficial effects on the progress of labour, with a clinically important reduction in the length of the second stage.

In our study, the patients in group A had minimal motor blockade when compared to patients in group B. Reduction in motor block allowing independent movement and awareness of contractions withoutpain has been shown to be popular with mothers.

Retention of pelvic floor sensation and motor function may allow appropriate coordinated pushing during the second stage, improving rotation and descent of the fetal head through the pelvis. Epidural local anaesthetic may attenuate endogenous oxytocin production reducing uterine contractility during the second stage.

Both a long second stage and instrumental delivery have associated morbidity for the mother, pose a controversial potential risk to the baby and negatively influence maternal satisfaction with the experience of labour. Although epidural analgesia produces excellent analgesia, this does not automatically produce maternal satisfaction with labour, and less effective methods of analgesia have produced higher satisfaction with scores. We demonstrated high maternal satisfaction with both epidural solutions, which was significantly greater in bupivacaine-fentanyl group.

Analgesia was established by 30 min in all women. Establishing analgesia with an epidural bolus is effective but takes longer than a combined spinal-epidural technique, which has been described widely. However, it avoids the complications of deliberate dural puncture.

The time difference between establishing spinal rather than epidural analgesia should be viewed in the context of the duration of labour and the potential complications of the spinal component of a combined technique.

The blood pressures (both systolic and diastolic) and pulse rate recorded during the analgesia in both the groups were not statistically significant. The APGAR score observed at 1 minute and 5 minutes showed no significant neonatal depression. Complications were only few, were minor and easily manageable.

Conclusion

- In our study, we have shown that establishing epidural analgesia in labour with 15ml of 0.0625% bupivacaine combined with fentanyl 30 microgram followed by top ups of 10ml of 0.0625% bupivacaine with 0.0002% fentanyl, produced similar analgesia to that obtained from the same volume of 0.125% bupivacaine alone, but motor block was minimized. This may influence the progress of labour, decreasing the duration of the second stage and produce high maternal satisfaction with the experience of labour.
- In our study, the APGAR score observed at 1 minute and 5 minutes showed no significant neonatal depression.

References

1. Pottecher J, Benhamou D. Labor pain and obstetric analgesia. J GynecolObstet Biol Reprod (Paris). 2004 May;33(3):179-91.
2. Vincent RD Jr, Chestnut DH. Epidural analgesia during labor. Am Fam Physician. 1998 Nov 15;58(8):1785-92.
3. Brownridge P, Cohen SE, Ward ME. Neural blockade for obstetrics and gynecologic surgery. In: Cousins MJ, Bridenbaugh PO, ed. Neural Blockade inClinical Anesthesia and Management of Pain, 3rd ed.. Philadelphia: Lippincott-Raven; 1998.pp.557-604.
4. Clement HJ, Caruso L, Lopez F, Broisin F, Blanc-Jouvan M, Derre-Brunet E, Thomasson A, Leboucher G, Viale JP. Epidural analgesia with 0.15% ropivacaine plus sufentanil 0.5 microgram ml-1 versus 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.
5. James KS, McGrady E, Quasim I, Patrick A. Comparison of epidural bolus administration of 0.25% bupivacaine and 0.1% bupivacaine with 0.0002% fentanyl for analgesia during labour. Br J Anaesth. 1998 Oct;81(4):507-10.
6. Riley ET. Neuroaxial analgesia for labor. Part III: Epidural drugs. In: Norris MC, ed. Obstetric Anesthesia, 2nd ed.. Philadelphia: Lippincott Williams & Wilkins; 1999:333-342.
7. Paull J: Epidural anesthesia for labor. In: Birnbach DJ, Gatt SP, Datta S, ed.Textbook of Obstetric Anesthesia, New York: Churchill Livingstone; 2000:145-156.

8. Polley LS, Columb MO, Naughton NN, et al. Effect of intravenous versus epidural fentanyl on the minimum local analgesic concentration of epidural bupivacaine in labor. Anesthesiology 2000;93:122-128.
9. 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 labor. Anesthesiology 1998; 89:626-632.
10. Janet A Picket. History of obstetric analgesia and anaesthesia. In: Collis R, Plaat F, Urquhart J, editors. Text book of obstetric anaesthesia. Cambridge university press, 2002.pp.1-20.
11. Thomas E. Epidural analgesia for patients in labour. Singapore Med J 1990;31:262-266.
12. Larson MD. History of anaesthetic practice. In: Miller RD, editor. Millers anaesthesia. Elsevier, 2005:27-28.
13. Brown DL. Spinal, epidural and caudal anaesthesia. In: Miller RD, editor.Millers anaesthesia. Elsevier, 2005.pp.1654-1658.
14. Igarashi T, Hirabayashi Y, Shimizu R, et. al. The lumbar extradural structure changes with age. British Journal of Anaesthesia 1997;78:149–152
15. Merskey H, Bogduk N. Classification of Chronic Pain. Descriptions of Chronic Pain Syndromes and Definitions of Pain Terms, 2nd ed. Seattle: International Association for the Study of Pain; 1994.
16. Stolte K. A comparison of women's expectations of labor with the actual event. Birth 1987;14:99-103.
17. Melzack R. The myth of painless childbirth. The John J. Bonica Lecture. Pain 1984;19:321-327.
18. Eltzchig HK, Lieberman ES, Camann WR. Regional anaesthesia and analgesia for labor and delivery. N Engl J Med 2003;348:319.
19. Brown ST, Campbell D, Kurtz A. Characteristics of labor pain at two stages of cervical dilation. Pain 1989; 38:289-95.
20. Mahomed K, Gulmezoglu AM, Nikodem VC et. al. Labour experience, maternal mood and cortisol and catecholamine levels in low-risk primiparous women. Journal of Psychosomatic Obstetrics and Gynaecology 1995;16:181-186.
21. Bonica JJ. The nature of pain in parturition. In Vanzundert A and Ostheimer GW (eds.) Pain relief and anaesthesia in obstetrics. 1996.pp.19-52. New York:Churchill Livingstone.
22. Irestedt L, Lagercrantz H and Belfrage P. Causes and consequences of maternal and fetal sympatho-adrenal activation during parturition. Acta Obstetrica et Gynecologica Scandinavica 1995;118(Supplement): S111-S115.
23. Birnbach DJ, Browne IM. Anaesthesia for Obstetrics. In: Miller RD, editor. Millers anaesthesia. Elsevier, 2005.pp.2308-2311.
24. Ross A. Physiological changes of pregnancy. In: Birnbach DJ, Gatt SP, Datta S, ed. Textbook of obstetric anaesthesia, New York: Churchill Livingstone; 2000.pp.31-45.
25. Chestnut DH, McGrath JM, Vincent RD Jr, Penning DH, Choi WW, Bates JN, et al. Does early administration of epidural analgesia affect obstetric outcome in nulliparous women who are in spontaneous labor? Anesthesiology 1994;80:1201-8.
26. Chestnut DH, Vincent RD Jr, McGrath JM, Choi WW, Bates JN. Does early administration of epidural analgesia affect obstetric outcome in nulliparous women who are receiving intravenous oxytocin? Anesthesiology 1994;80:1193-200.
27. Glosten B. Local anesthesic techniques. In: Chestnut DH, ed. Obstetricanesthesia: principles and practice. St. Louis: Mosby-Year Book, 1994.p.354.
28. AHFS Drug Information. Bupivacaine. 2008. Accessed on Oct 21,2008http//web.medicinescomplete.com / mc/ahfs/current/a382703.html.
29. Feldman HS, Arthue GR, Covino BG. Comparative systemic toxicity ofconvulsant and supreconvulsant doses of intravenous ropivacaine, bupivacaine and lignocaine in conscious dogs. Anaesth Analog. 1989; 69(6):794-801.
30. Scott DBB, Lee A, Fagan D, Bowler GMR, Bloomfield P, Lundh R. Acute toxicity of ropivacaine compared with that of bupivacaine. Anaesth Analog. 1989;69(6): 536-9.

Case Report

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Anaesthetic Management in a Patient with Huge Lymphoma Neck Having Retrosternal Extension for Caesarean Section

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Abstract

Anatomical and physiological changes of pregnancy make the airway management risky, which has resulted in the increased use of regional anaesthesia for caesarean section. Pathological conditions causing airway compromise in these patients can increase the risk making the situation life threatening during the perioperative period. Though regional anaesthesia avoids airway manipulation, it can often result in emergency situations necessitating airway control which can be catastrophic in them. We present the successful management of a patient with compromised airway due to huge lymphoma in front of the neck having retrosternal extension for elective caesarean section under continuous epidural anaesthesia with good maternal and neonatal outcome.

Keywords: Anaesthesia; Lymphoma; Retrosternal; Caesarean Section.

Introduction

Neck swelling with retrosternal extension causing airway compromise in the obstetric patient is a challenge for the anaesthesiologist. General anaesthesia can provide control of the airway, but can be risky due to airway distortion produced by the tumor over the difficult airway of pregnancy.

Neuraxial blockade though preferred for caesarean section can be catastrophic in the event of emergency airway intervention due to unexpected complications.

We report the anaesthetic management of a parturient with huge lymphoma in front of the neck having retrosternal extension producing significant tracheal narrowing who underwent caesarean section under continuous epidural anaesthesia uneventfully.

Case Report

A 33-year-old second gravida at 34 weeks of gestation who had uneventful caesarean section eleven years back was admitted for delivery. She had a huge swelling in front of the neck causing difficulty in breathing, making her to sit most of the time. The swelling was noted in the early second trimester, which rapidly enlarged to the present size. Histopathological examination proved it to be anaplastic large cell lymphoma, for which chemotherapy was planned at the earliest after delivery, for which caesarean section was planned.

She was 146cm, 49kg, had anxious look and congested facies with respiratory rate of 22/min. Pulse rate was 104 beats/ min and blood pressure, 124/84 mm Hg in sitting position. The huge multilobulated neck swelling was extending beyond the sternomastoids bilaterally [Figure 1] with a scar

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of recent biopsy over its lower part on the right side. There were dilated veins over the swelling and was not possible to get its lower margin due to retrosternal extension. Trachea and carotid arteries were not felt due to the swelling and it was dull to percussion over the manubrium sterni. Room air oxygen saturation was 96%, which dropped to 88% on lying supine. Uterine size corresponded to the gestational age and fetal heart rate was normal.

Due to respiratory distress, she requested not to make her unconscious, and opted for regional anaesthesia as done for her previous caesarean delivery.

Her routine hemogram and thyroid function tests were within normal limits. Electrocardiogram showed sinus tachycardia and echocardiography was normal. Ultrasound examination showed huge cervical, supraclavicular and pretracheal lymph nodes bilaterally. There were nodular masses along the jugular chains and compression over the brachiocephalic and internal jugular veins encasing the carotid vessels bilaterally. Radiographs showed

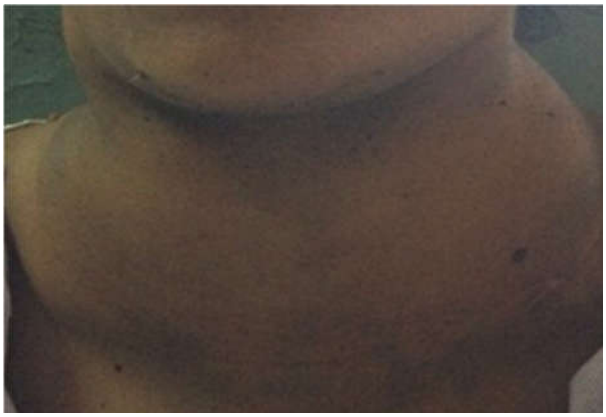

Fig. 1: Huge multilobulated neck swelling with retrosternal extension

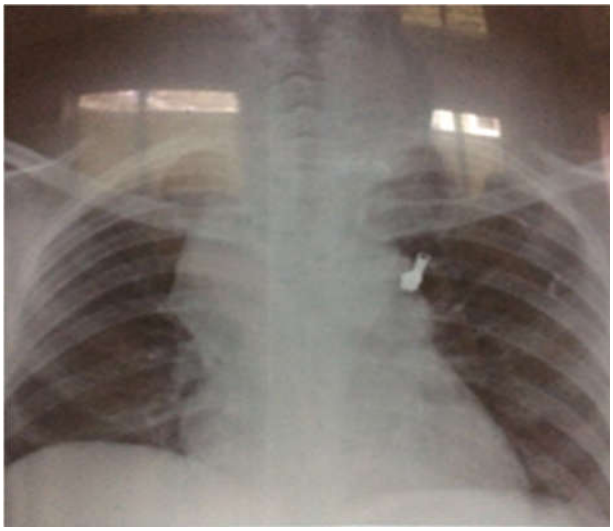

Fig. 2: Chest radiograph showing mediastinal tumor causing tracheal compression

the neck swelling extending down to the superior and middle mediastinum with severe tracheal compression at the thoracic level [Figure 2]. CT scan revealed multiple enlarged cervical, axillary and mediastinal lymph nodes causing compression and displacement of trachea with narrowest diameter of 9x3.7mm at the level of T3 veretebral body.

Informed consent was obtained in view of the possible airway problems and continuous epidural anaesthesia was planned as the patient opted regional technique. On the preoperative night, ranitidine was given orally and she was instructed nil by mouth for 6 hours before surgery.

On the day of surgery, 500ml ringer lactate was infused through 18 G cannula in the left forearm. Continuous supplemental oxygen was administered via facemask. Back up of difficult airway cart including pediatric size endotracheal tubes were kept ready. As the patient was dyspnoeic on lying down, she was positioned sitting. Under local infiltration with 3ml 2% lignocaine, epidural puncture was done at L2-3 interspace with 18G Touhy needle using loss of resistance technique and epidural cannula was passed 3 cm cephalad.

Epidural placement was confirmed by test dose of 3ml 2% lignocaine with 1:200,000 adrenaline, followed by 7 ml of the same drug over 10 minutes, maintaining her in the same position, which produced sensory blockade up to T4 level. She was then positioned semireclining at 45^0 head up with oxygen by face mask.

Lower segment caesarean section was done in this position delivering a male baby within five minutes of incision, and she smiled at her baby. The neonate weighed 2400 g and had APGAR scores 8 and 9 in the first and fifth minute respectively. 10 units of oxytocin was given through intravenous infusion after clamping the umbilical cord, which caused uterine contraction. Vital parameters (pulse, BP, SpO_2) were stable throughout the 45minute procedure with an approximate blood loss of 600 ml, which was replaced with ringer lactate.

Postoperatively she was shifted to intensive care unit (ICU), and nursed at 45^0 head up with oxygen by face mask. Epidural analgesia was initiated after 4 hours by 8 ml 0.125% bupivacaine with 50 µg fentanyl eighth hourly for 24 hours, after which the cannula was removed and was shifted to postoperative ward. She was symptomatically better in the postoperative period since the respiratory difficulty was partly relieved after evacuation of the uterus. On the 7^{th} postoperative day she was discharged and referred for oncology treatment.

Discussion

Retrosternal swellings that can significantly compromise the airway include goiters, thymomas, lymphomas, germ cell tumors and vascular lesions. Lesions arising from the sternum, lungs and pleura can also involve this space. Lymphomas are common primary anterior mediastinal tumors seen in adults, second only to thymomas. While Hodgkin's lymphoma has its peak occurrence in the female reproductive age group (1 in 1000-6000 pregnancies), non-Hodgkin's type occurs in all age groups [1].

Anaplastic large cell lymphoma is a non-Hodgkin's type which has a better prognosis with chemotherapy and/or radiation. Airway management in obstetric patient is often difficult due to the anatomical and physiological changes occurring during pregnancy, making the parturient vulnerable for early and rapid desaturation endangering both maternal and fetal lives [2].

This has resulted in wide spread use of neuraxial blockade in preference to general anaesthesia for caesarean section except in unavoidable situations. Other pathological conditions which compromise the airway make the situation worse causing failed intubation resulting in maternal and fetal morbidity and mortality [3].

Choice of anaesthesia for caesarean section in a patient with compromised airway poses additional risk in the setting of an already difficult airway caused by pregnancy. This patient has noted the neck swelling during her second trimester, which had rapidly increased in size with retrosternal extension causing dyspnea, orthopnea and superior vena cava (SVC) syndrome. This can be due to the tumor compressing the mediastinal structures like tracheobronchial tree, pulmonary arteries and SVC. Physiological dyspnea of pregnancy begins in the first trimester which plateaus or improves in the last trimester, whereas pathological dyspnea due to mediastinal compression is progressive and becomes worse as pregnancy advances.

Due to severe tracheal compression at the thoracic level, the patient was adopting sitting position most of the time for the maintenance of patent airway. She could not cooperate for awake blind nasal or fiber optic tracheal intubation.

Assuming supine position and induction of general anaesthesia can result in airway obstruction due to loss of muscle tone and airway compression due to the intrathoracic tumor. Decrease in functional residual capacity (FRC) and loss of muscle tone due to neuromuscular blockade can make the situation still worse. Hence there was possibility of cannot intubate-cannot ventilate (CICV) scenario on induction of general anaesthesia. Emergency cricothyrotomy or tracheostomy were not feasible due to the anatomical distortion produced by the neck tumor.

Anterior mediastinal tumors can cause severe airway and vascular compression, which can be exacerbated by general anaesthesia [4].

As general anaesthesia is risky in such situations, regional anaesthetic techniques were chosen in several cases in the literature. Yatish B etalused combined spinal epidural anaesthesia (CSE) for cesarean delivery in a patient with large anterior mediastinal mass tumor presenting as intrathoracic airway compression [5].

Crosby E conducted caesarean section under subarachnoid block in a parturient with large intrathoracic tumor filling the right hemithorax [6].

Though regional techniques are preferred over general anaesthesia in such situations, reports of sole epidural anaesthesia as done in this case is not available in the literature.

Since our patient could not lie supine due to orthopnea, she was positioned in the sitting "rescue" position. Continuos epidural anaesthesia was chosen due to its flexibility and slow achievement of the block, with minimal drug as against bolus drug administration in subarachnoid block. There was also less chance of higher block as the anaesthesia was gradually established with the patient sitting. Combined spinal epidural (CSE) was not preferred to avoid multiple punctures and unexpected high block due to subarachnoid puncture. To prevent undesired high level of neuraxial blockade, she was positioned semi-reclined with 45^{o} head up for the surgery. The patient was comfortable throughout the procedure with stable vital parameters. She was nursed in the postoperative ICU in this position and analgesia was provided through the epidural cannula.

We could successfully use continuous epidural anaesthesia for caesarean section in this patient with airway compromise, where general anaesthesia would have been catastrophic due to loss of airway during the perioperative period.

Conclusion

Neuraxialanaesthesia, especially continuous epidural anaesthesia if properly conducted can be safely used for caesarean section in patients with compromised airway as it avoids the airway risk of

general anaesthesia. However, meticulous selection of patients and expertise in anaestheticmanagement are crucial for a good outcome in such cases.

References

1. Rodriguez J, Gutierrez A, Piris M. Primary mediastinal B-cell lymphoma: treatment and therapeutic targets. Leuk. Lymphoma 2008;49:1050-61.
2. Ramkumar V, Dinesh E, Shetty SR, Shah A, Kundra P, Das S, et al. All India difficult airway association 2016 guidelines for the management of unanticipated difficult tracheal intubation in obstetrics. Indian J Anaesth 2016;60:899-905.
3. American society of anesthesiologists task force on obstetric anesthesia. Practice guidelines for obstetric anesthesia: an updated report by the American society of anesthesiologists task force on obstetric anesthesia. Anesthesiology 2007;106:843-63.
4. Gothard JW. Anesthetic considerations for patients with anterior mediastinalmases. AnesthesiolClin. 2008;26:305-14.
5. YatishBevinaguddaiah, ShivakumarShivanna, Vinayak Seenappa Pujari, Manjunath Abloodu Chikkapillappa. Anesthesia for caesarean delivery in a patient with large anterior mediastinal tumor presenting as intrathoracic airway compression. Saudi J Anaesth. 2014;8(4):556-558.
6. Crosby E. Clinical case discussion: Anesthesia for cesarean section in a parturient with a large intrathoracictumour. Can J Anaesth. 2001;48:575-83.

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Indian Journal of Research in Anthropology	Semiannual	12500	12000	977	938
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Indian Journal of Waste Management	Semiannual	9500	8500	742	664
International Journal of Food, Nutrition & Dietetics	Triannual	5500	5000	430	391
International Journal of Neurology and Neurosurgery	Quarterly	10500	10000	820	781
International Journal of Pediatric Nursing	Triannual	5500	5000	430	391
International Journal of Political Science	Semiannual	6000	5500	450	413
International Journal of Practical Nursing	Triannual	5500	5000	430	391
International Physiology	Triannual	7500	7000	586	547
Journal of Animal Feed Science and Technology	Semiannual	78500	78000	6133	6094
Journal of Cardiovascular Medicine and Surgery	Quarterly	10000	9500	781	742
Journal of Forensic Chemistry and Toxicology	Semiannual	9500	9000	742	703
Journal of Geriatric Nursing	Semiannual	5500	5000	430	391
Journal of Global Public Health	Semiannual				
Journal of Microbiology and Related Research	Semiannual	8500	8000	664	625
Journal of Nurse Midwifery and Maternal Health	Triannual	5500	5000	430	391
Journal of Organ Transplantation	Semiannual	26400	25900	2063	2023
Journal of Orthopaedic Education	Triannual	5500	5000	430	391
Journal of Pharmaceutical and Medicinal Chemistry	Semiannual	16500	16000	1289	1250
Journal of Practical Biochemistry and Biophysics	Semiannual	7000	6500	547	508
Journal of Psychiatric Nursing	Triannual	5500	5000	430	391
Journal of Social Welfare and Management	Triannual	7500	7000	586	547
New Indian Journal of Surgery	Bi-monthly	8000	7500	625	586
Ophthalmology and Allied Sciences	Triannual	6000	5500	469	430
Otolaryngology International	Semiannual	5500	5000	430	391
Pediatric Education and Research	Triannual	7500	7000	586	547
Physiotherapy and Occupational Therapy Journal	Quarterly	9000	8500	703	664
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The second page should carry the full title of the manuscript and an abstract (of no more than 150 words for case reports, brief reports and 250 words for original articles). The abstract should be structured and state the Context (Background), Aims, Settings and Design, Methods and Materials, Statistical analysis used, Results and Conclusions. Below the abstract should provide 3 to 10 keywords.

Introduction

State the background of the study and purpose of the study and summarize the rationale for the study or observation.

Methods

The methods section should include only information that was available at the time the plan or protocol for the study was written such as study approach, design, type of sample, sample size, sampling technique, setting of the study, description of data collection tools and methods; all information obtained during the conduct of the study belongs in the Results section.

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Present your results in logical sequence in the text, tables, and illustrations, giving the main or most important findings first. Do not repeat in the text all the data in the tables or illustrations; emphasize or summarize only important observations. Extra or supplementary materials and technical details can be placed in an appendix where it will be accessible but will not interrupt the flow of the text; alternatively, it can be published only in the electronic version of the journal.

Discussion

Include summary of key findings (primary outcome measures, secondary outcome measures, results as they relate to a prior hypothesis); Strengths and limitations of the study (study question, study design, data collection, analysis and interpretation); Interpretation and implications in the context of the totality of evidence (is there a systematic review to refer to, if not, could one be reasonably done here and now?, What this study adds to the available evidence, effects on patient care and health policy, possible mechanisms)? Controversies raised by this study; and Future research directions (for this particular research collaboration, underlying mechanisms, clinical research). Do not repeat in detail data or other material given in the Introduction or the Results section.

References

List references in alphabetical order. Each listed reference should be cited in text (not in alphabetic order), and each text citation should be listed in the References section. Identify references in text, tables, and legends by Arabic numerals in square bracket (e.g. [10]). Please refer to ICMJE Guidelines (http://www.nlm.nih.gov/bsd/uniform_requirements.html) for more examples.

Standard journal article

[1] Flink H, Tegelberg Å, Thörn M, Lagerlöf F. Effect of oral iron supplementation on unstimulated salivary flow rate: A randomized, double-blind, placebo-controlled trial. J Oral Pathol Med 2006; 35: 540-7.

[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.

Article in supplement or special issue

[3] Fleischer W, Reimer K. Povidone iodine antisepsis. State of the art. Dermatology 1997; 195 Suppl 2: 3-9.

Corporate (collective) author

[4] American Academy of Periodontology. Sonic and ultrasonic scalers in periodontics. J Periodontol 2000; 71: 1792-801.

Unpublished article

[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.

Personal author(s)

[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.

Reference from electronic media

[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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