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*Original Research Article*

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# A Comparative Clinical Study of Attenuation of the Pressor Response to Laryngoscopy and Intubation with Intravenous Fentanyl and Intravenous Butorphanol

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**Abstract**

*Introduction:* Rapid smooth induction, rapid recovery, perioperative hemodynamic stability, minimum post-operative pulmonary complications and effective analgesia intra-operatively and post-operatively are the main aspects of general anesthesia. *Aim:* To compare the attenuation of the pressor response to laryngoscopy and intubation with intravenous Fentanyl 2 mcg/kg and intravenous Butorphanol 40 mcg/kg. *Materials and Methods:* It is a randomized prospective comparative study comparing the two opioiddrugs. The patients were then randomly assigned into two groups of 30 each in Group F and Group B received Inj. Fentanyl 2 mcg/kg IV and Inj. Butorphanol 40 mcg/kg respectively. *Results:* There was no statistical significance between the Two groups (B / F) when the demographic parameters like age distribution (36.03 ± 7.73/36.23 ± 6.80), sex distribution (15/15 vs 16/14), weight (65.5 ± 7.72/66.63 ± 5.81) were compared. The comparison of parameters like pre operative pulse rate, systolic blood pressure, diastolic pressure, mean arterial pressure, rate pressure product, respiratory rate and sedation score was also found to be statistically insignificant between the two groups. Both the Butorphanol group and the Fentanyl group was comparable with respect to events of intra operative hypotension and intra operative Bradycardia. There was no significantly respiratory depression post extubation in both the groups. We observed that the post extubation sedation score was significantly higher with the Butorphanol group than with the Fentanyl group. A favourable side effect profile was observed with the Butorphanol group than with Fentanyl group with respect to the occurrence of post-operative shivering whilethe incidence of post-operative nausea and vomiting was similar between the groups. *Conclusion:* Intravenous Butorphanol prior to induction of anaesthesia helps in better attenuation of the hemodynamic response to laryngoscopy and intubation than intravenous Fentanyl. We conclude that Butorphanol could be an effective alternative to Fentanyl for attenuation of the hemodynamic stress response to laryngoscopy and intubation.

**Keywords:** Laryngoscopy; Intubation; Fentanyl; Butorphanol

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## Introduction

With the advent of newer drugs, the practice of anesthesia has revolutionized. Rapid smooth induction, rapid recovery, perioperative hemodynamic stability, minimum post-operative pulmonary complications and effective analgesia intra-operatively and post-operatively are the main aspects of general anesthesia. Laryngoscopy and intubation are noxious stimuli. The change in hemodynamics that arise from manipulation of the airway are attributed to the sympathoadrenal discharge that occurs as a result of stimulation of the epipharyngeal and parapharyngeal regions. This reflex increase in sympathetic activity may result in hypertension, tachycardia, and arrhythmia. A change in plasma catecholamine concentrations also has been demonstrated to be a part of the stress response to tracheal intubation. Various pharmacological methods are aimed at efferent, afferent or both limbs of response. It involves the use of inhalation agents, lignocaine, opiods, sodium nitroprusside, nitroglycerine, calcium channel blockers, adrenergic blockers.

The non-pharmacological methods aim at smooth and gentle intubation with a shorter duration of laryngoscopy. Insertion of LMA in place of endotracheal intubation blocking of the glossopharyngeal nerve and the superior laryngeal nerves. Since none of the above agents have proven to be the best choice to attenuate this pressor response the quest for the ideal agent still continue. Nevertheless opioids have been employed for this purpose for quite a long time and have proved to be extremely useful. Both the Fentanyl and Butorphanol group has haemodynamic stability, analgesia, sedation and decreases the requirement of other anesthetic drugs and are available at low cost. In this study we decided to compare the effects of the commonly used opioid Fentanyl with another opioid drug Butorphanol in attenuating the pressor responses to laryngoscopy and intubation.

## Aims and Objectives

To compare the attenuation of the pressor response to laryngoscopy and intubation with intravenous Fentanyl 2 mcg/kg and intravenous Butorphanol 40 mcg/kg.

## Materials and Methods

This is a randomized prospective comparative study comparing the two opioid drugs Fentanyl and Butorphanol conducted in the Department of Anesthesiology at Gandhi Hospital, Secunderabad and over a period of one year. This study includes 60 patients of ASA class I of either sex aged from 20 to 49 years scheduled for various elective surgeries under anaesthesia. All of them will require orotracheal intubation as part of their anaesthetic management and written informed consent was obtained to participate in the study.

*Sample size*

A sample size of 30 patients each, randomly allocated into two groups, using computerized randomization. The sample size was calculated based on the previous studies 73 Sample size calculation formulae.

The estimated sample size with an alpha-error of 0.05 and power of 80% for equivalence of groups, by substituting mean difference and standard deviation into the above formula was 21 in each group. Assuming 25% as loss to follow up in each group, we selected 30 patients in each group.

*Inclusion Criteria:* ASA class I with 20 to 49 years of both sexes posted for elective procedure under general anaesthesia with MP grade class I and II airway.

*Exclusion Criteria:* Valvular heart disease, Ischemic heart disease, Hypertension, Endocrine disorder, Metabolic disorders, Respiratory disease, Anaemic patients, Allergic diathesis, Unanticipated difficult airway.

This study was designed to study the difference between the two drugs Fentanyl and Butorphanol in attenuating the response to laryngoscopy and intubation. These two drugs were compared in terms of their effects on heart rate, systolic blood pressure, diastolic blood pressure, mean arterial pressure and rate pressure product. The influence of the drugs on the post extubation respiratory rate and sedation level was also recorded.

All patients were assessed pre operatively by history, physical examination routine laboratory tests, CXR and ECG. A pre-operative visit was made to allay the anxiety and to develop a good rapport. The Patients were instructed to fast overnight and aspiration prophylaxis was advised with Tab. Pantop 40mg on the day before surgery. On the day of surgery the patients were examined in the pre-operative room and the pulse rate(PR), systolic blood pressure (SBP), diastolic blood pressure (DBP) and mean arterial pressure (MAP) will be recorded as first pre-operative value (pre op

1). The patients were randomly allocated into two study groups of 30 patients each, using a sealed envelope technique into Group F and Group B.

On arrival in the operating room a 20 gauge intravenous cannula was placed and crystalloid infusion was started. Patients were monitored with a non invasive monitor throughout the study period. The parameters that were monitored include heart rate, blood pressure, oxygen saturation and ECG. All patients in two groups received Inj. Midazolam 0.05 mg/kg IV were given as premedication on arrival in the operating room. Thirty minutes later the heart rate, blood pressure and mean arterial pressure were recorded for all patients and noted as the pre op value (pre op 2). This value was taken as the baseline value for comparison of the different parameters at various time intervals. At this time point the respiratory rate and the sedation level of all the patients was also assessed and recorded (RR P1 and SS P1). The degree of sedation (Sedation Score 74) is graded as follows.

0- Patient awake and talkative

1- Patient awake but uncommunicative

2- Patient drowsy, quiet and easily arousable

3- Patient asleep

An anaesthesiologist who is not involved in the study administered the test drugs in a double-blinded fashion, before induction of anaesthesia. Patients in Group F and Group B received Inj. Fentanyl 2 mcg/kg IV and Inj. Butorphanol 40 mcg/kg respectively. The HR, SBP, DBP, MAP was measured for five minutes after the administration of the test drug and the fifth minute value was recorded as pre induction value (PI). Occurrence of any hemodynamic variability was observed for duration of five minutes.

All patients were induced with Thiopentone sodium 5-6 mg/kg IV till the loss of eyelid reflexes and Inj. Vecuronium 0.1 mg/kg IV was given to achieve muscle relaxation. Controlled positive pressure ventilation was done with 100% oxygen using bag and mask. A direct laryngoscopy was done 3 minutes after the injection of the muscle relaxant and the patients were intubated with appropriate size cuffed ETT. Intubation was done by same person for all the patients, who has experience in anaesthesia for 10 years. All patients who strained or took more than 15 seconds of laryngoscopy or required a second attempt of laryngoscopy were not included in statistical analysis. No surgical stimulation is allowed for the first 10 minutes after intubation.

HR, BP were recorded at the first, second, third, fourth, fifth and tenth minute following intubation and was recorded as T1,T2,T3,T4,T5 and T10 respectively. Intraoperatively the HR, BP, oxygen saturation, ECG was continuously monitored in all the patients. They were ventilated with IPPV to maintain $ETCO_2$ value of 35 mm - 40 mm Hg and anaesthesia was maintained with 50% oxygen, 50% nitrous oxide, Isoflurane (1%), intermittent inj. vecuronium bromide (0.02 mg/kg) IV and analgesia by intermittent doses of Fentanyl 1-2 mcg/kg, Inj. Diclofenac Sodium 75 mg IV was given to all patients. Inj. Ondansetron 0.1 mg/kg IV was given 30 min before extubation to all patients. After completion of surgery neuromuscular blockade was reversed with Inj.Neostigmine 0.05 mg/kg IV and Inj. Glycopyrrolate 0.01 mg/kg IV. Patients were extubated after thorough oral suctioning. The RR and sedation level five minutes after extubation was recorded (RR P2, SS P2 respectively). Patients in whom the surgical procedure lasted for more than 3 hours were excluded from the statistical analysis. The patients were then shifted to the recovery room and observed every 2 hours for upto 24 hours. The occurrence of postoperative nausea and vomiting and the postoperative shivering was observed in both the study groups upto two hours post extubation.

Postoperative nausea was measured on VAS scale (0-10) while emetic episode was defined as a single vomiting or retching event or any combination of these events separated by less than 2 mins. inj Ondansetron 4 mg IV was given as rescue antiemetic. The post-operative shivering was graded as follows.

Grade 0 = no shivering.

Grade 1 = mild fasciculation of face or neck and electrocardiogram disturbances in the absence of voluntary activity of the arms.

Grade 2 = visible tremor involving more than one muscle group.

Grade 3 = gross muscle activity involving whole body.

Oxygen through venturi mask was given to all patients with shivering. Injection Pethidine 0.25 mg/kg IV was given for grade 2 or 3 shivering.

Statistical analysis for intra and inter-group was carried out by paired t-test and unpaired t-test respectively. The software used for analysis of the data was Statistical package for Social Science (SPSS) package. A p – value of less than 0.05 will be considered to be statistically significant.

## Results

No significant difference was observed in sex wise distribution of the cases between the two groups (p>0.05). Overall frequency distribution in both the groups 51.67% males and 48.33% females. The mean values of the age with standard deviations are 36.06 ± 7.73 for group B and 36.23 ± 6.80 for group F. There was no significant difference between the two groups (p>0.05).

In the group B, the mean weight was 65.5 ± 7.72. In Group F the mean weight was 66.63 ± 5.81. No statistical significant difference was observed in the weight distribution in two groups (p>0.05).

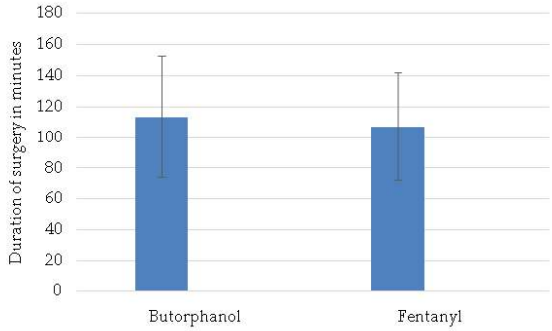


**Fig. 1:** Comparison of duration of surgery between two groups

In the group B, the mean duration (in minutes) was 113.5 ± 39.5 In Group F the mean duration (in minutes) was 107.3 ± 35.8. No statistical significant difference was observed in the duration of surgery between two groups (p>0.05).

**Table 1:** Comparison of pre operative baseline parameters (pre op 2)

| Parameter | Group B | Group F | p value |
|---|---|---|---|
| Pre op 2 HR | 80 ± 5.14 | 77.67 ± 4.95 | 0.2846 |
| Pre op 2 SBP | 120.96 ± 6.36 | 122.03 ± 4.99 | 0.2365 |
| Pre op 2 DBP | 79.83 ± 5.83 | 80.73 ± 3.44 | 0.235 |
| Pre op 2 MAP | 92.94 ± 5.52 | 94.5 ± 2.40 | 0.082 |

The pre-operative 2 (pre op 2) heart rate, systolic and diastolic blood pressures, mean arterial pressure is comparable between the two groups.

Heart rate was significantly higher at T1,T2,T3 when compared to the baseline and significantly lower when compared to the baseline values at other time intervals (T4,T5,T10) (Table 2).

The heart rate was significantly higher at T1, T2, T3 when compared to the baseline and significantly lower when compared to the baseline values at other time intervals (T5,T10).

The Mean Arterial Pressure was significantly higher at T1, T2, T3 when compared to the baseline and significantly lower when compared to the baseline values at other time intervals (T4, T5, T10) (Table 3).

The rate pressure product is significantly lower in group B when compared to group F from the

**Table 2:** Comparison of Heart Rate between two Groups

| Time | Groups | No. | Mean | S.D | % change wrt baseline | T value | p value |
|---|---|---|---|---|---|---|---|
| Pre op 1 | B | 30 | 81.4 | 4.65 | 1.75 | 0.837 | 0.4 |
| | F | 30 | 80.4 | 4.59 | 1.43 | | |
| Baseline | B | 30 | 80 | 5.14 | 0 | 0.572 | 0.56 |
| | F | 30 | 79.26 | 4.95 | 0 | | |
| Pre Induction | B | 30 | 77.13 | 5.30 | *3.58- | 0.182 | 0.85 |
| | F | 30 | 76,1 | 4.63 | 2.96- | | |
| T1 | B | 30 | 88.93 | 4.63 | *11.16 | 0.826 | 0.412 |
| | F | 30 | 89.8 | 3.40 | *13.2 | | |
| T2 | B | 30 | 84.73 | 4.97 | *5.91 | 2.74 | 0.005 |
| | F | 30 | 87.86 | 3.03 | *10.84 | | |
| T3 | B | 30 | 80.86 | 5.17 | 1.08 | 3.48 | 0.001 |
| | F | 30 | 84.7 | 3.09 | *6.85 | | |
| T4 | B | 30 | 77 | 5.38 | *3.75- | 3.86 | 0.001 |
| | F | 30 | 81.3 | 2.94 | *2.6 | | |
| T5 | B | 30 | 73.06 | 4.4 | *8.66- | 4.91 | 0.001 |
| | F | 30 | 77.63 | 2.55 | 2.06- | | |
| T10 | B | 30 | 68.13 | 2.72 | 14.83- | 5.72 | 0.001 |
| | F | 30 | 71.9 | 2.39 | *9.29 | | |

p value < 0.05 significant

second minute after intubation. At T1, both the groups showed increase in the rate pressure product which wasnot statistically significant. At T2 & T3, there was significant increase in the rate pressure product in Fentanyl group when compared to Butorphanol group ($p<0.05$). At T4, T5 & T10 there was significant reduction in the rate pressure product in Butorphanol group when compared to Fentanyl group which was highly significant ($p<0.001$) (Table 4).

**Table 3:** Comparison of MAP between two Groups

| Time | Groups | No | Mean ± S.D | % change wrt baseline | t value | p value |
|---|---|---|---|---|---|---|
| Mean pre op 1 | B | 30 | 95.07 ± 5.02 | 1.627 | 0.373 | 0.711 |
| | F | 30 | 65.44 ± 2.35 | 0.99 | | |
| Baseline | B | 30 | 92.94 ± 5.52 | 0.000 | 0.879 | 0.383 |
| | F | 30 | 94.5 ± 2.40 | 0 | | |
| Mean PI | B | 30 | 90.9 ± 4.83 | ∗3.041- | 2.019 | 0.048 |
| | F | 30 | 92.73 ± 2.45 | ∗1.90- | | |
| Mean T1 | B | 30 | 100.4 ± 4.19 | ∗7.115 | 3.752 | 0.001 |
| | F | 30 | 103.31 ± 1.52 | ∗9.32 | | |
| Mean T2 | B | 30 | 96.67 ± 4.07 | ∗3.338 | 5.994 | 0.001 |
| | F | 30 | 101.62 ± 1.68 | ∗7.44 | | |
| Mean T3 | B | 30 | 93.41 ± 4.60 | 0.166- | 6.126 | 0.001 |
| | F | 30 | 98.86 ± 1.71 | ∗4.62 | | |
| Mean T4 | B | 30 | 90.14 ± 4.27 | ∗3.635- | 8.048 | 0.001 |
| | F | 30 | 96.82 ± 1.53 | ∗2.45 | | |
| Mean T5 | B | 30 | 86.89 ± 4.02 | ∗7.115- | 8.674 | 0.001 |
| | F | 30 | 93.71 ± 154 | 0.835- | | |
| Mean T10 | B | 30 | 80.41 ± 15.54 | ∗10.904- | 8.187 | 0.002 |
| | F | 30 | 89.22 ± 1.90 | ∗5.58- | | |

p value < 0.05 significant;

**Table 4:** Comparison of Rate Pressure Product between two Groups

| Time | Groups | No. | Mean ± S.D | % change wrt baseline | t value | p value |
|---|---|---|---|---|---|---|
| Mean pre op 1 | B | 30 | 9988.03 ± 913.21 | 3.03917 | 0.196 | 0.845 |
| | F | 30 | 9943.67 ± 855.9 | 2.6700 | | |
| Baseline | B | 30 | 9550.96 ± 1002.83 | 0 | 0.035 | 0.972 |
| | F | 30 | 9489.9 ± 855.9 | 0 | | |
| Mean PI | B | 30 | 9124 ± 945.37 | ∗6.39436- | 0.402 | 0.689 |
| | F | 30 | 8909.7 ± 1487.18 | ∗5.3791- | | |
| Mean T1 | B | 30 | 11459.1 ± 888.94 | ∗18.2150 | 1.288 | 0.203 |
| | F | 30 | 11706.83 ± 564.61 | ∗20.875 | | |
| Mean T2 | B | 30 | 10657.6 ± 962.02 | ∗9.94659 | 3.040 | 0.004 |
| | F | 30 | 11278.43 ± 496.34 | ∗16.195 | | |
| Mean T3 | B | 30 | 9915.96 ± 1023.89 | 2.29571 | 2.991 | 0.004 |
| | F | 30 | 10546.27 ± 533.07 | ∗8.892 | | |
| Mean T4 | B | 30 | 9237.56 ± 1008.60 | 4.70284- | 3.097 | 0.003 |
| | F | 30 | 9864.73 ± 461.28 | 1.8551 | | |
| Mean T5 | B | 30 | 8553.96 ± 836.23 | ∗11.755- | 3.480 | 0.001 |
| | F | 30 | 9140.26 ± 389.94 | ∗5.6252- | | |
| Mean T10 | B | 30 | 7400.67 ± 1525.76 | ∗21.0723- | 3.856 | 0.0065 |
| | F | 30 | 8127.63 ± 289.26 | ∗16.081- | | |

p value < 0.05 significant

**Table 5:** Comparison of Respiratory Rate and Sedation Scorebetween two Groups

| Respiratory Rate | Group B | Group F | p value between B and F |
|---|---|---|---|
| P1 | 11.467 ± 0.9732 | 11.533 ± 1.041 | 0.3993 |
| P2 | 12.4 ± 1.734 | 12.2 ± 0.8469 | 0.2862 |
| | Sedation Score | | |
| P1 | 1 | 1 | NA |
| P2 | 2.3 ± 0.46 | 1.2 ± 0.40 | <0.001 |

p value < 0.05 significant

**Table 6:** Intra and post Operative variables distribution between two Groups

| Group | Intraoperative Hypotension | | Total | P value between B and F |
|---|---|---|---|---|
| | Yes | No | | |
| Group B No. of patients % within Group | 3 10% | 27 90% | 30 100.0% | 0.1869 |
| Group F No. of patients % within Group | 2 6.7% | 28 93.3% | 30 100.0% | |
| Total No. of patients % of study population | 5 8.3% | 55 91.7% | 60 100.0% | |
| *Intra Operative Bradycardia* | | | | |
| Group B No. of patients % within Group | 3 10% | 27 90% | 30 100% | 0.259 |
| Group F No. of patients % within Group | 1 3.3% | 29 96.7% | 30 100.0% | |
| Total No. of patients % of study population | 4 6.7% | 56 93.3% | 60 100% | |
| *Intra Operative Shivering* | | | | |
| Group B No. of patients % within Group | 2 6.7% | 28 93.3% | 30 100.0% | 0.0051 |
| Group F No. of patients % within Group | 6 20% | 24 80% | 30 100.0% | |
| Total No. of patients % of study population | 8 13.3% | 52 86.7% | 60 100.0% | |
| *Post Operative Nausea and Vomiting* | | | | |
| Group B No. of patients % within Group | 5 16.7% | 25 83.3% | 30 100.0% | 0.1704 |
| Group F No. of patients % within Group | 6 20% | 24 80% | 30 100.0% | |
| Total No. of patients % of study population | 11 18.3% | 49 81.7% | 60 100.0% | |

*p value: 0.1869

There is no significant difference between the groups B and F with regard tothe pre-operative and post extubation respiratory rate. While the sedation score was zero in both the groups pre operatively, the post extubation sedation score in Butorphanol group was 2.3 ± 0.46 and in Fentanyl group was 1.2 ± 0.4, which was significantly higher in group B than in group F (p<0.001) (Table 5).

In Butorphanol group, intra operative hypotension was observed in 3 patients (10%) and in Fentanyl group, intra operative hypotension was observed in 2 patients (6.7%). There is no significant difference in the occurrence of intra operative hypotension, Bradycardia in between the two groups (p >0.05). The incidence of post operative shivering is significantly more with the Fentanyl group than the Butorphanol group (p<0.005) (Table 6).

## Discussion

The purpose of conducting this study in healthy patients was to generate datato be used in a future study in those with a history or risks of coronary artery disease with ST – T monitoring in whom beneficial effects of Butorphanol and Fentanyl arelikely to out weigh adverse effects. Fentanyl has been tried in various bolus doses for control of hemodynamic changes of laryngoscopy. Kay et al. [3] found complete attenuation of hemodynamic response with 5 µg/kg Fentanyl. But this occurred at the cost of a significant decrease in blood pressure and heart rate and increase in respiratory depression. In clinical practice sympathetic reflexes resulting from surgical stimulation might maskany hypotensive, vagotonic respiratory effects of low dose fentanyl respiratory effects of low dose fentanyl.

McClain et al. [4] reported apnoeic episodes in four out of seven patients who received 3.2 to 6 µg/kg Fentanyl. Hence low dose Fentanyl (2 µ/kg) was used in the presentstudy. In the current study, the selection of dosages were based on the assumption that Butorphanol is equipotent to morphine. Fentanyl on an mg basis is about 80 times more potent than morphine and a dose of 2 µg/kg was therefore chosen to bealmost equipotent to

Butorphanol 40 mcg/kg. In the current study, dose of Butorphanol 40 mcg/kg was used because larger doses might have improved thequality of anaesthesia.

In the present study, there was no statistically significant difference in the distribution of age, sex and weight of patients and duration of surgery in both the groups. Variation of HR decrease with increasing age. Young patients show more extreme changes. Marked fluctuations in hemodynamic response are often seen ingeriatric patient. 87 In our study, we selected an optimal age range of 20 to 49 years.

The mean age in our study was 36.06 ± 7.73 for group B and 36.2 ± 6.80 for group F. There was no difference in the cardiovascular parameters at baseline in our study. A variable combination of drugs used for premedication, induction, relaxation and maintenance of anaesthesia can influence the sympathetic response tolaryngoscopy and intubation.

*Mean Arterial Pressure*

The mean arterial pressure which is a derived value is important for the maintenance of the auto regulatory functions of the heart, brain and kidney.

Forbes and Dally [5] observed that during induction of anaesthesia with thiopentone, suxamethonium and endotracheal intubation, normotensive patients showed a highly significant MAP (25 mmHg, S.E 2.2, range 2-45) with in 1 min of laryngotracheal stimulation which is explained on the basis of a reflex sympathetic response to a mechanical stimulation of larynx and trachea. Similarly in this study, in Group B at 1 min after laryngoscopy and intubation, a 7.11% increase in the MAP was observed with mean values of 100.4 ± 4.19 and then decreased with mean value of 96.67 ±4.7 at 2 minute subsequently and was statistically significant. A decrease trend in MAP was noted from 2 min to 10 min after laryngoscopy and intubation. The mean baseline MAP in this group was 94.5 ± 2.40. At 1 minute after laryngoscopy and intubation, 9.32% increase in the mean MAP was observed with mean values of 103.31 ± 1.52 which was further decreased to 101.62 ± 1.68 at 2 minute subsequently, a decreasing trend in MAP was noted starting from 2 min to 10 min after laryngoscopy. The MAP was significantly higher at T1, T2, T3, T4 when compared to the baseline and significantly lower when compared to the baseline value at other time intervals. At T1, T2, T3 both groups showed increase in MAP which was statistically significant ($p<0.001$). At T4, T5, T10 there was significant reduction in the mean arterial pressure in B group when compared to F group which was $p<0.05$.

*Heart Rate*

Pandit and colleagues [6] measured perioperative vital signs during laparoscopy using Butorphanol and fentanyl. They found that the patients who received Butorphanol experienced smaller increases in HR and SBP two mins after intubation which was in correlation with the present study. At T2 & T3, patients experienced smaller increases in the HR and SBP which was statistically significant ($p <0.05$). In the present study at T1, both the groups showed increase in the heart rate which was not statistically significant. At T2, T3, there was significant increase in the HR in F group when compared to B group ($p<0.05$). At T4, T5 & T10 there was significant reduction in the heart rate in B group when compared to F group which was highly significant ($p<0.001$).

*Rate Pressure Product (RPP)*

RPP also known as cardiovascular product is a measure of the stress put on the cardiac muscle based on the number of times it needs to beat per minute (HR) and the arterial BP that it is pumping against (SBP). It will be a direct demand of the heart and thus a good measure of the energy consumption of the heart. It allows youto calculate the internal work load or haemodynamic response. In a similar study conducted by Balasubramaniam S et al. [7] the RPP is significantly lower in Group B when compared to Group F from the 2$^{nd}$ min after intubation. The RPP in Group B after intubation becomes comparable to the preoperative RPP at the 4$^{th}$ min after intubation and it becomes significantly lower than the preoperative RPP from the 5$^{th}$ min after intubation. The RPP in Group Fafter intubation becomes comparable to the preoperative RPP at the 5$^{th}$ min after intubation and it becomes significantly lower than the preoperative RPP at 10$^{th}$ min after intubation. The RPP in both the groups increased following intubation. However the increase was significantly lower in the B group when compared to the F group. A rise of RPP by 18.2% was observed in B group as compared to 20.8% in F group. At T1, both the groups showed increase in the RPP which was not statistically significant.

At T2 & T3, there was significant increase in the RPP in F group when compared to B group ($p<0.05$). At T4, T5 & T10 there was significant reduction in the RPP in B group when compared

to F group which was highly significant (p <0.001). Intraoperative Hypotension: The occurrence of intraoperative hypotension was 10% and 6.7% in the B and F groups respectively, was not found to be significant between the two groups (p > 0.05). Intraoperative Bradycardia: The occurrence of intraoperative Bradycardia was 10% and 3.3 % in the B and F groups respectively, was not found to be significant between the two groups (p > 0.05).

Philip BK et al. [8] in their study comparing these two drugs also found the maintenance phase of anaesthesia to be uneventful in both the groups. In the present study, both the drugs provided stable hemodynamics throughout the intraoperative period.

Philp et al. [8] in their study found that there was no significant difference with regard to post operative respiratory depression both the groups which was incorrelation to present study.

Postoperative sedation was the most prominent side effect observed in the patients who received Butorphanol. The sedation score was significantly lower in the Fentanyl group (p<0.001). This finding is similar to that observed by Arora et al. [9] and Pandit et al. [6] PONV not only lead to patient discomfort but rarely can cause pulmonary aspiration when patients are recovering from the effects of anaesthetic drugs. Postoperative nausea and vomiting is one of the frequent side effects observed with opioids whether they are used in the intra operative or postoperative period [10]. The dose of the opioid used is of significance rather than the type of opioid in causing postoperative nausea and vomiting. Arora et al. [9] Observed that PONV was 18% in Fentanyl group and 12% in Butorphanol group which was statistically not significant. In ourstudy postoperative nausea and vomiting occurred in 16.7% of patients in the Butorphanol group and in 20% of percentage of patients in the Fentanyl group. Neither group was superior to the other with regard to the incidence of post operative nausea and vomiting (p >0.05).

Post anaesthesia shivering is another complication which can occur in 5-65% of patients in recovery period depending on age, sex, anaesthetic agent used forinduction and maintenance of anaesthesia and duration of surgery. Shivering notonly causes physical discomfort but also causes precipitous rise in oxygen consumption which may be poorly tolerated by a patient with diminished cardiorespiratory reserve. Arora et al. [9] Showed that post operative shivering was more in Fentanyl group when compared to Butorphanol group which was statistically significant. In the present study, the incidence of postoperative shivering was significantly less in the Butorphanol group (6.7%) when compared to the Fentanyl group (20%) (p <0.005). Both Butorphanol and Fentanyl effectively attenuates the hemodynamic response to laryngoscopy and intubation of trachea. Of the two, Butorphanol is effective in attenuation compared to Fentanyl.

## Conclusion

With this study we conclude that administration of intravenous Butorphanolprior to induction of anaesthesia helps in better attenuation of the hemodynamic response to laryngoscopy and intubation than intravenous Fentanyl. Neither of the drugs was associated with any adverse hemodynamic events. Hence, we conclude that Butorphanol could be an effective alternative to Fentanyl for attenuation of the hemodynamic stress response to laryngoscopy and intubation.

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# Comparative Study of Preanesthetic Single dose Dexmedetomidine versus Placebo in Patients Undergoing Elective Laparoscopic Cholecystectomy

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**Abstract**

*Background:* Laparascopic surgery is a routinely performed surgery and it is desirable to have a stable intraoperative haemodynamic states by avoiding hypertension and tachycardia. *Aim:* The present study has been conducted to compare the beneficial effect of alpha2 adrenergic receptor agoinist dexmedetomidine versus placebo in maintaining the perioperative haemodynamic parameters during laparoscopic cholecystectomy. *Materials and Methods:* The present Randomized double blind comparative study was conducted in the Department of Anaesthesiology. A total of 60 patients randomly allocated in two groups, to Group D (Dexmedetomidine) & Group P (Placebo) of 30 each undergoing elective laparoscopic cholecystectomy, under GA were studied. The patients recieved preloaded and coded study drug as infusion (Dexmedetomidine 0.5 mcg/kg & NS 10 ml) before induction. *Results:* Sex, age, and weight were comparable in the two groups. The study drug dexmedetomidine maintained cardiovascular stability during laparoscopic cholecystectomy. Mean arterial pressure and heart rate in Group D (Dexmedetomidine) were significantly less after intubation and throughout the period of pneumoperitoneum. In addition, other drugs requirement in placebo group was found to be considerably high when compared to dexmedetomidine group. *Conclusion:* Dexmedetomidine improves intraoperative and postoperative haemodynamic stability during laparoscopic surgery without prolongation of recovery. Dexmedetomidine was more effective in attenuating hemodynamic response to intubation and pneumoperitoneum when compared with placebo.

**Keywords:** Dexmedetomidine; Placebo; Elective Laparoscopic Cholecystectomy

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## Introduction

Laparoscopic surgeries involves insufflation of a $CO_2$ gas into the peritoneal cavity producing a pneumoperitoneum. This causes an increase in intra-abdominal pressure. Carbondioxide is insufflated into the peritoneal cavity at the rate of 4-6 lit/min to a pressure of 10-15 mm Hg. [1] The pneumoperitoneum is maintained by a constant gas flow of 200-400 mL/min. Peritoneal insufflation induces alterations of haemodynamics,

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characterized by decrease in stroke volume and cardiac output, elevation of mean arterial pressure, and increase of systemic and pulmonary vascular resistance [2]. Haemodynamic changes are accentuated in high-risk cardiac patients. General anaesthesia has been supplemented on ocassions with intraoperative infusions of propofol due to its intrinsic ability to inhibit catecholamine secretion, infusions of nitroglycerine or beta blockers to control perioperative stress. Again combined GA with epidural anaesthesia is yet another strategy employed by anaesthesiologists to control perioperative haemodynamic instability, with limited success. But the search for the ideal agent to control this instability in haemodynamics is still on [3]. The pathophysiologic haemodynamic changes can be attenuated or prevented by optimizing preload before pneumoperitoneum and by vasodilating agents, $\alpha_2$-adrenergic receptor agonists, high doses of opioids, and β-blockers. Alpha 2 agonists produce diverse responses including analgesia, anxiolysis, sedation and sympatholysis, each of which has been reported in the treatment of surgical and chronic pain patients and in panic disorders as well.The food and drug administration (FDA) registered two novel α2-adrenergic agonists Clonidine and Dexmedetomidine. The α2 agonists, including clonidine and dexmedetomidine, decrease central sympathetic outflow and modify intraoperative cardiovascular responses to surgical stimuli and laryngoscopy. The reduction in tachycardia, hypertension, and sympathetic activity may be of benefit in patients at risk of myocardial ischemia. Clonidine is a centrally acting selective partial α2 agonist (220:1 α2: α1) with a elimination half-life of 6-10 hours. It is known to induce sedation, decrease anaesthetic day requirement and improve perioperative haemodynamics by attenuating BP & HR responses to surgical stimulation and protection against perioperative myocardial ischemia. It provides sympathoadrenal stability and suppresses renin angiotensin activity. Dexmedetomidine is an α2 adrenergic receptor agonist with high selectivity for the α2 receptor (α2 to α1 1620:1) and it is seven to ten times more selective for α2 receptors compared to clonidine, and has a shorter duration of action with a elimination half-life of 2-3 hours. Dexmedetomidine is considered full agonist at α2 receptors as compared to clonidine, which is considered as a partial agonist. The purpose of this study was to compare the effects of a single IV dose of dexmedetomidine by administering 10 minutes before induction of anesthesia with placebo group on induction and haemodynamic parameters in patients undergoing elective laparoscopic cholecystectomy.

## Materials and Methods

The present study conducted from 1st September 2014 to 1st June 2015. The study protocol was approved by the Institutional Ethical committee and informed consent was taken from each of the patients. It was prospective, randomized and double blinded study. The study included total 60 patients belonging to ASA grade I and II of either sex with age between 20-55 years posted for laparoscopic cholecystectomy. A prospective, randomized, double blind comparative study consisting of 30 patients in group D (Dexmedetomedine) and 30 patients in group P (Placebo group) is undertaken to compare the haemodynamic parameters in patients undergoing elective laparoscopic cholecystectomy, requirement of rescue drugs and adverse effects. A sample size of 30 patients each, randomly allocated into two groups, using computerized randomization.

*Inclusion Criteria* was patients planned for elective laparoscopic cholecystectomy surgery, age group of 20-55 years and ASA I and II patients.

*Exclusion criteria* was patients unwilling for the study, patients who had hypertension and diabetes, obese with BMI greater than 30, ASA III, IV, V patients, patients with cardiovascular, pulmonary, hepatic, neurological and endocrine abnormalities, pregnant patients, known case of pre-op hypotension, surgeries converted to open cholecystectomy, inability to understand protocol due to language barrier, hypersensitivity to dexmedetomidine.

A Pre-anaesthetic evaluation comprising of history of previous medical and surgical illnesses, previous anaesthetic exposures, drug allergies; and baseline investigations of blood, radiograph of the chest and airway examination will be done. Informed written consent will be taken from the patient. Patient will be kept nil by mouth for atleast 6 hours prior to surgery. Preoperative vital parameters in the form of baseline pulse, blood pressure and oxygen saturation will be recorded. NIBP, pulse oximeter, $EtCO_2$, ECG, anaesthesia machine was checked, resuscitation equipment and drugs were checked and kept ready, before undertaking the procedure. On arrival to operation theatre, routine monitors (ECG, Pulse oximetry, NIBP) attached and baseline vital parameters like heart rate, mean arterial blood pressure (MAP) and arterial oxygen

saturation ($SpO_2$) were recorded. An intravenous line with 18G secured. After baseline parameters were noted, patients were allocated randomly to the two groups using a computer generated random numbers table. An anesthesiologist who was not one of the study participants prepared syringes containing either dexmedetomidine or 0.9% saline. Both syringes were labeled "study drug" and coded to maintain the double-blinded nature of the study. Dexmedetomidine 0.5 µg kg−1 was prepared in a 10-mL isotonic solution and 10-mL isotonic 0.9% normal saline was taken and labeled as study drug. All patients premedicated with Fentanyl 2 µg/kg, Glycopyrrolate 4 µg/kg, Ondansetron 15 µg/kg were given slowly intravenously, 20 minutes before induction. Patients in Group D received Dexmedetomidine 0.5 µg/kg by IV infusion, 10 minutes before induction. Patients in Group P recieved 10 ml of 0.9% normal saline by IV infusion, 10 minutes before induction. All patients were preoxygenated with 100% $O_2$ for 3 minutes and were induced with Propofol 2 mg/kg IV. Intubation was facilitated by using Vecuronium bromide 0.1 mg/kg. The lungs were ventilated with 100% oxygen for 3 minutes. Intubation was achieved with an appropriate size oral cuffed, portex endotracheal tube by the aid of Macintosh laryngoscope blade. $CO_2$ was insufflated into the peritoneal cavity (at a rate of 2 lit/min) to create pneumoperitoneum. Intra-abdominal pressure was restricted to 10-14 mmHg throughout the laparoscopic procedure. The patients were mechanically ventilated to keep ETCO2 between 35-40 mmHg. Anaesthesia was maintained with Vecuronium bromide and intermittent positive pressure ventilation with nitrous oxide and oxygen in the ratio of 50:50 with 1% Isoflurane using circle absorber system connected to the Boyle's anesthetic work station. The parameters recorded were heart rate, systolic blood pressure, diastolic blood pressure, mean arterial pressure, $SpO_2$, $EtCO_2$. The recordings were noted at various intervals from the study conducted; pre-operatively i.e. before pre-medication, after induction, after intubation, 15 mins, 30 mins, 45 mins, 60 mins, 75 mins, 90 mins, extubation, post op first hour.

*Statistical analysis:* The data was expressed as mean and standard deviation. The homogenicity in two groups of mean and standard deviation was analysed using SPSS version, Analysis of variance (ANOVA) for each parameter. Comparison between two groups at a time (inter-group comparison) was done using student's unpaired t- test. $p < 0.05$ was considered statistically significant, value < 0.01 was considered highly significant, > 0.05 was considered insignificant.

## Results

A total of 60 patients randomly allocated in two groups, to Group D (Dexmedetomidine) & Group P (Placebo) of 30 each undergoing elective laparoscopic cholecystectomy, under GA were studied. Sex, age, and weight were comparable in the two groups.

Table 1 shows that There were no significant differences between the two groups with regard to demographic data such as age, sex, and weight. Both groups have a sex ratio which are comparable. The average age in Group D (Dexmedetomidine) was 38.06 years and average age in Group P (Placebo) was 41.56 years. The average weight in Group D (Dexmedetomidine) was 64.06 kgs and average weight in Group P (Placebo) was 67.5 kgs. Both the groups were comparable with respect to demographic profile. No significant differences were found with respect to age, sex, and weight.

Figure 1 shows that heart rates were on lower side in Group D (Dexmedetomedine) after induction, intubation, pneumoperitoneum and maintained throughout the intraoperative and post-operative period compared to Group P (Placebo). There is highly significant difference in heart rate between both groups during intraoperative and post-operative period. Heart rate significantly lower in Group D compared to Group P throughout the intraoperative period.

Figure 2 shows that systolic blood pressure(SBP) is lower in Group D patients after induction,

Table 1: Demographic profile (Mean ± SD):

| Characteristics | Group D | Group P | p value | Significance |
|---|---|---|---|---|
| Age in years | 38.067 ± 7.306 | 41.567 ± 6.961 | 0.062 | NS |
| Sex (F:M) | 13:17 (1.433 ± 0.504) | 10:20 (1.333 ± 0.479) | 0.434 | NS |
| Weight | 64.067 ± 8.642 | 67.5 ± 9.347 | 0.145 | NS |
| Sex (Female) | 13 (43%) | 10 (33.33%) | | |
| Male | 17 (57%) | 20 (66.67%) | | |

NS-Non Significant

intubation, 15 mins, 30 mins, 45 mins and 60 mins after pneumoperitoneum and throughout the intraoperative period and post operative recovery period compared to Group P. In Group P Systolic blood pressure (SBP) is higher in preoperative, intraoperative period and post operative recovery period compared to Group D.

Figure 3 shows that in Group D (Dexmedetomidine), DBP (Diastolic blood pressure) is significantly lower during intubation, 15 mins after pneumoperitoneum, extubation and in the post operative method compared to Group P (Placebo).

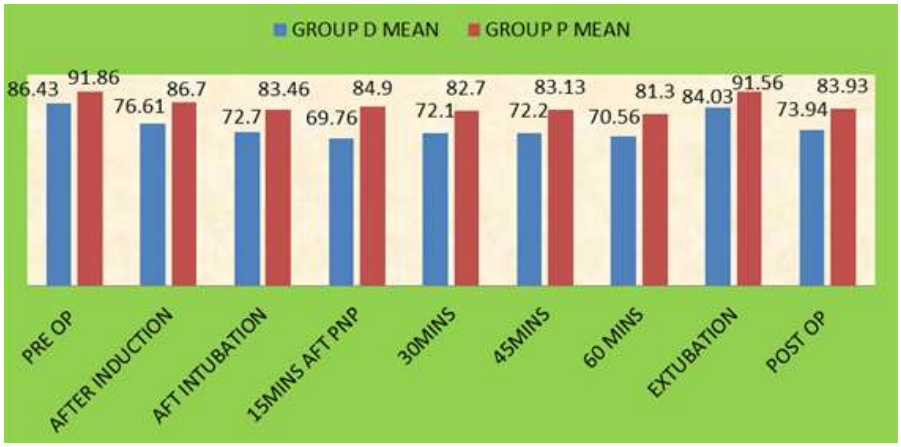


**Fig. 1:** Changes in heart rate

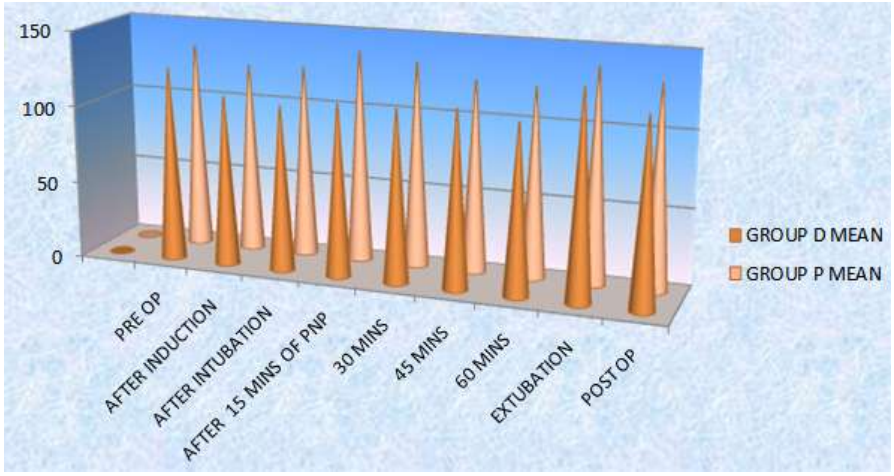


**Fig. 2:** Changes in systolic blood pressure (Mean ± SD)

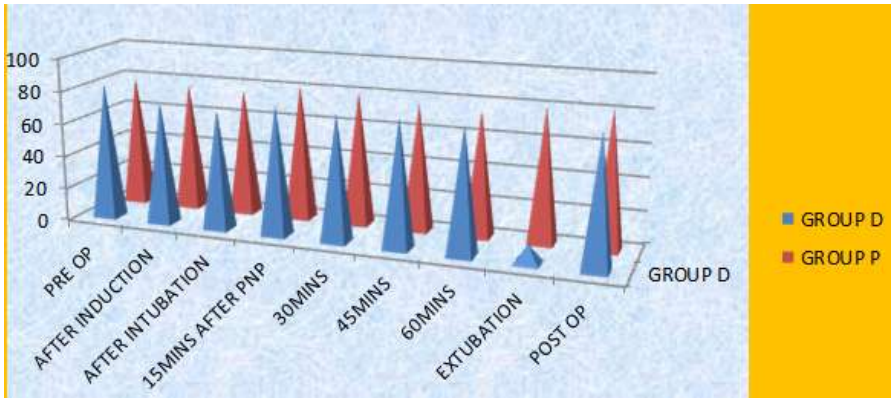


**Fig. 3:** Changes in DBP (Mean)

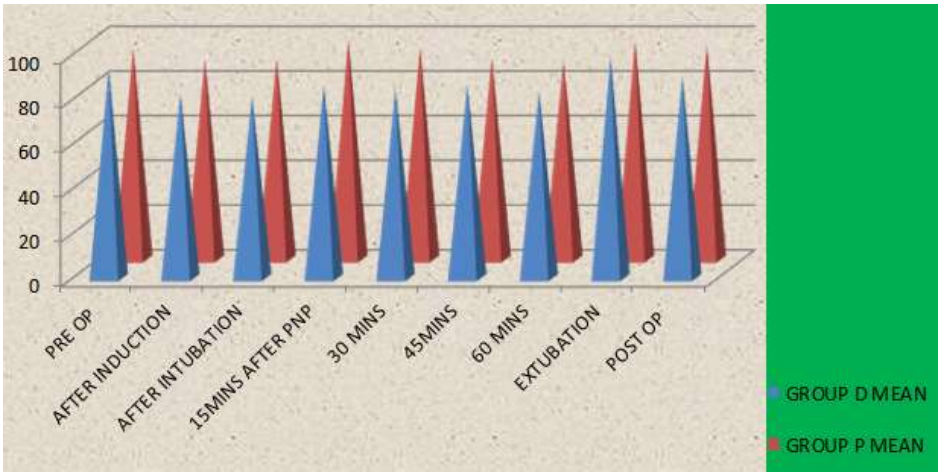


**Fig. 4:** Changes in mean arterial pressure (Mean ± SD)

Figure 4 shows that mean arterial pressure (MAP) is lower in Group D patients after induction, intubation, 15 mins, 30 mins, and 60 mins after pneumoperitoneum and in the post operative recovery period. In Group P patients, mean arterial pressure (MAP) is higher compared to Group D after induction, intubation pneumoperitoneum and throughout the intraoperative period. There was no significant difference in the preoperative Mean values of MAP between the two groups. MAP values in group D were significantly lower after induction than in group P ($p < 0.05$ ). MAP values in group D were highly significantly lower ($p < 0.01$) after intubation and pneumoperitoneum and remained lower throughout the pneumoperitoneum and in the postoperative period.

**Table 2:** Recovery time following extubation.

| Time (Mins) | Group D (Mean ± SD) | Group P (Mean ± SD) | p value |
|---|---|---|---|
| Ability to vocalize following extubation | 3.7667 ± 1.8880 | 6.1667 ± 1.4404 | < 0.0001 |

Table 2 shows that ability to vocalize following extubation was significantly prolonged in Group P (Placebo) when compared to Group D (Dexmedetomidine). In our study, a single dose of 0.5 µg kg−1 of dexmedetomidine given preoperatively 10 minutes before induction led to significant sedation, but it does not caused delay in the recovery time following extubation. It caused delay in recovery time in Group P, when compared to Group D due to higher consumption of isoflurane, to maintain haemodynamic stability after creation of pneumoperitoneum and throughout the intraoperative period.

**Table 3:** Comparison of adverse effects between two groups.

| Adverse Effects | Group D (N=30) | Group P (N=30) |
|---|---|---|
| Bradycardia | 0 (0%) | 0 (0%) |
| Hypotension | 0 (0%) | 2 (6.6%) |

Table 3 shows that the study didn't encountered episodes of bradycardia in any case of both the study groups. But we have seen two cases of hypotension in our placebo group (Group P).

In Group D other drugs like Inj.Paracetamol has been used only for 4 cases for additive analgesia and it clearly explains that dexmedetomidine is highly effective in providing adequate analgesia throughout the intraoperative period. In Group P other drugs like clonidine, metoprolol have been used in 28 cases to maintain haemodynamic stability throughout the intraoperative period after creation of pneumoperitoneum. p value is less than 0.0001 and is highly significant.

## Discussion

In the present study, we compared the effects of dexmedetomedine and placebo administered before induction on haemodynamic parameters in patients undergoing elective laparoscopic cholecystectomy. In laparoscopic surgery, $CO_2$ is routinely used to create pneumoperitoneum. Elevated intra abdominal pressure induced by pneumoperitoneum and $CO_2$ itself produce some adverse effects on the cardiovascular system. In the present study, found statistically significant changes between Group D (Dexmedetomidine) and Group P (Placebo) as regards to heart rate, mean arterial pressure after induction, intubation, 15 mins, 30 mins, 45 mins, 60 mins after pneumoperitoneum,

and throughout intraoperative period and in post operative period, changes in heart rate and mean arterial pressure were found to be significant. The present study confirms that haemodynamic changes (rise in mean arterial pressure and heart rate) are attenuated by dexmedetomidine infusion given 10 minutes before induction during laparoscopic cholecystectomy. The decrease in heart rate appears more in the Group D (Dexmedetomidine) at all intervals when compared to Group P (Placebo), but the fall was found to be significant. Similarly the fall in mean arterial pressure (MAP) appeared more in Group D (Dexmedetomidine) compared to Group P (Placebo) and the fall was found to be significant. In present study, we didn't encountered episodes of bradycardia and hypotension in any case of Group I (Dexmedetomidine). In the present study, requirement of other drugs was very less in Group D (Dexmedetomidine) as it maintained stable haemodynamics and adequate analgesia throughout the intraoperative period. In Group P (Placebo) requirement of other drugs was very high to maintain haemodynamic stability throughout the intraoperative period. Various studies have been conducted with various pharmacological interventions that results in reduced incidence of tachycardia, hypertension during laparoscopic cholecystectomy and provide a stable haemodynamic state, without significant undesirable effects.

In a study, Jaakola et al. [4] found decreased BP and HR during intubations following the administration of 0.6 μg/kg bolus of dexmedetomidine preoperatively. In our study, we found significant fall in HR after intubation with a mean of (72.70) in Group D (Dexmedetomidine) compared to Group P (Placebo) with a mean of (83.46) and significant fall in MAP after intubation with a mean of (81.33) in Group D (Dexmedetomidine) compared to Group P (Placebo) with a mean of (89.90). In a study, Lawrence and De Lange [5] found decreased hemodynamic response to tracheal intubation or extubation following a single high dose of dexmedetomidine (2 μg/kg). In our study, we found decreased hemodynamic response to tracheal intubation or extubation following a single dose of dexmedetomidine (0.5 μg/kg) given in infusion over 10 mins before induction. In a study, Ghodki et al. [6] used dexmedetomidine 1 μg/kg intravenously over 15 min before induction followed by maintenance infusion of 0.2 μg/kg/h and observed favorable vasopressor response during laryngoscopy, with minimal change in BP with pneumoperitoneum. In our study, we used single dose of dexmedetomidine 0.5 μg/kg in infusion over 10 mins before induction, and observed hemodynamic stability after laryngoscopy, intubation, and pneumoperitoneum. In a study, Dutta et al. [7] showed that when propofol, another induction agent was used, dexmedetomidine decreased the propofol concentration necessary for sedation by approximately 60% to 80%. In a study, Aho et al. [8] found that opioid requirement decreases following 0.4 μg $kg^{-1}$ dexmedetomidine. Plasma noradrenaline concentration was markedly reduced in patients receiving dexmedetomidine. This decrement in neuronal noradrenaline release may explain in part the reduction in thiopental requirements. The response to thiopental is shown by three clinical signs: loss of eyelid reflex, loss of corneal reflex, and absence of movement in response to squeezing the trapezius muscle. The eyelid reflex was lost at significantly lower levels of thiopental than the corneal or movement response. The presence of an endotracheal tube leads to reflex sympathetic responses during both intubation and extubation. Sympathetic responses include hypertension, tachycardia, increased intraocular and intracranial pressures, bronchospasm, and myocardial ischemia. The use of α2 agonists in the preoperative period has been associated with attenuated HR and BP responses to stressful events.

In a study, Jaakola et al. [4] showed that dexmedetomidine attenuated the increase in HR and BP during intubation. In our study, single-dose 0.5 μg/kg preoperative dexmedetomidine given in infusion, and maintained hemodynamic stability after intubation and in the intraoperative period. In a study, Lawrence et al. [5] found that a single dose of dexmedetomidine before induction of anesthesia attenuated the hemodynamic response to intubation and extubation. They used a large dose (2 μg kg−1) of dexmedetomidine; bradycardia was observed on the first and fifth minutes after administration. In our study, single-dose 0.5 μg/kg preoperative dexmedetomidine given in infusion, maintained hemodynamic stability after intubation, extubation and in the intraoperative period, without causing bradycardia in any one of our study cases. In a study, OLeary E, Hubbard K et al. [9] studied hemodynamic and neuroendocrine responses after pneumoperitoneum, and changes in position in laparoscopic cholecystectomy and concluded that there were much hemodynamic fluctuations with rise in BP and HR due to catecholamine release. In our study dexmedetomidine showed a favorable outcome in Group I (Dexmedetomidine) patients. Dexmedetomidine decreased BP and HR during pneumoperitonium. thus, maintaining haemodynamic stability. In a study,

According to Bhattacharjee et al. [10], effects of dexmedetomidine 0.2 µg/kg/hr were studied in sixty patients undergoing elective laparoscopic cholecystectomy. Mean arterial pressure and heart rate were significantly less after intubation and throughout the period of pneumoperitoneum. In our study too, MAP and HR were significantly less after intubation and throughout the period of pneumoperitoneum. In a study Yildiz M, Tavlan A, Tuncer S, Reisli R et al. [11], studied effects of dexmedetomidne on haemodynamic responses to intubation on fifty patients scheduled for elective minor surgery were randomised into two groups (dexmedetomidine group and placebo group, n = 25 in each group. Fentanyl 1 microg/kg was administered to all patients and thiopental was given until lash reflex disappeared. Anaesthesia continuation was maintained with 50%:50%, oxygen : nitrous oxide. Haemodynamic parameters and adverse effects were recorded every 10 minutes for 1 hour after surgery. Arterial blood pressure and heart rate in intraoperative period were significantly lower in the dexmedetomidine group compared with the placebo group ($p < 0.05$). In our study, a single dose 0.5 µ/kg of Dexmedetomidine administered before induction resulted in blunting of haemodynamic responses during laryngoscopy, and reduced opioid and anaesthetic requirements. Tufanogullari B, White PF, et al. [12] studied effect of Dexmedetomidine infusion during laparoscopic bariatric surgery and the effect on recovery outcome variables. There was significant difference in MAP and heart rate between two groups during intraop and postop period with favourable outcome with dexmedetomedine. In our study, we found similar results. There was significant difference in MAP and heart rate between both groups during intraoperative period. It can be concluded that dexmedetomedine provides a good haemodynamic stability by attenuating haemodynamic response during laparoscopic cholecystectomy.

## Conclusion

To conclude,. dexmedetomidine reduces the elevation of mean arterial pressure and heart rate during and after pneumoperitoneum and thereby improving perioperative haemodynamic stability during laparoscopic surgery. The haemodynamic stability provided by dexmedetomidine should be helpful in patients with compromised cardiac function by allowing these patients to get the benefits of the laparoscopic approach. In our study, we found that in Group D (Dexmedetomedine), the heart rate and MAP remained similar to the preoperative value during pneumoperitoneum (PNP), thus indicating the haemodynamic stability during PNP with Dexmedetomidine group when compared to Group P (Placebo group).

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*Original Research Article*

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# Evaluation of Preemptive Intramuscular Phenylephrine vs Ephedrine for Prevention of Hypotension Induced by Spinal Anesthesia in Lower Segment Caesarean Section

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**Abstract**

*Background:* Hypotension is the commonest side effect after giving spinal anaesthesia in lower segment caesarean section (LSCS). Various drugs are being used to prevent hypotension due to spinal anaesthesia. *Aim:* The present study was planned to compare role of preemptive (used just after giving spinal anaesthesia) Phenylephrine and Ephedrine intramuscularly (IM) in reducing spinal anaesthesia induced hypotension and other adverse effects in LSCS. *Settings and design:* After approval from ethical committee (Reference No: SGRR/IEC/16/18) a prospective, double blind randomized control clinical study was conducted. *Material and method:* Total 90 pregnant females with single pregnancy, term gestation and aged between 18-45 years and American Society of Anaesthesiologist (ASA) class I, posted for LSCS were selected and randomly divided by using envelope technique into three groups each having 30 patients. In Group A Phenylephrine 4 mg, in Group B Ephedrine 30 mg and in Group C normal saline was given by intramuscular route. *Statistical Analysis:* One way ANOVA test was used to compare means of different groups whereas Chi- square test was used to compare proportions of different group. p value <0.05 was considered statistically significant. *Results:* Mean blood pressure values were found maximum in Phenylephrine group followed by Ephedrine group and least in control group. Incidence of hypotension and nausea/vomiting was seen least in Phenylephrine group in comparison to other groups. *Conclusion:* Phenylephrine and Ephedrine both were effective in maintaining mean blood pressure, lowering incidence of hypotension and associated adverse effects related to spinal anaesthesia however Phenylephrine was found more effective.

**Keywords:** Hypotension; Caesarean; Pre-emptive Phenylephrine; Ephedrine; Spinal Anaesthesia.

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## Introduction

There are many views regarding the ideal anaesthetic technique for Lower segment caesarean section [1]. Subarachnoid block (SAB) is usually preferred over general anaesthesia in caesarean section to avoid the airway difficulty in pregnant ladies [2]. Hemodynamic changes specially hypotension is the commonest side effect after giving SAB [3]. Hypotension sometimes may be associated with nausea and vomiting, which might

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cause interference in the surgical procedure [4]. Vasopressors are considered as the best way for prevention of hypotension after spinal anaesthesia. The present study was planned to compare the role of preemptive (just after giving spinal anesthesia) intramuscular Ephedrine, Phenylephrine and normal saline (NS) to prevent hypotension and associated nausea and vomiting.

## Material and Method

A prospective study was conducted after approval from the ethical committee of the institution and 90 patients (pregnant females) were selected. This study was a double blind randomized control clinical trial. Pregnant females belonging to age limits of 18-45 years, with ASA class I physical status, single pregnancy, on term gestation, posted for LSCS were included in the study. Pregnant females with refusal for procedure, any contraindications to spinal anaesthesia, having eclampsia, being known case of diabetes mellitus or gestation diabetes mellitus, having history of any cardiovascular or cerebrovascular diseases, detected with foetal anomalies in antenatal period were excluded from the study. Patients were randomly divided into three groups of 30 patients each; by using sealed envelope technique. In Group A Phenylephrine 4 mg, in Group B Ephedrine 30 mg and in Group C Normal saline was given through intramuscular route.

Firstly all patients were taken in the operation theatre and their vitals were monitored with the help of non-invasive blood pressure monitoring, pulse oximeter and ECG (electrocardiogram) monitor. For preoperative measurement of baseline systolic arterial pressure, average of two readings (taken two minutes apart) was calculated. An 18G cannula was used for intravenous access through non dominant hand and preloading was done at 10 ml/kg body weight with ringer lactate. Afterwards spinal block was given in the left lateral position using 2.2 ml sensoricaine (heavy) in L3-L4 space with the help of a 25G Quincke spinal needle. Just after inducing subarachaniod block, intramuscular injection of the drug to be investigated was administered in the left vastus lateralis muscle. Particular study medication for each group was prepared to a dose of 2 ml with 0.9% normal saline and administered by one anaesthetist, not involved in any data collection or patient care. Another anaesthetist, who was blind to identification of any of the study medication, managed all the patients during whole procedure.

In this study serial measurement of Mean Blood Pressure (MBP), Heart rate (HR), Blood Oxygen saturation ($SpO_2$) was done and readings were recorded at the interval of two minutes in initial 20 minutes, then at the interval of five minute till 45 minutes. The frequency, onset, time and duration of hypotension was analyzed. If Mean blood pressure fall was more than 20% of the initial value, rescue dose of intravenous Ephedrine 6 mg was administered. Incidence of hypotension, nausea and vomiting was noted down in all the groups and compared.

### *Statistical Analysis*

The collected data was entered in SPSS version 23 software and analyzed. Quantitative variables were expressed as mean and standard deviation whereas categorical variables were expressed in terms of percentages and proportions. To compute results, the mean and standard deviation of blood pressure and mean changes of their values over period of time along with standard deviation were calculated statistically. One way ANOVA test was used to compare the mean of different groups whereas Chi- square test was used to compare proportions of different groups. P-value of tests was used to ascertain statistical significance to the tests. p-value $<0.05$ was considered as significant and p value $<0.005$ was considered as highly significant. Microsoft Excel software was used for making graphs.

## Results

Total 90 patients (pregnant females) were registered in the study. All the patients (n=30 in each group) completed the study. In Group A patients received Phenylephrine 4 mg, in Group B patients received Ephedrine 30 mg and in Group C which was a control group normal saline was given; via intramuscular route.

While comparing the demographic profile; the age, weight, height and body mass index (BMI) measurements of all the three groups were similar (p value $>0.05$). [Table 1]

All the patients in each group were in ASA I category with no pre-existing co-morbid condition and got good quality of surgical anaesthesia.

Regarding the mean value of Mean Blood Pressure, all the groups were comparable in base line values. The mean value of Mean Blood Pressure starting from two minutes and up to 45 minutes;

was found highest (less fall) in Phenylephrine group followed by Ephedrine group and least in control group. (p value < 0.05). [Figure 1]

Mean value of Heart Rate was also comparable in base line values in all the three groups, Ephedrine showed statistically significant rise in heart rate throughout caesarian section (from two minutes up to 45 minutes) in comparison to Phenylephrine and control group (p value <0.05). Decrease in heart rate was not observed in any of the group. [Figure 2]

While comparing incidence of hypotension in Phenylephrine group with Control group, it was 23.3% against 70% and this difference was found statistically highly significant (p value=0.000). On comparing Ephedrine group with the Control group, the incidence of hypotension was 43.3% against 70%, this difference was found significant (p=0.037). On comparing Phenylephrine group with Ephedrine group, the incidence of hypotension was found 23.3% against 43.3% and the difference came to be statistically insignificant (p value= 0.085). [Table 2]

On Comparing Phenylephrine Group with Control group the difference was found statistically significant (p<0.01) in nausea, vomiting. On Comparing Group B (Ephedrine) with Group C (Control) for nausea and vomiting, the difference was found statistically insignificant (p=0.096). When Phenylephrine Group with Ephedrine group were compared the difference was found statistically significant (p value=0.053). [Table 3], [Fig. 3]

The mean value of rescue dose of Ephedrine administered in three groups was found to be 1.6 mg in Phenylephrine group, 3 mg in Ephedrine group and 5.2 mg in control group. The amount was significantly lower in Phenylephrine and Ephedrine group as compared with control group. (p value =0.001). [Table 4], [Fig. 4]

**Table 1:** Demographic Profile of the patients enrolled (n=90)

| Group | | Age | Wt (Kg) | Ht (Cm) | BMI |
|---|---|---|---|---|---|
| Group A | Mean | 26.17 | 59.70 | 160.13 | 23.3362 |
| | S D | 2.768 | 7.340 | 5.993 | 3.05531 |
| Group B | Mean | 26.33 | 64.90 | 164.60 | 24.0211 |
| | S D | 3.133 | 6.116 | 6.078 | 2.58280 |
| Group C | Mean | 25.17 | 60.40 | 162.63 | 22.9155 |
| | S D | 2.755 | 5.519 | 5.353 | 2.65282 |
| p value | | 0.245 | 0.886 | 0.458 | 0.301 |

Wt=weight, Ht=height, BMI=body mass index, SD= standard deviation

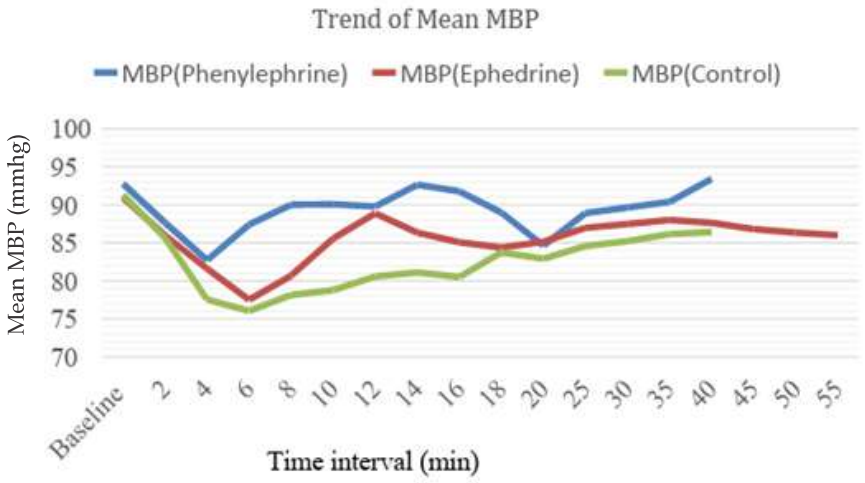


**Fig. 1:** Line diagram showing trend of mean values of mean blood pressure

**Table 2:** Intergroup comparison of incidence of hypotension

| | % of hypotension in each group | % of hypotension within Groups | p value | Significance |
|---|---|---|---|---|
| Group A | 23.3% | Group A vs Group C 46.7% | 0.000 | Highly significant |
| Group C | 70% | | | |
| Group B | 43.3% | Group B vs Group C 56.7% | 0.037 | Significant |
| Group C | 70% | | | |
| Group A | 23.3% | Group A vs Group B 33.3% | 0.085 | Not significant |
| Group B | 43.3% | | | |

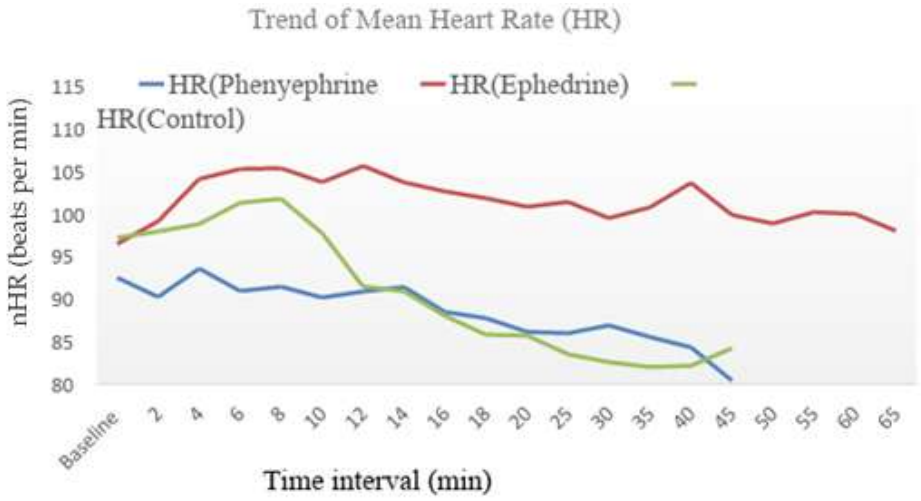


**Fig. 2:** Line diagram showing trend of mean heart rate

**Table 3:** Intergroup comparison of incidence of nausea/ vomiting

| | % nausea/vomiting in each group | % of nausea/vomiting within Groups | p value | Significance |
|---|---|---|---|---|
| Group A | 13.3% | Group A vs Group C 33.3% | <0.01 | Significant |
| Group C | 53.3% | | | |
| Group B | 33.3% | Group B vs Group C 43.3% | 0.096 | Not significant |
| Group C | 53.3% | | | |
| Group A | 13.3% | Group A vs Group B 23.3% | 0.053 | Significant |
| Group B | 33.3% | | | |

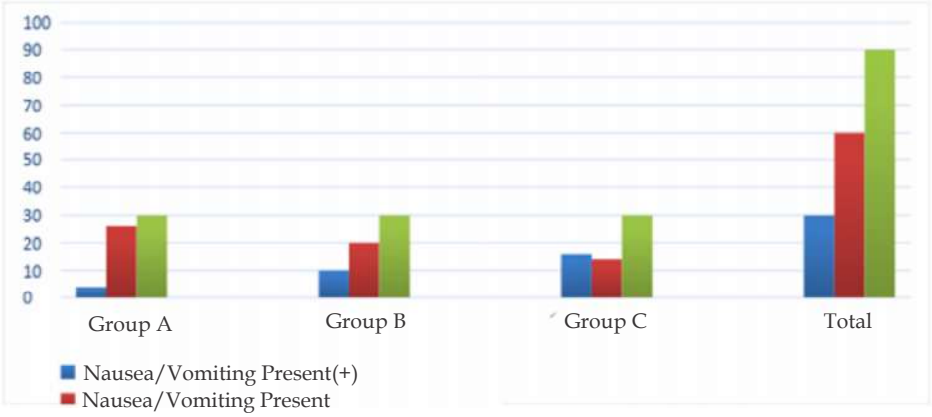


**Fig. 3:** Bar diagram showing presence of nausea/vomiting in different groups

**Table 4:** Comparison of mean dose of rescue ephedrine in different groups

| Group | Mean dose of Rescue Ephedrine (mg) | Standard Deviation | p-value | Significance |
|---|---|---|---|---|
| Phenylephrine | 1.600 | 3.1250 | 0.001 | Significant |
| Ephedrine | 3.000 | 3.7783 | | |
| Control | 5.200 | 4.0887 | | |
| Total | 3.267 | 3.9371 | | |

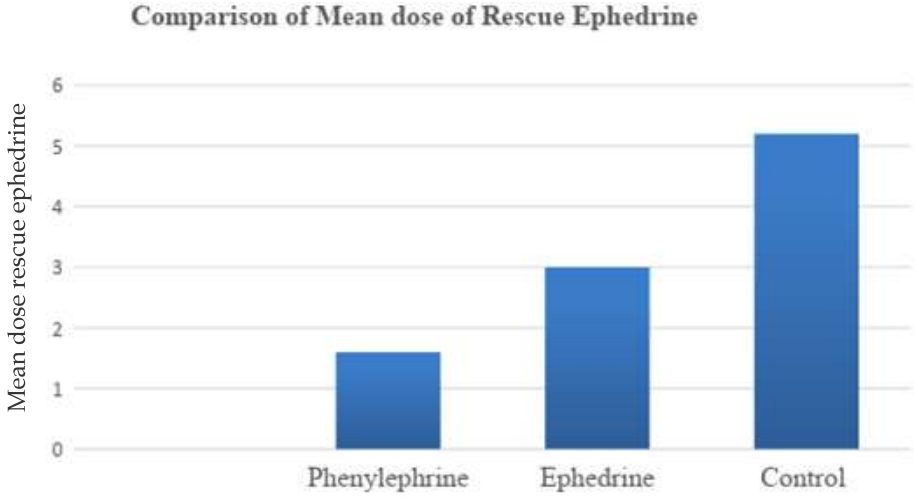


**Fig. 4:** Bar diagram showing mean rescue ephedrine dose in different groups

## Discussion

The incidence of hypotension after spinal anaesthesia is about 70% as reported in many studies. Preloading with crystalloid and keeping left lateral position may be helpful in reducing its incidence but still hypotension is a major side effect [5]. Spinal anaesthesia causes sympathetic blockage which produces vasodilatation and decrease in preload resulting in hypotension. It can further get aggravated by effect of aorto-caval compression in supine position and hypovolemia resulting from loss of blood volume. So to combat this, fluid preloading is being used widely [6].

Dyer and Langesaester colleagues have found that cardiac output and stroke volume increases few minutes after spinal anaethesia [7,8]. It shows that arteriolar dilatation is the main cause responsible for hypotension after spinal anaesthesia. Thus vasopressor drugs like Ephedrine and Phenylephrine may have a role in reducing incidence of hypotension. Ephedrine is an indirectly acting sympathomimetic amine and commonly used vasopressor in obstetric anaesthesia. Phenylephrine is an α1 adrenergic agonist, vasoconstrictor which may counteract the vasodilatation caused by spinal anaesthesia. Various studies have highlighted that continuous infusion of intra venous Phenylephrine (vasopressor) during cesarean section in spinal anaesthesia is preferred for prevention of maternal hypotension and foetal acidosis [9].

In the present study the drugs Phenylephrine, Ephedrine and normal saline were given by intramuscular route just after spinal anaesthesia. It was observed that Phenylephrine and Ephedrine both reduce the incidence of hypotension significantly however Phenylephrine was found more effective than Ephedrine in reducing the episodes of hypotension. These Findings are consistent with a study done by B.T. Ayorinde et al. [10]. in which 4 mg Phenylephrine, 2 mg Phenylephrine and 45 mg Ephedrine (via intramuscular route) were compared, there Phenylephrine 4 mg group showed maximum reduction in episode of hypotension without any rebound hypertension. The findings of lesser consumption of rescue dose of Ephedrine in Phenylephrine group than in Ephedrine group is also consistent with the above study where rescue dose was least required in Phenylephrine 4 mg group.

The lesser incidence of hypotension in Phenylephrine group than Ephedrine group in the present study may be due to the stronger vasoconstrictor action of Phenylephrine, while Ephedrine acts primarily by increasing cardiac

output and heart rate. Yet the incidence of hypotension could not be eliminated completely, this might be because in this study the vasopressor drug was injected after spinal anaesthesia and the onset of peak effect might take time via intramuscular route. It might also be due to lesser amount of vasopressor drug used. Previous studies have shown that effort to eliminate the hypotensive episodes completely might cause increased episodes of hypertension.

In this study it was also found that Ephedrine was more efficacious in reducing hypotension when compared to normal saline group. A previous study done by Webb AA et al. [11] has also shown that intramuscular Ephedrine (37.5 mg) decreases incidence of hypotension significantly than normal saline and that too without causing much side effects. In an another study Sternlo and collegues also found that when Ephedrine was given in a dose of 0.6 mg/kg IM, there was found decreased incidence of hypotension in patients undergoing hip joint surgery [12].

The incidence of nausea, vomiting was highest in control group followed by Ephedrine group and least in the Phenylephrine group. It can be very well explained on the basis of decreased episode of hypotension in Phenylephrine group.

## Conclusion

This study concludes that Phenylephrine and Ephedrine (on preemptive use) both when used via intramuscular route reduce the incidence of hypotension and associated nausea/vomiting which would have been inevitable otherwise as seen in control group. However Phenylephrine was found more efficacious.

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# Comparative Study of Intravenous Butorphanol and Intravenous Tramadol for Control of Intra-operative Shivering Under Spinal Anesthesia

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**Abstract**

*Background:* Shivering is one of the complications of central neuraxial blockade due to impairment of thermoregulatory control. Control of post spinal anesthesia shivering is essential for optimal peri-operative care which can be achieved by non-pharmacological and pharmacological means. *Aim:* The present study was designed to evaluate and compare the efficacy of intravenous Butorphanol and Tramadol for control of intra-operative shivering under spinal anesthesia. *Material & Methods:* In this prospective, interventional double blind, randomized study, 60 ASA I/II patients, aged 18–60 years, undergoing elective lower abdominal, urological and lower limb surgeries under spinal anesthesia, who subsequently developed shivering of grade 3 or 4, were randomized into two groups, to receive Tramadol 1 mg/kg or Butorphanol 0.03 mg/kg. Time taken to control shivering, response rate, recurrence rate and side effects such as nausea, vomiting, dry mouth, respiratory depression and sedation were observed. *Results:* Butorphanol had rapid onset of action for control of shivering as compared to Tramadol ($p<0.05$). The incidence of recurrence was significantly higher with Tramadol compared to Butorphanol while as sedation was found to be significantly higher with Butorphanol as compared to Tramadol. Side effects such as nausea, vomiting was significantly higher with Tramadol. *Conclusion:* Both Intravenous Butorphanol and Tramadol are effective treatment for control of shivering following spinal anaesthesia. Butorphanol is superior to Tramadol for control of shivering post spinal anaesthesia in several respects like rapid onset of action, lesser recurrence and lesser incidence of nausea and vomiting.

**Keywords:** Spinal anaesthesia; Shivering; Butorphanol; Tramadol.

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## Introduction

Shivering is a common problem during the intra-operative period under regional anaesthesia. The reported incidence of shivering is 55% following regional anaesthesia [1]. Shivering is an oscillating involuntary muscular activity that increases basal metabolic rate for heat production. It is a physiological response to core hypothermia [2]. Shivering is caused by a lowering of core body temperature which is due to several factors like

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impairment of thermoregulatory autonomic control under anaesthesia, cold temperature of operating rooms and infusion of crystalloids [3].

Shivering can be very distressful and unpleasant for the patients. Mild shivering increases the consumption of oxygen which may be increased by 200 to 500% in severe shivering. Intraocular and intracranial pressures may be raised by shivering. Involuntary muscular activity in shivering interferes with monitoring of parameters like blood pressure, heart rate, oxygen saturation and ECG [4]. Shivering may also contribute to increased wound pain, delayed wound healing and delayed discharge from Post anaesthesia care3. These all factors prompt primary prevention and control of shivering once it occurs.

Effective and prompt treatment for control of shivering is achieved by non-pharmacological and pharmacological methods. Various drugs used for control of shivering include Pethidine, Clonidine, Ketamine, Nalbuphine, Butorphanol, Tramadol etc. However debate for an ideal anti- shivering continues [2,3].

Butorphanol Tartrate is a centrally acting opioid analgesic with potent antishivering property mediated through κ (kappa) and μ (mu) receptors agonistic modulation [5]. Tramadol Hydrochloride is a synthetic opioid with opioid action preferably mediated via μ (mu) receptor and has been effective in controlling post spinal shivering [6].

This clinical study was set out to compare the efficacy of Butorphanol and Tramadol for controlling peri-operative shivering of surgical patients under spinal anaesthesia as primary outcome. Secondary outcomes included peri-operative variations in hemodynamic parameters and incidence of adverse effects among the groups.

**Methodology**

This randomized, prospective double blind study was conducted in a multi-specialty tertiary care Hospital associated with a medical college from September 2016 to May 2018 and was approved by institutional ethical committee. 60 patients aged between 18 to 60 years with American Society of Anaesthesiologists physical status I/II, posted for elective Lower abdominal, Urological and Lower limb surgeries under spinal anaesthesia were taken up for the study. These patients were divided in two groups of 30 patients each (Group B and Group T) by sealed envelope technique. Group B – Patients were administered Inj. Butorphanol 0.03 mg/kg while Group T – Patients were administered Inj Tramadol 1 mg/kg.

Written informed consent was obtained from all patients. Patients having fever, thyroid disease, neuromuscular diseases, compromised cardio-respiratory conditions, patients on long term phenothiazines and MAO inhibitors and patients with hepatic, renal insufficiency and any contra-indication to spinal anaesthesia were excluded from study.

In the operation theatre, Intravenous access was secured, standard monitors were attached and baseline heart rate, blood pressure, respiratory rate, electrocardiograph (ECG), oxygen saturation ($SpO_2$) and base line axillary temperature were noted. Sedatives and hypnotics inclusive of opioids were avoided in premedication as well as intra operatively. Ambient temperature of the operating room and recovery room were maintained at 20-23$^0$C. All the patients were preloaded with ringer lactate 10 ml/kg before administration of neuro-axial blockade. All the fluids and drugs were stored and administered at room temperature. Spinal Anesthesia was performed with a 25 gauge quincke spinal needle in a sitting position, at L3-L4/ L4-L5 interspace (midline approach) with bupivacaine (hyperbaric 0.5%) in a dose range of 15-20 mg to achieve a desirable level of T6-T10 dermatome, in accordance with surgical procedure. After induction of spinal anesthesia, patients were observed for the occurrence of shivering, its disappearance, hemodynamic status, axillary temperature and complications (if any) until the post-operative period and parameters were observed and noted. The intensity of shivering was graded on a scale of 0-4 as per Crossley and Mahajan scale.

Shivering grades (Crossley and Mahajan scale)

| | |
|---|---|
| Grade 0 | No Shivering. |
| Grade 1 | One or more of the following: Piloerection or peripheral vasoconstriction, with peripheral cyanosis, but without visible muscular activity. |
| Grade 2 | Visible muscular activity confined to one muscle group. |
| Grade 3 | Visible muscular activity in more than one muscle group but not generalized. |
| Grade 4 | Gross muscle activity involving the whole body. |

All the patients who developed intra operative shivering post-spinal anesthesia of grade 3 or grade 4, lasting for a minimum period of two

minutes were included in the study and were given treatment on an intention to treat basis. A double blind technique was used. The principal investigator, who was administering the drug and monitoring the patient, was not aware of the type of drug handed over to him by a senior faculty member of the department. Patients were also unaware of the type of drug administered to them for control of shivering. A record sheet was maintained by the faculty member where in details of patient along with drug administered was maintained. At the end of study un-blinding was done.

At the onset of shivering (grade 3 or 4), all the patients were given oxygen via face mask at six litre/minute and study drug was diluted up to ten ml as per group allocation, in the dose of Tramadol 1 ml/kg and Butorphanol 0.03 ml/kg given over 20 seconds. Shivering control was defined as complete when the shivering grade declined to grade 0, incomplete when the grade was decreased but shivering was not abolished completely after five minutes of drug administration and failed if no change in grades were observed after five minutes of drug administration.

The time taken for complete control of shivering after drug administration was accurately noted in seconds with a stop watch. Patients were monitored for failure of drug, incomplete control, and recurrence of shivering. Time taken for onset of shivering following spinal anesthesia was observed and noted.

Recurrence of shivering was observed until patient left the operation theatre and was treated with tramadol 0.5 mg/kg or butorphanol 0.015 mg/kg. diluted in ten ml normal saline and given over 20 seconds. Hemodynamic parameters were noted during recurrence along with time taken for control of recurrence.

Significant hypotension (MAP < 65 mmhg) would have been treated with intravenous ephedrine six mg in increments and significant bradycardia (HR< 60 beats/minute) with atropine sulphate 0.64 mg intravenously.

Sedation was observed in patients after the administration of study drug and was assessed with a sedation score as per Filos.

Sedation score as per "Filos":

| | |
|---|---|
| Grade 1 | Awake and alert. |
| Grade 2 | Drowsy, responsive to verbal stimulus. |
| Grade 3 | Drowsy, arousable to physical stimuli. |
| Grade 4 | Unarousable. |

*Statistical Analysis*

The entire data is statistically analyzed using Statistical Package for Social Sciences (SPSS version 21.0, IBM Corporation, USA) for MS Windows. The inter-group comparison of categorical variables is done using Chi-square test or Fisher's exact probability test for 2 x 2 contingency table. The statistical significance of inter-group difference of means of normally distributed continuous variables is tested using independent sample t test or unpaired t test. In the entire study, the p-values less than 0.05 are considered statistically significant.

## Results

**Table 1:** Demographic profile of patients

| Demographic Characteristics | Mean ± SD | | p-value |
|---|---|---|---|
| | Group B | Group T | |
| Age (years) | 35.6 ± 13.5 | 39.0 ± 13.6 | 0.335 |
| *Sex* | | | |
| Male | 19 ± 63.3 | 20 ± 66.7 | 0.787 |
| Female | 11 ± 36.7 | 10 ± 33.3 | 0.787 |

In our study both the groups were comparable with regards age and sex (Table 1).

**Table 2:** Comparison of duration of surgery, baseline temperature and shivering grade in both groups

| Variables | Mean ± SD | | p-value |
|---|---|---|---|
| | Group B | Group T | |
| Duration of surgery (Minutes) | 88.0 ± 23.9 | 90.3 ± 26.4 | 0.721 |
| Baseline axillary temperature ($^0$C ) | 36.8 ± 0.22 | 36.8 ± 0.25 | 0.741 |
| *Shivering Grade* | | | |
| Grade III | 15 (50%) | 13 (43.3%) | 0.605 |
| Grade IV | 15 (50%) | 17 (56.7%) | |

Duration of surgery and baseline temperature were comparable between two study groups (p>0.05). The distribution of grade of shivering among the cases studied did not differ significantly between two study groups (p>0.05) (Table 2).

**Table 3:** Comparison of anti-shivering effects of drugs in both groups.

| Variables | Mean ± SD | | p-value |
|---|---|---|---|
| | Group B | Group T | |
| Mean time for onset of shivering (Minutes) | 13.27 ± 2.32 | 13.03 ± 2.53 | 0.711 |
| Time to control shivering (Seconds) | 81.17 ± 37.38 | 170.23 ± 48.15 | 0.001 |
| *Control of shivering* | | | |
| Complete | 27 (90%) | 22 (73.3%) | 0.226 |
| Incomplete | 2 (6.7%) | 4 (13.3%) | |
| Failure | 1 (3.3%) | 4 (13.3%) | |
| Recurrence rate | 3 (10%) | 12 (40%) | 0.015 |

The distribution of mean time for onset of shivering did not differ significantly between two groups (p>0.05). Mean time for control of shivering is significantly higher in Group T compared to Group B (p<0.001). The distribution of control of shivering among the cases studied did not differ significantly between two study Groups (p>0.05). Incidence of recurrence was significantly higher in Group T as compared to Group B (p<0.05) (Table 3).

**Table 4:** Incidence of sedation

| Incidence of Sedation | Group B | Group T | p-value |
|---|---|---|---|
| Present | 13 (43.3%) | 4 (13.3%) | 0.020 |
| Absent | 17 (56.7%) | 26 (86.7%) | |

The incidence of sedation was significantly higher in Group B compared to Group T. (p<0.05 ).

Mean heart rate, mean systolic and diastolic blood pressure along with mean arterial pressure did not significantly alter from their respective baseline values in both the groups, throughout the procedure, barring a few statistically insignificant changes. (p>0.05) (Table 4).

**Table 5:** Comparison of side effects

| Side effects | Group B | | Group T | | p-value |
|---|---|---|---|---|---|
| | n | % | n | % | |
| Itching | 0 | 00 | 2 | 6.7 | 0.492 |
| Nausea/Vomiting | 1 | 3.3 | 8 | 26.7 | 0.026 |
| Respiratory depression | 0 | 0.0 | 0 | 0.0 | 0.999 |
| Hypotension | 0 | 0.0 | 0 | 0.0 | 0.999 |
| Bradycardia | 0 | 0.0 | 0 | 0.0 | 0.999 |

In Group B, one patient (3.3%) had nausea/ vomiting. None of the patient in Group B had itching, respiratory depression, bradycardia or hypotension.

In Group T, two patients (6.7%) had itching, eight patients (26.7%) had nausea/vomiting, none had hypotension, bradycardia or respiratory depression.

Incidence of nausea/ vomitting was significantly higher in Group T as compared to Group B. (p< 0.05). Incidence of other side effects did not differ significantly between two groups (Table 5).

## Discussion

The safety profile of spinal anesthesia compared with general anesthesia makes it the anesthesia of choice whenever possible. Shivering is a very distressing complaint in many of patients intra-operatively after spinal anesthesia. The probable mechanism of shivering under regional anesthesia could be either a result of decreased core body temperature or misinformation from receptors [7].

Various pharmacological and non-pharmacological methods have been used to prevent and control shivering. Pharmacological intervention is an effective measure to control shivering under spinal anesthesia because these drugs are easily available at all centers and they prove to be practical in many settings.

This study was formulated with an aim to compare the efficacy of two drugs; Butorphanol and Tramadol given intravenously for control of shivering under spinal anesthesia.

The mean time for onset of shivering following spinal anesthesia was comparable in both groups. In group B it was 13.27 ± 2.32 minutes while in group T it was 13.03 ± 2.53 minutes. Similar observations were made in a study conducted by Koay CK, Chan WY et al. in 1991. They observed that if shivering under spinal anesthesia occurs, it usually occurs within ten minutes after administration of spinal anesthesia [8].

Time taken for control of shivering was significantly lower in group B than group T. While the mean time taken to control shivering was 81.17 seconds ± 37.38 seconds in group B, it was 170.23 ± 48.15 seconds in group T. The results were in accordance with studies conducted by Joshi SS, Arora A et al. [9] in 2013 and Krithika V, Selvarajan R et al. [10] in 2017. However a study by Maheshwari BS, Shah SK et al. [11] in 2008 showed contrasting results.

In our study, control of shivering was comparable in both groups after the administration of study drugs which accords with the observation made by Joshi SS, Arora A et al. [9] and Bansal P, Jain G [12] in their studies. However we observed that the incidence of failure rate and incomplete control of shivering was higher in Tramadol group.

We observed in our study that the mean axillary temperature at onset of shivering was 36.2 in group B and 36.1 in group T which was similar to a study by Dhimar AA, Patel MG et al. [13] in 2007.

Recurrence of shivering was higher in group T (40%) as compared to group B (10%). This was in accordance with the conclusion of a study by Bansal P, Jain G [12] in 2011 while Maheshwari BS, Shah SK et al. [11] has contrasting findings/results.

The incidence of sedation was significantly higher in group B (43.3%) than group T (13.3%). This finding was similar to finding of the study by Bansal P, Jain G [12] in 2011.

In our study both the drugs gave good hemodynamic stability throughout the course of the study in all the patients. The incidence of nausea/ vomiting as a side effect was significantly higher in group T (26.7%) compared to group B (3.3%). Similar observations were made by Joshi SS, Arora A et al. [9] in their study. None of the cases in both groups had hypotension, bradycardia or respiratory depression.

In our study a dose-response using a single drug may have delineated its antishivering profile and corresponding increase in side effects. Further studies can investigate these aspects or compare the efficacy of combination of drugs for control of shivering under spinal anesthesia.

The limitation of our study includes a relatively small sample size in proportion to the burden of this peri-operative problem.

## Conclusion

From our study we can conclude:

1. Both intravenous butorphanol and tramadol are effective treatment for control of shivering following spinal anesthesia.
2. Butorphanol is superior to tramadol for control of post spinal shivering in several respects like more rapid onset of action, lesser recurrence and less incidence of nausea and vomiting with comparable level of safety.
3. Butorphanol causes more sedation than tramadol.

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*Original Research Article*

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# Randomised Double Blind Study of Dexmedetomidine Versus Tramadol for Post Spinal Anaesthesia Shivering

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**Abstract**

Shivering is one of the most common complications of a central neuraxial blockade. Shivering is defined as involuntary, spontaneous, oscillatory mechanical activity of skeletal muscle associated with increased oxygen consumption. Shivering can be thermo regulatory or non thermo regulatory. Its mere presence per operatively is very unpleasant and even physiologically stressful. It is managed per operative either by non pharmacological means such as warm blankets, drapes, warm intravenous fluids or by pharmacological means using various drugs like intravenous opioids, HT3 antagonists, Dexmedetomidine (α-2 agonist). Our study was planned to study the efficacy of Dexmedetomidine with that of Tramadol for control of shivering after spinal anesthesia given in patients for various surgical indications. 60 Patients of age group 15-70 years of ASA grade I & II were divided in two groups Group D (to receive Inj. Dexmedetomidine 0.5 µg/kg intravenously slowly) and Group T (to receive Inj. Tramadol 1 mg/kg intravenously slowly) intra operatively who developed shivering of the Grade 3 and 4. We found that Dexmedetomidine in the dose of 0.5 µg/kg intravenously controls shivering faster than Tramadol 1 mg/kg, reduces patient discomfort experience time, and also induces sedation without any nausea and vomiting. Hence Dexmedetomidine seems to be a better alternative to Tramadol for per operative and post operative shivering during central neuraxial blockade.

**Keywords:** Dexmedetomidine; Tramadol; Shivering Grade.

**How to cite this article:**

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## Introduction

A Safe and widely used subdural anesthesia (spinal anesthesia) has a incidence of per operative and post operative shivering in almost 40-70% of patients. Shivering is one of the most common complications of a central neuraxial blockade. Shivering is defined as involuntary, spontaneous, oscillatory mechanical activity of skeletal muscle associated with increased oxygen consumption. Shivering can be thermo regulatory or non thermo regulatory. Its mere presence per operatively is

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very unpleasant and even physiologically stressful. Complications or side effects of shivering may be increased oxygen requirement along with increased $CO_2$ production leading to adverse cardiac event, increased chances of infection and increased surgical bleeding. In Central neuraxial blockade (spinal anesthesia), thermoregulatory control may be hampered secondary to autonomic blockade [2]. Intra operative shivering is managed both by non pharmacological and pharmacological means. Non pharmacological aids like increasing ambient temperature of OR, covering the patient with warm blanket or surgical drapes, warm intravenous fluids.

Many drugs have been tried to reduce this not properly explained per operative shivering after central neuraxial blockade. These include opioids like alfentanyl, pethidine, tramadol, 5HT3 antagonists [3]. Dexmedetomidine a α-2 agonist also has been tried exploring its sedative properties. In our study efficacy of Dexmedetomidine and Tramadol were compared in terms of efficacy to reduce or curb the shivering in patients subjected to various surgeries under spinal anesthesia. The drugs were compared in aspect of onset, degree of control and any recurrence along with any systemic side effects.

## Methodology

After approval from the hospital ethical committee, this present was planned to include 60 patients of age 18-70 years and ASA gr I and II, posted for various surgeries under spinal anesthesia randomly distributed to receive either:

Group D: Inj. Dexmedetomidine 0.5 µg/kg intravenously diluted to 10 ml in normal saline

Group T: Inj. Tramadol 1 mg/kg intravenously diluted to 10 ml in normal saline.

Patients with psychological disorders, allergy to study medications, already given any adjuvant in spinal anesthesia were excluded from this study.

Securing an appropriate size of intravenous cannula, preloading patient with 500 ml of Inj. Ringer Lactate, and premedicating patients with Inj. Ondansetron 0.08 mg/kg intravenously. Preoperative vital parameters of patients were noted. Spinal anesthesia was given using 23G Quincke needle, inj. Bupivacaine 0.5% in sitting position under proper anti septic precautions. Sensory and motor level of anesthesia was noted. Ambient temperature of OR was maintained to around $21^0$- $23^0$C and all the intravenous fluids and drugs were administered at room temperature. Patients were included in study only if shivering occurred. Once shivering occurred, the patients were randomly selected to receive either drug (Group D and Group T). If at all the shivering occurred the grade of shivering was decided as per "Tsai and Chu Grading":

0 – No shivering

1 – Pilo erection or peripheral vasoconstriction with no visible shivering.

2 – Visible muscular activity in only one muscle group.

3 – Visible muscular activity in more than one muscle group, but not generalized

4 – Shivering involving the whole body.

Patients with grade 3 & 4 of shivering were subjected to treatment with either of the drug. Patients were observed and time noted from the time of giving of study drug to the disappearance of shivering. Other parameters noted were reappearance of shivering, adverse events if any, hemodynamic monitoring (the time of administration of study drug was considered to be zero and hemodynamic monitoring was done every five minutes there after). If shivering did not subside in 10 minutes, the study drug was considered not effective for this study and further rescue dose of either drug was given. Continuous variables, hemodynamic parameters, respiratory rate, adverse events were noted and compared in between two groups using chi-square test. $p < 0.05$ was considered to be statistically significant.

## Results

The present study of 60 patients who developed per operative shivering after spinal anesthesia were treated with either of the drug in our study.

Group D: Inj. Dexmedetomidine 0.5 µg/kg intravenously diluted to 10 ml in normal saline

Group T: Inj. Tramadol 1 mg/kg intravenously diluted to 10 ml in normal saline.

Demographically there was no any statistical difference between the groups in regards to age, sex, and ASA grading (Table 1).

The dose of bupivacaine given intrathecally was as per body weight and the sensory block achieved was up to T6 in majority of the patient except for one patient in which escalated to T4 level. But overall the statistical difference was not significant between both the groups (Table 2).

If shivering occurred post spinal in any of the patient the variable and degree of shivering was noted in both the groups and only patients with shivering grade 3 & 4 were included as case study. Table 3 and Graph 1 shows the number of patients who had shivering of 3 or 4 grade, with values near about similar (p>0.05). When subjected to treatment with either dexmedetomidine or tramadol, it was observed that shivering subsided in 29/30 patients receiving Inj. Dexmedetomidine while it subsided in 26/30 patients receiving Inj. Tramadol. (p=0.001) these results are shown in table 4 and graph 2.

Table 5 shows the time duration for the shivering to subside after giving the study drug. It was 139 ± 76.02 seconds in Group D as compared to 329 ± 162.87 seconds in Group T. This difference was highly significant statistically. More over there was reappearance of shivering in both the group but the incidence was low in Group D (1 patient) as compared to Group T (3 patients).

Hemodynamic changes of pulse rate and Blood pressure in both the groups were compared from the time of giving drug onwards every five minutes. There was a slight fall in the pulse rate and blood pressure with Inj. Dexmedetomidine which was not seen with Inj. Tramadol. Though the fall was significant it didn't deviate >20% from the base line.

Graph 5 and Graph 6 display the adverse events in Group T and Group D respectively. Incidence of nausea after Tramadol injection was bit high as compared to dexmedetomidine. Bradycardia and hypotension occurred in around 3-8 patients receiving dexmedetomidine but it was not that alarming.

**Table 1:** Demographic Variables

| Parameters | Group D (n=30) | Group T (n=30) | p value |
|---|---|---|---|
| Mean Age (years) | 39.47 ± 16.027 | 39.73 ± 14.300 | 0.946 |
| Sex Ratio (M:F) | 20:10 | 22:8 | 0.317 |
| ASA grading (I/II) | 14:16 | 14:16 | 1 |

Values are Mean ± SD or numbers

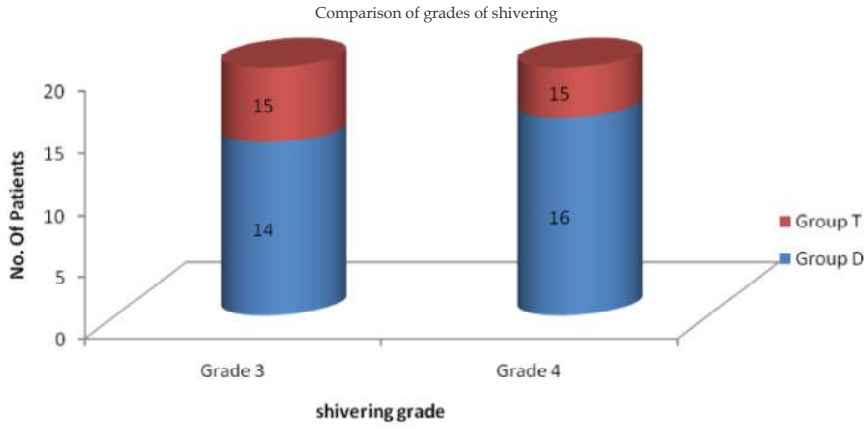
**Table 2:** Sensory Block Level

| Parameter | | Group D (n=30) | Group T (n=30) | p value |
|---|---|---|---|---|
| Volume of Inj. Bupivacaine 0.5% intrathecally | | 3.47 ± 0.305 | 3.473 ± 0.330 | 0.968 |
| Sensory Block | T4 | 1 | 0 | 0.313 |
| | T6 | 1 | 9 | 0.781 |
| | T8 | 6 | 8 | 0.541 |
| | T10 | 9 | 9 | 1 |
| | T12 | 4 | 4 | 1 |

Values are Mean ± SD or numbers

**Table 3:** Comparison of the Grade of Shivering

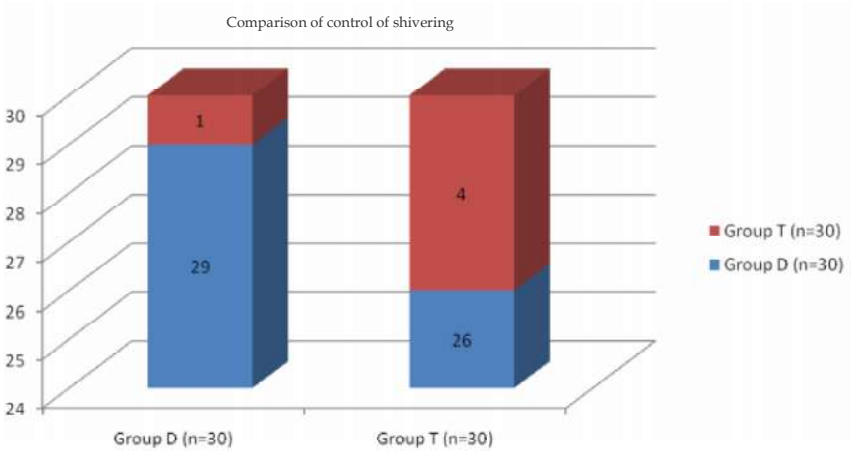
| Shivering Grade | Group D (n=30) | Group T (n=30) | p value |
|---|---|---|---|
| 3 | 14 | 15 | 0.796 |
| 4 | 16 | 15 | 0.796 |




**Graph 1:**

**Table 4:** Showing Comparison of Control of Shivering

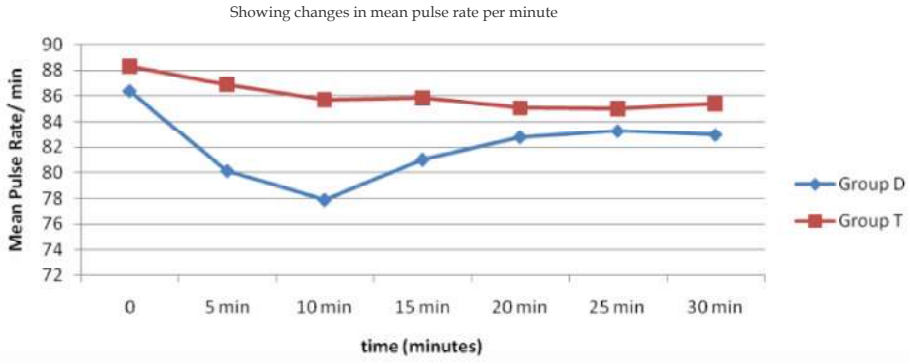
| Control of Shivering | Group D (n=30) | Group T (n=30) |
|---|---|---|
| Yes | 29 (96.67%) | 26 (86.67% |
| No | 1 (3.33%) | 4 (13.33%) |



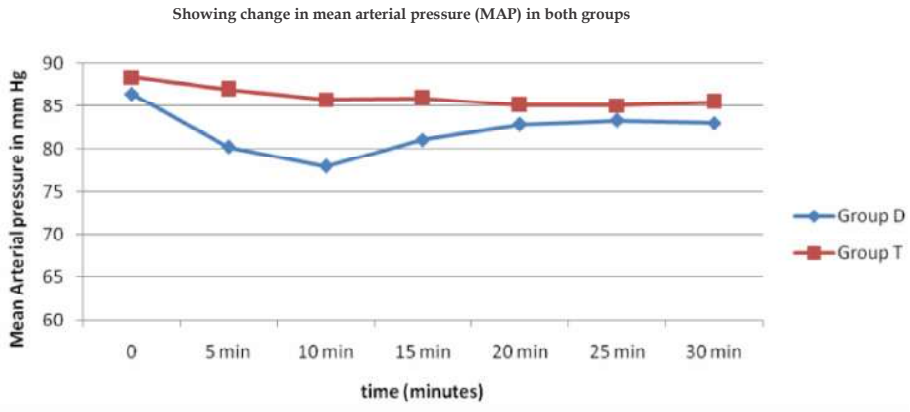

**Graph 2:**

**Table 5:** Time Required for Complete Loss of Shivering

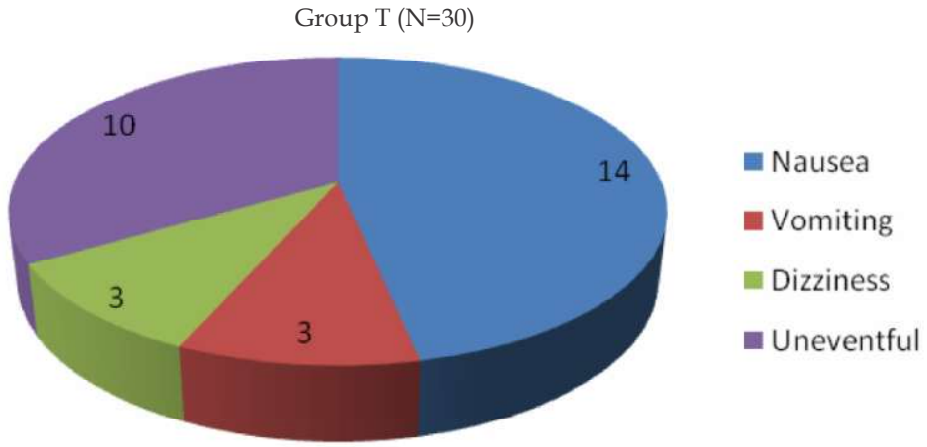
| Time of Complete loss of shivering | Group D | Group T | p value |
|---|---|---|---|
| In seconds | 139.17 ± 76.02 | 329.73 ± 162.87 | 0.0001 |



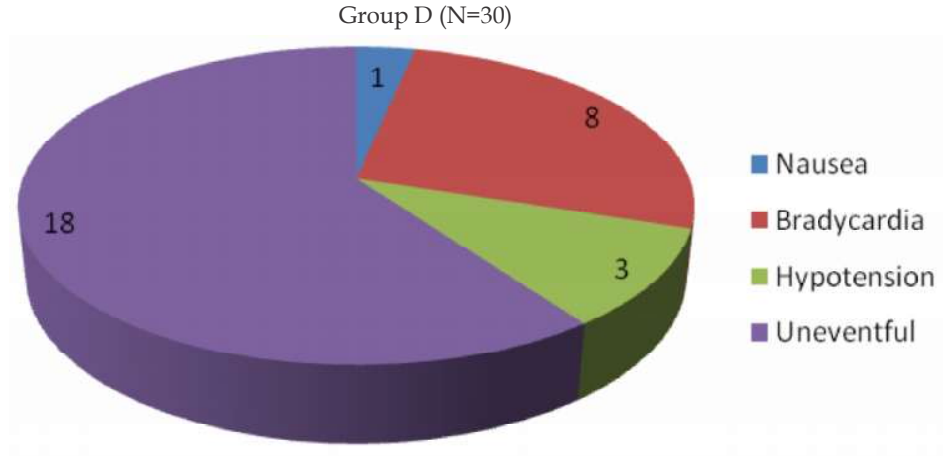

**Graph 3:**




**Graph 4:**




**Graph 5:** Adverse Events in Group T




**Graph 6:** Adverse events in Group D

## Discussion

A large number of studies have been done to assess the role of prophylactic pharmacological intervention for post spinal anesthesia shivering. In spite of high incidence (40-60%) of shivering we chose to do pharmacological interventions only after shivering develops post spinal anesthesia. We included only those patients in our study that developed grade – 3 or 4 shivering. There was a widespread muscular contraction which may increase metabolic requirement and affect core body temperature significantly. Keeping all the non pharmacological variables like ambient or temperature, use of warm blankets, warm iv fluids to a standard level we aimed at only treatment of the shivering if it occurred. S. Mathew et al compared prophylactic 1 mg/kg of Inj. Tramadol with placebo for per operative shivering and concluded that Tramadol considerably reduces the incidence of shivering. Horn EP et al. (1998) studied Dexmedetomidine 0.5 µg/kg for post operative shivering and concluded that dexmedetomidine if given before emergence of anesthesia considerably reduces the incidence of post operative shivering.

In our study we found that there was a significant statistical significance in response rate for treating shivering between dexmedetomidine and tramadol (Table 4). Moreover the incidence of reappearance of shivering was also quite less with dexmedetomidine (3.45%) as compared to tramadol (11.54%). The effectiveness of dexmedetomidine in treating shivering was also faster as compared to tramadol (Table 5).

In similar studies with Tramadol 0.5 mg/kg the response rate of disappearing of shivering was 92.5% (Shukla et al.) [5], 87% (Tsai and Chu) [6] and with a dose of 1 mg/kg we had 100% response

in treating the shivering. Similarly we had 100% response with dexmedetomidine in a dose of 0.5 µg/kg [1] (similar results were also observed by Easley in pediatric patient) along with sedation which was an additional benefit.

Hemodynamically the changes in pulse rate and Mean arterial blood pressure (Graph 3 & 4) were studied only after administration of the study drug (trying not to consider the hemodynamic changes secondary to spinal anesthesia). Shivering leads to tachycardia and we found a drop in heart rate after administration of drug in both the group. No significant change in the Blood pressure (SBP, DBP and MAP) was seen after administration of study drug and results were comparable.

The incidence of side effects of both the drugs as shown in Graph 5 and Graph 6 were also not much which are similar to other studies done by Shukla U [5] et al., Kulshrestha S et al. [4] (2013)

Only limitation to our study was that we could not measure core body temperature as putting a esophageal probe in awake patients was bit cumbersome and we didn't try the rectal probe.

We observed the study cases only for 120 minutes after the administration of the study drugs. It was also found that shivering re appeared after 3-4 hours more commonly in surgeries that lasted long and this can probably be because of the excess heat loss in such cases.

## Conclusion

Dexmedetomidine in a dose of 0.5 µg/kg intravenously controls shivering faster that Tramadol 1 mg/kg thereby reducing patient discomfort time. The success rate with dexmedetomidine is also more with less chance of recurrence as compared to Tramadol. Slight sedation with dexmedetomidine proves beneficial. Hence can be concluded that dexmedetomidine is faster, more effective with lesser side effects when compared to Tramadol in control of per operative shivering after giving of spinal anesthesia.

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# Efficacy and Safety of Promethazine Hydrochloride as a Local Analgesia in Comparison with Bupivacaine Hydrochloride, in Various Peripheral Nerve Blocks

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**Abstract**

Abolishing the pain conduction in sensory nerves – this idea would have definitely come from progressive physicians. Various local anesthetic agents since 1860 have been isolated and synthesized till dates which have their action mediated through nerve conduction blockade. But there are other agents who can inhibit conduction to varying degrees, in a nerve and other excitable tissues – like H1 – blockers, Antihistaminics, Anti convulsants, opioids, Marine Biotoxins. Phenothiazine derivative of H1 – blocking agents viz. Promethazine and Diphenhydremine have potent local anesthetic activity as compared to procaine (a amide local anesthetic) when injected locally. Promethazine is widely used as anti emetic, anti histaminic and hypnotic agent by oral, introa muscular, intra venous and trans rectal route but its local anesthetic property has not been fully utilized and advocated in clinical practice. A careful search to literature was done and this study was undertaken to study the use of promethazine in aspect to onset of action, intra operative analgesia, post operative analgesia, sedation along with other complications as compared to Bupivacaine. Sixty patients of ASA status I & II, undergoing elective surgery like Hydrocelectomy, circumcision and others to be operated under regional blocks were randomly divided in two groups: Group I to receive Inj. Promethazine hydrochloride (2 mg/kg) diluted to make a volume of 15 ml, Group II to receive Inj. Bupivacaine 0.25% (2 mg/kg) to a maximum of 15 ml and patients were observed for onset of analgesia, duration, requirement of rescue analgesic using 4 point pain score and post operative sedation using Cook's Sedation Score along with hemodynamic stability and any other known complications. It was found that there was good analgesia in both the groups per operatively with good hemodynamic stability all throughout the surgery and surgery accomplished satisfactorily with no side effects except drowsiness seen in Group I specially of age > 45 years. Hence, promethazine can be considered as a safe alternative to standard local anesthetics for superficial surface surgeries where sensitivity to local anesthetics is a problem.

**Keyword:** Promethazine; Bupivacaine; Cook's Sedation Score; 4 Point Analgesia Score.

**How to cite this article:**

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## Introduction

"The thought of producing anaesthesia by abolishing conduction in sensory nerves, by suitable means, should have arisen in the minds of progressive physicians" [6].

Local anesthetic agents reversibly depress the nerve conduction beyond the point of application. It was first demonstrated by Karl Kollar in 1860 by use of Cocaine in practice of regional anesthesia. There are diverse group of drugs other than local anesthetic drugs having the ability of inhibit nerve conduction in varying degrees in nerves and other excitable tissues. Of which H1 blockers are 2-4 times potent to few local anesthetic agents.

Phenothiazine derivative of H1 blockers like promethazine and diphenhydremine have potent local anaesthetic activity.

Fitzpatrick and Stabbart (1950) [2] used promethazine hydrochloride solution for urethral dilatation but patients had lot of local irritation

Dundee and Moore (1951) [5] used Promethazine as local infiltration and found it to be potent but the dose required was associated with deep sedation.

S. Kumar (1997) [4] did study promethazine as local infiltration for hernia repair and found its local anesthetic property as comparable to lignocaine.

Not much is known about the dose and action of Promethazine used as local analgesic.

A thorough search in the literature and to explore the unusual action of promethazine we undertook this study to compare the efficacy of Promethazine as local infiltration for superficial surface surgeries as compared to Bupivacaine in aspect to onset of analgesia, quality of analgesia, duration of analgesia and degree of sedation with optimally minimum dose of Promethazine.

## Methodology

This prospective randomized study was conducted after approval from institution and written informed consent from the patients. For the study 60 patients posted for elective surgeries of ASA grade I & II, aged 5 to 55 years of either sex were selected. After thorough preoperative check up, fitness sought after the necessary systemic examination and relevant blood investigations, they were randomly divided in two groups (n=30): Group I to receive regional nerve block with Inj. Promethazine hydrochloride (maximum 2 mg/kg of body weight) diluted in saline up to 15 ml. Group II to receive Inj. Bupivacaine (maximum 2 mg/kg body weight) 0.25% to a volume of 15 ml. All regional blocks were performed after informed consent obtained from patients. The patients were fasted for sufficient time and subjected to Inj. Glycopyrrolate 0.01 mg/kg body weight intramuscularly.

The surgery was allowed only after there was loss of pin prick sensation of the particular dermatome infiltrated with the drug. Fasting period and preoperatively intravenous fluids were administered to cover the deficit. Patients were observed for hemodynamic changes, respiration, other vital parameters and analgesia using Four point Pain Score (Melzeck and Wall, 1983) (Table 1).

In the post operative period the duration of analgesia was noted from the time of infiltration of regional block to the demand of first rescue analgesic. Patients were also observed for the sedation post operatively using Cook's Sedation Score (Table 2).

The result of both group were tabulated and mean and standard deviation value were taken out. Statistical analysis was done using chi-square test and t – test. $p<0.05$ was regarded as statistically significant.

## Results

The two groups were comparable in age, sex, type of surgery, type of anesthesia and duration of surgery as showed in table 4, 5, 6 & 8 respectively.

**Table 1:** Four Point Pain Score (Melzeck and Wall, 1983)

| Score | Interpretation |
|---|---|
| 0 | No Pain |
| 1 | Wincing With/Or Facial Grimace |
| 2 | Verbalization |
| 3 | Withdrawal |

**Table 2:** Cook's Sedation Score

| Command | Response | Score |
|---|---|---|
| Eyes Open | Spontaneously | 4 |
| | To Speech | 3 |
| | To Pain | 2 |
| | None | 1 |
| Response to Nursing Procedure | Obeys Commands | 5 |
| | Purposeful Movements | 4 |
| | Non Purposeful Flexion | 3 |
| | Non Purposeful Extension | 2 |
| | None | 1 |
| Cough | Spontaneous Strong | 4 |
| | Spontaneous Weak | 3 |
| | On Suction Only | 2 |
| | None | 1 |

The type of cases selected were those of superficial surgeries, Table 6 shows the types of surgeries considered for both the groups and the type of anesthesia given for them. Field blocks, local infiltration, regional blocks like wrist, ankle block, penile block were performed for the cases selected for the study.

The time duration of onset of effect was observed by the observer who was blind to the type of drug used. Table 7 shows that in majority of patients the onset was quick (within 3 minutes) in group I whereas the onset was bit delayed in Group II (from 4 minutes onwards) with a mean onset of 1.95 ± 0.70 minutes in Group I as compared to 3.35 ± 1.25 minutes in group II. This comparison was statistically significant.

The patients were observed for their compliance during surgery in terms of feeling of pain, discomfort or totally comfortable with no pain. These observations were made using the four point Pain Score (Melzeck and Walls). Table 8 shows that 18 patients were comfortable during the surgery in Group I with the score of '0' whereas 19 patients had score of '0' in group II. The score was 1 in 10 and 8 patients and it was 2 in one and two patients in Group I and Group II respectively. Patients with score of 3 were needed to be supplemented with either $O_2$+$N_2O$ through mask ventilation or Inj. Ketamine but the proportion of such patients was very less in both the groups. When compared statistically there was not much difference as far as the pain relief and efficacy of both drugs were taken in consideration.

**Table 3:** Interpretation of Cook's Score

| Score | Interpretation |
|---|---|
| 11-13 | Very Mild or No Sedation |
| 8-10 | Mild Sedation |
| 6-7 | Moderate Sedation |
| <6 | Deep Sedation |

**Table 4:** Distribution of Patients Age Wise

| Age Group (Years) | Group I (N=30) | Group II (N=30) |
|---|---|---|
| 15-25 | 16 | 14 |
| 26-35 | 07 | 07 |
| 36-45 | 04 | 04 |
| 46-55 | 03 | 05 |
| Mean ± Sd | 28.4 ± 12.24 | 30.07 ± 12.54 |
| p Value | >0.05 | |

**Table 5:** Distribution of Patients Sex Wise

| Sex | Group I (N=30) | Group II (N=30) |
|---|---|---|
| Male | 19 (63.3%) | 21 (70%) |
| Female | 11 (36.7%) | 9 (30%) |
| Ratio | 6.3:3.7 | 7:3 |
| p Value | >0.05 | |

**Table 6:** Distribution of Patients as Per Type of Surgery and Anesthesia

| Sr. No. | Type of Surgery | Group I (n=30) | Group II (n=30) |
|---|---|---|---|
| 1 | Skin Grafting (Local infiltration) | 4 | 3 |
| 2 | Gynecomastia (local infiltration) | 5 | 5 |
| 3 | Fibroadenoma breast excision (local infiltration) | 8 | 7 |
| 4 | Lord's Plication (Block for hydrocele) | 5 | 6 |
| 5 | Lipoma excision (local infiltration) | 5 | 6 |
| 6 | K wiring # metacarpal (wrist block) | 1 | 2 |
| 7 | Skin grafting (femoral nerve block) | 2 | 1 |

**Table 7:** Time for Onset of Action

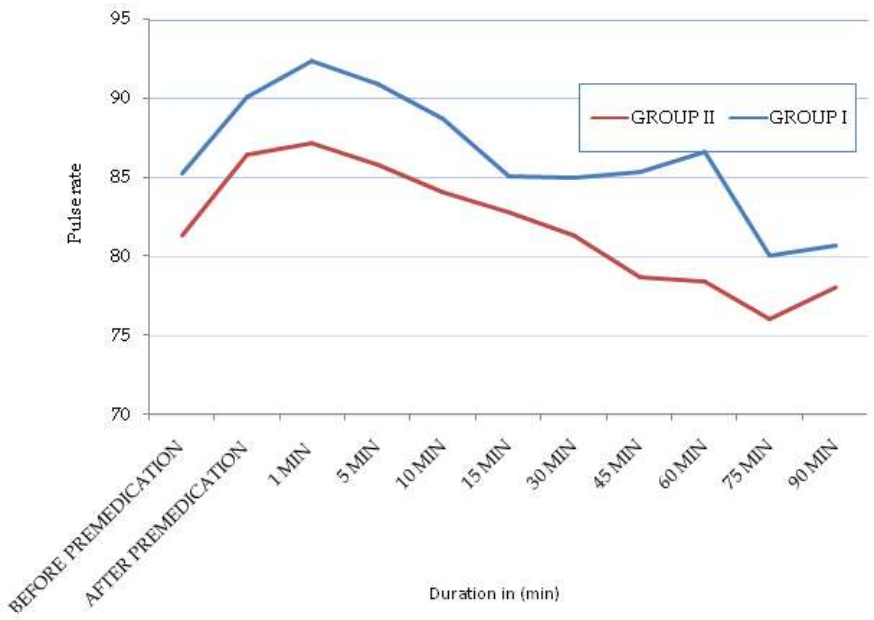
| Duration (Min) | Group I (N=30) | Group II (N=30) |
|---|---|---|
| 0.0-1.0 | 04 | 00 |
| 1.1-2.0 | 12 | 00 |
| 2.1-3.0 | 11 | 07 |
| 3.1-4.0 | 03 | 20 |
| 4.1-5.0 | 00 | 02 |
| 5.1-6.0 | 00 | 01 |
| 6.1-7.0 | 00 | 00 |
| Mean ± SD | 1.95 ± 0.70 | 3.35 ± 1.25 |
| t value | 5.38 | |
| p value | <0.05 | |

**Table 8:** Time for Surgery

| Duration (Min) | Group I (N=30) | Group II(N=30) |
|---|---|---|
| 21-40 | 18 | 14 |
| 41-60 | 07 | 10 |
| 61-80 | 02 | 04 |
| 81-100 | 03 | 02 |
| Mean ± SD | 46.17±18.06 | 47.17±15.14 |
| t value | 0.19 | |
| p value | >0.05 | |

**Table 9:** Intra Operative 4 Point Pain Score

| Pain Score | No. of Cases | |
|---|---|---|
| | Group I | Group II |
| 0 | 18 | 19 |
| 1 | 10 | 08 |
| 2 | 01 | 02 |
| 3 | 01 ($O_2$ + $N_2O$) | 01 (Ketamine) |
| p Value | >0.05 | |




**Graph 1:** Showing the Changes in Mean Pulse Rate


**Graph 2:** Showing the Changes in Mean Systolic Blood Pressure

Hemodynamically the patients stayed well controlled as compared to the pre operative values which are shown in Graph 1 (changes in pulse rate) and Graph 2 (change in systolic blood pressure). Post operatively patients were also observed for the sedation caused by use of these drugs using Cook's sedation score (Table 2) almost all the patients had a score of more than 11 all through out suggestive of no sedation.

## Discussion

The basic mechanism behind the local analgesic effect of Promethazine Hydrochloride is similar to other local analgesics drugs. It exhibits its action through membrane stabilization and directly blocking the sodium channels. It was in 1943 Watrous WG [1] explored the local anesthetic property of promethazine in animals and was of

conclusion that it was more potent than procaine a ester local anesthetic preparation. But owing to its antanalgesic property when given intravenously its property of local analgesic action was not much studied. In 1997, Kumar S. [2] published a pilot case study showing the use of Promethazine as an infiltrative local analgesic agent in direct inguinal hernia repair.

In our study, we used Inj. Promethazine hydrochloride in dose of 2 mg/kg diluted to a volume of 20 ml (Group I) to explore its use as local analgesic agent in superficial surgeries in comparison to Inj. Bupivacaine 0.25% diluted to a volume of 20 ml (Group II) (a routinely used local anesthetic).

It was found that the onset time of analgesia in Group I (mean of 1.95 ± 0.7 min) was significantly earlier than Group II (3.325 ± 1.25 min). As far as the efficacy of the drug was concerned in terms of feeling of pain, discomfort and patient compliance, both drugs were comparable. We observed the patients for any pain during the surgery using four point pain score which was around score '0' for 18 & 19, score '1' for 10 & 8, score 2 for 1 & 2 and score 3 for one patient in each group respectively. We supplemented with mask ventilation of $O_2$+$N_2O$ and intravenous Inj. Ketamine in analgesic dose to alleviate the pain. This suggests that both drugs do provide a good pain free comfort to the patients. Kumar et al. (1997) [2] observed mild sedation during use of Promethazine as local infiltrant for inguinal surgeries. Sedation is commonly seen with intravenous use of Promethazine but it was not found in any of our case when used in regional and local blocks.

Hemodynamically the patients stayed stable as they didn't perceive the pain and had bare minimum stress sympathetic response keeping the pulse, Blood pressure as near as pre operative values. No any other complications like respiratory depression were observed except for burning sensation felt during the infiltration of drug in group I but this was not hampering to the patients compliance.

Our study concluded that Promethazine is a safe and efficacious local analgesic in peripheral nerve blocks given individually and even along with other local anesthetics. So it can turn out to be a safe alternative in patients where use of local anesthetics may be limited owing to the known hypersensitivity. The mild sedation if at all occurs can be an added advantage along with its anti emetic and anti histaminic effect.

## Conclusion

Analgesic effect of Promethazine is as comparable to local anesthetics when used solely in peripheral nerve blocks along with field block and local infiltration. It can turn out to be a safe alternative in patients where use of local anesthetics may be limited owing to the known hypersensitivity. The mild sedation if at all occurs due to systemic absorption from the infiltration site can be an added advantage along with its anti emetic and anti histaminic effect.

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*Original Research Article*

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# Intravenous Magnesium Sulphate ($MgSO_4$) for Postoperative Analgesia in Patients Undergoing Hip Surgeries Under Spinal Anaesthesia

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**Abstract**

*Objective:* This study is conducted to assess the analgesic effects of intravenous magnesium sulphate (50 mg/kg) in hip surgeries under spinal anaesthesia. *Methods:* This prospective, randomised, double blinded control study was done on 60 patients posted for hip surgeries (Dynamic hip screw fixation, Proximal femur nailing and Hemiarthroplasty) under spinal anaesthesia. The patients were randomly divided into two groups with 30 patients each. Group S (Study) received magnesium sulphate 50 mg/kg intravenously in 250 ml Normal saline, 15 minutes before spinal anaesthesia and group C (Control) received same volume of normal saline. Hemodynamic variability, duration of analgesia and analgesic requirements were evaluated upto 12 hours after surgery. (30 minutes, 2, 4, 8 and at 12 hours). *Results:* Postoperative pain scores were significantly lower in Group S ($p<0.05$) at 2nd hour after surgery and was not significant at other time intervals. Time to first analgesic requirement was significant ($p=<0.005$) between two groups. Rescue analgesic requirement was lower in Study group compared to Control group, and was statistically significant ($p=0.009$). The two groups had no significant differences with regards to hemodynamic variability and had no side effects. *Conclusion:* Intravenous magnesium sulphate 50 mg/kg when given as a bolus reduced the postoperative pain and decreased the need of rescue analgesics after spinal anaesthesia for hip surgeries.

**Keywords:** Anaesthesia; Bupivacaine; Magnesium sulphate; Postoperative; Rescue analgesia.

## Introduction

Postoperative pain following hip surgeries is usually severe in nature, adequate pain management in the postoperative period is essential for early rehabilitation and to improve functional recovery [2,3].

Neuroendocrine responses, catecholamine release, increased morbidity and central sensitization are thought to be among the mechanisms implicated in persistence of postoperative pain [4,5]. Excitatory amino acid transmitters such as aspartate and

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glutamate are associated with central sensitisation by activation of N-methyl-D-aspartate (NMDA) receptors [5,6].

Magnesium blocks NMDA receptor in a voltage-dependent way [7], NMDA receptor antagonists causes pre-emptive analgesia when administered before tissue injury occurs, as they prevent central sensitisation from peripheral nociceptive stimulation [8,9].

The main purpose of this study is to evaluate the efficacy of magnesium sulphate (50 mg/kg) to prolong postoperative analgesia and subsequent analgesic requirement in hip surgeries, when administered intravenously 15 minutes before induction of spinal anaesthesia.

## Methods

The present study was conducted at Apollo Institute of Medical Science and Research (AIMSR), Chittoor, over a period of one year. Institutional Ethical Committee approval was obtained. Informed written consent were obtained from participating patients.

In the present randomised controlled double blinded study, 60 patients of ASA 1 and 2 undergoing hip surgeries were included. Patients with neurological, respiratory, cardiac, renal diseases, bleeding disorders, known hypersensitivity to magnesium, local anesthetics, patients on treatment with calcium channel blockers and magnesium, infection at lumbar spine were excluded from the study.

Patients were randomly assigned into two groups (30 patients each). Standard monitoring included ECG (Electrocardiogram), pulse oximetry, and NIBP (Non-invasive blood pressure).

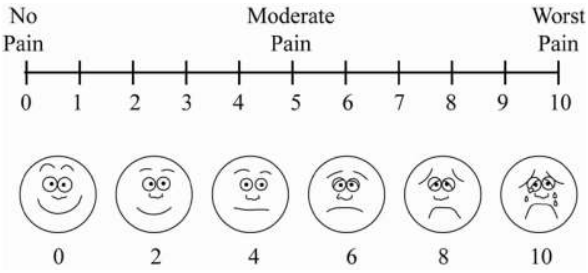
After obtaining the baseline values of hemodynamic variables, the Group S received 50 mg/ kg magnesium sulphate ($MgSO_4$) in 250 ml of Normal saline intravenously (IV) over 15 minutes before induction of spinal anaesthesia, and the Group C received the same volume of Normal saline over 15 minutes before induction of spinal anaesthesia.

An injection of 0.3 mg/kg of 0.5% hyperbaric bupivacaine was given intrathecally in $L_3$-$L_4$ interspace using 25 G spinal (quincke) needle in sitting position. The anaesthesiologist and the patient were not aware of study and control groups. Baseline Heart Rate (HR), NIBP, $SpO_2$ were recorded immediately after spinal anaesthesia, and at 5, 10, 15, 30, 60, 90 and at 120 minutes. Bradycardia (HR<45) is treated with atropine 0.6 mg and hypotension (mean arterial pressure <65 mmhg) treated with injection mephentermine 6 mg IV bolus. At the end of the surgery patients were shifted to postoperative ward.

The level of pain was assessed immediately after the surgery and at 30 minutes, 2,4,8 and at 12 hours post surgery, based on visual analogue score (VAS), where 0 = no pain and 10 = severe pain. Rescue analgesia (tramadol 100 mg IV) was administered when VAS score was 4 and above. Patients were monitored and managed appropriately for any side effects (nausea, vomiting, pruritus).

Descriptive statistical analysis was represented as Mean ± SD and results on categorical measurements are represented as percentages. Appropriate tests of significance like the independent t- test and chi-square test were used depending on nature and distribution of variables. Values of $p<0.05$ were considered significant.

*Visual analogue scale*




## Results

The patient's characteristics like age, sex, height, ASA grade and anaesthetic time were matched in the two groups and they were not statistically significant. (Table 1).

**Table 1:** Patient characteristics and anaesthetic time. Values shown are for mean for age, or patient numbers (n) and group S for study and group C for control.

| | Group S (N=30) | Group C (N=30) |
|---|---|---|
| Age (years) | 57 (45-70) | 54 (43-65) |
| Sex (M/F) | 20/10 | 18/12 |
| Height (cm) | 166.5 | 166 |
| Weight (kgs) | 65 | 67 |
| ASA 1,2 | 18/12 | 21/9 |
| Anaesthetic time(min) | 125 | 120 |

The height of spinal block achieved in the two groups were not statistically different, with average

level at T6 for Group S and T8 for Group C, whereas the time to first pain between the two groups were statistically significant (p=<0.05) with average time of 199.2 minutes for Group S and 179.2 minutes for Group C. The doses of bupivacaine used in the two groups were not statistically different (Table 2).

**Table 2:** Characteristics of spinal block. Values are presented as means (range) for height of spinal block or means (sd). Group S for study group and group C for control group.

| | Group S (N=30) | Group C (N=30) | p Value |
|---|---|---|---|
| Height of spinal block | T6 (T4-T8) | T8 (T6-T10) | 0.32 |
| Time to first pain (min) | 199.2 (41) | 179.2 (38) | <0.05* |
| Dose of bupivacaine (mg) | 15.7 (0.8) | 16.08 (0.9) | 0.9 |

The postoperative VAS score compared between the two groups was only significant at the 2nd hour with p value 0.002, whereas it was not significant at other intervals. (Table 3).

**Table 3:** Postoperative VAS score

| Time interval | Group S | | Group C | | p value Chi square test |
|---|---|---|---|---|---|
| | VAS 0-3 | VAS 4-6 | VAS 0-3 | VAS 4-6 | |
| Immediate postoperative period | 29 | 1 | 27 | 3 | 0.30 |
| 30 min | 27 | 3 | 25 | 5 | 0.44 |
| 2 hours | 26 | 4 | 15 | 15 | 0.002 * |
| 4 hours | 20 | 10 | 17 | 13 | 0.42 |
| 8 hours | 24 | 06 | 22 | 08 | 0.54 |
| 12 hours | 24 | 06 | 22 | 08 | 0.54 |

VAS – Visual Analogue Scale

The time to rescue analgesia between the two groups was not significant (p=0.177), whereas the rescue analgesia requirement was more in the control group and was statistically significant with p =0.009 (Table 4).

**Table 4:** Time for rescue analgesia

| Parameter | Study, S | Control, C | p value |
|---|---|---|---|
| Time to rescue analgesia(hr),mean+/-.SD | 7.5+/-4.5 | 4.5+/-4 | 0.177 |
| Rescue analgesia (n) (%) | 9(30%) | 19(63%) | 0.009* |

## Discussion

Our study showed that IV magnesium sulphate (50 mg/kg) bolus given 15 minutes before spinal anaesthesia reduced postoperative pain and rescue analgesia requirement, without any significant hemodynamic variations (Table 5).

Following hip surgeries, postoperative pain is usually severe in nature, adequate postoperative pain management is required for early rehabilitation and recovery [2,3]. Regional anaesthesia is usually preferred over general anaesthesia for lower limb surgeries for certain advantages like spontaneous breathing during intraoperative period and easy recovery. Pre-emptive analgesics before exposure to painful stimulus has shown to prevent the central sensitisation and amplification of postoperative pain [2,3].

In a study done by Prerana N. Shaw et al., shown that intravenous magnesium sulphate when given as bolus followed by infusion, delayed and decreased the need of rescue analgesics after spinal anaesthesia [1].

Our study findings were partly similar to the study done by Apan A et al. where they compared 5 mg/kg of magnesium sulphate immediately after spinal block followed by 500 mg/hr infusion in the same volumes for 24 hours showed reduced analgesic requirement in spinal aneaesthesia [10].

In a study done by Ryu JH et al., it was noted that pre and intraoperative administration of

**Table 5**: Patients post-operative hemodynamic variables

| Time interval | Heart rate (per minute) | | | Blood pressure (MAP) mmhg | | |
|---|---|---|---|---|---|---|
| | Group S | Group C | p Value | Group S | Group C | p Value |
| Immediate postoperative period | 82 | 90 | 0.10 | 62 | 66 | 0.55 |
| 30 min | 87 | 92 | 0.24 | 65 | 70 | 0.45 |
| 2 hr | 75 | 85 | 0.07 | 62 | 70 | 0.23 |
| 4 hr | 92 | 95 | 0.38 | 66 | 74 | 0.21 |
| 6 hr | 90 | 98 | 0.0515 | 70 | 76 | 0.339 |
| 8 hr | 95 | 98 | 0.24 | 68 | 72 | 0.537 |
| 12 hr | 92 | 96 | 0.23 | 72 | 80 | 0.185 |

MAP = mean arterial pressure

magnesium sulphate at 50 mg/kg bolus and 15 mg/kg/hr infusion in gynaecological patients undergoing surgery under total intravenous anaesthesia reduced rocuronium requirement and improved postoperative analgesia [11].

In a study done by Dabbagh A et al., it was shown that VAS scores were significantly lower in patients receiving perioperative magnesium undergoing lower limb orthopaedic surgery [12].

In the present study, VAS score was significantly lower in Group S ($p<0.002$) at postoperative 2nd hour. Rescue analgesia requirement was significantly lower ($p=0.009$) in Group S when compared to Group C and there was significant difference between two groups with regards to time to first analgesic requirement ($p=<0.05$). There was no significant difference between the Group S and Group C in terms of height of spinal block. There was no significant hemodynamic variation in the two groups in postoperative period and there were no complications.

## Conclusion

Intravenous magnesium sulphate 50 mg/kg when given as a bolus reduced the postoperative pain and decreased the need of rescue analgesics after spinal anaesthesia for hip surgeries.

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# Effects of Dexmedetomidine Infusion in different Concentrations on Intraoperative and Postoperative Hemodynamic Response and Analgesic Requirement in Laparoscopic Cholecystectomy Patients

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**Abstract**

*Background:* Dexmedetomidine is a newer α2 agonist with sedative, sympatholytic and analgesic properties. This study was carried out to evaluate the effect of two different concentrations of intravenous dexmedetomidine infusion on haemodynamic response to critical incidents like laryngoscopy, endotracheal intubation, creation of pneumoperitoneum and extubation in patients undergoing laparoscopic cholecystectomy. *Methods:* The study was conducted at our institute in 60 ASA grade I & II patients undergoing laparoscopic cholecystectomy. They were randomly allocated into two groups of 30 patients each 'Group Dex 0.25' and 'Group Dex 0.5'. The patients received dexmedetomidine infusion at the rate of 0.25 /kg/hr and 0.5 mcg/kg/hr respectively, starting 15 minutes before induction and continued till the end of surgery. Standard anaesthesia technique was used. Comparison of the effect of infusion on haemodynamic changes seen in laparoscopic cholecystectomy was done. *Results:* Haemodynamic response to laryngoscopy and creation of pneumoperitoneum was blunted more in group Dex 0.5 as compared to group Dex 0.25. The intraoperative and post operative analgesic requirement was also reduced in group Dex 0.5. The time to first analgesic demand was later in the group Dex 0.5 as against group Dex 0.25. No significant side effects were noted in either group. *Conclusion:* Dexmedetomidine infusion at the rate of 0.5 mcg/kg/hr given perioperatively can serve as a very useful anaesthetic adjunct for premedication, maintenance of haemodynamic stability and postoperative analgesia without any significant adverse effects.

**Keywords:** Dexmedetomidine; Laparoscopic cholecystectomy; Hemodynamics.

## Introduction

Laparoscopic cholecystectomy is one of the most commonly practiced surgeries for gall bladder diseases in today`s era. However, like any other surgery, laparoscopic cholecystectomy is also associated with haemodynamic stress induced by surgery and anaesthesia, the two leading to an endocrine response starting adrenaline and nor adrenaline secretion by stimulation of sympathetic

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nervous system [1]. Anesthetic maneuvers like direct laryngoscopy, tracheal intubation and even extubation involve severe sympathetic stimulation leading to increase in serum catecholamine and nor epinephrine levels [2].

All these changes lead to increased blood pressure and heart rate, increased systemic and pulmonary vascular resistance and reduced cardiac output [3]. The reverse Trendelenberg position leads to diminished venous return and thereby further reduction in cardiac output [4]. The hyperdynamic changes predispose the myocardium to ischemia especially in the patient population with decreased reserve for coronary blood flow. Perioperative ischemia is associated with a significant increase in postoperative morbidity and mortality.

Modern anaesthesia practices aim to prevent sympathetic discharge and provide haemodynamic stability perioperatively. Various agents in the form of opioid analgesics, benzodiazepines, beta blockers, calcium channel blockers and vasodilators have been used to attenuate this stress response and to provide haemodynamic stability with variable success [1,2].

Several clinical studies suggest that α2 adrenergic agonists might be effective in blunting the perioperative haemodynamic response. Intravenous use of Dexmedetomidine in the intraoperative period decreases catecholamine by ninety percent, blunts the haemodynamic response to laryngoscopy, tracheal intubation, pneumoperitoneum and extubation, increases the haemodynamic stability, and decreases anaesthetic requirements and post operative analgesic requirements [2]. The analgesic, sedative, hypnotic and anxiolytic properties of dexmedetomidine make this drug potentially useful for painful surgical procedures.

Low dose infusion of 0.25–0.5 μg $kg^{-1}$ $hr^{-1}$ results in a monophasic response of 10-15% fall in mean arterial blood pressure and pulse rate. Furthermore, in low dose, dexmedetomidine exhibits linear kinetics, meaning that a constant amount of drug is eliminated per hour rather than a constant fraction.

In this study, we evaluated the effect of two different doses of Dexmedetomidine infusion (0.25 μg $kg^{-1}$ and 0.5μg $kg^{-1}$) on haemodynamic response to various critical incidences like laryngoscopy, intubation, pneumoperitoneum and extubation and analgesic requirements in patients undergoing laparoscopic cholecystectomy. We hypothesise that dexmedetomidine infusion 0.5 μg/kg/hr provides better haemodynamic profile but may have increased incidence of side effects.

## Material and Methods

This study was conducted with due approval by the Hospital ethics committee. Sixty ASA physical grades I and II patients between 18 and 65 years, of either sex and scheduled for laparoscopic cholecystectomy under general anaesthesia were enrolled in study and written informed consent was taken. Exclusion criteria were allergy to dexmedetomidine, respiratory disease, severe cardiovascular disease and BMI > 35 kg $m^{-2.}$

It was a prospective, randomized, comparative study carried out from February 2015 to November 2015.

A thorough preoperative evaluation of each patient was done. All patients were explained about the anaesthetic technique and perioperative course. All routine biochemical, hematological and radiological investigations were done.

Routine preoperative preparation consisted of fasting for 6-8 hours prior to surgery. All the patients were premedicated with tablet alprazolam 0.5 mg night before surgery.

At the time of this check up they were acquainted with the Visual analogue scale (VAS) for pain scoring.

All the monitoring was done on anesthesia work station Datex-Ohmeda with IntelliVue MP20 monitor calibrated to measure all hemodynamic parameters required for the study. The parameters monitored included heart rate and rhythm by three lead ECG, noninvasive blood pressure (systolic, diastolic and mean arterial pressure), oxygen saturation, end tidal concentrations of anesthetic agents and $CO_2$ level by capnograph and temperature monitoring.

The patients were allocated into two groups of 30 patients each, Group Dex 0.25 (patients receiving dexmedetomidine infusion 0.25 μg/kg/h) and Dex 0.5 (patients receiving dexmedetomidine infusion 0.5 μg/kg/h) based on a computer generated method.

A suitable size intravenous cannula was secured for intravenous fluids, and another line for drug infusion. Ringer Lactate was started @ 4 ml $kg^{-1}$ $hr^{-1}$. Test drug infusion was started via infusion pump at the predetermined rate, according to the allocated group. The infusion was continued till the removal of scope from the abdominal cavity. Fifteen minutes after starting the drug infusion; patients were given midazolam 1 mg intravenous as premedication. After preoxygenation, induction was done with

Fentanyl 2.0 μg $kg^{-1}$ body weight intravenously and Propofol 2 mg $kg^{-1}$ body weight intravenously. Vecuronium bromide 0.1 mg $kg^{-1}$ body weight intravenously was used for intubation. Anaesthesia was maintained with Isoflurane and Nitrous oxide in oxygen and vecuronium bromide with controlled ventilation using circle system maintaining a MAC of 1.2. Intraabdominal pressure was maintained between 12 and 14 mmHg throughout the procedure. During maintenance of anesthesia, administration of Fentanyl 0.5 to 1 μg $kg^{-1}$ body weight was added depending upon clinical condition and alteration of hemodynamic parameters (tachycardia and hypertension). Drug infusion and anaesthetic agents were stopped at the end of surgery, as soon as the scope was taken out of the abdominal cavity. Neuromuscular blockade was reversed with Neostigmine (0.04 mg $kg^{-1}$) and Glycopyrrolate (0.01 mg $kg^{-1}$). At the end of the surgery all patients were given Ondansetron 4 mg for prevention of post operative nausea and vomiting.

Vital parameters were observed at regular intervals including before starting the infusion, 10 minutes after starting the infusion, after induction, after creation and release of pneumoperitoneum and after extubation.

After surgery, the following parameters were recorded every hour for the first 6 hours and then at 12 hours and 24 hours post operatively in the ward - heart rate, mean blood pressure (MBP), oxygen saturation, time to first analgesic demand, VAS and total post operative analgesic requirement. Sedation was assessed at 1, 15, 30, 60 to 120 minutes after extubation using Ramsay sedation score (RSS).

When pain reported by patient was ≥ 4 on visual analogue scale [VAS], Injection diclofenac sodium 1.5 mg $kg^{-1}$ intramuscular was used as rescue analgesic and repeated thereafter whenever the VAS score became ≥4.

Throughout the study, patients were observed for any adverse effects like bradycardia, tachycardia (PR less than or more than 20% of preoperative level respectively on two consecutive readings), hypo and hypertension (MBP less than or more than 20% of preoperative level respectively on two consecutive readings), sedation score more than RSS 4, respiratory depression ($SaO_2$ < 90%) and dryness of mouth and they were managed conventionally.

*Statistics*

Sample size was calculated using MedCalc Software version 11.5.0.0. (MedCalc Software bvba, Acacialaan 22, 8400 Ostend, Belgium). Based on minimum mean difference of 25% in parameters (mean heart rate and mean blood pressure) with α =0.01 and β =0.20, sample size for each group was estimated as 28. Rounding up this figure, a sample size of 30 per group was required to detect a significant difference between the groups.

The results were tabulated and statistically analysed using SPSS (Statistical Package for Social Sciences) Software version 15.0, Chi-square test was used for qualitative data (sex, ASA grade), heart rate, Mean blood pressure, were compared within the group against baseline values using paired *t*test. p >0.05 was considered insignificant, p<0.05 as significant and highly significant if p<0.001.

## Results

Both groups were comparable in terms of age, weight, sex, ASA grade distribution and duration of surgery as shown in table 1.

The mean baseline variables (HR, SBP, DBP, MBP, $SpO_2$) were comparable in both groups.

On Comparison, the mean heart rate and the mean blood pressure at initiation of the drug infusion decreased significantly from the base line value in both the groups, the fall being more in the DEX 0.5 group. Thereafter the mean heart rate and mean blood pressure in the DEX 0.5 group was less than that in DEX 0.25 group at all the above mentioned time points. The difference being statistically significant as shown in table 2 and table 3. Also the mean heart rate and mean blood pressure post operatively in the post anaesthesia care unit in the DEX 0.5 group was less than the mean heart rate and mean blood pressure in DEX 0.25 group at all the above mentioned time points (Table 4).

None of the patients in either group had significant bradycardia or hypotension, requiring a rescue medication.

In our study fentanyl citrate top-ups of

**Table 1:** Demographic data

| | Group DEX 0.25 (n =30 ) | Group DEX 0.5 (n =30 ) |
|---|---|---|
| Age (yrs) | 39.2 ± 8.6 | 39.2 ± 8.8 |
| Sex (M/F) | 21/9 | 20/10 |
| Height (cms) | 159.2 ± 6.3 | 158.3 ± 6.3 |
| Weight (kg) | 63.5 ± 5.4 | 60.43 ± 7.5 |
| ASA (I/II) | 21/9 | 20/10 |
| Duration of surgery (mins) | 73.5 ± 18.5 | 69.3 ± 19.3 |

**Table 2:** Mean Intra Operative Heart Rate (BPM) in the two Groups

| Time | Group Dex 0.25 Mean SD | Group Dex 0.5 Mean ± SD | Inter group p value |
|---|---|---|---|
| Before starting infusion | 87.4 ± 9.45 | 91.53 ± 10.66 | 0.1323 |
| 10 min after starting infusion | 82.3 ± 7.44 | 72.8 ± 3.15 | < 0.0001 |
| 1 min after Induction | 77.33 ± 14.29 | 67.8 ± 4.65 | < 0.0001 |
| 1 min after Intubation | 83.463 ± 3.10 | 73.13 ± 8.57 | < 0.0001 |
| 5 min after Intubation | 83.93 ± 3.70 | 75.13 ± 5.78 | < 0.0001 |
| 1 min after Pneumoperitoneum | 85.36 ± 1.96 | 78.26 ± 6.92 | < 0.0001 |
| 15 min after Pneumoperitoneum | 86.8 ± 5.98 | 77.8 ± 6.44 | < 0.0001 |
| 30 min after Pneumoperitoneum | 86.6 ± 3.68 | 77.9 ± 7.43 | < 0.0001 |
| 45 min after Pneumoperitoneum | 84.1 ± 4.87 | 75.3 ± 7.58 | < 0.0001 |
| 60 min after Pneumoperitoneum | 84.53 ± 7.14 | 76.43 ± 7.06 | < 0.0001 |
| 1 min after Release of pneumoperitoneum | 81.9 ± 5.80 | 74.9 ± 6.46 | < 0.0001 |
| 15 min after Release of pneumoperitoneum | 82.36 ± 4.94 | 75.9 ± 5.30 | < 0.0001 |
| After extubation | 87.9 ± 4.47 | 77.06 ± 4.4 | < 0.0001 |

**Table 3:** Mean Intra Operative Mean Blood Pressure in the two Groups (mmHg)

| Time | Group Dex 0.25 Mean ± SD | Group Dex 0.5 Mean ± SD | Inter group P value |
|---|---|---|---|
| Before starting infusion | 93.46 ± 5.02 | 93.83 ± 4.10 | 0.0195 |
| 10 min after starting infusion | 87.5 ± 5.48 | 75.2 ± 3.43 | 0.3445 |
| 1 min after Induction | 83.47 ± 5.66 | 71.03 ± 4.78 | < 0.0001 |
| 1 min after Intubation | 85.03 ± 3.45 | 73.3 ± 12.48 | <0.001 |
| 5 min after Intubation | 84.97 ± 3.42 | 73.93 ± 2.52 | <0.001 |
| 1 min after Pneumoperitoneum | 86.07 ± 14.81 | 75.7 ± 2.08 | <0.001 |
| 15 min after Pneumoperitoneum | 86.43 ± 2.06 | 76.4 ± 3.05 | < 0.0001 |
| 30 min after Pneumoperitoneum | 86.33 ± 2.61 | 75.8 ± 3.04 | < 0.0001 |
| 45 min after Pneumoperitoneum | 85.10 ± 4.96 | 73.6 ± 4.18 | < 0.0001 |
| 60 min after Pneumoperitoneum | 82.7 ± 4.02 | 74.3 ± 5.10 | < 0.0001 |
| 1 min after Release of pneumoperitoneum | 83.07 ± 14.62 | 71.0 ± 5.42 | < 0.0001 |
| 15 min after Release of pneumoperitoneum | 84.87 ± 3.05 | 72.2 ± 5.56 | 0.0011 |
| After extubation | 86.87 ± 3.38 | 74.8 ± 4.97 | < 0.0001 |

**Table 4:** Mean Post Operative Mean Blood Pressure in the two Groups (mmHg)

| Time | Group Dex 0.25 Mean ± SD | Group Dex 0.5 Mean ± SD | Inter group p value |
|---|---|---|---|
| Post operative 1 hour | 86.87 ± 3.38 | 75.4 ± 4.11 | 0.1323 |
| Post operative 2 hour | 87.7 ± 4.57 | 76.4 ± 5.27 | 0.7125 |
| Post operative 3 hour | 87.3 ± 3.12 | 77.2 ± 4.40 | 0.0546 |
| Post operative 4 hour | 86.9 ± 3.22 | 78.9 ± 6.34 | < 0.0001 |
| Post operative 5 hour | 87.37 ± 5.87 | 77.6 ± 6.11 | < 0.0001 |
| Post operative 6 hour | 87.90 ± 3.83 | 78.5 ± 3.23 | < 0.0001 |
| Post operative 12 hour | 86.57 ± 4.26 | 78.1 ± 6.71 | < 0.0001 |
| Post operative 24 hour | 92.97 ± 4.91 | 77.96 ± 4.9 | < 0.0001 |

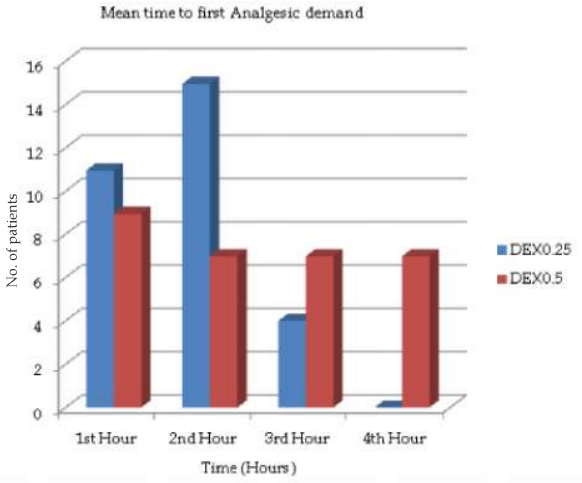


**Fig. 1:** Mean Post Operative Time to First Analgesic Demand in the two Groups

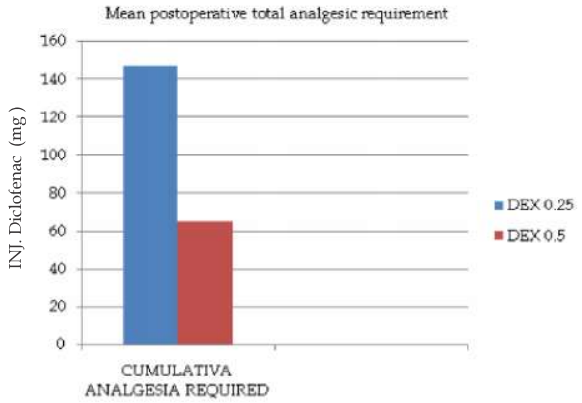


**Fig. 2:** Mean Post Operative Total Analgesic Consumption (Inj. Diclofenac) Mg

0.5–1.0 μg $kg^{-1}$ were given intraoperatively whenever required to keep mean blood pressure within 20% of baseline value. In group Dex 0.25 total 25 patients (83.3%) required single top up, where as in DEX 0.5 group only 2 patients (6.7%) required single dose of fentanyl top up and the

difference being statistically significant.

Comparing the VAS between the two groups, the mean VAS was less in DEX 0.5 group than in DEX 0.25 group at all observed time points.

The time to first analgesic demand was later in the DEX 0.5 group as compared to the DEX 0.25 group (Fig. 1)

The mean total analgesic consumption of Diclofenac in Group Dex 0.25 was 147.50 ± 68.42 mg and in Group Dex 0.5 it was 65.0 ± 25.49 mg as depicted in figure 2.

Sedation scores were higher in group DEX 0.5 as compared to groups DEX 0.25 during the postoperative period.

Two patients in the DEX 0.5 group experienced dryness of mouth which was relieved by wetting of lips and oral mucosa with a sip of water.

**Discussion**

The hemodynamic alterations due to intense sympathetic stimulation accompanying laparoscopic surgery comprising of elevation in heart rate and rise in systolic, diastolic and mean arterial pressure are well known. Immediately after pneumoperitoneum, plasma level of norepinephrine, epinephrine and plasma renin activity is increased. Increased catecholamine level activates the renin-angiotensin-aldosterone-system (RAAS) leading to some characteristic hemodynamic alterations. The potential for life-threatening complications associated with such a response is also well documented.

Laparoscopic cholecystectomy is performed in reverse Trendelenberg position. This particular position causes diminished venous return which ultimately leads to further decrease in cardiac output. Patients with compromised cardiac function may not be able to tolerate the changes in afterload produced by pneumoperitoneum and it may have deleterious effects on their hemodynamics.

There is a strong relationship of both perioperative myocardial ischemia and postoperative myocardial infarction with anaesthetic and surgical events known to produce intense sympathetic stimulation, with or without hemodynamic abnormalities [5]. Thus, it is logical to look for methods to reduce sympathetic stimulation per se.

Various drugs and methods have been studied to prevent hemodynamic alterations due to stress of surgery and anaesthesia. Dexmedetomidine, a highly selective α2 agonist, has been used by many workers for attenuation of hemodynamic responses in various doses and along with various anaesthetic regimens for various types of surgeries. Dexmedetomidine infusion in the perioperative period in laparoscopic cholecystectomy provides better intraoperative and postoperative hemodynamic stability [6].

Keniya et al. showed that the increase in the heart rate during endotracheal intubation and laparoscopic insufflation was significantly attenuated in the dexmedetomidine group as compared to the control group. [6-11]. Mean heart rate was lower than in Group Dex 0.5 as compared to the group Dex 0.25 and significant differences were found at all-time points of the study period. Significant bradycardia was not noted in any of the cases in either group.

Bhatacharjee et al. noted that the MBP was significantly reduced during the intraoperative period and the reduction in MBP was significantly more in patients receiving dexmedetomidine than in patients receiving propofol. In the recovery room, MBP of both treatment groups was significantly lower than before surgery. MBP was significantly lower throughout the period of recovery in the Dexmedetomidine group as compared to the propofol group. They attributed it to the to additive sympatholytic effect of dexmedetomidine over hypotensive effect of propofol at the dosages used in their study. [6,11-15].

In both DEX 0.25 and DEX 0.5 baseline MBP fell to lowest mean after loading dose of dexmedetomidine. After that minimal change in MBP was observed in post intubation and after pneumoperitoneum, with the MBP being significantly lower in the DEX 0.5 group at all the study time intervals as compared to the DEX 0.25 group.

We observed in our study that none of the patients had any episode of bradycardia and hypotension in either of the dexmedetomidine groups which could be because we used lower maintenance dose without any loading dose. Studies using dexmedetomidine have commonly reported cardiovascular side effects such as bradycardia, sinus arrest and hypotension mainly because of sympatholytic effect. In several study reports, dexmedetomidine infusion rates ranging from 0.1 to 10 μg kg-1 hr-1 have been used. The studies with higher infusion rates had more incidences of adverse effects like hypotension and bradycardia [16].

Patients who received dexmedetomidine 0.5 infusion had lesser requirement of fentanyl and the hemodynamic parameters were much more stable than dexmedetomidine 0.25 infusion

group. Bajwa SS et al. in their study showed that dexmedetomidine decreased the dose of intraoperative opioids and isoflurane in achieving adequate analgesia and anaesthesia respectively [8,10,12,17,18,19].

Waleed M. et al. in their study found that, compared with placebo group, patients in the dexmedetomidine group had significantly lower visual analogue scale scores. [9,19-21].

The mean sedation score is more in DEX 0.5 group than in DEX 0.25 group at all observed time points (using modified ramsay sedation score) and patient satisfaction higher [12,21].

Dexmedetomidine lowers the cumulative analgesic consumption at all times during the post operative period and also delays time to first analgesic demand. Gourishankar Reddy Manne et al. in their study concluded that the rescue analgesia was required early (55.5 minutes.) in Group NS compared to dexmedetomidine groups (173 minutes in Dex 0.2 and 249 minutes in Dex 0.4 group) [11,14,21, 22].

Tufanogullari B et al., Turgut N et al., Massad M I et al. also demonstrated that patients receiving dexmedetomidine had lesser incidence of postoperative nausea and vomiting [14,15,23].

## Conclusion

We conclude from our study that dexmedetomidine intravenous infusion in the dose range of 0.25 μg $kg^{-1}$ $hr^{-1}$ and 0.5 μg $kg^{-1}$ $hr^{-1}$ reduces the rise in heart rate and mean arterial pressure associated with the creation and maintenance of pneumoperitoneum during the laparoscopic surgical procedures. Thus, it provides perioperative hemodynamic stability in ASA I and II grade patients during laparoscopic surgeries because of their sedative, hypnotic, anxiolytic and sympatholytic properties [24]. Hence, dexmedetomidine infusion at 0.5 μg $kg^{-1}$ $hr^{-1}$ can be used as an anaesthetic adjuvant in laparoscopic surgeries to provide hemodynamic stability and facilitate smooth emergence from anaesthesia. It also affords added advantage of opioid sparing properties and in preventing post operative nausea and vomiting. However further study is required to evaluate its effect on hemodynamic parameters in high risk group patients with compromised cardio-respiratory function undergoing laparoscopic surgical procedures.

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# Comparative Study of Efficacy of Caudal Ropivacaine plus Dexmedetomidine Vs Ropivacaine Alone For Postopertive Analgesia in Children Undergoing Infraumbilical Surgeries

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**Abstract**

*Introduction:* Caudal analgesia is reliable, safe and has become most popular and commomly performed regional blocks in pediatric infraumbilical surgeries but has a short duration of action without adjuvants. Dexmedetomidine a potent alpha 2 adernergic agonist, provides better hemodynamic stability and longer post operative analgesia than many other adjuvants. Ropivacaine a amide local anaesthetic, provides pain relief with less motor blockage with reduced central and cardiotoxic effects than bupivacaine. Hence study conducted with 2 groups ropivacaine alone (R) and ropivacine plus dexmedetomidine (RD) an adjuvant. *Aims:* Primary objective is to compare post operative analgesia between two groups, secondarily sedation. *Methods:* prospective, randomized study was carried out in 60 patients of ASA grade 1 and 2, aged between 2 and 8 yrs weighing <20 kg, scheduled in elective infraumbilical surgeries. In our study patients were divided into two groups of 30 each with the help of computer generated table of random numbers. Group R received 0.2% ropivacaine 1 ml/kg and Group RD received ropivacaine 0.2% 1 ml/kg plus dexmedetomidine 1 mcg/kg. Mean duration of caudal analgesia, mean duration of sedation and any other side effects were recorded in both the groups and compared. *Result:* The mean duration of caudal analgesia in group RD was 10.41 hrs while group R was 5.89 hrs and difference is statistically significant ($p<0.001$) and quality of sleep was better in group RD. *Conclusion:* Addition of dexmedetomidine to caudal blocks significantly prolongs post operative analgesia with arousable sedation without significant side effects.

**Keywords:** Caudal; Paediatric; Ropivacaine; Dexmedetomidine.

## Introduction

Pediatric patients are undertreated in terms of pain. In addition to various differences between children and adults, there are barriers unique to pediatric patients which interfere with effective postoperative pain control [1]. The impact of painful experience on young nervous system is so significant that long term effects can occur, including a lowered pain tolerance for months

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after a pain producing event [2]. The benefits of adequate analgesia include attenuation of the surgical stress response, decreased perioperative morbidity, improved outcome of surgery, facilitates rehabilitation and accelerates recovery from surgery [3,4]. Regional anaesthesia techniques can be used as sole anaesthetic technique or adjuvant to general anaesthesia for intra-operative and post operative analgesia. Caudal epidural analgesia is the most common regional technique performed in children [5]. Ropivacaine is a long acting amide local anaesthetic used for caudal anaesthesia. It provides pain relief with less motor blockage but has a improved safety profile over bupivacaine with reduced central nervous and cardiotoxic effects, thus making it more suitable for caudal analgesia [6]. Prolongation of caudal analgesia using a single shot technique has been achieved by addition of various adjuvant, such as epinephrine, opioids, ketamine and alpha-2 agonists [7]. Dexmedetomidine is a highly selective alpha agonist with sedative and analgesic properties. It has alpha2/alpha1 selectivity ratio of 1600:1 which is 8 times more potent than clonidine 200:1.

Various studies are being done to evaluate the use of dexmedetomidine in regional anaesthesia to improve quality and duration of analgesia [8]. Very few studies have been done to evaluate the effect of dexmedetomidine in caudal anaesthesia in children with Ropivacaine. Hence this study was to compare dexmedetomidine with ropivacaine and ropivacaine alone in children under going infraumbilical surgeries.

**Materials and Methodology**

After obtaining clearance from institutional ethical committee and informed consent from all the parents of patients, this study was conducted over a period of 6 month. Sixty pediatric patients of either gender, belonging to ASA I and II aged between 2 to 8 yrs scheduled for elective infra umbilical surgeries under general anaesthesia were enrolled for the study. Patients with bleeding disorders, spinal anomalies, anticipated difficulty airway and heart blocks, patients with liver and renal diseases were excluded from study. The patient and the observer were blinded to the study drugs. The patients were allocated to either of the two groups ropivacaine group (R) and ropivacaine plus dexmedetomidine (RD) by computer generated randomization technique.

A standard anaesthesia technique was followed. Children were premedicated with 0.4 mg/kg midazolam syrup 45 minutes prior to surgery and intravenous access with appropriate size cannula was obtained and Ringer lactate infusion was started as per the calculated fluid requirements. Patients were shifted to operative theatre and baseline values of heart rate (HR), noninvasive blood pressure (NIBP), and pulse oximetry ($SpO_2$) was noted. Electrocardiogram (ECG) and all vital parameters were monitored throughout the study. General anaesthesia was induced using propofol 2 -2.5 mg over 20-30 sec as tolerated. Loss of eye lash reflex was considered as the end point of induction. At this point Injection Atracurium 0.5 mg/kg given. After three minutes of mask ventilation, endotracheal intubation was performed with appropriate size endotracheal tube. Bilateral air entry was confirmed. Anaesthesia was maintained with sevoflurane delivered in 50% nitrous oxide and 50% oxygen.

The child was positioned in left lateral position and caudal block was performed using aseptic technique with a short beveled 22-23g needle. After negative aspiration for blood and CSF, one of the following drug combination was injected into the caudal epidural space.

Group R received 1 ml/kg of 0.2% ropivacaine with 1 ml normal saline and Group RD received 1 ml/kg of 0.2% ropivacaine plus 1 mcg/kg of dexmedetomedine diluted to 1ml with normal saline.

Dexmedetomidine 100 µg/ml preparation was used. The dosage was calculated according to the patients weight, loaded using an insulin syringe rounded off to the closest unit and diluted to one ml with normal saline.

Patients heart rate and blood pressure were monitored after administration of caudal block every 5 min for the first 30 min and every 15 min subsequently up to 90 min by an observer who was blinded to the study drug.

No narcotics, analgesics or sedatives were administered intraoperatively. An increase in heart rate and mean blood pressure (>20%) with skin incision indicates that caudal block was inadequate, analgesia was supplemented with injection fentanyl 2 µg/kg and the plane of anaesthesia was deepened by increasing Sevoflurane 1-3% These cases were excluded from study as it is implied that block itself had failed. At the end of procedure, neuromuscular blockade was reversed by neostigmine and glycopyrolate. After the surgery, patients were observed in the post anaesthesia care unit and FLACC pain scale assessment was carried out at 1, 2, 3, 4, 6, 8, 12 and 24 hrs after caudal block.

Duration of post-operative analgesia was defined as the time interval between the administration of caudal block and the first requirement of supplementary analgesia for the patient.

When the FLACC pain scale score was more than 4, analgesia was supplemented with diclofenac sodium suppository (1-2 mg/kg) or syrup ibuorofen (4-6 mg/kg). The study concluded when the first supplementary analgesic was administered or at the end of 24 hours, whichever was earlier.

Side effects such as nausea, vomiting, urinary retention, shivering, agitation and deep sedation were noted and recorded.

## Results and Statistics

In our study, patients were divided into two groups of 30 each with the help of a computer generated table of random numbers. Data was analyzed using SPS22 version software categorical data was represented in the form of frequencies and proportions. Chi square test was used as test of significance for qualitative data. Continuous data was represented as mean standard deviation.

Both the groups were comparable with respect to age, sex, body weight and duration of surgeries.

There were no significant differences in the heart rates and mean blood pressures between both the groups intraoperatively and postoperatively.

Total duration of post operative analgesia (time to first analgesic requirement) in Group RD was 425.33 ± 33.37 min, whereas in the group R was 219.33 ± 19.06 min. The difference is statistically highly significant ($p<0.001$). About 68% of cases in the Group RD did not require any rescue analgesics. All the cases in the Group R received rescue analgesics within 24 hrs. Group R children had significantly high FLACC score than group RD children. Difference was statistically significant ($p<0.001$). In group R, most of the patients have FLACC score of 4 between 3 to 6 hrs compared to group RD patients having FLACC score of 4 between 7 to 10 hrs of post operative period.

There was no incidence of bradycardia, respiratory depression or urinary retention intra or postoperatively in both the groups. Whereas vomiting was noted in 2 children of group R and 3 children of group RD post operatively. Sedation scores were comparable between the groups.

**Table 2:** Demographic profile

| Variable | Group R | Group RD |
|---|---|---|
| Age (months) | 49.2 ± 12.2 | 51.56 ± 21.3 |
| Weight (kg) | 14.80 ± 3.23 | 14.43 ± 3.42 |
| Sex (male/female) | 22/08 | 25/05 |
| Duration of Surgery (min) | 52.65 ± 2.12 | 51.96 ± 28.07 |

**Table 3:** Duration of post operative analgesia

| | Group | N | Mean | Std. Deviation | p |
|---|---|---|---|---|---|
| Duration of analgesia | R | 30 | 219.33 | 19.061 | <0.001 |
| | RD | 30 | 425.33 | 33.372 | |

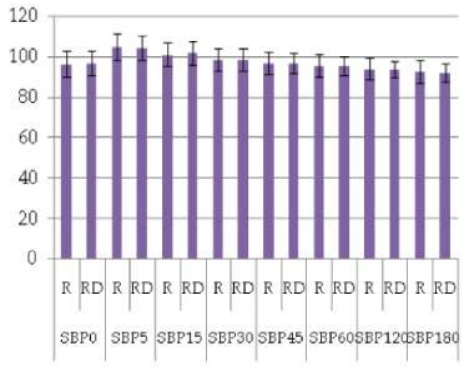


**Fig. 1:** Changes in Systolic blood pressure

**Table 1:** FLACC Behavioral Pain Assessment Scale

| Categories | Scoring | | |
|---|---|---|---|
| | 0 | 1 | 2 |
| Face | No particular expression or smile | Occasional grimace or frown; withdrawn, disinterested | Frequent to constant frown, clenched jaw, quivering chin |
| Legs | Normal position or relaxed | Uneasy, restless, tense | Kicking or legs drawn up |
| Activity | Lying quietly, normal position, moves easily | Squirming, shifting back and forth, tense | Arched, rigid, or jerking |
| Cry | No cry (awake or asleep) | Moans or whimpers, occasional complaint | Crying steadily, screams or sobs; frequent complaints |
| Consolability | Content, relaxed | Reassured by occasional touching, hugging or being talked to; distractable | Difficult to console or comfort |


**Fig. 2:** Changes in Heart rate

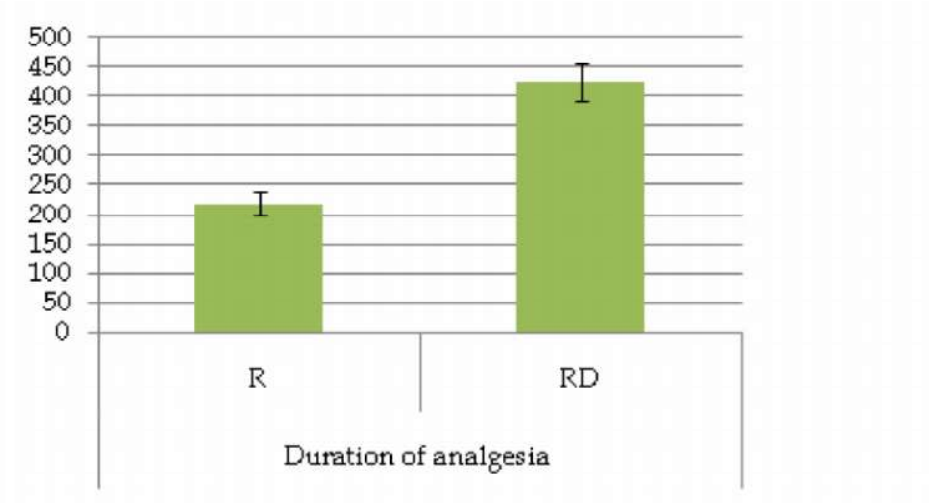


**Fig. 3:** Showing mean duration of post operative analgesia between the two groups (min)

## Discussion

Caudal analgesia in one of the most commonly performed pediatric regional analgesia technique to provide intraoperative and post operative analgesia. It has a very high success rate, reduces the incidence of side effects associated with general anaesthesia, attenuates the stress response, and reduces the hospital stay [9]. Most common disadvantage of caudal block is short duration of action of local anaesthetics. For this reason various adjuvant have been used to prolong the duration of action of local anaesthetics. Various additives used for caudal block are alpha -2 adrenergic agonist's clonidine and dexmedetomidine, opioids like fentanyl, ketamine and epinephrine. Sedation, stable hemodynamics and an ability to provide smooth and prolonged post operative analgesia are the main qualities of alpha-2 adrenergic agonists. Dexmedetomidine is a safe and highly selective alpha-2 agonist, has been described safe and effective additive in many studies. It is available as a preservative free solution.

Ropivacaine is a long acting amide local anaesthetic with greater safety margin and reduced systemic toxicity, although still toxicity has been noted in adults following regional techniques. The main aim of our study was to evaluate the efficacy of caudal dexmedetomidine with ropivacaine in providing intra and postoperative analgesia along with prolongation of post operative duration of caudal block.

Ropivacaine produces lesser post operative motor blockade as compared to bupivacaine when used in lower concentration. There was no apparent motor deficit in our patients probably due to lower concentration of ropivacine used [10].

The analgesic activity of dexmedtomidine is mediated by both supraspinal and spinal mechanisms. It is assumed that central alpha 2 adernorecptors in the locus cerulus and in dorsal horn of the spinal cord are involved in the activity [10].

The dose of dexmedetomidine used in our study was 1 μg/kg. Many studies have used dexmedetomidine in the dose of 0.5 μg /kg, 1 μg /kg, 1.5 μg /kg [11]. They noted in their study patients receiving dexmedetomidine 1.5 μg /kg were more sedated when compared to other groups ($p<0.001$). So in our study caudal dexmedetomidine dose selected at 1 μg /kg.

In this study, the duration of analgesia was significantly prolonged in group RD (425.33 + 33.37 min) compared to group R (219.33 + 19.06 min). The difference between the two groups was highly significant, both clinically and statistically. About 68% of cases in the Group RD did not require any rescue analgesics. All the cases in the Group R received rescue analgesics within 24 hrs. Similar results were noted in studies by our was similar to that conducted by EL-Hennawy et al. [12], Parameshwari et al. [13], Xiang et al. [14], Kauppiah et al. [15].

We choose the FLACC pain score to evaluate post operative pain as it is easy to use, validated and useful for an objective evaluation [16]. Group R children had significantly high FLACC score than group RD children. Difference was statistically significant ($p<0.001$). In group R, most of the patients have FLACC score of 4 between 3 to 6 hrs compared to group RD patients having FLACC score of 4 between 7 to 10 hrs of post operative period.

After addition of dexmedetomidine 1 μg/kg to caudal ropivacaine, the magnitudes of hemodynamics changes between the groups were similar. No respiratory depression or urinary retention was noted. Whereas vomiting was noted in 2 children of group R and 3 children of group RD post operatively, sedation scores were comparable between the groups.

## Conclusion

We conclude that single caudal injection of dexmedetomidine 1 μg/kg added to ropivacaine 0.2% offer an advantage over plain ropivacaine 0.2% for post operative pain relief in children undergoing infraumbilical surgeries without increasing the incidence of adverse effects.

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*Original Research Article*

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# Comparative Study of Intranasal Dexmedetomidine v/s Midazolam as a Premedication in Pediatric Patients Undergoing Cardiac Surgery

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**Abstract**

*Background:* Intranasal midazolam is a novel technique for administering premedication in children. It has been shown to be more effective than parental presence or placebo in reducing anxiety and improving patient's compliance at induction of anesthesia. Dexmedetomidine is selective α2 agonist with sedative, anxiolytic and analgesic properties with favorable pharmacokinetics. We designed this prospective randomized double-blinded study to compare the safety and efficacy of midazolam and dexmedetomidine administered intranasally as premedication in children undergoing cardiac surgery for CHD. *Method:* Sixty-two children belonging to the American Society of Anaesthesiologists (ASA) class I and II, scheduled for elective cardiac surgery were divided into two groups by standard randomization technique. Patients belonging to group M received intranasal midazolam 0.2 mg/kg whereas patients in group D received intranasal dexmedetomidine 1 µgm/kg 30 min prior to surgery in an adequately monitored condition. Patient's sedation score, behaviour scores, attitude, heart rate, respiratory rate, oxygen saturation, intravenous cannula acceptance and face mask acceptance at the time of induction were studied by an observer till induction of anesthesia. *Results:* There was no significant difference in sedation score in both the groups except at 20 minutes, when it was significantly lower in patients belonging to Group D as compared to those of Group M. There was no significant difference inheart rate, respiratory rate, $SpO_2$, behavior score, parental separation acceptance, behavior at separation and level of sedation atinduction of anaesthesia between the two groups. There was a significant difference in the number of patients with a change of behaviour (6.4% v/s 34.4%) and change of sedation (7.1% v/s 37.5%) in Group M and Group D respectively. Patients inGroup M were calmer and allowed face mask application at the time of induction of anesthesia. *Conclusion:* Intranasal route is safe and effective for administering both, midazolam and dexmedetomidine as premedication in children undergoing corrective surgery for congenital heart disease. However, we observed better behaviour with midazolam at induction of anesthesia.

**Keywords:** Intranasal midazolam; Intranasal Dexmedetomidine; Cardiac Surgery.

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## Introduction

For pediatric cardiac anaesthesiologist, it is a challenge to minimize distress among children and to facilitate smooth induction anesthesia in the operating room environment, particularly in presence of severe pulmonary artery hypertension or cyanosis is associated with congenital heart diseases. Each year approximately 10,000 infants require anesthesia for corrective or palliative surgery for congenital heart disease [1,2]. The surgical injury may be followed by stress-induced catabolism, which can lead to delayed convalescence and increased morbidity and mortality [3,4]. Furthermore, postoperative mortality is higher and recovery is slower in patients who have delirium after surgery, than in those without delirium, which leads to prolonged ICU stay and higher cost of treatment [5,6].

The pre-aesthetic management of infants and children undergoing surgery for congenital heart disease can be a challenge for the anesthesiologist. Fear of operation theatre, injections and separation from parents prior to anesthesia produces traumatic experiences in tender mind of young children [7].

Premedication by the atraumatic method can minimize such problems. To provide effective anxiolysis and conscious sedation and to facilitate parental separation, were the objective of our study. The ideal premedication for children should have a rapid and reliable onset, should be atraumatic, palatable with minimal side effects and rapid recovery [8,9].

Thus, the intranasal route was selected, as all the criteria for an Ideal\premedication were satisfied [10]. Midazolam has already been used aspremedication by various routes. Oral and rectal roots for midazolam [11] are wildly used in this age group. The onset of action is slow via oral route (15-30 min) [12], and its first pass metabolism results in lower and unpredictable systemic availability. [13,14]. Intranasal midazolam for premedication in preschool children was first described and advocated by Wilton and colleagues [15].

Clonidine, an alpha-2 agonist has been used as an effective premedication in paediatrics. Oral clonidine premedication has also been shownto reduce the incidence of sevofluraneinduced emergence agitation [16] Dexmedetomidine is a newer alpha-2 agonist with a more selective action on the alpha-2 adrenoreceptor and a shorter half-life. Its bioavailability is 81.8% (72.6-92.1%) when administrated via buccalmucosa [17].

Many studies have reported, dexmedetomidine tobe an effective agent for sedation in pediatric population when given intravenously (IV) or intramuscularly (IM) [18,19] or intra-nasally (IN) [20]. The primary objective of our study was to evaluate and compare the efficacy and safety of intranasal midazolam 0.2 mg/kg with intranasal dexmedetomidine 1 μg /kg in paediatric patients Posted for cardiac surgery for CHD. Our secondary objectives were to evaluate the effects of the two drugs on the level of sedation, behavioral changes, parental separation reaction, and face mask acceptance.

## Materials and Methods

After approval from hospital's scientific and ethical committees and after obtaining written informed consent fromthe patient's parents, sixty -two Children in the age group of 1 to 12 years, belonging to ASA grade Ior II scheduled for elective cardiac surgery for CHD were selected for this prospective randomized double-blinded study. Patients with known allergy, organ dysfunction, cardiac arrhythmias, bradycardia and mental retardation were excluded from the study.

Children were randomly allotted to either of the two groups (Group-M and Group-D) by computer generated random numbers. Children in Group-M received intranasal midazolam (0.2 mg/kg) while Group D children received intranasal dexmedetomidine 1 μg /kg via 1 ml syringe 30 min prior to surgery in the preoperative holding area in the presence of one parent with monitored anesthesia care.

Intranasal midazolam was prepared from the 5 mg/ml parenteral preparation in a 1 ml syringe, after appropriate dilution with 0.9% saline to make a final volume of 0.4 ml. Intranasal dexmedetomidine was prepared from the 100 μg /ml parenteral preparation diluted with 0.9% saline to make the final volume of 0.4 ml. All drugs were prepared by an independent investigator not involved in the study or conduct of anesthesia. Observers and attending anaesthesiologist were blinded to the study drug given.

The drug was instilled into both nostrils using 1 ml syringe with the patient in recumbent position. Baseline heart rate (HR), Oxygen saturation ($SpO_2$) and Respiratory rate (RR) were recorded, and observations were made at 2.5 min, 5 min, 10 min, 20 min and 30 min after test drug administration. Sedation status was assessed by 5 point Wilton

and Colleagues sedation score [21] and behaviour was evaluated with a 4 point behaviour score [22] Table 1. Other parameters observed were attitude (co-operative or not), Separation reaction crying, apprehensive or good, change of behaviour from satisfactory to unsatisfactory at the time of parental separation and face mask acceptance. Adverse effects, if any, especially odd behaviour, excessive salivation, nausea, vomiting, pane, desaturation, bradycardia (20% decreases in baseline value), restlessness etc. were recorded.

**Table 1:** Sedation and behaviour scores

*Wilton and Colleagues sedation score.*
1. Agitated.
2. Alert
3. Calm
4. Drowsy
5. A sleep

*Behaviour Score*
1. Calm and co-operative
2. Anxious but reassurable
3. Anxious and non- reassurable
4. Crying and resisting

Outcome measures: Primary endpoints were behaviour and sedation status atseparation from the parent and at induction of anesthesia. Secondary end point included Heart rate, Respiratory rate and $SpO_2$.

*Statistical Analysis*

Statistical analysis was carried out using SPSS version 20.0 software (SPSS Inc., USA). This data was presented as mean ± SD or proportion as appropriate.Chi-square test and Independent sample t test was used to compare categorical and continuous variables respectively. The "p" value less than 0.05 was considered to be significant.

## Results

Between July 2016 to January 2017 sixty-two (62) children posted for congenital heart surgery were enrolled for the study and evaluated for various parameters. All children accepted the intranasal drug instillation well without anyvomiting. All children were studied in two groups, group M (IN midazolam) and group D (IN dexmedetomidine). Demographiccharacteristics are summarized in Table 2. Patients in both the groups were comparable with respect to age, weight, height, BSA, gender and numbers. No children complained of pain or discomfort with intranasal drug administration.

There were no statistically significant differences in heart rate, respiratory rate and $SpO_2$ in both the groups during premedication sedation period (Fig. 1).

Assessment of sedation and behaviour score after intranasal drug administration (Table 3,4).

Table 3 shows the sedation score at various time points. There was no significant difference in sedation score between the groups except at 20 min when the sedation score was significantly lower in group D as compared to group M (P-value 0.010). The onset of sedation was at 5 min in both the groups (sedation score >2), and patients became calm at 20 min in group M (Mean sedation score 3.32 ± 0.65 min), while in group-D, it is at 30 min (Mean sedation score 3.22 ± 0.61 min).

Table 4 shows behavior score after IN premedication. Behavior scores were comparable in both the groups at various time periods with onset time within 5 min and accepted score at 10 minutes of IN premedication administration.

**Table 2:** Demographic details

| | Group M | Group D | P value |
|---|---|---|---|
| Age | 5.52 ± 2.84 | 4.42 ± 2.61 | 0.118 |
| Weight | 14.48 ± 4.09 | 12.36 ± 5.18 | 0.078 |
| Height | 108.26 ± 14.11 | 100.2 ± 19.98 | 0.071 |
| BSA | 0.66 ± 0.13 | 0.59 ± 0.17 | 0.094 |

**Table 3:** Sedation Score after IN Premedication

| Willton score | Group M | Group D | p value |
|---|---|---|---|
| 2.5 willton score | 1.48 ± 0.50 | 1.48 ± 0.50 | 1.000 |
| 5 willton score | 2.38 ± 0.61 | 2.25 ± 0.63 | 0.412 |
| 10 willton score | 2.83 ± 0.52 | 2.64 ± 0.48 | 0.140 |
| 20 willton score | 3.32 ± 0.65 | 2.93 ± 0.51 | 0.010 |
| 30 willton score | 3.54 ± 0.72 | 3.22 ± 0.61 | 0.063 |

**Table 4:** Behaviour Score after IN Premedication

| Behaviour score | Group M | Group D | p value |
|---|---|---|---|
| 2.5 Behaviour score | 1.90 ± 0.59 | 2.19 ± 0.60 | 0.059 |
| 5 Behaviour score | 1.19 ± 0.40 | 1.35 ± 0.48 | 0.159 |
| 10 Behaviour score | 1.06 ± 0.24 | 1.19 ± 0.40 | 0.126 |
| 20 Behaviour score | 1 ± 0 | 1.03 ± 0.17 | ------- |
| 30 Behaviour score | 1 ± 0 | 1 ± 0 | -------- |

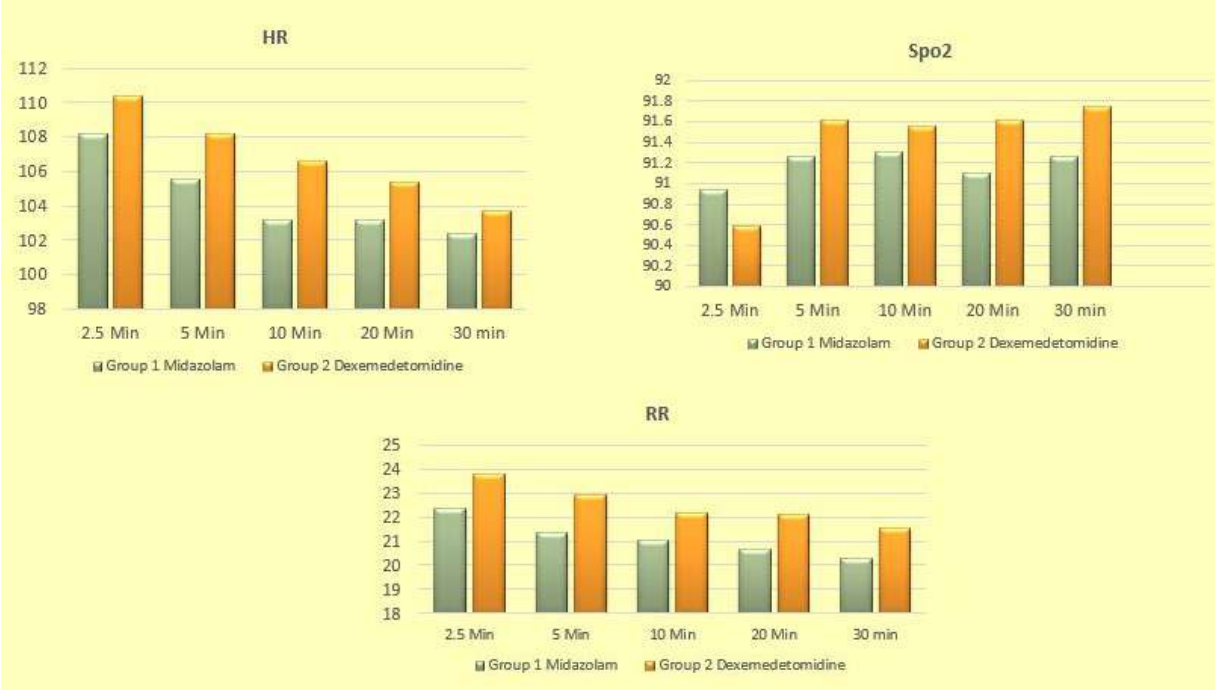


**Fig. 1:** Comparison of Heart Rate, Respiratory rate and $SpO_2$

**Table 5:** Behaviour and sedation status at parental separation and at induction

| | Group M (No %) | Group D (No %) | p value |
|---|---|---|---|
| Sedation at Separation | 31 (100%) | 30 (96.7%) | 1.000 |
| Behaviour at Satisfactory | 30 (96.7%) | 29 (93.5%) | 1.000 |
| Sedation at Induction | 30 (96.7%) | 26 (83.8%) | 0.197 |
| Change of Behaviour | 02 (6.4%) | 10 (32.2%) | 0.024 |
| Change of Sedation | 02 (6.4%) | 09 (29.03%) | 0.046 |

Assessment of sedation and behaviour at separation and at Induction: (Table 5).

We observed sedation at separation in 28 children (90.32%) in group M, while in 24 children (77.4%) in group D, but it was not statistically significant. The behavior seemed to be satisfactory in 30 children (96.7%) in group M and in 29 children (93.5%) in group D. There was no statistically significant difference in behaviour score at separation in both the groups.

We observed that in 96.7% patients (no=30) in group M, there was sedation at induction of anesthesia, while in group D 83.8% patients (no=26) had sedation at induction time (no significant difference between the groups).

During induction change of behaviour from satisfactory to unsatisfactory was observed to be significantly lower in group M (6.4%/2 patients) as compared to group D (32.2% / 10 patients). Similar changes in the level of sedation during induction, from satisfactory to unsatisfactory was also significantly lower in group M (6.4% / 2 patients) as compare to group D (29.03% / 9 patients). Children in group M were significantly calmer during induction of anesthesia. Face mask acceptance was without cry in 22 children in group M, while in 14 children in group D.

## Discussion

There is a continuous search for safe premedication for children posted for congenital cardiac surgery, which would make separation of children from parents peaceful. As suggested by weksler et al. [23], ideal premedication for children should be easy to administer, with rapid onset and faster recovery. Ketamin, midazolam, clonidine, dexmedetomidine etc possess ideal criteria for premedication such as rapid onset, good anxiolysis, sedation and rapid recovery [24].

Oral, rectal, intravenous and intranasal routes are documented for premedication in children. The problem with the oral route is delayed and unpredictable effect due to first-pass hepatic metabolism, while for the intravenous route, intravenous line should be required and chances of respiratory depression are there.

Previous studies have shown that in administration is an effective way to administer premedication and it provide rapid and reliable onset of action,

predictable effect, good quality of sedation to children, it's relatively easy and non-invasive route with high bioavailability (25, 26, and 27).

Intranasal midazolam and intranasal dexmedetomidine are safely used as premedicant in various paediatric surgeries. In this prospective, randomized double-blinded study, we compared IN dexmedetomidine with IN midazolam as premedication in 62 paediatric cardiac surgery patients in the age group of 1 to 12 years.

Dexmedetomidine is an alpha-2 agonist, can beadministrated intranasally or transbuccally, has recently been introduced as a sedative in paediatric patients [28]. Primarily it has been used forpaediatric sedation by intravenous route [29]. It has minimal effects on the respiratory drive and upper airway dynamics [30]. It is odourless, intranasal administration is not irritating and well tolerated by children [28]. Limited animal studies suggested dexmedetomidine may not be associated with neurodegeneration [29]. Dexmedetomidine has a half-life of 2 hours, which may lead to faster recovery. However, as an alpha-2 adrenergic receptor agonist, it decreases heart rate and blood pressure [31].

Most children tolerated the intranasal study drugs. Primary end points were behaviour and sedation status at separation from the parent and at induction of anesthesia. We observed onset of sedation at 5 min in both the groups with little delay in group D but without statistical significance. Satisfactory sedation achieved at 20 min in group M (3.32 ± 0.65 minat 20 min in group M), while it is at 30 min in the group- D (3.22 ± 0.61 min at 30 min in group-D), which was statistically significant. Behaviour score was satisfactory at all time intervals in group M, while it was satisfactory at 5 min, 10 min, 20 min and 30 min in group D, but there was no statistical difference at 2.5 min interval in both groups. We observed good sedation and satisfactory behaviour at separation of children from parents in both the groups.

When compared with group D, the number of patients with change of behaviour and change of sedation were significantly lower in group M. Change of behaviour 6.4% (2 patients) in group M v/s 32.2% (10 patients) in group D, which is statistically significant (p=0.024). Change of sedation 6.4% (2 patients) in group M v/s 29.03% (9 patients) in group D, that is statistically significant (p=0.046). These observations were also noted by A L Menakshi et al. (32a), unlike conventional gabaminergic sedative drugs, such as midazolam dexmedetomidine's site of action in thecentral nervous system is primarily in the locus coeruleus where it induces electroencephalogram activity Similarto natural sleep [32]. Dexmedetomidine induces arousable sedation, undereffect of which, the patient can be awakened by background noise and movement [33] and patients are less likely to become disoriented and uncooperative. Attitude and facemask acceptance were excellent in group M as compared to group D. Secondary end point like intraoperative pulse rate, oxygen saturation, respiratory rate had no significant difference in group M and group D.

Post-operative oral secretions were minimal in both groups. Nystagmus and other sideeffects like vomiting and increased salivation were not observed in any patients. None of the patients had any reaction in our study, consistent with the study done by Agrawal Nidhi et al. [34].

## Conclusion

Intranasal drug administration for premedication in children posted for congenital heart surgery is simple, rapid and with predict sedation. We have observed that this route is feasible for dexmedetomidine and midazolam–both the drugs are safe and effective premedicants in pediatrics with better sedation and behaviour at induction of anesthesia in midazolam group as compare to dexmedetomidine group.

In summary, 0.2 mg/kg intranasal midazolam and 1 µg/kg intranasal dexmedetomidine both produce significant sedation in children between 1 and 12 years of age. The behavior of the children at parental separation and at induction of anesthesia was satisfactory inboth the groups.

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# A Comparative Study of Supraclavicular versus Infraclavicular Approach for Right Subclavian Vein Catheterization

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**Abstract**

*Background and Aim:* Supraclavicular approach to subclavian vein catheterization has become one of the forgotten techniques in anaesthesia practice. The aim of this study is to compare supraclavicular approach with infraclavicular approach to subclavian vein cannulation, with respect to time taken to identify and cannulate vein, number of attempts taken to cannulate, success rate and complications. *Method:* In this study, 60 patients were enrolled and their right subclavian veins were catheterized by either Supraclavicular approach (Group-A, n=30) or infraclavicular approach (Group-B, n=30). Parameters including time to locate the subclavian vein, number of attempts needed to successfully cannulate the vein, success rate, total access time and complications were recorded. *Results:* The mean time to identify Right Subclavican Vein in first attempt in Group A was 10.652 ± 3.926 seconds as compared to 15.550 ± 8.325 seconds in Group B. In Group A, 23 out of 30 patients (76.7%) were successful in first attempt compared to 20 out of 30 patients (66.7%) in Group B. The average number of attempts needed to successfully identify the right subclavian vein in Group-A was 1.24 ± 0.511 and in Group-B was 1.37 ± 0.688. The total access time for Group A was 197.069 ± 35.12 seconds and for Group B was 227.481 ± 61.22 seconds. Arterial puncture is more common in Group-A (3 out of 30) whereas malposition of the catheter was more common in Group-B (3 out of 30). *Conclusion:* Supraclavicular approach can be used as an effective alternate to infraclavicular approach for Subclavian Vein cannulation.

**Keywords:** Central Venous Cannulation; Subclavican vein; Supraclavicular approach; Infraclavicular approach.

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## Introduction

Central Venous Catheterization is one of the commonly performed interventions in Critical Care Units and Operating theatres. The indications for central venous catheterization are difficult peripheral venous catheterization, volume resuscitation, emergency transvenous pacemaker placement, flow directed Pulmonary artery catheterization, administering total parenteral

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nutrition, hemodynamic monitoring, central venous oxygen saturation monitoring, access for renal replacement therapy and for administration of ionotropes and veno-irritant medications.

The common sites of central venous catheterization are Internal Jugular vein, Subclavian vein and Femoral vein. The Subclavian vein catheterization has some advantages over other sites for central venous access because of easily identifiable bony landmarks, large size of vein, patient comfort, long term catheter maintenance with comparably lower rate of catheter related infections and thrombosis [1-4]. Subclavian vein cannulation is preferred in patients with hypovolemia, for long-term total parenteral nutrition (TPN) and in patients with elevated intra-cranial pressure who require hemodynamic monitoring. However, it should not be considered the primary choice in the presence of thrombocytopenia (platelets < 50,000), for acute hemodialysis and in patients ventilated with high PEEP (i.e., > 12 cm $H_2O$) [5].

The subclavian vein cannulation was initially performed by Aubaniac in 1952. Infraclavicular approach for Subclavian vein catheterization was introduced in 1962 by Wilson and colleagues and is widely practiced till now [6]. In 1965, Yoffa introduced the supraclavicular approach for Subclavian vein cannulation [7]. Supraclavicular approach for Subclavian vein cannulation was not widely practiced for a long time because of fear of directly entering into the pleural cavity, damage to vital structures, difficulty in identifying the landmarks and difficulty in positioning the needle, resulting in failures. However supraclavicular approach to subclavian vein cannulation can be equally performed in view of well defined anatomical landmark (the claviculosternomastoid angle); shorter distance from skin to vein; a larger target area; a straighter path to superior vena cava; less proximity to the lung and fewer complications.

Hence we conceptualized this study to compare supraclavicular approach with infraclavicular approach to subclavian vein cannulation, with respect to time taken to identify and cannulate vein, number of attempts taken to cannulate, success rate and complications.

## Materials and Methods

This prospective randomised control trial was conducted in a tertiary care teaching institute after getting Institutional ethical committee clearance. Sixty patients of either sex in the age group 18-75 years, who were in need of central venous catheterisation were enrolled into the study. Patients with local infection, coagulopathy, neck deformity (anatomical), trauma to chest, clavicle, neck, cervical spine and pregnancy were excluded from the study. Written informed consent was obtained from all the patients included in the study. Patients were allotted to either Group-A (Supraclavicular) or Group-B (Infraclavicular) by random number generation by computer, with 30 patients in each group. [Fig. 1]

After securing Peripheral Venous Access with 18G cannula and attaching monitors (ECG, NIBP, $SpO_2$), patients were premedicated with Inj. Midazolam 0.05 mg/kg. Patients were positioned in $15^0$ Trendelenberg position, head turned slightly to left, with arms kept to the side of the body. Patient's neck was cleaned with 7.5% Povidone Iodine and anaesthetised with 2 ml of 2% Lignocaine at site of skin puncture.

In Group-A, after preparing the patient, the 18G finder needle mounted on 5 ml heparin saline loaded syringe, was inserted 1 cm cephalad and 1 cm lateral to the junction of the lateral border of the clavicular head of sternocleidomastoid muscle with the superior border of clavicle (angle between clavicle and sternocleidomastoid). The needle was directed towards the line that bisects the claviculosternocleidomastoid angle with elevation $5^0$–$15^0$ below the coronal plane. The vein was usually occured between clavicle and the attachment of anterior scalene muscle with the first rib. Venipuncture was confirmed by free back flow of venous blood in the syringe. Once subclavian vein was punctured, catheterization was done by seldinger technique.

In Group-B, after preparing the patient, the 18G finder needle mounted on 5 ml heparin saline loaded syringe, was inserted 1cm below the midpoint of the clavicle and advanced towards the suprasternal notch under the posterior surface of the clavicle. After confirming free back flow of venous blood, catheterization was done by standard seldinger technique.

Each Skin Puncture was defined as an attempt and maximum 3 attempts were allowed in each approach for subclavian vein catheterization (i.e., Supraclavicular or infraclavicular approach). In cases of failure, Right internal jugular venous catheterization was done. Successful Catheterization was confirmed by free back flow of venous blood through all the ports.

## Results

Demograpic datas like age, gender between the two groups were comparable. The mean time to identify Right Subclavican Vein in first attempt [Table 1] in Group-A was 10.652 ± 3.926 seconds and in Group-B was 15.550 ± 8.325 seconds which was found to be statistically significant (p = 0.015). In Group-A, subclavian vein catheterisation was successful in 23 patients in first attempt, 5 needed second attempt and 1 patient needed third attempt whereas Group-B, it was successful in 20 patients in first attempt, 4 needed second attempt and 3 needed third attempt [Table 2]. There was failure to identify right subclavian vein by supraclavicular approach in 1 patient and by infraclavicular approach in 3 patients. The average number of attempts needed to successfully identify the right subclavian vein in Group-A was 1.24 ± 0.511 and Group-B was 1.37 ± 0.688 [Table 3]. The total access time for Group-A was 197.069 ± 35.12 seconds and for Group-B was 227.481 ± 61.22 seconds [Table 4]. The Complications observed during this study included, arterial Puncture in 3 cases (3 in Group-A and 0 in Group-B) and malposition of the catheter in 4 cases (1 in Group-A and 3 in Group-B) [Table 5].

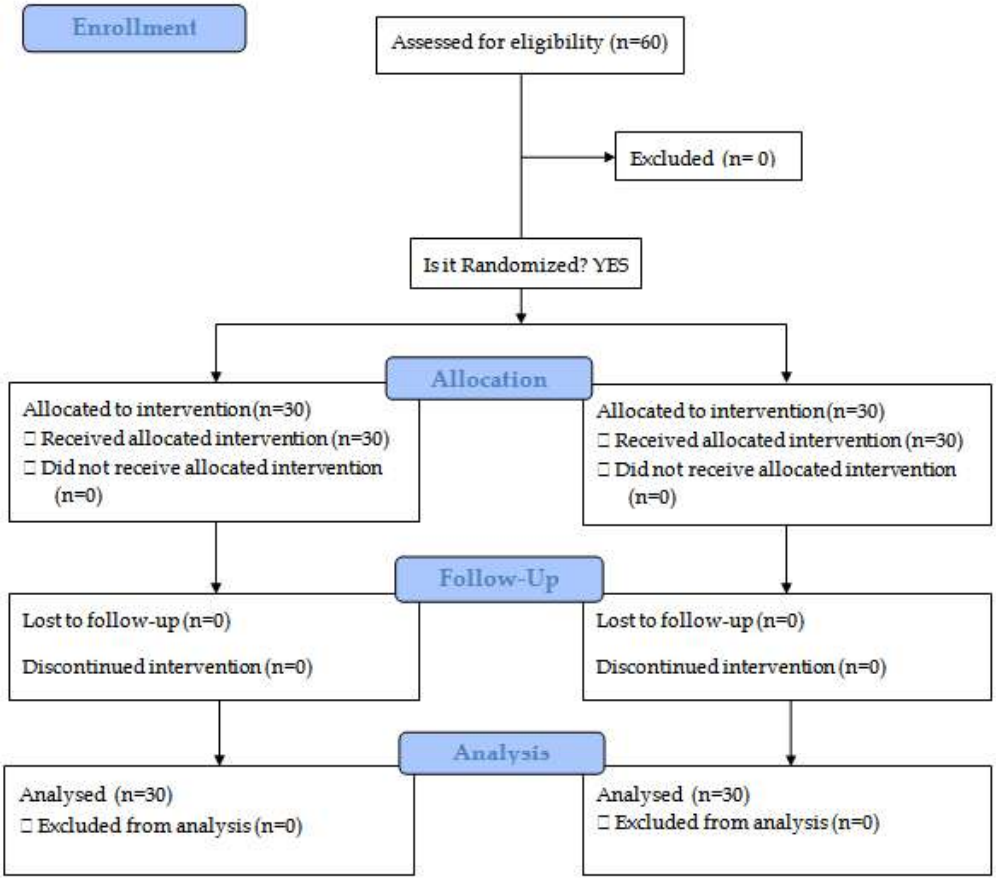


**Table 1:** Comparison of Time to identify Right Subclavian Vein in First Attempt

| Subclavian Vein | Group A (n=23) In secs | Group B (n=20) In secs | Total (43) In secs | t Value | P Value |
|---|---|---|---|---|---|
| Mean ± SD | 10.652 ± 3.926 | 15.550 ± 8.325 | 12.930 ± 6.748 | 2.5208 | 0.015* |

*- There is a Statistically Significant difference between Group A and Group B with respect to time to Subclavian Vein at 95% [p < 0.05]

**Table 2:** Comparison of number of attempts needed to successfully identify subclavian vein

| Attempts | Approaches n (%) | | Total n (%) n = 60 | Chi Square Test | p Value |
|---|---|---|---|---|---|
| | Group A n = 30 | Group B n = 30 | | | |
| One | 23 (76.7) | 20 (66.7) | 43 (71.7) | 2.320 | 0.509 NS |
| Two | 5 (16.7) | 4 (13.3) | 9 (15) | 3 df | |
| Three | 1 (3.3) | 3 (10) | 4 (6.7) | | |
| Unsuccessful | 1 (3.3) | 3 (10) | 4 (6.7) | | |

**Table 3:** Comparison of Successful Attempts

| Attempts | Group A (n=29) | Group B (n=27) | Total (56) | t Value | p Value |
|---|---|---|---|---|---|
| Mean ± SD | 1.24 ± 0.511 | 1.37 ± 0.688 | 1.3 ± 0.601 | 0.800 | 0.427 NS |

**Table 4:** Comparison of Total Access Time

| Total Access Time | Group A (n=29) In Secs | Group B (n=27) in Secs | Total (46) In Secs | t Value | p Value |
|---|---|---|---|---|---|
| Mean ± SD | 197.069 ± 35.12 | 227.481 ± 61.22 | 211.732 ± 51.33 | 2.300 | 0.0253* |

**Table 5:** Comparison of Complications

| Complications | Group A n (%) | Group B n (%) | Total n (%) | Chi Square Test | p Value |
|---|---|---|---|---|---|
| Nil | 25 (86.2) | 24 (88.9) | 49 (87.5) | 6.958 | 0.138 |
| Arterial Puncture | 3 (10.3) | 0 (0) | 3 (5.4) | 4 df | NS |
| Malposition into Lt. SCV | 0 (0) | 2 (7.4) | 2 (3.6) | | |
| Malposition of Catheter to Rt. IJV | 0 (0) | 1 (3.7) | 1 (1.8) | | |
| Malposition to ipsilateral axillary vein | 1 (3.4) | 0 (0) | 1 (1.8) | | |
| Total | 29 (100) | 27 (100) | 56 (100) | | |

## Discussion

The time taken to identify the subclavian vein by supraclavicular and infraclavicular approaches was not compared in any of the studies conducted so far. We have measured time to cannulate subclavian vein in our study, since it is one of the important factors in deciding route of central venous cannulation, especially in emergencies. The time to identify right Subclavian vein by supraclavicular approach was 10.65 ± 3.926 secs, whereas in infraclavicular approach, it was 15.55 ± 8.325 secs, which was statistically significant with the p-value of 0.015.

The number of attempts required to successfully cannulate right Suclavian vein by Supraclavicular approach was 1.24 ± 0.511 whereas by infraclavicular approach was 1.37 ± 0.688. Even though, the number of attempts needed to successfully identify subclavian vein was statistically insignificant (p-value-0.427), the percentage of patients in whom cannulation was successful in first attempt was comparatively greater in supraclavicular approach. The percentage of patients in whom subclavian vein was cannulated in first, second and third attempt in supraclavicular approach was 76.6% (23/30), 16.6% (5/30), 3.33% (1/30), where as in Infraclavicular approach it was 66.6% (20/30), 13.3% (4/30), 10% (3/30) respectively. These findings are comparable to the results obtained by SafdarHussain et al. [8], where first attempt success rate with supraclavicular approach was 86.11% (62 out of 72 patients) whereas with infraclavicular approach was 68.05% (49 out of 72 patients). The mean numbers of attempts needed were 1.13 ± 0.42 and 1.35 ± 0.69 in the supraclavicular and infraclavicular approach groups respectively. In the case series reported by Tomarz Czarnik et al. [9] on 370 mechanically ventilated patients, the first attempt success rate was even higher (88.9%) for Right subclavian vein cannulation.

The total access time to cannulatesubclavian vein was 197.069 ± 35.12 seconds and 227.481 ± 61.22 seconds in Supraclavicular approach and Infraclavicular approach respectively. There is a statistically significant difference (p-value of 0.0253) in the total time to access vein between

supraclavicular and infraclavicular approaches. This value is comparable with the results of the study conducted by Anil Thakur et al. [10], in which the mean access time was 4.30 ± 1.02 minutes in Supraclavicular approach and 6.07 ± 2.14 minutes in Infraclavicular approach.

In our study, success rate in subclavian vein cannulation by Supraclavicular approach is better than infraclavicular approach, though it was not statistically significant. Among the 30 cases done in each group, cannulation was successful in 29 cases (96.7%) in Group A and 27 cases (90%) in Group B. Aysu Kocum [11] achieved 98% and 92% success rate in subclavian vein cannulation by Supraclavicular and infraclavicular approach respectively. Study conducted by Sterner S et al. [12] have shown success rate of 84.5% in supraclavicular approach and 80% in infraclavicular approach. Hussain S et al. [8], conducted study on 144 patients and concluded that the overall success rate was 95.83% for right supraclavicular approach and 87.50% for right infraclavicular approach for subclavian vein cannulation. Dronen S et al. [13] have proved that supraclavicular approach to the subclavian vein cannulation is associated with fewer failures that by infraclavicular approach even during cardiopulmonary resuscitation. The case series conducted so far by different people between 1965 to 2004 have shown varying failure rates by supraclavicular approach ranging between 0.0% to 20.6%, with an average of 3.2% failure in the total of 13,309 pts (422 cases failure).

The complications observed during the course of this study were Arterial puncture and malposition of the central venous catheter. Statistically, there was no difference among the two groups with respect to complication rate. In our study, complication rate in Supraclavicular approach was 13.8% while in Infraclavicular approach was 11.1%. We encountered three instances of arterial puncture and one instance of malposition of Catheter to right axillary Vein in supraclavicular approach, whereas we had three instances of malposition of Catheter (catheter tip was found to be in Lt. Subclavian vein in two instances whereas catheter tip was in right internal jugular vein in one patient). The commonest complication during subclavian vein cannulation by supraclavicular approach was inadvertent arterial puncture (160 patients), as per data collected from 13,309 patients between 1965 to 2004. Arterial puncture is more common when the needle insertion site is more lateral and cephalad than usual. Other complications included 39 cases of Pneumothorax, 37 cases of Malposition of the Catheter and 9 cases of lymph leak.

## Conclusion

The Supraclavicular approach to Right Subclavian vein is found to be a better technique compared to infraclavicular approach with regard to the time taken to identify & catheterise the vein, number of attempts taken and the success rate with comparable complication rate. Hence, Supraclavicular approach to subclavian vein cannulation can be used as alternate method to conventional infraclavicular approach.

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*Original Research Article*

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# Comparative Study on Ultrasound Guided Shoulder Block Versus Interscalene Brachial Plexus Block in Patients Undergoing Arthroscopic Shoulder Surgery

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**Abstract**

*Background:* Ultrasound (US)-guided Interscalene or Shoulder blocks are commonly used for Shoulder arthroscopic surgeries. *Aim:* The aim of this randomized study were to compare the block performance and onset times, effectiveness, incidence of adverse events and patient's acceptance of US-guided Interscalene or Shoulder blocks. *Methods:* 68 patients were randomized to two equal groups: Shoulder block (SB) and Interscalene group (ISN). Each patient received a mixture containing 0.75% Ropivacaine. The block performance and latency times, surgical effectiveness, adverse events and patient's acceptance were recorded. *Results:* The mean block performance time was 5.529 ± 1.022 mins in the ISN group and 8.559 ± 1.260 mins in the SB group. Onset of sensory block and motor block was early in ISN group. However, duration of sensory and motor block was higher in SB group. The total requirement of analgesic was higher in SB group and patients' satisfaction was slightly more in ISN group. Also, ISN group had more complications than SB group. The haemodynamic parameters (H.R, systolic BP, diastolic BP, RR and $SpO_2$) were recorded at 0, 4, 6, 12 & 24 hours. These parameters were all comparable in both the groups, thus statistically insignificant. *Conclusion:* Shoulder block can be considered in patients with Acute or Chronic respiratory distress, decreased pulmonary reserve, elderly patients, COPD patients and in patients with absolute contraindication to any degree of phrenic nerve block which almost always occurs in Interscalene nerve block.

**Keywords:** Brachial Plexus; Arthroscopic Shoulder surgery.

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## Introduction

Major surgery such as Shoulder arthroscopy are associated with moderate to severe postoperative pain. These procedures are amenable to regional anaesthesia techniques which decrease neuroendocrine stress responses, central sensitization of nervous system and muscle spasms

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which occur in response to pain stimuli. Inadequate relief of postoperative pain may result in harmful physiological and psychological consequence that lead to significant morbidity. This may delay recovery and return to daily activities. Also, the presence of postoperative symptoms including pain contributes to patients' dissatisfaction with their surgical and anaesthetic experience. In addition, inadequately treated postoperative pain may lead to chronic pain. Various analgesic techniques for Shoulder arthroscopic surgeries such as intra-articular injection of local anaesthetics, parenteral opioids, brachial plexus block have been used with varying effectiveness, but not without side effects [1]. Continuous intra-articular Bupivacaine infusion is associated with Glenohumeral chondrolysis. Parenteral opioids are effective, but may result in adverse reactions such as nausea, vomiting, sedation and dizziness [1]. Regional anaesthetic techniques have specific advantages both for stand alone anaesthesia or as analgesic supplements for intraoperative and postoperative care [2,3]. Brachial plexus blockis preferred as analgesic supplement for its rapid onset, reliable anesthesia and as a safe technique for Shoulder arthroscopic surgeries for Rotator cuff tear (Supraspinatus, Infraspinatus, Subscapularis and Teres minor) [4,5]. There are many advantages of supplementing brachial plexus block with general anaesthesia for Shoulder arthroscopic surgeries, namely effective analgesia with good motor blockade, extended post-operative analgesia, early ambulation, early resumption of oral feeding, minimum number of drugs used so that polypharmacy is avoided, less incidence of post-operative nausea and vomiting, ideal operating conditions can be met, PACU and ward nurses particularly appreciate the use of regional anaesthesia. The Interscalene block (ISN) technique is more effective in controlling postoperative pain causing lower pain scores and less rescue opioid consumption for pain relief [4,5,6]. However, it is essentially associated with complications such as unintentional injection of local anaesthetic into the epidural space, spinal cord and brachial plexus injury, brain damage or adverse effects such as blockade of phrenic nerve, vagus nerve, recurrent laryngeal nerve, stellate ganglion, cervical sympathetic ganglion, Horners syndrome and respiratory complications such as respiratory distress and pneumothorax [7,8]. Phrenic nerve block occurs almost in all patients undergoing Interscalene nerve block. These side effects and complications lead to the development of an alternative regional anaesthetic technique or shoulder arthroscopic surgery. The combination of Suprascapular nerve block (SSN ) and Axillary nerve (AXN) block called as Shoulder block (SB) has been reported to provide safe and effective intra-operative and post operative analgesia for Shoulder arthroscopic surgeries for Rotator cuff tear. Shoulder block could be considered especially in older patients with pulmonary comorbidities such as chronic obstructive pulmonary disease, restrictive lung disease, prior pneumonectomy on the opposite side and so on [9]. Since its introduction into clinical practice, Ultrasonography has become a valuable adjunct for peripheral nerve blocks. Initially used in conjunction with nerve stimulation, ultrasound guidance has increasingly been used as the sole modality to locate and anaesthetize the brachial plexus. By allowing the operator to visualize in real time, the nerve, needle, and local anesthetic spread, it has resulted in success rates equal or superior to 95% for the Interscalene, Suprascapular, Supraclavicular, Infraclavicular and axillary approaches**.** Nowadays; the intraoperative use of ultrasonography becomes more popular and much easier. Its use in these blocks increases the success rate and decreases complications. This is a prospective randomized controlled study to compare Shoulder block and Interscalene approaches for brachial plexus block using ultrasound guidance in patients undergoing Shoulder arthroscopic surgery for Rotator cuff tear.

## Materials and Methods

The present study conducted in patients at Yashoda Hospital, a multi speciality hospital in Secunderabad, during the period of February 2016 to May 2017.

The study protocol was approved by the Institutional Ethical committee and informed consent was taken from each of the patients.

The study included total 68 patients belonging to ASA grade I, ASA grade II and ASA grade III with age between 18 to 60 years posted for Shoulder arthroscopic surgeries. It is a prospective, randomized, double blinded and controlled study. After obtaining written informed consent, patients satisfying the inclusion criteria were randomized into 2 groups using a computer generated random number list.

Group I received USG guided SB with 20 mL of 0.75% ropivacaine (max 150 mg).

Group II received USG guided ISN block with 20 mL of 0.75% ropivacaine.

Group allocation was concealed in sealed, opaque envelopes. A pain nurse who had undergone prior education in assessment of postoperative analgesia and who was unaware of group assignment, collected data on each patient. Thus both the patients and the observer were blinded. A sample size of 34 patients each, randomly allocated into two groups, using computerized randomization. We planned for an inclusion of 34 patients in each group to compensate for any dropouts and the uncertainty in our estimated standard deviation.

*Group SB:* patients receiving ultrasound guided Shoulder block.

*Group ISN:* Patients receiving ultrasound guided Interscalene Nerve block. Patients of either sex between 18-60 years. Patients with American Society of Anaesthesiologists grade I, II and III physical status. Patients planned electively for Shoulder Arthroscopic surgery under general anaesthesia. Patients capable of giving an informed consent. Patients with ability to follow study protocol were included in the study.

*Exclusion criteria:* Patients with age less than 18 yrs and Age greater than 60 years, patients with ASA IV or V adults, patients with hypersensitivity to amide local anaesthetics, patients with uncontrolled anxiety, patients with significant cardiovascular disease, patients with uncontrolled diabetes, patients with schizophrenia or bipolar disorder, patients with peripheral neuropathy, patients with renal Impairment (Creatinine greater than 2.0 mg/dl), patients with liver impairment, patients with BMI greater than 35, patients with preexisting nerve damage (sensory or motor) in the extremity to be blocked, patients with history of chronic pain condition or daily intake of analgesics and steroids, patients with history or Ongoing drug abuse or alcohol abuse, patients with pregnancy, patients with daily use of gabapentin, pregabalin, tricyclic antidepressant, serotonin- norepinephrine reuptake inhibitor, tramadol were excluded from the study.

Obtained ethical clearance from the instituitional ethical committee. Each patient was visited pre-operatively, procedure was explained and written informed consent was obtained. Pre-anaesthetic evaluation was done on the evening before surgery. A routine examination was conducted assessing general condition of the patients, airway assessment by Mallampatti grading and rule of 1-2-3, nutritional status, weight and height of the patient, a detailed examination of the cardiovascular system, a detailed examination of the respiratory system, the surface anatomy where the block was going to be given.

The following investigations were done in all the patients: Haemoglobin estimation, urine examination for albumin, sugar and microscopy, standard 12 lead ECG, X-ray chest, fasting and post prandial blood sugars, blood urea and serum creatinine. All patients included in the study were premedicated with the tablet Alprazolam 0.5 mg and Ranitidine 150 mg orally at night before surgery and were kept nil orally 11 PM onwards.

On arrival of patients in the operating room, a 20 guage intravenous cannula was inserted on the non-operating hand and infusion of normal saline was started. All patients were pre-medicated with I.V. 1 mg midazolam 20 minutes before giving the block. The patients were connected with monitor to record heart rate, non-invasive measurement of systolic blood pressure (SBP), diastolic blood pressure (DBP), continuous electrocardiogram monitoring and hemoglobin oxygen saturation ($SpO_2$). The baseline blood pressure, heart rate and $SpO_2$ level were recorded. Descriptive and inferential statistical analysis has been carried out in the present study.

Results on continuous measurements are presented on Mean ± SD (Min-Max) and results on categorical measurements are presented in Number (%). Significance is assessed at 5% level of significance. Significance levels (ascending order): * = $p<0.05$; ** = $p<0.01$; *** = $p<0.001$. The following assumptions on data are made: 1. Dependent variables should be normally distributed, 2. Samples drawn from the population should be random, and cases of the samples should be independent. 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. ANOVA (analysis of variance test) has been used to find the significance of study parameters on categorical scale between two or more groups. The Statistical software namely Windostat version 9.2 was used for the analysis of the data and Microsoft word and Excel have been used to generate graphs, tables etc. p value < 0.05 is considered to be significant and p value > 0.05 is considered to be non significant.

## Results

**Table 1:** Demographic profile of patients.

| Parameters | Group ISN (Mean ± SD) | Group SB (Mean ± SD) | p value |
|---|---|---|---|
| Age in years | 26.529 ± 6.752 | 28.000 ± 6.719 | 0.140 |
| Weight in Kgs | 59.794 ± 3.844 | 58.853 ± 5.695 | 0.191 |
| Height in cms | 158.324 ± 4.367 | 157.353 ± 4.424 | 0.277 |

The p value was is not significant showing that the groups are comparable with regards to Age, Weight and height. There was statistically no difference between two groups.

**Table 2:** Comparison of onset of sensory block, comparison of onset of motor block.

| | Group ISN (Mean ± SD) | Group SB (Mean ± SD) | p value |
|---|---|---|---|
| Onset of sensory block (min) | 3.5 ± 0.862 | 13.676 ± 2.142 | 0.000 |
| | **Group ISN (Mean ± SD)** | **Group SB (Mean ± SD)** | **p value** |
| Onset of motor block (min) | 5.941 ± 1.071 | 11.765 ± 1.793 | 0.000 |

Onset time is the time from the completion of injection of the local anaesthetic to first loss of pinprick sensation in any of the dermatomes C5-T1. In group ISN, it was 3.500 ± 0.862 min and 13.676 ± 2.142 min in group SB. p value is 0.000 which is significant. This shows that Interscalene nerve block provides faster sensory block than Shoulder block. The total time required to achieve complete paralysis of the upper limb was considered as onset of motor block. In group ISN, it was 5.941 ± 1.071 min and 11.765 ± 1.793 min in group SB. P value is 0.000 which is significant.

**Table 3:** Comparison of duration of motor block, comparison of duration of sensory block.

| | Group ISN (Mean ± SD) | Group SB (Mean ± SD) | p value |
|---|---|---|---|
| Duration of motor block (hrs) | 11.559 ± 1.418 | 13.059 ± 1.757 | 0.000 |
| | **Group ISN (Mean ± SD)** | **Group SB (Mean ± SD)** | **p value** |
| Duration of sensory block (hrs) | 13.000 ± 1.348 | 13.882 ± 1.552 | 0.015 |

Duration of motor blockade was longer in group SB (13.059 ± 1.757 hrs) compared to group ISN (11.559 ± 1.418 hrs) and this difference was statistically significant. The above mentioned values compare the duration of sensory blockade in the two groups. Duration of sensory blockade was longer in group SB (13.882 ± 1.552 hrs) compared to group ISN (13.000 ± 1.348 hrs) and this difference was statistically significant.

**Table 4:** Comparison of tramadol requirements in 24 hrs, comparison of block performance time (BPT), comparison of patient satisfaction.

| | Group ISN (Mean ± SD) | Group SB (Mean ± SD) | p value |
|---|---|---|---|
| Total amount of rescue tramadol in 24 hrs | 24.265 ± 32.266 | 25.000 ± 27.524 | 0.920 |
| | **Group ISN (Mean ± SD)** | **Group SB (Mean ± SD)** | **p value** |
| BPT | 5.529 ± 1.022 | 8.559 ± 1.260 | 0.000 |
| | **Group ISN (Mean ± SD)** | **Group SB (Mean ± SD)** | **p value** |
| Patient Satisfaction | 2.088 ± 0.712 | 1.382 ± 0.652 | 0.000 |

Total amount of rescue analgesic i.e. Tramadol injections required in 24 hours in the two groups. The requirement of rescue injections in 24 hours was less in group ISN (24.265 ± 32.266) than group SB (25.000 ± 27.524). The difference was not statistically significant. Duration in group ISN was 5.529 ± 1.022 min and in group SB was 8.559 ± 1.260 min and this difference was statistically significant as p value is 0.000. The above mentioned values compare the satisfaction of patients in the two groups. It was 2.088 ± 0.712 in ISN group and 1.382 ± 0.652 in SB group and this difference was statistically significant as p value is 0.000.

Haemodynamic parameters (HR, systolic BP, diastolic BP, RR & $SpO_2$ ) were recorded at 0, 4, 6, 12 and 24 hours to record any incidence of bradycardia or hypotension. ANOVA test was used to compare all these variables over different intervals of time.

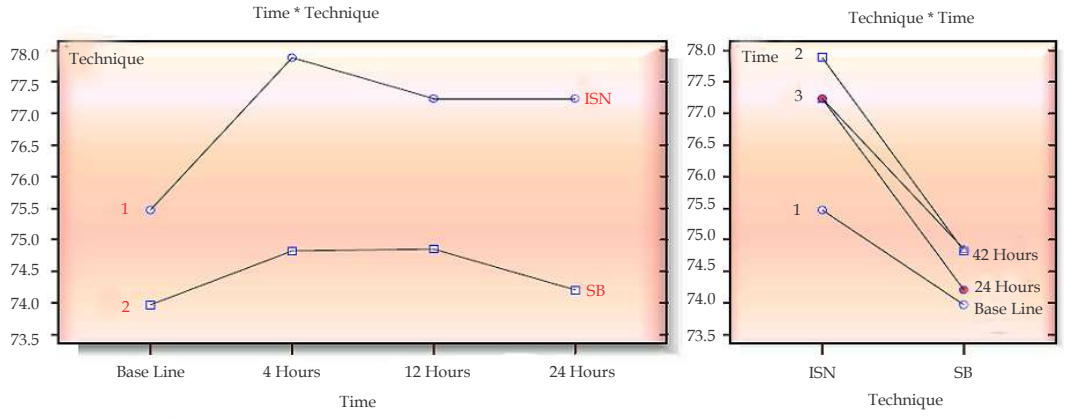


**Fig. 1:** ANOVA for heart rate

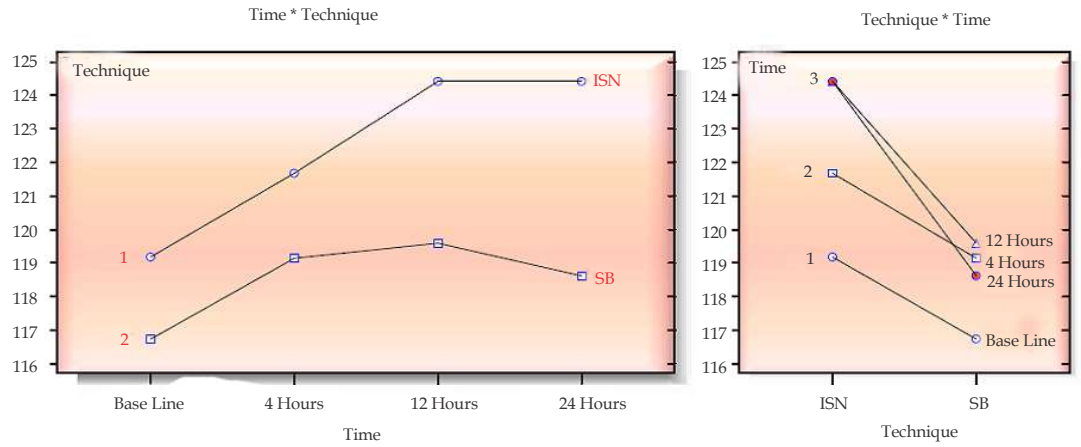


**Fig. 2:** ANOVA for systolic BP

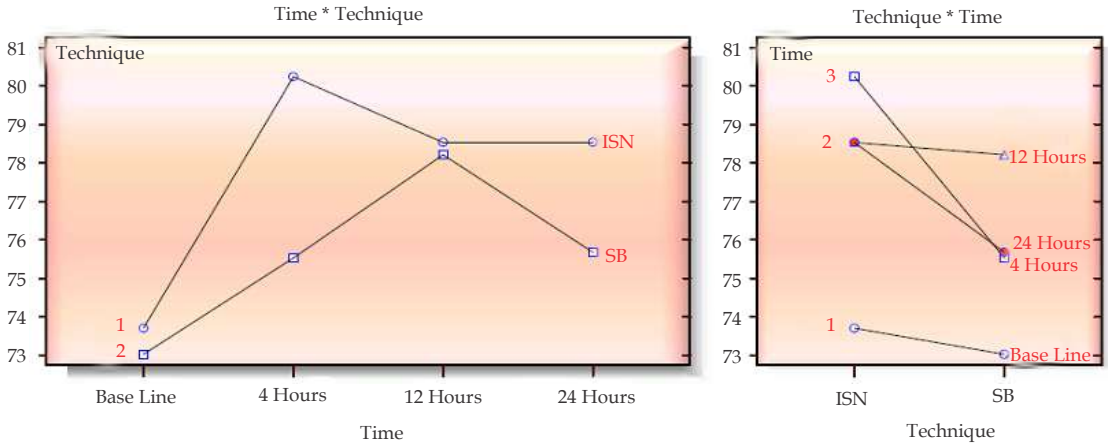


**Fig. 3:** ANOVA for diastolic BP

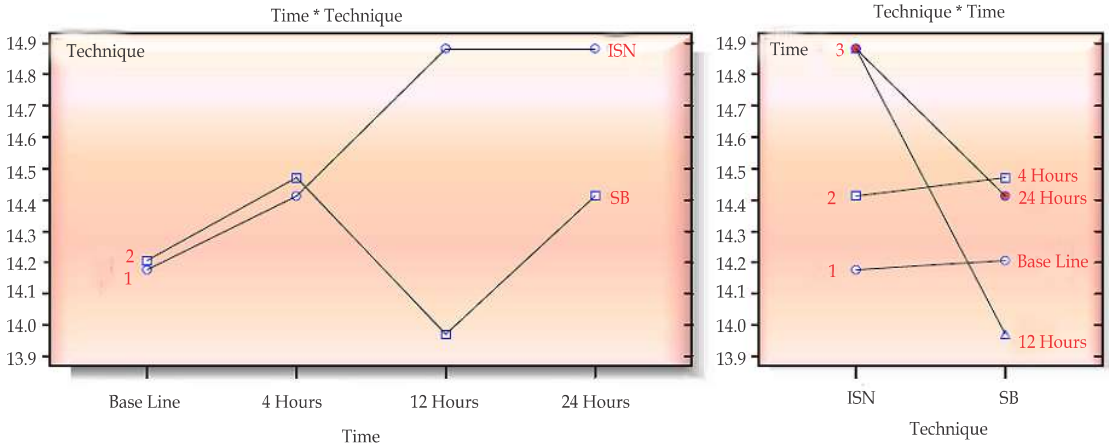


**Fig. 4:** ANOVA for respiratory rate

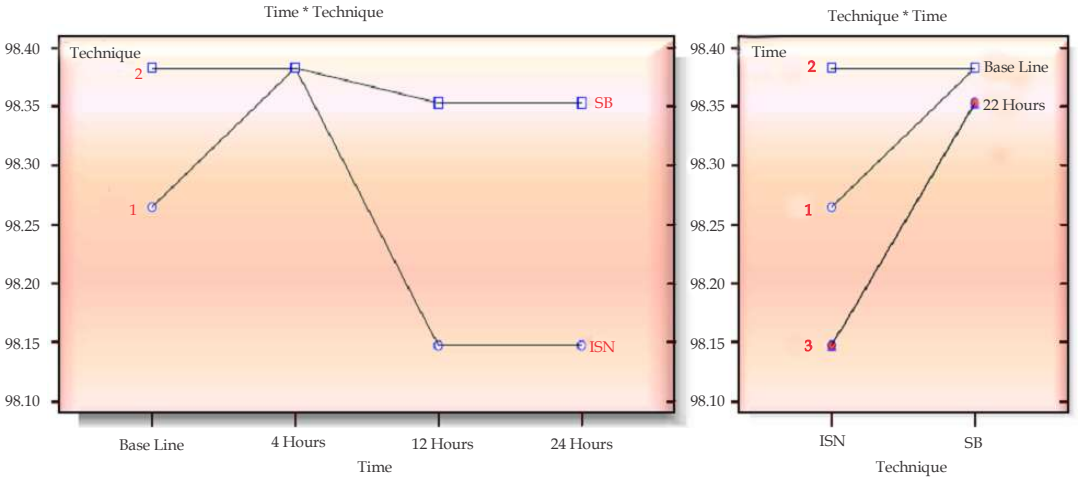


**Fig. 5:** ANOVA for $SpO_2$

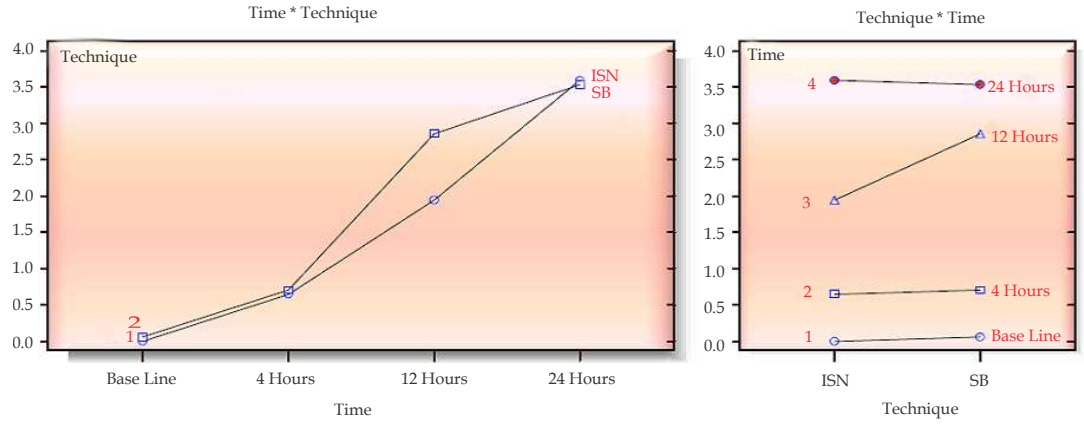


**Fig. 6:** ANOVA for numerical rating scale

There was no significant statisitical difference among the two groups in HR, Systolic BP, Diastolic BP, RR and $SpO_2$ during the first 24 hours. Numerical rating scale (NRS) scores were also recorded at 0, 4, 6, 12 and 24 hours. ANOVA was applied for statistical analysis of NRS scores in the two groups over the various time intervals. Data displayed on graph are mean NRS scores of that time interval. In our present study we found that NRS scores were initially higher in SB group but in the total 24 hour period post surgery, NRS scores of both the groups remained comparable. Differences in NRS scores of the two groups was statistically significant. (p=0.030). However, clinically this significance is not of much importance as during the first 24 hours post surgery, NRS scores remain less than 4 on a scale of 10.

Bromage scale scores were also recorded at 0, 4, 6, 12 and 24 hours. ANOVA was applied for statistical analysis of Bromage scores in the two groups over the various time intervals. Bromage scores were initially higher in ISN group indicating a denser motor block in ISN group but in the total 24 hour period post surgery, Bromage scores of both the groups remained comparable. Differences in Bromage scores of the two groups was statistically significant. (p=0.000). However, clinically this significance still remains debatable.

In ISN group of patients, there were incidences of Horners syndrome, hoarseness of voice, respiratory distress, pneumothorax, paraesthesia in arm and nausea & vomiting. While in SB group of patients there were procedural complications such as intravascular injection, haematoma, nausea & vomiting and LAST (local anaesthetic systemic toxicity).

## Discussion

In our study, the two groups were comparable in age, sex, weight, height and ASA physical grade. All this imply that there was no statistically significant difference in age, sex, weight, height

and ASA physical grading among both the groups with p= 0.140, p= 0.810, p = 0.191, p= 0.277, p= 1.000 respectively. Analgesic requirement i.e. Tramadol in first 24 hours was low in ISN than SB, still it was non significant (p= 0.920).

Onset of sensory block, onset of motor block was earlier in ISN than SB which were statistically significant (p= 0.000 & p= 0.000 respectively). Duration of sensory and motor block was more in SB at p values of 0.015 & 0.000 respectively, thus statistically significant.

However, block performance time was less and patient satisfaction was more in ISN which were also statistically significant (p= 0.000 & p= 0.000 respectively).

In our study, haemodynamic parameters (H.R, systolic BP, diastolic BP, RR and $SpO_2$) were recorded at 0, 4, 6, 12 & 24 hours. These parameters were all comparable in both the groups, thus statistically insignificant.

Numerical rating scale (NRS) scores were also recorded at 0, 4, 6, 12 and 24 hours. Numerical rating scale scores were initially higher in SB but in 24 hour period it were comparable with the scores of ISN. NRS scores were statistically significant p= 0.030. However, clinically this significance is not of much importance as during the first 24 hours post surgery, NRS scores remain less than 4 on a scale of 10 in both the groups.

Bromage scale scores were also recorded at 0, 4, 6, 12 and 24 hours. In our present study we found that Bromage scores were initially higher in ISN group indicating a denser motor block and in ISN group but in the total 24 hour period post surgery, Bromage scores of both the groups remained comparable. Differences in Bromage scores of the two groups was statistically significant. (p=0.000). However, clinically this significance still remains debatable.

*1. Onset of sensory block*

In our study, we observed that onset time was 3.500 ± 0.862 min in group ISN and 13.676 ± 2.142 min in group SB. (P =0.000 ). Onset time is the time from the completion of injection of the local anaesthetic to first loss of pinprick sensation in any of the dermatomes C5-T1. This shows that Interscalene nerve block provides faster sensory block than Shoulder block.

*2. Onset of motor block*

In our study, we observed that onset of motor block was earlier in study group ISN having the mean value of 5.941 ± 1.071 min and in comparison, the SB group had a mean value of 11.765 ± 1.793, which is statistically significant (p = 0.000). The total time required to achieve complete paralysis of the upper limb was considered as onset of motor block. This shows that Interscalene nerve block provides faster motor block than Shoulder block.

*3. Duration of motor block*

The duration of motor block, in our study was 11.559 ± 1.418 hours in group-ISN and 13.059 ± 1.757 hours in group-SB, which is statistically significant (p= 0.000). This shows that SB has a longer duration of motor block than ISN block.

*4. Block performance time*

The block performance time in our study was 5.529 ± 1.022 mins in group-ISN and 8.559 ± 1.260 mins in group-SB, which is statistically significant (p= 0.000). This shows that ISN block is performed in a shorter time than SB.

*5. Duration of sensory block*

In our study, we observed that duration of sensory block was longer in study group SB having the mean value of 13.882 ± 1.552 hours and in comparison, the ISN group had a mean value of 13.000 ± 1.348 hours, which is statistically significant (p = 0.015). This shows that SB provides a longer duration of pain relief in patients than ISN block but clinically it still remains insignificant.

*6. Duration of analgesia*

Pain was assessed using a standard Numeric Rating Scale (NRS) by an independent anaesthesiologist. Time for first request for postoperative analgesic (duration of analgesia) was noted when NRS score was 4. In our present study we found that NRS scores were initially higher in SB group but in the total 24 hour period post surgery, NRS scores of both the groups remained comparable. Differences in NRS scores of the two groups was statistically significant. (p=0.030). However, clinically this significance is not of much importance as during the first 24 hours post surgery, NRS scores remain less than 4 on a scale of 10. The duration of analgesia, in our study was 13.000 ± 1.348 hoursin group-ISN and 13.882 ± 1.552 hours in group-SB, which is statistically significant (p = 0.015).

Patricia Falcao Pitombo et al. [1], in his study found that the duration of analgesia was longer in Shoulder block group compared with Interscalene

nerve block group, 26.3 ± 7.7 hours versus 20.4 ± 6.8 hours respectively ( p=0.002).

This shows that Shoulder block group provided prolonged analgesia than Interscalene group in shoulder arthroscopic surgeries.

*7. Patient satisfaction*

In our study patient satisfaction was 2.088 ± 0.712 in ISN group and 1.382 ± 0.652 in SB group and this difference was statistically significant as p value is 0.000.

Hala E. Zanfaly et al. [10] in his study evaluated the patients with a questionnaire on a 10 point scale for pain. He found that patient satisfaction was higher in the Interscalene nerve block group of patients {9 (9-10)} than the Shoulder block group of patients {8 ( 8-9 )} ( p< 0.001).

*8. Requirement of rescue analgesic*

In our study we found that the requirement of rescue injections i.e Tramadol in 24 hours was less in group ISN (24.265 ± 32.266) than group SB (25.000 ± 27.524). The difference was not statistically significant.

Hala E. Zanfaly et al. [10] in his study found that the time to first analgesic request, was significantly longer in Interscalene group of patients {10 ( 9-10) hours} than Shoulder group of patients {9 (9-10) hours} (p< 0.001). He also concluded that the total mean morphine consumption (rescue analgesic) over 24 hours postoperatively was significantly higher in Shoulder block group {6 (6-7) mg} than Interscalene group of patients {6(5-6) mg} (p< 0.001).

*9. Haemodynamic variables*

In our study we found that there was no significant statisitical difference among the two groups in HR, Systolic BP, Diastolic BP, RR and $SpO_2$ during the first 24 hours.

*10. Adverse effects*

In our study, incidence of haematoma, nausea and vomiting (because of opioids), intravascular injection and LAST (local anaesthetic systemic toxicity) were reported in Shoulder block group of patients during the first 24 hours post surgery.

In the Interscalene group, almost all patients had ipsilateral diaphragmatic palsy because of the phrenic nerve involvement leading to respiratory distress or respiratory arrest. Also incidence of Horners syndrome due to the involvement of stellate ganglion, pneumothorax, hoarseness of voice because of recurrent laryngeal nerve involvement, paraesthesia in arm and nausea & vomiting (because of opioids), were reported.

All the complications were managed efficiently.

Waleed Abdalla et al. [11] in his study recorded more complications in Interscalene group i.e dyspnea (13.33%), Horner's syndrome (16.67%), hoarseness of voice (6.67%), major weakness of upper arm (53.33%), pain during needle entry (10%), and postoperative nausea and vomiting (PONV) (6.7%). On other hand fewer number of complications were recorded in Shoulder block group of patients pain during needle entry (16.67%) and postoperative nausea and vomiting (PONV) (13.33%).

Hala E. Zanfaly [11] et al. in his study found that the Shoulder block group of patients had the lowest incidence of complications compared with the Interscalene group. In Interscalene group, patients reported Horner's syndrome (36%) and weakness in the arm postoperatively (28%). The difference was significant (p < 0.001). He stated that the higher incidence of the potentially serious complications in Interscalene group was due to unpredictable spread of local anaesthetic to important adjacent neural structures such as phrenic and vagus nerves and the stellate ganglion.

Patrícia Falcao Pitombo et al. [1] in his study too reported complications with Interscalene group of patients such as unintentional injection of local anaesthetic into the vertebral artery, epidural space, spinal cord and brachial plexus injury; or adverse effects such as blockade of phrenic nerve, vagus nerve, recurrent laryngeal nerve, stellate ganglion, pneumothorax and transient neurological complications

Hence, Shoulder block can be considered in patients with Acute or Chronic respiratory distress [12], decreased pulmonary reserve [12], elderly patients, COPD patients [12] and in patients with absolute contraindication to any degree of phrenic nerve block which almost always occurs in Interscalene nerve block.

## Conclusion

This study shows that onset of sensory and motor time is earlier in Interscalene nerve block group. Duration of sensory and motor time is more in Shoulder block group. Performance time of the block technique is less for Interscalene approach than combined Suprascapular and Axillary

approach for brachial plexuses block. Patients were well satisfied in both groups with more adverse effects observed in interscalene nerve block group.

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*Original Research Article*

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# Efficacy of Transversus Abdominis Plane Block for Post-operative Analgesia Following Lower Segment Cesarean Section

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**Abstract**

*Background and Objective:* Transversus abdominis plane (TAP) block is a recently introduced regional technique that blocks abdominal wall neural afferents between T6 and L1 and thus can relieve pain associated with an abdominal incision of lower segment cesarean section. This study was conducted in 60 female patients to assess visual analogue scale (VAS) for pain score, requirements of rescue analgesics, patient's and surgeon's satisfaction score, side effects and complications if any. *Method:* After institutional review board approval and informed written consent from patients, Patients were randomly allocated to one of the two groups of 30 patients each. In Group T (TAP block with 15 ml of 0.25% Bupivacaine bilateral + Diclofenac Sodium 75 mg intravenous 8 hourly) given and in Group C (Diclofenac Sodium 75 mg Intravenous 8 hourly) given. The assessment of presence and severity of pain was done for 24 hours. At any point of time if VAS is ≥ 4, intravenously Paracetamol 1 gm was given to the patient as a rescue analgesic. *Result:* The mean VAS pain Score was comparable in each group and difference was significant statistically at 6, 8, 10, 12 hours ($p<0.05$). Requirement of rescue analgesia was reduced in patients of group T as compared to patients of group C. Hemodynamics remained stable in both the groups. *Conclusion:* TAP block as a part of multimodal analgesic regimen for post cesarean delivery provided reliable and effective analgesia in this study, and no complications due to the TAP block were detected.

**Keywords:** Transversus abdominis plane (TAP); Visual analogue scale; Diclofenac; Postoperative pain; Analgesia.

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## Introduction

Cesarean section is one of the most commonly performed surgical procedures [1]. It accounts for more than one-fourth of all births worldwide [2]. After cesarean delivery substantial postoperative discomfort and pain is usually described as moderate to severe by most patients [3]. The provision

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of effective postoperative analgesia is of key importance to reduce postoperative stress response and associated morbidity and accelerates recovery from surgery [4,5,6]. It facilitate early ambulation and infant care which includes breast feeding, care of baby and mother-baby bonding. Risk of thrombo-embolism is increased during pregnancy which is aggravated by immobility due to pain to the patients [7]. The analgesic regimen needs to meet the goals of providing safe, effective analgesia, with minimal side effects to the mother and her child [8].

Pain of cesarean section essentially has two components: somatic (from abdominal wall incision) and visceral (from the uterus). A significant component of pain experienced by the patients is derived from abdominal wall incision [9]. Systemic or neuraxial opioids are the mainstay for treating postoperative pain, as they are effective against both the components. However, they are associated with a number of undesirable side effects such as nausea, vomiting, pruritus, constipation, and respiratory depression [10,11].

Non- steroidal anti- inflammatory drugs (NSAIDS) like Diclofenac Sodium relieves visceral component of pain through their action via inhibition of Prostaglandin (PG) synthesis, but it is insufficient for relieving somatosensory pain of abdominal wall incision.

Transversus abdominis plane (TAP) block is a recently introduced regional technique that blocks abdominal wall neural afferents between T6 and L1 and thus can relieve pain associated with an abdominal incision [12,13].

TAP is a neurovascular plane located between the internal oblique and transverse abdominis muscles and nerves supplying abdominal wall pass through this plane before supplying anterior abdominal wall [14]. Therefore, if the local anaesthetic is deposited in this space, myocutaneous sensory blockade results [12,13]. The benefits of TAP block include the avoidance of neuraxial analgesic techniques and their associated risk, as well as a reduction in opioid consumption. As the side-effects of opioids are dose dependent, reducing postoperative opioid requirements could significantly reduce the incidence of opioid-related problems, such as sedation, nausea, vomiting, urinary retention, respiratory depression, delayed recovery of colonic mobility, and prolonged postoperative ileus [15,16].

This study was aimed to assess duration of post-operative analgesia, haemodynamic parameters & complications after lower segment cesarean section with primary objectives were,

1) Visual Analogue Scale (VAS) score to assess the quality of pain.
2) Frequency and duration of rescue analgesia required in 24 hours.
3) Patient's satisfaction score.
4) Surgeon's satisfaction score.
5) Time of ambulation & time of starting of breast feeding.

And the secondary objectives were,

1) Effect on hemodynamic variables like Heart Rate (HR), Mean Arterial Pressure (MAP), Oxygen saturation ($SpO_2$).
2) Side effects & Complications if any.

**Materials and Methods**

After Institutional Review Board (IRB) approval and informed written consent from the patient, this randomized controlled, double blind clinical study was carried out in sixty patients in tertiary care hospital from April 2016 to May 2017 with the following inclusion criteria.

1. Informed written consent for participation in study.

2. Age: 20-35 years.

3. Gender: Antenatal female patients scheduled for elective or non-urgent lower segment cesarean section.

4. ASA physical status I and II.

And the patients who refusing to give consent, have contraindications to Spinal anaesthesia like, local infection or sepsis at the site of Lumbar puncture, bleeding disorders, thrombocytopenia, space occupying lesions of the brain, anatomical disorders of the spine, hypovolaemia e.g. following massive haemorrhage, allergy to local anaesthetic drugs and NSAIDS, patient on any form of analgesics therapy and BMI ≥ 25 $kg/m^2$ were excluded from the study.

*Preoperative preparation:*

Patients were randomly allocated to one of the two groups of 30 patients each by computer generated random no.

Group T (n=30) – TAP block with 15 ml of 0.25 % Bupivacaine bilateral

+ Diclofenac Sodium 75 mg intravenous 8 hourly.

Group C (n=30) – Diclofenac Sodium 75 mg Intravenous 8 hourly.

In preanaesthetic preparation room, Standard monitoring for Heart Rate (HR), Non Invasive Blood Pressure (NIBP), Peripheral oxygen saturation ($SpO_2$) was established and baseline vital parameters was recorded then peripheral intravenous line was secured with 18G venous cannula.

*Premedication*

All patients were pre-loaded with Ringer Lactate (10 ml/ kg body weight) before starting the surgery and were received subarachnoid block with 2 ml of 0.5% heavy hyperbaric bupivacaine in L3-L4 Inter spinous space with 23 G spinal needle. Surgery was started after adequate sensory and motor block was achieved.

At the end of surgery, Patients in group T were received TAP block. After keeping the Patients in the supine position, the iliac crest was palpated from anterior to posterior until latissimus dorsi muscle insertion could be felt. Triangle of Petit was located (anteriorly bounded by external oblique and posteriorly by latissimus dorsi muscle and inferiorly by iliac crest). A 22 gauge 5 cm long blunt tip regional anesthesia needle was inserted in the triangle of Petit just above the iliac crest at right angle to the coronal plane until first resistance was felt. This indicated that the needle tip pierced external oblique muscle. The needle was further advanced gently in the same direction until "pop" sensation was felt, which signaled entry into facial plane between external and internal oblique muscles. Further advancement resulted in 2nd "pop" and this indicated entry into TAP. After careful negative aspiration 15 ml of 0.25% Bupivacaine (group T) was slowly injected in 5 ml increments. The block was given on the other side using the same method.

In all the patients, incision site was covered with a pressure dressing and was shifted to Post Anaesthetic Care Unit.

In both groups, the patients received standard analgesia according to obstetric department protocol consisting of Diclofenac sodium 75 mg intravenous 8 hourly, first dose was given at the end of surgery. (i.e. time 0).

The assessment of presence and severity of pain (both on rest and on passive Flexion of hip and knee) was done immediately after transfer to Post Anaesthetic Care Unit (PACU) and at 0, 1, 2, 4, 6, 8, 10, 12, 16, 20 and 24 hours after completion of surgery. Pain severity was measured by Visual Analog Scale (VAS 0=No pain, 10=Worst pain). At any point of time if VAS was ≥ 4, intravenously Paracetamol 1 gm was given to the patient as a rescue analgesic.

*Visual Analogue Scale (VAS) For Pain*

VAS is a continuous scale comprised of a horizontal (HVAS) or vertical (VVAS) line, usually 10 centimeters in length. It is self completed by the respondent, is asked to place a line perpendicular to the VAS line at the point that represents their pain intensity.

*Scoring:* Using a ruler, the score is determined by measuring the distance on the10 cm line. *Figure 1:*

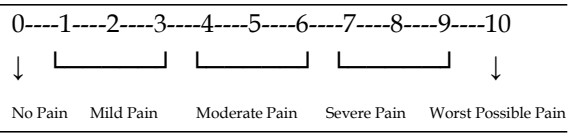


**Fig. 1:** Visual Analogue Scale (VAS) For Pain

Patient's and Surgeon's satisfaction score were shown in table below:

**Table 1:** Patient's and surgeon's satisfaction score

| Score | Poor | Good | Excellent |
|---|---|---|---|
| Patient's satisfaction score | 1 | 2 | 3 |
| Surgeon's satisfaction score | 1 | 2 | 3 |

*Statistical analysis*

Data collected was analysed as mean ± SD and % which ever applied. Statistical analysis was done by graph pad instat 3.0 software. Inter group comparison between two groups was done using the unpaired student T test for quantitative data and chi square test for qualitative data ($p < 0.05$ was considered as statistical significant).

## Observations and results

*Demographic profile*

*Age Distribution*

**Table 2:** Mean age distribution in each group

| Patient characteristic | Group T | Group C | p value |
|---|---|---|---|
| Age (years) (mean ± SD) | 24.43 ± 2.70 | 23.5 ± 2.95 | 0.2068 |

The mean age of the patients in Group T and Group C was 24.43 ± 2.70 years and 23.5 ± 2.95 years respectively and difference was not significant

statistically (p>0.05) (Table 2).

*Comparison of weight*

**Table 3:** Mean weight distribution in each group

| Patient characteristic | Group T | Group C | P value |
|---|---|---|---|
| Weight (kg) (mean ± SD) | 55 ± 5.24 | 53.93 ± 4.38 | 0.3964 |

The mean weight in Group T and Group C was 55 ± 5.24 and 53.93 ± 4.38 kgs respectively and difference was not significant statistically (p>0.05) (Table 3).

*VAS pain score*

**Table 4:** Mean VAS pain score comparison in each group

| Vas Score | Group T (n=30) (mean ± SD) | Group C (n=30) (mean ± SD) | p Value |
|---|---|---|---|
| 0 hr | 0.00 ± 0.00 | 0.00 ± 0.00 | 0.00 |
| 1 hr | 0.00 ± 0.00 | 0.03 ± 0.18 | 0.00 |
| 2 hr | 0.00 ± 0.00 | 0.73 ± 0.52 | 0.00 |
| 4 hr | 0.00 ± 0.00 | 1.26 ± 0.44 | 0.00 |
| 6 hr | 0.03 ± 0.18 | 1.9 ± 0.54 | <0.0001 |
| 8 hr | 0.1 ± 0.40 | 2.66 ± 0.95 | <0.0001 |
| 10 hr | 0.23 ± 0.56 | 1.2 ± 0.61 | <0.0001 |
| 12 hr | 1.16 ± 0.64 | 2.0 ± 0.45 | <0.0001 |
| 16 hr | 2.16 ± 1.02 | 2.46 ± 0.62 | 0.17 |
| 20 hr | 1.56 ± 0.50 | 1.7 ± 0.46 | 0.29 |
| 24 hr | 2.3 ± 0.46 | 2.3 ± 0.46 | >0.99 |

The mean VAS pain Score at 0, 1, 2, 4, 6, 8, 10, 12, 16, 20, 24 hours was comparable in each group and difference was significant statistically at 6, 8, 10, 12 hours (p<0.05) (Table 4).

*Rescue analgesics*

Group T- Test group

Group C- Control group

In group T, 6 patients required rescue analgesia at 16 hours while in group C, 8 patients required rescue analgesia at 8 hours, 1 patient required rescue analgesia at 10 hours, 1 patient required rescue analgesia at 12 hours, 1 patient required rescue analgesia at 16 hours (Fig. 2).

*Patient's satisfaction score:*

**Table 5:** patient's mean satisfaction score comparison in each group

| Patient's satisfaction Score | Group T (n=30) (mean ± SD) | Group C (n=30) (mean ± SD) | P Value |
|---|---|---|---|
| POD1 | 2.7 ± 0.46 | 2.5 ± 0.50 | 0.1177 |

Patient's mean satisfaction score at POD1 was comparable in each group and not significant statistically (p>0.05) (Table 5).

*Surgeon's satisfaction score*

**Table 6:** surgeon's mean satisfaction score comparison in each group

| Surgeon's satisfaction Score | Group T (n=30) (mean ± SD) | Group C (n=30) (mean ± SD) | p Value |
|---|---|---|---|
| POD1 | 2.86 ± 0.34 | 2.83 ± 0.37 | 0.7232 |

Surgeon's mean satisfaction score at POD1 was comparable in each group and not significant

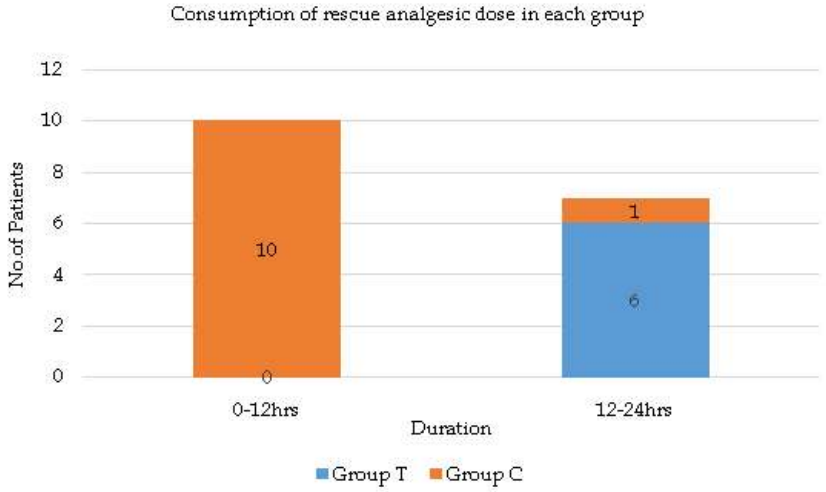


**Fig. 2:** Consumption of rescue analgesic dose in each group

statistically (p>0.05) (Table 5).

Comparison of Patients heart rate, mean arterial blood pressure and oxygen saturation at 0 min, 30 min, 1, 2, 4, 6, 8, 10, 12, 16, 20 and 24 hours was comparable in each group and difference was not significant statistically (p>0.05).

In our study there was no any side effects and complication noted after TAP block given.

## Discussion

Effective postoperative pain control is an essential component of the care of the surgical patient. Inadequate pain control, may result in increased morbidity or mortality [21,22]. Evidence suggests that surgery suppresses the immune system and this suppression is proportionate to the invasiveness of the surgery [23,24]. Good analgesia can reduce this deleterious effect. The advantages of effective postoperative pain management include patient comfort and therefore satisfaction, early mobilization, fewer pulmonary and cardiac complications, a reduced risk of deep vein thrombosis, faster recovery with less development of neuropathic pain, and reduced cost of care.

Postoperative pain should be cured to alleviate nociception induced responses, such as the endocrine, metabolic and inflammatory responses to surgery which activates autonomic reflexes with adverse effects on organ function and reflexes leading to muscle spasm [25]. The autonomic over activity results in increase in heart rate, peripheral vascular resistance, arterial blood pressure and myocardial contractility which culminate in increased oxygen consumption from increased cardiac work. The combination of increased myocardial oxygen demand and decrease oxygen supply can be detrimental in patients with coronary artery disease and may lead to myocardial ischemia and infarction [26]. Untreated or poorly treated postoperative pain increases incidence of nausea and vomiting. Increased sympathetic activity can lead to increased urinary sphincter tone and subsequent urinary retention [26,27[. The somatic pathway stimulation activates hypothalamic-pituitary axis which is followed by secretions of pituitary hormones. The limitation of movement caused by pain lead to marked impairment in muscle metabolism resulting in muscle atrophy, fatigue and delayed return to normal muscle function [26,27]. Psychological consequences due to inadequate pain relief include anxiety, fear, anger, depression and reduced patient satisfaction as well. So, it is a prime duty of an anaesthesiologist to provide postoperative analgesia to make patient more comfortable and relax after surgery.

Pain after cesarean section is usually described as moderate to severe by most patients [17]. The provision of analgesic regimen needs to meet the goals of providing safe, effective analgesia, with minimal side effects to the mother and her child [8]. Pain of cesarean section essentially has two components: somatic (from abdominal wall incision) and visceral (from the uterus). A significant component of pain experienced by the patients is derived from abdominal wall incision [17].

A multimodal analgesic regimen is most likely to achieve these goals. single-shot neuraxial analgesic techniques using long-acting opioids, or patient-controlled epidural opioid administration produce effective analgesia but they are associated with a frequent incidence of side effects like nausea, vomiting and pruritus which reduce overall patient satisfaction.

Non- steroidal anti- inflammatory drugs (NSAIDS) like Diclofenac Sodium relieves visceral component of pain through their action via inhibition of Prostaglandin (PG) synthesis, but it is insufficient for relieving somatosensory pain of abdominal wall incision.

Transversus abdominis plane (TAP) block is a relatively new technique used in a multimodal approach that decreases the need of post operative analgesia after lower segment cesarean section by relieving somato sensory component of pain [20].

The present study was conducted to compare efficacy of TAP block along with Diclofenac sodium and Diclofenac sodium alone following lower segment cesarean section to assess post operative analgesia. We also compared amount of rescue analgesia required, patient's and surgeon's satisfaction score, side effects and Complications.

There is no significant difference statistically between the groups with regard to age and weight (p>0.05).

While comparing analgesic efficacy, in the present study VAS score was comparable in both the groups. The result was comparable with the previous study done by Uma Srivastava et al., [17] (2015) who showed vas scores were significantly lower up to 24 hours in patients received TAP block with 0.25% bupivacaine compared to no TAP block with 75 mg diclofenac 8 hourly and intravenous tramadol and the difference was found significant (p < 0.0001). The study done by John G. McDonnell et al., [8] (2008) showed

TAP block with ropivacaine compared with placebo reduced postoperative visual analogue scale pain scores. The study done by Mayank Chansoria et al., [18] (2015) showed the mean vas score was less in patients received TAP block with ropivacaine compared to patients received 0.9% saline and the difference was found highly significant ($p<0.05$) compared to control group. The study done by Maitreyi Gajanan Mankikar et al., [19] (2016) showed VAS score was reduced after TAP block with 0.5% ropivacaine for the first 8–10 hour post-operatively as compared to patients receiving placebo block. In the present study VAS score was comparable in both the groups and difference was significant statistically at 6,8,10,12 hours ($p<0.05$).

While comparing rescue analgesic requirement, in the present study, the number of patients requiring rescue analgesics compared in both the groups. The study done by Uma Srivastava et al., [17] showed requirement of rescue analgesia was reduced in study group as compared to control group and difference was significant statistically ($p < 0.0001$). The study done by John G. McDonnell et al., [8] showed requirement of rescue analgesia was reduced in study group as compared to control group and difference was significant statistically ($p < 0.001$). The study done by Roshan John et al. [28] (2017) showed the difference in mean time to rescue analgesia was not statistically significant when both the groups were compared ($p>0.05$). In the present study, the number of patients requiring rescue analgesics compared in both the groups, in group T, 6 (20%) patients against 11 (36.6%) patients in group C required rescue analgesics, though difference was not significant ($p>0.05$).

While comparing patient's and surgeon's mean satisfaction score, in the present study patient's mean satisfaction score at POD1 was comparable in each group ($p>0.05$). Surgeon's mean satisfaction score at POD1 was also comparable in each group ($p>0.05$).

## Conclusion

This study concluded that, the Transversus abdominis plane block as a component of multimodal analgesic regimen provide reliable and effective post-operative analgesia, when combine with Diclofenac sodium relieves both somatosensory and visceral component of pain following lower segment cesarean section. It's also reduces requirements of rescue analgesia over 24 hours postoperatively. There were no any side effects and complication detected after TAP block given.

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# How well are we Prepared? - An Observational Study of Basic Life Support Knowledge amongst Doctors, Interns and Medical Students from Gujarat

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**Abstract**

*Background:* Successful Cardio Pulmonary Resuscitation for a good patient outcome requires teamwork and appropriate knowledge amongst health professional is necessary. Uniform protocols can be put in place only if hospital personnel have sound knowledge of Basic Life Support, which is achievable with regular training alone. We conducted this study to assess the knowledge and attitude among medical faculties, interns and students regarding BLS at our institute. *Methods:* An observational study was conducted at a tertiary care hospital from Gujarat, India. A self-prepared questionnaire was distributed to the participants and based on their responses; the percentage of knowledge and attitude regarding BLS was assessed. *Results:* Total 230 participants (94 faculties/senior residents, 36 junior residents/medical officers and 100 students/interns) were included in the study. For the purpose of analysis the faculty/SRs were divided in two groups based on their involvement in emergency services. The mean score (out of 15) for Faculty/ SR (Emergency) was 7.3, Faculty/ SR (Non- emergency) was 6.5, JR/ Mo was 8.1 and Student/ Intern was 8.0., indicating that Faculty/ SR (Non-emergency) scored significantly lower. Only one participant scored between 91-100%, five between 81-90%, 20 (8.7%) between 71-80%, 89 (38.69%) scored 51-70% and 115 (50%) scored less than 50%. Trained participants scored better versus those who were untrained (p = 0.0012). Years of clinical experience did not affect the knowledge scores (p = 0.3905). *Conclusion:* Overall knowledge of the doctors and students of our Institute was not satisfactory which warrants an Institutional policy for regular BLS training.

**Keywords:** BLS (Basic Life Support); CPR (Cardiopulmonary resuscitation); Questionnaire; Training; Knowledge; Attitude.

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## Introduction

Cardiac arrest is a very important critical event within and outside the hospital and has a high level of mortality [1]. Early initiation of Basic life support (BLS) – cardio pulmonary resuscitation (CPR) is known to improve the survival rates [2]. Successful CPR requires appropriate teamwork

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and hence knowledge of BLS amongst medical and paramedical staff becomes necessary. In developing countries like India, CPR training is not yet a routine practice and there are only few publications addressing the level of knowledge among the health care professionals in India [1,3,4]. Institutions where BLS training is not a mandatory part of job profile, the staff are unable to follow uniform protocols. We assessed the knowledge and attitude among medical faculties and students regarding CPR at our institute as a preliminary step to formulate a future plan for their regular training.

## Materials and Methods

### *Ethics consideration*

The study was conducted after Institutional Human Ethics Committee approval. Written and informed consent of the participants was taken. The information collected from all the participants was kept confidential.

### *Study design*

An observational study was conducted at a tertiary care teaching hospital from Gujarat, India.

### *Study setting*

This medical college and hospital is relatively new in its operations as it was started recently in the year 2011. The hospital is a 750 bedded public hospital with all speciality departments being operational. At present the college runs undergraduate medical course with yearly intake of 150 MBBS students since 2011.

### *Study population*

We planned to include all doctors and students from our medical college in this study. Our sampling frame included Faculties and Senior Residents (178), Junior Residents (48) and third MBBS students and Interns (180) from our college. Those on leave and / or unwilling to participate were excluded from the study. Hence, we were able to reach 120 Faculties and Senior Residents (SRs), 40 Junior Residents (JRs) and Medical Officers (MOs) and 126 students and interns who were distributed the questionnaire. Data was collected from on-duty, above mentioned participants from hospital and college during two months of study period. Participants were given a maximum of two reminders to return the filled questionnaire at two days interval through a phone call. The questionnaires which were not returned by this time or were incomplete were excluded from analysis. Therefore, the total participants available for study analysis were 94 faculty/SRs, 36 JRs/MO and 100 students /interns.

### *Study instrument*

A structured questionnaire was prepared to measure the knowledge and attitude of the participants based on American Heart Association Guidelines 2010/2015 [5]. The questionnaire consisted of 20 questions out of which 14 were Multiple Choice Questions and 6 short answer questions. We also collected the basic demographic details of the participants.

Face validation as well as content validation was done by three independent experts in this field for the prepared questionnaire and changes were made according to their suggestions in the second version of the questionnaire and this was sent to two participants from each group for pilot testing. Based on this the final version of the questionnaire was prepared.

### *Outcome Measures*

Primary outcome measures: Following analysis of the data, we assessed the following:

The percentage of knowledge score among faculties/senior residents, junior residents/medical officers and students/interns.

Difference in knowledge scores amongst BLS trained (within 5 years) vs not trained.

Effect of number of years of experience on knowledge scores.

Effect of frequent or infrequent exposure to patients requiring CPR on knowledge scores.

### *Data analysis*

The collected data was entered in Microsoft office excel 2007 and then statistical analysis was done using Open Epi Software Version 3.01. Descriptive analysis was done using percentage, mean and median as appropriate. Comparison between various groups was done using ANOVA and Chi square test. A p value of $< 0.05$ was considered statistically significant.

## Results

The following section presents the findings from the survey done among 230 participants

(94 Faculties/SRs, 36 JRs/MOs and 100 Students/ Interns). For the purpose of analysis the faculty/SRs were divided in two groups based on whether their department was involved in emergency services or not. Table 1 shows the basic demographic profile of the participants.

Among the faculty/SRs from emergency departments (Faculty E), only one third had received any prior training in CPR during the five years preceding the survey. Among non-emergency department (Faculty NE) less than one in five faculty members was trained in CPR. Among those who had received training majority had taken AHA or Non-AHA certified training with hands on component. Among the students who reported to have been trained, for majority this exposure was as part of their curriculum in anaesthesia. The self-reported level of involvement in CPR among these categories of study participants is also presented in Table 1. The knowledge assessment was done using 15 questions. Table 2 shows the average marks obtained by different categories of study participants. On applying one way ANOVA test, a significant difference was found among the mean marks obtained by participants of different categories. We applied post ANOVA Student-Newman-Keuls test for all pair wise comparisons. The marks obtained by the faculty from non-emergency departments were significantly lower than the Junior Residents and students on this test.

For ease of interpretation of the findings we first converted the obtained marks in percent. Then, we classified the obtained marks in three categories. Poor score was defined as <50% marks, Average score as 50-85% marks and Good score as >85% marks. Figure 1 shows the distribution of study participants as per their obtained marks across these categories. As can be seen from the figure very few study participants belonged to the good score category. Among the study participants scoring more than 50% marks, again, majority were in category of 51-60% marks. (Not shown as a separate range in figure 1).

We analysed whether the type of the prior training received, the years of experience or prior involvement in CPR were associated with good knowledge among study participants. Since the number of participants with good score category are very few, we have clubbed the average score and good score categories to simplify the interpretation of this analysis. Table 3 shows the findings of this analysis. The prior training experience significantly affected the knowledge score. As can be seen from the table, only a small proportion of participants with prior experience of AHA and Non-AHA certified training had poor score. Whereas almost half participants among those having training exposure in form of CME / lecture or no training exposure had poor score. With regard to the cumulative years of experience, there was a deterioration seen in knowledge score as the experience increased, though this was not statistically significant. Those having higher involvement in CPR had better scores but the difference was not statistically significant.

Important highlights of BLS includes rate of chest compression, ratio of compression to breathing in adults and paediatrics, location of hand placement and AED. Table 4 presents the details on proportion of the study participants who could correctly answer individual questions. Around 54% participants did not know the correct rate of chest compression.

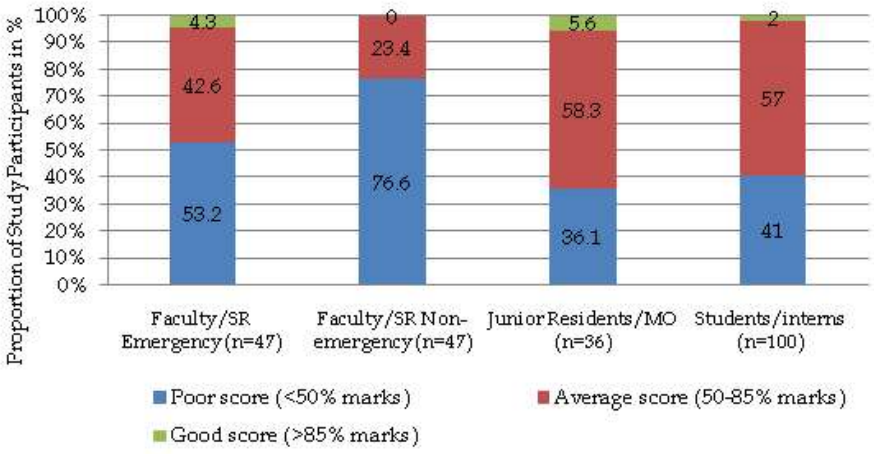


**Fig. 1:** Distribution of the study participants as per their category of obtained marks

For ratio of chest compression to breathing, 43% participants didn't know the correct ratio in adults and 76% didn't know the ratio in paediatric patients. Approximately 72% participants were not clear about the correct location of chest compression. 78% participants didn't know the step after AED (Automated External Defibrillator). These questions require special mention as they are utmost basic and vital if a person is involved in performing CPR.

The participants' responses on the questions measuring their attitude towards CPR are presented in table 5.

**Table 1:** Demographic profile of the study participants

| Demography | Faculty/SR Emergency (n=47) | Faculty/SR Non-Emergency (n=47) | Junior Residents/ MO (n=36) | Intern/ Students (n=100) |
|---|---|---|---|---|
| Age [Mean (SD) years] | 36.5 (6.4) | 35.4 (6.5) | 28.3 (6.2) | 22.3 (0.5) |
| Gender | | | | |
| Male (%) | 30 (63.8) | 22 (46.8) | 23 (63.9) | 31(31) |
| Female (%) | 17 (36.2) | 25 (53.2) | 13 (36.1) | 69(69) |
| Median years of experience | 12 | 9 | 2 | NA |
| Prior Training received in CPR (%) | 15 (31.9) | 8 (17) | 8 (22.2) | 60 (60) |
| Involvement in CPR (%) | | | | |
| Very frequent | 14 (29.8) | 1 (2.1) | 8 (22.2) | 3 (3) |
| Occasional | 27 (57.4) | 12 (25.5) | 23 (63.9) | 23 (23) |
| Only observed | 4 (8.5) | 15 (31.9) | 4 (11.1) | 56 (56) |
| Never | 2 (4.3) | 19 (40.4) | 1 (2.8) | 18 (18) |

*SD = Standard Deviation; NA= Not Applicable

**Table 2:** Marks obtained by study participants (out of 15)

| Category | Mean (+/-SD) | Statistical significance |
|---|---|---|
| Faculty/SR Emergency (n=47) | 7.3 (4.2 – 10.5) | F ratio = 5.2 * p= 0.002 |
| Faculty/SR Non-emergency (n=47) | 6.5 (4.4 – 8.6) | |
| Junior Residents/MO (n=36) | 8.1 (5.9 – 10.4) | |
| Students/interns (n=100) | 8 (6 – 10) | |

* One way ANOVA

**Table 3:** Analysis of predictors of good knowledge among the study participants

| | Fair score (>50%) | Poor score (<50%) | Statistical test |
|---|---|---|---|
| Training (duration of training) | | | |
| AHA certified (four hours with hands on practice) | 16 (84.2) | 03 (15.8) | $\chi2$= 13.5 * p= 0.0012 |
| Certified Training Non-AHA (two-four hours with hands on practice) | 4 (80) | 1 (20) | |
| CME / Lecture (one-two hours, without hands on practice) | 37 (54.4) | 31 (45.6) | |
| Non trained | 58 (42) | 80 (58) | |
| Experience (n=130) + | | | |
| <5 years | 22 (51.2) | 21 (48.8) | $\chi2$= 1.881 p= 0.3905 |
| 5-10 years | 15 (41.7) | 21 (58.3) | |
| >10 years | 19 (37.3) | 32 (62.7) | |
| Involvement in CPR | | | |
| No involvement | 14 (35) | 26 (65) | $\chi2$= 6.390 p= 0.0941 |
| Only observed | 42 (53.2) | 37 (46.8) | |
| Occasional | 42 (49.4) | 43 (50.6) | |
| Very frequent | 17 (65.4) | 09 (34.6) | |

* The categories of certified non-AHA training and CME/lecture were clubbed while calculating $\chi2$ test, + Students and interns are not included in this analysis, Numbers in bracket indicate row percent.

**Table 4:** Question-wise proportion of the study participants able to answer correctly (n=230)

| No | Question | Correct (%) | Incorrect (%) | Blank (%) |
|---|---|---|---|---|
| 1 | Full form of BLS | 221 (96.1) | 2 (0.9) | 7 (3) |
| 3 | First step in outside hospital arrest situation | 141 (61.3) | 87 (37.8) | 2 (0.9) |
| 4 | Rate of chest compression in adult CPR | 105 (45.7) | 118 (51.3) | 7 (3) |
| 5 | Ratio of chest compression to breathing in adult CPR | 130 (56.5) | 98 (42.6) | 2 (0.9) |
| 6 | Airway manoeuvre for unresponsive polytrauma patient | 105 (45.7) | 118 (51.3) | 7 (3) |
| 7 | About rescue breaths | 57 (24.8) | 168 (73) | 5 (2.2) |
| 8 | Chest compression to breathing ratio in pediatric CPR | 53 (23) | 168 (71.3) | 13 (5.7) |
| 9 | Depth of chest compression in adults | 172 (74.8) | 56 (24.3) | 2 (0.9) |
| 10 | Location for chest compression in adult | 65 (28.3) | 164 (71.3) | 1 (0.4) |
| 11 | Need to check carotid pulse | 201 (87.4) | 27 (11.7) | 2 (0.9) |
| 12 | Ventilation rate in intubated patient | 94 (40.9) | 123 (53.5) | 13 (5.7) |
| 13 | Full form of AED | 96 (41.7) | 88 (38.3) | 46 (20) |
| 14 | Step after AED | 50 (21.7) | 164 (71.3) | 16 (7) |
| 15 | Components of high quality CPR | 71 (30.9) | 151 (65.7) | 8 (3.5) |
| 16 | Manoeuvre for choking | 129 (56.1) | 100 (43.5) | 1 (0.4) |

BLS- basic life support, AED-automated external defibrillator, CPR-cardio-pulmonary resuscitation.

**Table 5:** Participant responses on the attitude questions (n=230)

| Attitudinal attribute | Number (%) |
|---|---|
| Attitude of the participants regarding mouth to mouth breathing* | |
| Prefer to use some barrier device | 126 (55) |
| Would stay back and let someone else to volunteer | 2 (0.8) |
| Willing to perform without any hesitancy | 85 (37.1) |
| Will just give chest compressions | 16 (6.9) |
| Proportion of participants expressing readiness to take a lead | 181 (78.7) |
| Proportion of participants recommending to include CPR as part of curriculum | 229 (99.6) |

*One student didn't give any answer for this question hence, n=229

## Discussion

All healthcare professionals should have the knowledge as well as skills for performing effective CPR. Effective CPR needs proper training [6], and that too regularly and repeatedly. Our institute is relatively new with just two batches of MBBS graduates and no post graduate students. No formal BLS training is mandatory before recruitment within the hospital for health care professionals. Moreover refreshment of their knowledge regarding BLS does not occur on a regular basis.

We conducted this questionnaire based study to assess current knowledge of BLS among doctors and students so as to make a future plan for training. It showed that overall knowledge of doctors and students of our institute was inadequate. Other studies done previously on different study population have similar conclusions [3,7–9].

In our study, only one (0.43%) participant obtained a score between 91-100% who was from intern/student group. Total five (2.17%) participants (two Faculty/SR E, two JR/MO and one intern/student) obtained a score in range of 81-90%. 20 (8.7%) participants scored between 71-80% marks. 89 (38.69%) participants scored 51-70% marks. Total 115 (50%) participants scored less than 50% marks.

In a study conducted at Quassim University, Kingdom of Saudi Arabia, published in 2014, the results were similar to our study. They assessed knowledge of BLS among clinical practitioners, medical students, interns and medical science students. They found only two responders (1.4%), scored 90–99%. Six responders (4.3%) scored 80–89%. Medical students achieved a higher score than students of allied health college [8].

In a study conducted in Iran, the authors assessed the knowledge of the general dental practitioners with a questionnaire and their practical CPR skills on a manikin by giving them a hypothetical cardiac arrest scenario. They concluded that the dental practitioners were lacking in appropriate knowledge and skills regarding CPR; 39% did not answer any question correctly and only 4% performed CPR properly on manikin [10].

A cross sectional study was conducted in Tamilnadu, India on 1054 medical practitioners, medical, dental, homeopathy students and nurses. No one had complete knowledge on BLS. Only two out of 1,054 (0.19%) had secured 80–89% marks, Ten out of 1,054 (0.95%) had secured 70–79% marks, Forty-three of 1,054 (4.08%) had secured 60–69% marks. 894 (84.82%) secured less than 50% marks. The study results showed that medical, dental and nursing students and faculty in the study group had poor knowledge of BLS [3].

In our study we collected information regarding the speciality of the faculties/SRs and made a broad division into the emergency and non-emergency group. Those who work in emergency branches, come across arrest scenarios more often. We found that knowledge of Non Emergency (NE) group of faculties was the lowest (mean 6.5, P value 0.002), the probable reason being that they are not involved in clinical emergency work in hospital and CPR/ BLS may not have been included in their post graduate curriculum. We couldn't find any other report of such comparison of knowledge of CPR among the emergency and non-emergency faculties in currently available data.

We collected information regarding participants' training status in the last 5 years. Total 91 participants out of 230 had received a prior training (39.56%). We also collected data regarding the type of training received. Various training that the participants mentioned were broadly classified into four groups; AHA certified training, non-AHA certified training, CME or Lecture and lecture with hands on training. 60% of students and interns reported having received training which was mostly lecture with hands on practice during their clinical posting in anaesthesia department. This may have helped them in attaining relatively higher mean knowledge score 8/15 (table 2). In our study the participants who had received prior training, received a significantly higher score as compared to those who were untrained (p value 0.0012) as shown in Table 3.

In a study conducted in Nepal by Roshana et al., in 2012, the participants were asked about any resuscitation training after their basic degree. The participants who had been trained in CPR in last five years had significantly more mean knowledge score than those who had been trained more than five years ago and those who had not been trained at all (no training vs. training <5 years, $p<0.001$; training <5 years vs. training >5 years $p=0.001$ [7].

Hence, it can be concluded that training in some form, whether structured or non-structured helps to build the knowledge base of an individual but due to limited retention capacity, there is definitely a need for re-training in BLS. Some studies show that the retention of this knowledge after training is between three to six months [11,12].

Partiprajak et al., 2016, showed that the training had an immediate significant effect on the knowledge, self-efficacy and skill of chest compression; however, the same significantly declined after three months post-training. Chest compression performance after training was positively retained for three months compared to the first post-test but was not statistically significant. So they emphasized on retraining programme after three months post-training [11].

Cooper S et al., 2007, studied impact of Immediate life support (ILS) training in a primary setting. They suggested there was a significant deterioration in skills six months after the ILS course ($p = 0.02$). However, skills measured six months after attending the course remained significantly higher than before the course ($p < 0.001$), hence it indicates, skills do not decrease to pre-course levels [12].

Sharma et al., 2012 studied Adult basic life support awareness and Knowledge among medical and dental interns after completion of their internship. Majority of the responses mentioned non availability of professional training as the prime reason for lack of BLS knowledge [1].

Ajjappa et al. conducted a study on effectiveness of BLS Training in improving the knowledge and skills among medical interns in Karnataka, India. The study was done amongst 91 interns who were previously not aware about the BLS skills. As per AHA schedule, the course book was provided to the participants and they were required to give a pre-test prior to the training. The BLS training was based on theoretical and practical teaching (2010 AHA guidelines). After the training, a post-test was conducted to re-assess their BLS skills theoretically as well as practically. The mean pre test score was 75.09%, with a minimum of 24% and maximum of 82%. The mean post test score was 92.7%, with a minimum of 90% and maximum of 95% [13].

Although formal practical training might be the best way to teach BLS, other means such as internet, electronic media or smart phone applications can be used to teach or reinforce knowledge of BLS. This training should be provided not only to the health care professionals but also to lay persons. A study conducted in Australia by Gavin et al. on high school students concluded that the online course improved participant's knowledge of

BLS significantly, but not their skills to perform CPR [14].

In our study, With regard to the cumulative years of experience, there was a deterioration seen in knowledge score as the experience increased, though this was not statistically significant. This observation warrants repeated training. Similar observation was found in another study where no association was found between knowledge of the participants and the duration of their clinical work (p=0.91) [7].

In our study, 99.4% of participants suggested inclusion of CPR training in curriculum. 76.9% were ready to take a lead in CPR. 47.8% preferred barrier device for mouth to mouth breathing, 12.5 % were ready to give just chest compression. Since there is a high motivation to take the lead, the health care professionals, in general, seem to be receptive for such atraining. Roshana et al observed that 95% of the participants favoured BLS to be included in the undergraduate curriculum, 82.6% of the participants were not reluctant to perform CPR, 64% preferred to use some type of barrier for mouth to mouth breathing, and 7% refused to perform that [7].

An important issue raised in our study by one of the participating faculties was that, not only should the BLS training be mandatory but it should also be sponsored by the Institute. In India, in most of the government institutes, various trainings are mandatory during the person's tenure, for example medical education training (MET), computer training etc. Equal importance should be given to achieving a high score in the BLS training and evaluation.

## Conclusion

Overall knowledge of BLS is very poor among the doctors and students (third MBBS) of our institute. Knowledge among the participants who were trained is better than untrained participants, so there should be some institutional policy regarding regular training sessions for students, doctors and paramedical staff for BLS. Retraining every six months should also be stressed upon for retention of knowledge.

*Limitation*

The practical skills to perform CPR were not assessed in this study.

*Future implication*

On the basis of the results of our study, we would like to formulate a plan for regular BLS training in our institute. A multicentric observational study can be conducted across the state or even country to know the current status of knowledge of BLS among the doctors to sensitize them regarding the need of BLS training and retraining.

Equal importance should be given to lay person's training for basic life support and first aid for example police personnel, ambulance drivers, teachers, high school students etc. Hence future plans can include community BLS training as a regular practice apart from in hospital trainings.

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# Low Back Ache, Methyl Prednisolone, Interferential Current, General Health Questionnaire

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**Abstract**

Low back pain is a symptom and not a disease which can lead to suffering, sadness and sleeplessness and hence physical limitation and disability. It's a universal problem the etiology of it can be viscerogenic, neurogenic, vascular, psychogenic, spondylogenic, ergonomic, obesity. The major pitfall is to miss a treatable cause in the rush to treat the symptoms. Kelly et al. 1956 postulated that inflammation of nerve root from the compression causes pain and neurological changes. Various modalities of treatment are available including injection therapy, current therapy and surgery with a conservative approach before going for definitive treatment. Epidural injection of local anesthetics (Viner 1925), steroids (Kepes and Duncalf 1960), interferential current therapy (Tidy 1968) were the various modes tried for treatment of symptoms – the aim being to reduce the inflammatory response, restore the electric equilibrium of the affected cell membranes. This present study was undertaken to break the cycle of pain and thus providing better life style to the patient which in turn helps early mobility relieving the muscle spasm and further reducing the pain. Patients with low backache of neurogenic and spondylogenic in nature were taken in consideration. Those patients who didn't respond to conservative approach were subjected to receive either epidural steroids (Methyl prednisolone) or Interferential Current therapy. Epidural Methyl Prednisolone 80 mg with Inj. Bupivacaine 0.125% and Inj. Buprenorphine 0.1 mg was used followed by NSAIDS orally for whole duration of treatment of 30 days. The other group received interferential therapy at a dose of 30 mv medium frequency at the maximum point of tenderness followed by physiotherapy and NSAIDS for a period of 90 days. The patients were observed for the effectiveness of both modalities of treatment in terms of symptom free life style, early rehabilitation and psychological well being using General Health Questionnaire both pre and post procedure.

**Keywords:** Low Back Ache; Methyl Prednisolone; Interferential Current; General Health Questionnaire.

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## Introduction

Low back pain (LBP) is a very common symptom which can affect about 80% of the population at least once in lifetime. Each year, 15–20% of the population will have back pain. It is usually a self-limiting condition but can go into chronicity in about 10% of the individuals. It is the most common

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cause of disability for people less than 45 years of age. Low backache which is acute and has red flag signs should be evaluated urgently to look for emergency and catastrophic causes. Chronic pain does cause physical disability and along with that the psyche of the patient is also affected.

Kelly 1956 postulated that inflammation of nerve root from compression causes pain and neurological changes. This is how the concept of using steroids to reduce inflammation came into picture. Various studies have come up for use of steroids in combination of local anesthetics and other adjuvant like opioids for the treatment of low backache given epidurally. In 1989, Goldberg et al studied the usefulness of 28 point GHQ in detecting the psychiatric co morbidity in patients with acute and chronic pain. This questionnaire is quite predictive in screening the patients for the psychological component if involved due to pain.

Use of interferential current (IFT) also has gained popularity in management of acute back aches and is better than other techniques like rubbing ice, ultrasound and early mobilization (Tidy 1968) and is of more value in patients having residual pain after healing (Flower [3] et al. 1982). Use of IFT in low back ache of varied etiology has proved its efficacy in many cases like fibromyalgia, herniated discs, myogenic pain and residual pain after healed fractures, surgery.

So proper examining and evaluating the patient for all aspects pertaining to cause of pain, associated factors and the psychological changes if any and then subjecting them to definitive therapy was the key approach to the patients in this study.

## Materials and Methods

60 patients from pain OPD having pain restricted to low back or radiating to lower limbs with or without paraesthesia were selected for this study. After thorough history for co existing diseases, physical examination pain mapping was done with a note of aggravating and alleviating factors. Radiological investigations if required were carried out. The patients were subjected to SLR (Straight Leg Raising) test and examined for Mobility Score (Table 1). The psychological component was assessed using GHQ-28 and if found significant were subjected to treatment with imipramines.

Patients were divided in two groups (n=30) each to receive epidural Methyl Prednisolone with Inj. Bupivacaine 0.125% 10 ml and Inj. Buprenorphine 0.1 mg (Group A) or IFT (Endomed 582) in the strength of 30 mA at point of maximum tenderness. (Group B).

Group A: The Epidural injection was given in operation theatre with 18G toughy needle under strict aseptic and antiseptic precautions. (inj. Methyl Prednisolone 2 ml + Inj. Bupivaine 0.125% 10 ml + Inj. Buprenorphine 0.1 mg diluted to 20 ml). Patients were kept under observation for one hour and monitored for vital parameter, relief in pain and at the end of one hour they were sent home with NSAIDS cover to be taken twice a day. They were called up for follow up after 10 days. During the follow up these patients were asked about the pain relief pointing to the VAS (visual analogue scale) (0-10 to suggest the relief). SLR was performed and improvement if any was noted. Second and third injections were given at interval of 10 days with complete NSAIDS analgesic cover in between. Regular follow-up of these patients was done monthly there after up to six months.

Group B: The patients were subjected to IFT in physiotherapy department using ENDOMED 582 and 30 mA current was delivered using rubber probe of multiple stimulator for 3 minutes under aseptic precautions. Patients were kept under observation for 10-15 minutes and then discharged with advice to come for follow up twice a week for first month, weekly for second month and fortnightly in the third month. These patients were asked to do strict physiotherapy of back extension, flexion, stretching and traction regularly. They were called up for follow up regularly for three months and even up to six months with good physiotherapy cover at home.

## Results

In this study of 60 patients with chronic backache being localized to low back with or without radiating to lower limbs were selected to receive either epidural steroids (Methyl Prednisolone) or Interferential current (n=30 each).

We had patients of varied etiology as shown in table 1 with few patients were under investigations for the cause of low back ache.

Table 2 shows symptomatic distribution of patients having either localized backache or radiating to both lower limbs with or without paresthesia. We divided the patients equally for the modality of treatment as per symptoms also.

Patients were mainly of the age group 20-60 years of either sex (statistically not significant). The mean weight of patients in Group A was about 53.66 ±

7.81 and that in group B was 49.7 ± 5.77 kg which was also in statistically not significant. Mostly patients from different economic class were selected including those having sedentary life style, moderate worker and labor class in both the groups (Table 3).

Table 4 shows the comparison of onset of analgesia on the first visit which was earlier for epidural injection as compared to interferential current. Subsequently on second to 30th day there was progressive improvement in pain relief in both groups with percentage improvement almost of same efficacy and when compared were statistically comparable.

Table 5 shows the improvement in the pain relief on subsequent visits of the patients in the follow up schedule (as discussed in methodology), it was seen that there was progressive pain relief in both the groups as compared to the previous visits and when compared with each other it was found to be statistically insignificant suggesting definitive improvement seen in both the groups. Going further for evaluation of pain relief we used VAS, SLR and observed Mobility of the patients with Modified Bromage Scale (Tables 5, 6, & 7 respectively). All values were suggestive of progressive improvement in the pain relief in both the groups clinically manifested as better patient's compliance, improvement in the SLR and increased mobility which was restricted due to the pain. We even observed the patients for any psychological component by subjecting the patients to the General Health Questionnaire (GHQ-28) [6] on first follow up visit. A GHQ score >8 was suggestive of disturbed psychological behavior. The score was less than 8 for majority of the patients in both the groups as shown in Table 8

**Table 1:** Showing Causative Faactors for Low Back Pain

| Causes | Group A | Group B | Total |
|---|---|---|---|
| PID | 14 | 03 | 17 |
| LCS | 12 | 02 | 14 |
| Post Laminectomy | - | 02 | 02 |
| Compression Fracture | 02 | - | 02 |
| Ankylosing Spondyitis | - | 04 | 04 |
| Myofascial Backache | - | 13 | 13 |
| Under Investigation | 02 | 06 | 08 |
| Total | 30 | 30 | 60 |

**Table 2:** Showing Symptom Wise Distribution of Patients

| Site of Pain | Group A | Group B |
|---|---|---|
| Low Back | 08 | 04 |
| Low Back Radiating to Lower Extremeties | 22 | 26 |
| Paraesthesia/ Numbness | 14 | 10 |

**Table 3:** Occupation of the Patients

| Type of Occupation | Group A | | | Group B | | | $X^2$ | p |
|---|---|---|---|---|---|---|---|---|
| | M | F | T | M | F | T | 1.18 | >0.05 NS |
| Category A Sedentary Work | 02 | 04 | 06 | 00 | 03 | 03 | | |
| Category B Moderate Work | 10 | 06 | 16 | 14 | 04 | 18 | | |
| Category C Labor | 06 | 02 | 08 | 06 | 03 | 09 | | |

**Table 4:** Onset of Pain Relief and Improvement (%) (Vas Score)

| Days | Group A Mean ± SD | Group B Mean ± SD | $X^2$ | p value |
|---|---|---|---|---|
| 1st | 40.3 ± 24.88 | 15.0 ± 4.43 | 12.177 | <0.05 S |
| 2-4 | 42.0 ± 14.5 | 25.3 ± 10.78 | 8.61 | >0.05 NS |
| 5-7 | 35.3 ± 12.27 | 29.48 ± 8.38 | 9.23 | >0.05 NS |
| 7-10 | 35.6 ± 12.57 | - | 9.38 | >0.05 NS |
| 10-15 | - | 40.0 ± 11.95 | 10.06 | >0.05 NS |
| 30th | - | 59.48 ± 15.83 | 8.32 | >0.05 NS |

except for 2 patients in Group A and 1 patient in group B. Adding Imipramine 150 mg o.d. to their treatment cart helped them to be more procreative and less depressed. This improvement in GHQ which became <8 after imipramine after the third follow up this improvement being more in Group B as compared to A was statistically significant.

Table 10 indicates the follow up of the patients after 3 and 6 months. We couldn't do the long term follow up with all the patients involved in the study. Looking to the percentage of patients coming for followup with improvement in the pain relief was more significant in Group B as compared to Group A. This indicates a better persistent effect of Interferential current therapy as compared to epidural injection. As the improvement was progressive the intake of oral analgesics also reduced with the time. Table 11 shows the increased working ability after the pain relief in both the groups which had been restricted due to pain. The pattern of improvement varies with the etiology of the pain. As table suggest the improvement was better with epidural injections in patients of PID, LCS, compression fracture whereas interferential current proved to be more effective in patients with myofascial pain syndrome, ankylosing spondylitis and post surgery. This suggests that epidural injection of Methyl prednisolone is better for chronic pain whereas the IFT is beneficial in alleviating acute pain.

**Table 5:** Percentage Improvement in Pain Relief After 1st, 2nd and 3rd Visit

| Days | Group A Mean ± SD | Group B Mean ± SD | $X^2$ | p value |
|---|---|---|---|---|
| 1st | 34.8 ± 12.42 | 40.0 ± 11.95 | 1.41 | >0.05 Ns |
| 2nd | 49.66 ± 14.47 | 45.12 ± 15.03 | 1.82 | >0.05 Ns |
| 3rd | 54.82 ± 17.14 | 59.00 ± 17.19 | 1.84 | >0.05 Ns |

**Table 6:** Mean Changes in SLR After Each Visit

| Days | | Group A Mean ± SD | Group B Mean ± SD | $X^2$ | p value |
|---|---|---|---|---|---|
| 1st | Rt | 2.00 ± 4.00 | 2.00 ± 4.00 | - | Ns |
| | Lt | 2.00 ± 4.00 | 2.00 ± 4.00 | - | Ns |
| 2nd | Rt | 3.33 ± 4.41 | 2.00 ± 3.68 | 0.68 | >0.05 Ns |
| | Lt | 2.67 ± 4.47 | 2.00 ± 5.40 | 1.17 | >0.05 Ns |
| 3rd | Rt | 4.00 ± 4.42 | 2.00 ± 4.00 | 0.26 | >0.05 Ns |
| | Lt | 4.00 ± 4.90 | 2.00 ± 4.42 | 0.77 | >0.05 Ns |

**Table 7:** Mean Changes in Modified Bromage Score for Mobility after Each Visit

| Days | Group A Mean ± SD | Group B Mean ± SD | $X^2$ | p value |
|---|---|---|---|---|
| 1st | 1 ± 0.82 | 1 ± 0.84 | 4.45 | >0.05 NS |
| 2nd | 2 ± 0.67 | 1 ± 0.87 | 4.12 | >0.05 NS |
| 3rd | 2 ± 0.71 | 2 ± 0.62 | 3.18 | >0.05 NS |

**Table 8:** Showing Evaluation of Psychological Component on First Visit

| GHQ Score (Total Score = 28) | No. of Patients | | |
|---|---|---|---|
| | Total | Group A | Group B |
| <8 | 57 | 28 | 29 |
| >8 | 03 | 03 | 01 |
| | 60 | 30 | 30 |

**Table 9:** Showing Percentage Improvement in Psychiatric Component after Imipramine

| Visit | Group A Mean ± SD | Group B Mean ± SD | GHQ Score | $X^2$ | p value |
|---|---|---|---|---|---|
| 1st | 19.64 ± 8.23 | 29.76 ± 9.04 | 5 | 6.04 | <0.05 S |
| 2nd | 30.12 ± 10.04 | 30.19 ± 8.12 | >8 | 7.21 | <0.05 S |
| 3rd | 39.83 ± 12.06 | 39.21 ± 10.38 | <8 | 7.74 | <0.05 S |

**Table 10:** Follow UP of Pain Relief after 3 and 6 Months

| Visit | No. of Patients | Group A | No. of Patients | Group B |
|---|---|---|---|---|
| 3 | 09 | 50% | 12 | 60% |
| 6 | 05 | 35% | 07 | 45% |

**Table 11:** Showing Evaluation of Treatment Efficacy

| Causative factor | No. of patients | Group A | Ability on activity | Work after injection | Group B | Ability on activity | Work after current therapy |
|---|---|---|---|---|---|---|---|
| PID | 17 | 14 | Sedentary | Exertional | 03 | Sedentary | Sedentary |
| LCS | 14 | 12 | Moderate | Exertional | 02 | Sedentary | Sedentary |
| Compression # | 02 | 02 | Sedentary | Moderate | 00 | - | - |
| Post Laminectomy | 02 | 00 | Sedentary | Sedentary | 02 | Sedentary | Moderate to hard |
| Myo Fascial Backache | 13 | 00 | - | - | 13 | Sedentary | Exertional |
| Ankylosing Spndylitis | 04 | 00 | - | - | 04 | Moderate | Exertional |
| Under Investigation | 08 | 02 | Moderate | Moderate | 06 | Sedentary | Sedentary to moderate |
| Total | 60 | 30 | - | - | 30 | - | - |

## Discussion

Low back pain (LBP) is a very common symptom which can affect about 80% of the population at least once in lifetime. This is even more in the industrial nations where over all life time prevalence of back pain exceeds 70%.

It can be acure (<7 days origin), sub acute (1 week to 3 months) and chronic (> 3 months) of duration. Anesthesiologists have been prime movers in this comparatively neglected field. Despite the frequency of this complain, back pain has been treated partly with total compliance seen in only 10-15% of patients.

The present study of sixty patients between 20-60 years of age with chronic low back pain not responding the conservative approach involved two modalities of treatment. Group A to receive epidural methyl prednisolone and Group B to receive IFT. Various drugs to be used epidurally have been changed from time to time expecting a good result. Injecting a good volume in epidural space helps to break in the adhesions, reduce inflammation, and reduce compression and covers spaces ascending even up to L1 level, Burns [1] (1985). Derby and White [2] (1986) explained the effectiveness of epidural steroids in low back ache of various causes where it was more effective in chronic causes like herniated disc but transient relief in spondylosis and functional backache. Flower RJ et al found that steroids decrease the inflammatory response by preventing prostaglandin production. It has even been found that combination of various drugs like opioids, saline, α-2 blockers as adujvants to local anesthetics and steroids prove to be more effective in relieving acute on chronic back ache even of the refractive nature (MT Bhatia).

Interferential Current on the other hand also has its role in management of low back ache which are more localized. Tidy (1968) [7] was of opinion that IFT is better than conventional modalities like USG, ice packs for treatment of low back ache. The stimulation and relaxation after the current application gives a sinusoidal effect triggering the production of endogenous opioids, encephaline which naturally inhibit the pain response. Yadav NS [8] suggested that co techniques like intermittent traction, biofeed re-education along with IFT do improve the efficacy.

Interferential Current Therapy with medium frequency has a long lasting pain relief cause of its programmable computerized unit where relaxation and contraction of muscles can be controlled in the 1:1 or 2:4 ratio specially the pain which is of acute nature or has localized. In our study, the patients of both the groups showed progressive improvement in pain relief which started early in the steroidal group given epidurally, but when followed up at long intervals was comparable to each other. A follow up at 3 months and 6 months showed that 5-10 patients in group A and 7-12 patients in group B had an acceptable pain relief up to 60%. Hence further management with NSAIDS was discontinued after 3 months whereas physiotherapy was continued in patient receiving IFT. All the patients were allowed to resume their routine activity avoiding strenuous work. 2 patients in Group A and one patient in group B were psychologically disturbed and tricyclic antidepressants (imipramine 150 mg o.d.) when given to them did show significant recruitment and compliance to the treatment for backache.

Thus, epidural treatment particularly with steroids constitute a successful modality in pain

management of cases where there is reasonable evidence that inflammation, irritation and compression of nerve roots is the cause whereas interferential therapy proves to be highly beneficial in relieving acute back pain by improving muscle tone and reducing muscle stiffness.

## Conclusion

Epidural methyl prednisolone – prolonged persistent effect – better for back aches with chronic causes like PID, LCS disc herniation.

Interferential current Therapy – consistent and effective by breaking the pain cycle helped by relaxation of the muscle spasms – helps in backaches with spondylotic changes and of localized nature.

Overall help in reducing the pain, improving psyche of the patient, early rehabilitation, early mobilization and thus living a near normal routine life.

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# Efficacy of Intraoperative Dexmedetomidine on Emergence from Anesthesia and on Recovery Characteristics after FESS (Functional Endoscopic Sinus Surgery)

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**Abstract**

*Context:* Emergence agitation is a post anesthetic phenomenon commonly associated with ENT surgeries. We studied the effects of maintenance infusion of Dexmedetomidine on prevention of Emergence agitation in adult patients undergoing FESS. *Aims:* To see the effects of intraoperative dexmedetomidine infusion on incidence of emergence agitation and recovery characteristics in terms of cough, pain and nausea vomiting scores. *Settings and Design:* A prospective, randomized, controlled, double blinded comparative study done at our institute. *Methods and Material:* One hundred patients undergoing FESS surgery were randomized into two groups. Group D (n=50) received dexmedetomidine infusion at a rate of 0.5 μg $kg^{-1}$ $hr^{-1}$ from induction of anesthesia until extubation, while group C (n=50) received volume-matched normal saline infusion. The incidence of agitation and recovery characteristics in terms of Cough score, Nausea vomiting score and Pain scores were evaluated in both groups. *Statistical analysis used:* Parametric data were analyzed using one-way ANOVA and the Student's paired t-test where appropriate. Non parametric data were analyzed using Chi-square test. A value of $p < 0.05$ was considered statistically significant. *Results:* The incidence of Emergence Agitation (Ricker sedation agitation score ≥ 5) was higher in group C compared to group D ($p < 0.001$). Recovery characteristics in terms of Cough score ($p=0.118$) and Nausea vomiting score ($p=0.589$) were similar in both groups, while Pain score was higher in Group C compared to Group D ($p<0.001$). Increase in Heart rate and MAP at emergence was more in Group C compared to Group D. Conclusions: Dexmedetomidine as an adjuvant to general anesthesia for FESS is an excellent drug to reduce Emergence agitation, provide better postoperative pain relief and also maintains stable hemodynamics at emergence.

**Keywords:** Dexmedetomidine; Emergence agitation; Nasal surgery.

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## Introduction

Emergence agitation is a post anesthetic phenomenon that develops in the early phase of general anesthesia recovery and is characterized by agitation, confusion, disorientation and possible violent behavior [1]. Though emergence agitation is observed more frequently in pediatric patients, its incidence in adults has been reported [2].

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Emergence agitation can lead to consequences such as self extubation or removal of catheters, which can cause serious complications such as hypoxia, aspiration pneumonia, bleeding and sometimes can cause severe injuries [3].

Previous studies have reported that ENT (ear, nose, and throat) surgical procedures have a higher incidence of emergence agitation which can be due to sense of suffocation during emergence from anesthesia caused by intranasal packing [3,4,5].

Dexmedetomidine is a selective α2-receptor agonist is known to reduce agitation from general anesthesia in children [6] and from ventilator weaning in ICU patients [7]. However, the data related to the effects of dexmedetomidine on reducing agitation from general anesthesia in adults is limited. Perioperative use of dexmedetomidine also decreases perioperative opioid consumption, post operative pain intensity and need of antiemetic therapy [8,9]. Therefore it is known to improve quality of recovery after surgery [10].

In this study, we hypothesized that intraoperative use of dexmedetomidine until extubation would reduce emergence agitation in adult patients undergoing Functional Endoscopic Sinus Surgery (FESS).

## Materials and Methods

After obtaining the Institutional Ethics Committee approval, 100 patients belonging to the American Society of Anesthesiologists physical status Classes I and II, aged between 18–60 years, belonging to either sex, scheduled for elective FESS under general anesthesia were enrolled into the study.

Patients with uncontrolled Hypertension, Diabetes mellitus, coronary artery diseases and any other renal, respiratory, hepatic or cerebral insufficiency were excluded from the study. Patients who were allergic to drugs used in the study and those receiving β-blockers were excluded from the study. Patients with history of any psychiatric disorders or drug abuse were also excluded.

The study was conducted over a period of 8 months in the Operation theater complex, Department of Anesthesia in our Institute. Study design was prospective, randomized, controlled, double blinded trial.

Primary aim of the study was to see the effect of intraoperative dexmedetomidine infusion on incidence of emergence agitation from anesthesia recovery after Functional endoscopic sinus surgery. Secondary goals were to study the effect of intraoperative dexmedetomidine infusion on recovery characteristics from anesthesia by evaluating cough score at emergence, Pain score and Nausea vomiting score in post anesthesia care unit (PACU) and also study its effect on intraoperative hemodynamics.

The sample size calculation was based on previous study, which showed the incidence of emergence agitation after ENT surgery was 55.4%. [3] A sample size was calculated based on these findings, with a value of $\alpha = 0.05$ and power $(1-\beta)$ of 0.80. It was calculated that 48 patients were required per group. We included fifty patients in each group (total of 100 patients) for better validation of results. Data values are presented as mean (standard deviation), median (range), or number (percentage). Parametric data were analyzed using one-way ANOVA and the Student's paired t-test where appropriate. Non parametric data were analyzed using Chi-square test. A value of $p < 0.05$ was considered statistically significant. The statistical software Windostat Version 9.2 was used for the analysis of the data.

After obtaining informed consent, 100 patients who met inclusion criteria were allocated randomly using a closed envelope technique into one of the two groups. The consort flow diagram is given in Figure 1. Patients were allocated to Group D (n = 50) or Group C (n = 50) to receive intraoperative dexmedetomidine or Saline infusion respectively. Patient and the anesthetists conducting the case were unaware of drug dilution and group allocation.

All patients were kept nil by mouth for at least 6 hours prior to surgery. On arrival to operation theatre, an intravenous line was secured and all patients were started on maintenance intravenous fluid 0.9 percent sodium chloride/ringer lactate. All patients were monitored with non-invasive blood pressure (NIBP), ECG (lead II and V5), and pulse oximeter ($SpO_2$), End-tidal $CO_2$ ($ETCO_2$), end-tidal anesthetic agent (EtAA) and MAC (Minimum alveolar concentration) throughout intra operative period.

All the patients were pre medicated with injection Glycopyrrolate 0.2 mg intravenously (IV). After pre-oxygenating the patient, they were induced with injection Fentanyl 2 $\mu g.kg^{-1}$ IV and injection Propofol in titrated doses to around 1.5-2 $mg.kg^{-1}$ IV and intubation facilitated with injection Atracurium 0.5 $mg.kg^{-1}$ IV. After induction, trachea was intubated with cuffed oral endotracheal tube of appropriate size. Patients were ventilated with

volume control mode and minute ventilation adjusted to maintain $EtCO_2$ between 33 and 38 mmHg. Oro-pharyngeal packing was done and patients were positioned for surgery. For topical vasoconstriction and local anesthesia, epinephrine soaked cotton was placed in the nasal cavity for 5 min. Group D received Dexmedetomidine IV infusion at rate of 0.5 $\mu g.kg^{-1}.hr^{-1}$ after induction of anesthesia and was continued until extubation, while the control group (Group C) received volume-matched normal saline infusion. Anesthesia was maintained with 50 percent oxygen in air, isoflurane concentration to achieve MAC of 1. Additional muscle relaxant was given as needed. All patients were given Paracetmol 1 gm IV as routine analgesic intraoperatively. Inj Ondansetron 4 mg slow IV was given as emesis prophylaxis half hour before end of surgery. At the end of surgery reversal agents (Glycopyrrolate 0.004 $mg.kg^{-1}$ and Neostigmine 0.05 $mg.kg^{-1}$) was given and then oral suction was performed and throat pack was removed.

Following these steps, inhalation agent was turned off (defined as 'time zero' in the emergence process) in both groups, and mechanical ventilation was then converted to manual ventilation with 100% oxygen at 8 litres/min. The patients were not disturbed, except by continual verbal requests to open their eyes. All other stimuli were prevented. Extubation was performed when patients started to breathe spontaneously and were able to respond to verbal requests. After extubation, dexmedetomidine or saline infusion was stopped.

Emergence is defined as the time interval from 'time zero' to 2 min after extubation. During emergence, the level of agitation was evaluated using the Ricker sedation-agitation scale and each patient's maximum agitation score was recorded accordingly: [11].

1- Minimal or no response to noxious stimuli.

2- Arousal to physical stimuli but does not communicate.

3- Difficult to arouse but awakens to verbal stimuli or gentle shaking.

4- Calm and follows commands.

5- Anxious or physically agitated and calms to verbal instructions.

6- Requiring restraint and frequent verbal reminding of limits.

7- Pulling of tracheal tube, trying to remove catheters or striking at staff.

Emergence agitation was defined as any score on the sedation-agitation scale ≥5. Dangerous agitation was defined as a sedation-agitation scale score=7.

Other parameters observed were Heart rate (HR), Systolic blood pressure (SBP), Diastolic blood pressure (DBP), Mean arterial pressure (MAP) at baseline, 10 min and 30 min after induction, at the end of surgery, at extubation, and at 2 min, 15 min and 60 min post extubation. Respiratory rate at extubation was observed in both groups.

Grade of cough during emergence was assessed using a four-point scale (0-no cough; 1-single cough; 2-persistent cough lasting less than 5 sec; and 3-persistent cough lasting ≥5 s or bucking).

In PACU, Pain score on numerical rating scale (NRS) for pain (0-no pain to 10-worst pain) was recorded and a Four point nausea and vomiting scale (0-no nausea; 1-mild nausea; 2-severe nausea requiring antiemetic; and 3- retching, vomiting, or both) was evaluated.

Desaturation ($SpO_2$ < 90%), laryngospasm and other complications if any were recorded during emergence and postoperative period. Heart rate less than 50 bpm was treated with 0.6 mg of IV Atropine. Mean arterial pressure (MAP) less than 60 mmHg was treated with IV Mephentramine 6 mg. Patients with pain score more than 4 were given Injection Tramadol 1 $mg.kg^{-1}$ as rescue analgesic and patients with Nausea vomiting score ≥2 were given Injection Dexamethasone 8 mg as rescue drug.

**Results**

The demographic data (Table 1) of the patients belonging to two groups were comparable and did not show any statistical significance.

Emergence Agitation was assessed in both the groups based on Ricker sedation agitation score (Table 2). It was observed that Emergence Agitation (score ≥ 5) was higher in patients belonging to Group C compared to patients belonging to group D which is statistically significant (p value <0.001). Similarly the incidence of Dangerous Agitation (score = 7) was observed in four patients in group C and in one patient belonging to group D. (Fig. 2).

Heart rate and MAP was compared between two groups at various intervals (Fig. 3). Their values at various intervals and P values between the two groups at those intervals are mentioned in Table 3. Their baseline values were comparable. The Heart rates and MAP values in group D were significantly lower compared to group C at various intervals from 10 min post induction to 15 min post extubation (p values in Table 3). However their

1 hour post extubation values were comparable and did not show significance.

Recovery characteristics were assessed in terms of Cough Score at emergence, Pain score and Nausea vomiting score in PACU between two groups (Table 4). We observed that there was no difference between Cough score (p= 0.118) and Nausea Vomiting score (p =0.589) between two groups, but the Pain score was more in group C compared to group D with a p value <0.001, which is statistically significant.

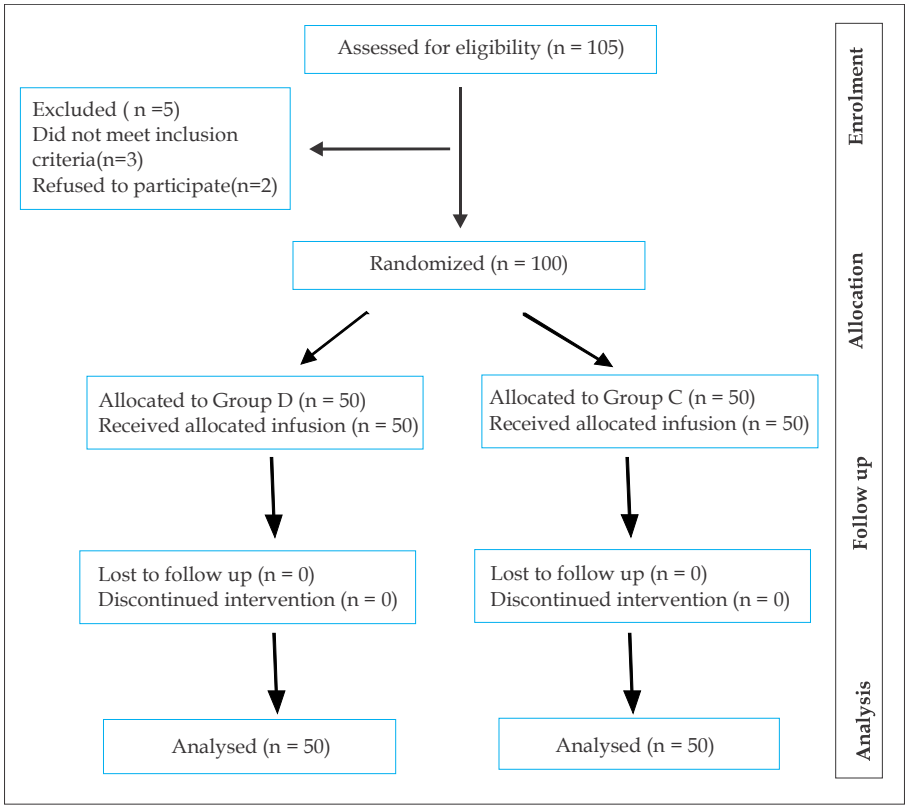


**Fig. 1:** Consort flow diagram of Randomization, group allocation and Number of patients analyzed

**Table 1:** Comparing patient demographics between two groups, (Std.Dev – Standard deviation)

| Variable | Group D Mean | Std. Dev. | Group C Mean | Std. Dev. | p value |
|---|---|---|---|---|---|
| Age | 32.160 | ± 10.082 | 32.240 | 9.584 | ± 0.968 |
| Sex | 1.360 | ± 0.485 | 1.340 | 0.479 | ± 0.836 |
| Weight kg | 68.000 | ± 10.467 | 69.240 | 10.344 | ± 0.553 |
| ASA Grade | 1.240 | ± 0.431 | 1.260 | 0.443 | ± 0.820 |

**Table 2:** Ricker Sedation Agitation score among two groups (n=Number)

| Ricker Sedation-Agitation score(Grade 1-7) | Group D (n=50) | | Group C (n=50) | |
|---|---|---|---|---|
| | Number | Percent | Number | Percent |
| 1-minimal or no response to noxious stimuli | 0 | 0 | 0 | 0 |
| 2-arouse to physical stimuli but does not communicate. | 1 | 2 | 0 | 0 |
| 3-difficult to arouse but awakens to verbal stimuli or gentle shaking | 15 | 30 | 4 | 8 |
| 4-calm and follows commands | 21 | 42 | 13 | 26 |
| 5-anxious or physically agitated and calms to verbal instructions | 9 | 18 | 25 | 50 |
| 6-requiring restraint and frequent verbal reminding of limits | 3 | 6 | 4 | 8 |
| 7-pulling at tracheal tube, trying to remove catheters or striking at staff | 1 | 2 | 4 | 8 |
| Total | 50 | 100 | 50 | 100 |

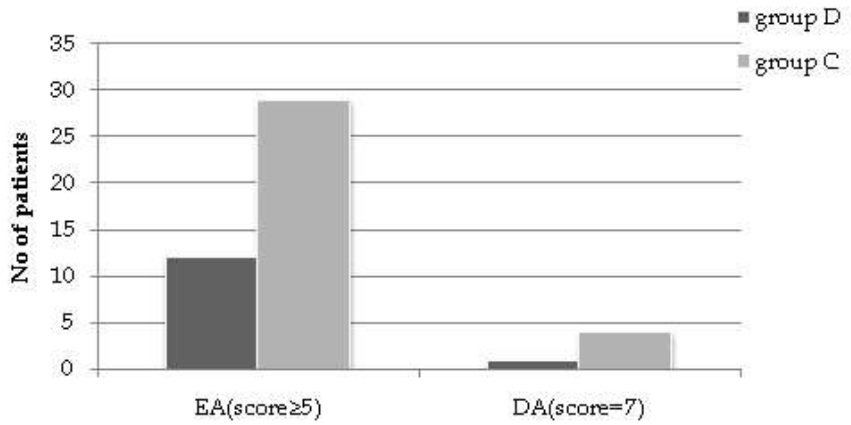


**Fig. 2:** Incidence of Emergence agitation and Dangerous agitation among two groups (EA –Emergence Agitation, DA- Dangerous Agitation)

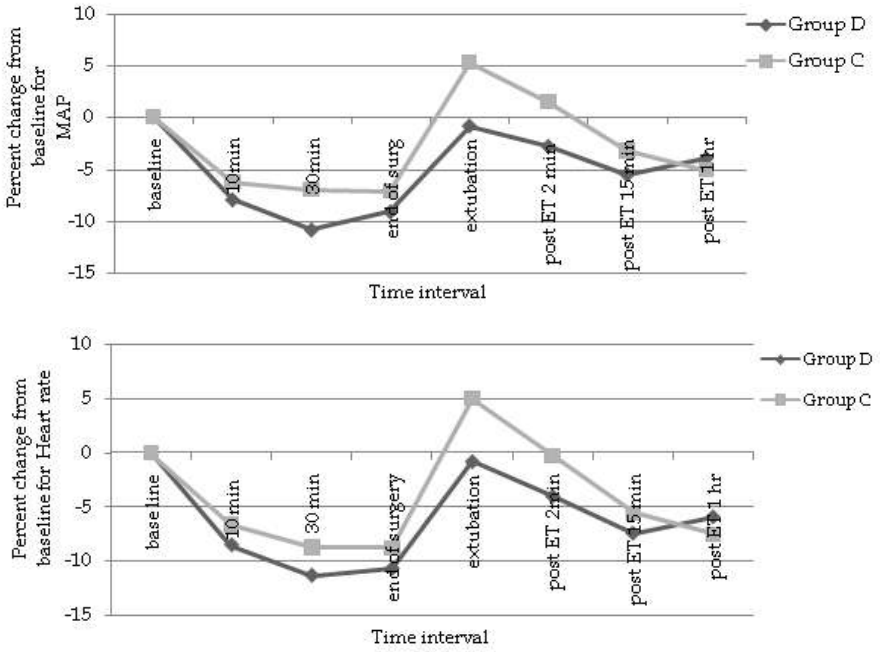


**Fig. 3:** Comparison of percentage change from baseline for Heart rate and MAP in two groups studied

**Table 3:** Comparing Mean Heart Rate (in beats/min) and Mean MAP (in mmHg) between two groups and P values

| | HR Group D | HR Group C | HR P value | MAP Group D | MAP Group C | MAP p value |
|---|---|---|---|---|---|---|
| BaseLine | 77.80 ± 6.57 | 78.46 ± 5.59 | 0.590 | 89.72 ± 5.70 | 90.2 ± 5.16 | 0.660 |
| 10 min | 71.18 ± 4.85 | 73.20 ± 4.56 | 0.035 | 82.62 ± 4.92 | 84.58 ± 4.56 | 0.042 |
| 30 min | 68.98 ± 4.07 | 71.56 ± 4.13 | 0.002 | 80.04 ± 4.34 | 82.920 ± 4.11 | 0.003 |
| End of Surgery | 69.48 ± 3.89 | 71.52 ± 4.09 | 0.012 | 81.58 ± 4.39 | 83.80 ± 4.92 | 0.019 |
| Extubation | 77.18 ± 5.36 | 82.34 ± 9.55 | 0.001 | 88.96 ± 5.15 | 94.96 ± 5.64 | <0.001 |
| Post ET 2 min | 74.68 ± 5.06 | 78.22 ± 6.68 | 0.004 | 87.20 ± 4.73 | 91.52 ± 4.87 | <0.001 |
| Post ET 15 min | 72.02 ± 4.80 | 74.02 ± 4.85 | 0.041 | 84.78 ± 3.64 | 87.28 ± 3.97 | 0.001 |
| Post ET 1 hr | 73.2 ± 4.50 | 72.48 ± 4.67 | 0.435 | 86.18 ± 4.03 | 85.60 ± 3.68 | 0.454 |
| μ Groupi | 73.06 ± 5.80 | 75.22 ± 6.83 | | 85.135 ± 5.66 | 87.60 ± 6.18 | |

**Table 4:** Distribution of Cough score, Pain score and Nausea vomiting score among both groups

| Variable | Group D | Std. Dev. | Group C | Std. Dev. | p value |
|---|---|---|---|---|---|
| Cough Score | 0.600 | ± 0.728 | 0.840 | ± 0.792 | 0.118 |
| Pain Score | 2.140 | ± 0.756 | 2.820 | ± 0.873 | <0.001 |
| Nausea Vomiting Score | 0.300 | ± 0.544 | 0.360 | ± 0.563 | 0.589 |

## Discussion

Emergence agitation is characterized by agitation, confusion, disorientation, and possible violent behavior leading to various complications [1]. Male gender, type of surgery, inhalation anesthetics, presence of tracheal tube and presence of urinary catheter are risk factors for postoperative agitation in adults. Emergence agitation is especially common after ENT surgery, where 55.4% of patients experienced agitation [3].

In our study, we expected patients undergoing FESS to have a higher risk of emergence agitation because patients required general anesthesia and packing of both nostrils after surgery. Demographic data like age, sex, weight and ASA physical status was comparable between two groups. Inducing agents and maintenance agents for anesthesia also remained same in both the groups except for the study drug. Urinary catheter was not used in any of the patients. Bilateral nasal packing was placed in all patients after surgery.

Dexmedetomidine, a selective α2-receptor agonist with sympatholytic, analgesic, and sedative properties is known to reduce emergence agitation without causing respiratory depression [12]. In previous studies involving use of dexmedetomidine for preventing emergence agitation, the protocols used for administration were diverse (one study used loading dose of 1 µg.kg-1 in 15 min followed by maintenance infusion of 0.7 µg.kg-1.hr-1 [6] and other study used only bolus dose of 1 µg.kg-1 [13]). It is known that hypotension and bradycardia are common after administration of the loading dose of dexmedetomidine [14]. In the present study, only continuous infusion of dexmedetomidine at 0.5 µg.kg-1.hr-1 was administered without loading dose to prevent complications associated with it.

Present study showed that the incidence of Emergence Agitation (Ricker sedation agitation score ≥ 5) was higher in patients belonging to group C compared to that of group D which is statistically significant (p value <0.001). These findings were similar to a study which concluded that use of dexmedetomidine as intraoperative infusion in nasal surgeries resulted in smooth emergence with better hemodynamic stability [15]. The incidence of Dangerous Agitation (scale =7) was seen in 1 patient belonging to group D and in 4 patients belonging to group C.

Our study showed that, intraoperative administration of dexmedetomidine reduced emergence agitation by 40% in group D. These results were comparable to study, which showed dexmedetomidine was effective in reducing emergence agitation by around 30% in adults [15].

Recovery characteristics in terms of Cough score at emergence, Pain score and Nausea vomiting score in PACU was observed in our study. We found that, Cough score at emergence was similar in both groups (p=0.118) and Nausea and vomiting score in PACU was similar in both groups (p=0.589). We observed in our study, that patients belonging to group D had less pain scores in PACU than those in group C which is statistically significant (p<0.001). This can be attributed to the analgesic property of dexmedetomidine [12]. Our findings were consistent with other studies, which showed that intraoperative infusion of dexmedetomidine, reduces perioperative analgesic requirements and post operative pain intensity [8,9].

It was observed that increase in Heart rate and MAP at extubation and 2 min post extubation was more in patients belonging to group C compared to group D. It was also observed that mean Heart rate and MAP at different intervals after induction up to one hour post extubation was always below baseline in group D which is desirable in nasal surgeries. This can be explained by the fact that dexmedetomidine has better hemodynamic stability due to its $\alpha_2$-agonistic action. Our findings were comparable to other studies, which observed that the increase in heart rate and MAP was much less and in turn more stable hemodynamics was achieved in group receiving dexmedetomidine [16,17].

As dexmedetomidine does not depress respiratory drive inspite of its sedative property and hence does not interfere with criteria for extubation. So, maintaining its infusion until extubation is considered safe [12]. It was observed that mean respiratory rates at extubation was similar in both groups (p value=0.463). There were no complications, including desaturation or laryngospasm, during emergence or while in PACU. Only two patients

in group D had significant bradycardia in the intraoperative period, though they did not have an episode of hypotension associated with the bradycardia. Both patients responded to single dose Injection of Atropine 0.6 mg IV.

Limitations of the study were that dose reduction effect of anesthetic agents when Dexmedetomidine was used could not be studied because we did not have a depth of anesthesia monitor. Our study population consisted of American Society of Anesthesiologists physical status Classes I and II. The organ protective effects of perioperative dexmedetomidine infusion would potentially be more pronounced in higher risk patients.

*Further Scope of Study:* Larger randomized studies need to be conducted to test the effect of intraoperative maintenance dose of dexmedetomidine infusion on emergence from anesthesia in adult patients. The use of depth of anesthesia monitors such as Bispectral Index or Entropy monitoring along with the use of dexmedetomidine intraoperatively could potentially reduce the anesthetic and analgesic requirements and their consequent side-effects.

## Conclusion

Our results allow us to conclude that the use of Dexmedetomidine as an adjuvant to general anesthesia for Functional Endoscopic Sinus Surgery is an excellent drug to reduce Emergence agitation and provide better recovery in terms of reduced postoperative pain and also maintains stable hemodynamics at emergence.

## Key Message

Prevention of Emergence agitation in patients undergoing nasal surgeries is very essential to avoid various complications associated with it. Maintainance dose of dexmedetomidine alone as an adjuvant to other general anesthetics is sufficient to prevent it along with other benefits of reducing post operative pain and also maintaining stable hemodyanmics at emergence.

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*Original Research Article*

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# Efficacy of Ultrasound-guided 3-in-1 Femoral Nerve Block for Pain Management in Elderly Patients Presenting to the Emergency Department with hip Fractures: A Randomized Controlled Trial

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**Abstract**

*Background:* Hip fractures in elderly is a common occurrence around the world and is associated with increased morbidity and mortality. Adding to this burden is the inadvertent pain management occurring frequently in the Emergency Department due to the fear of adverse effects of the administered pharmacotherapy. Hence, newly developed, safer Ultrasound guided nerve block modality is the cornerstone in the management of pain in these special populations attending the Emergency Department. *Objectives:* To determine the efficacy of Ultrasound (US)-guided three-in-one femoral nerve block as compared to intravenous opioids alone for analgesia in the elderly patients presenting to the Emergency Department (ED) with hip fractures. *Methods:* This was a single centre, pragmatic randomised controlled open-label trial. Older adults (age>55 yrs) with radiologically confirmed hip fractures were randomized into either of the two treatment arms: US-guided three-in-one Femoral Nerve Block plus Intravenous Morphine (FNB group) vs Intravenous Morphine alone Standard Care (SC group). Pain relief was measured with a 11-point numerical rating scale (NRS). Secondary outcome measures included the amount of rescue analgesia received and occurrence of adverse events (respiratory depression, hypotension, nausea/vomiting). *Results:* Thirty patients in each arm completed the study. There was no significant difference between the two groups with respect to baseline characteristics. There was a significant decrease in pain intensity over time in FNB group ($p<0.001$). The primary outcome measure, SPID over 1 hour was significantly greater in the FNB group [292.0(225-330) vs 106.5(45-195), $p<0.001$]. With regard to second outcome measure, parenteral opioid use, FNB group received significantly less parenteral opioid than those in the SC group [0.8 mg vs 9.5 mg, $p<0.001$]. *Conclusion:* US-guided femoral nerve block as an adjunct to intravenous opioids resulted in: 1) Significantly reduced pain intensity; 2) Decreased amount of rescue analgesia received; 3) Significantly reduced adverse events due to opioids. Hence, our study supports the routine use of US-guided three-in-one femoral nerve block for pain management in hip fractures in the ED.

**Keywords:**Femoral Nerve Block; FNB group; Numerical rating scale (NRS); SC group; Opioids.

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## Introduction

Hip fractures are very common, with an incidence of around 1.6 million cases/year worldwide [1]. This high incidence is expected to rapidly increase in the coming decades, driven by population aging [2,3]. It remains one of the most serious injuries that occur in older people [4-6] and is associated with mortality rate of 10% at one month, 20% at four months and 30% at one year [7]. Approximately half of patients who were previously functionally independent become partly dependent, while one third become totally dependent [8].

Hip-fracture patients are in severe pain upon arrival at the emergency department [9,10]. It is well known that control of pain in Emergency Department is often inadequate [11]. Persistent, unremitting pain may adversely affect the body's endocrine (overstimulation of hypothalamic-pituitary-adrenal-axis), cardiovascular (altered insulin and lipid metabolism – increased cardiovascular deaths), immune (adrenal exhaustion and decreased serum levels of glucocorticoids, including cortisol and pregnenolone), neurologic (anxiety, depression, delirium) and musculo-skeletal systems (muscle atrophy, neuropathies, contractures, arthropathies, myopathies and neuropathies) and require aggressive treatment of the pain as well as the resulting complications. Untreated pain is also associated with delirium [12,13]. And thus adequate treatment of pain is a primary goal and should be continued throughout until the patient is pain free [10].

A wide variety of options are available for the treatment of pain; NSAIDs for mild to moderate pain and opioids for severe pain. Despite having effective treatments available for both acute and chronic pain therapy, the treatment of pain can be difficult and is often one of the most challenging and frustrating aspects of the practice of emergency medicine [14-17]. Pain management for moderate pain is usually based on systemic opioids that have many side effects, [18] more commonly, nausea, vomiting and constipation and a few serious side effects like delirium, respiratory depression and death. These are more common particularly among frail, elderly populations [19].

Given the adverse effects of systemic opioids, regional anaesthesia has been advocated as an alternative and/or supplement to conventional treatment [20]. Femoral nerve blocks have been shown to be a safe, fast, and effective means of providing analgesia [21-26]. Use of ultrasound would be expected to improve the success rate of regional techniques and evidence does support this [27]. Anaesthesiology research also suggests that US-guided femoral nerve blocks may be superior to other nerve block techniques in regard to onset of action and amount of anaesthetic required [28,29].

Therefore we set out to determine if the patients who receive ultrasound-guided femoral nerve block have better pain relief when compared with the patients who received parenteral opioids alone. Secondary aim of this study was to determine if femoral nerve block reduces the total dose of parenteral opioids received. Lastly, we aimed to explore the incidence of adverse events.

## Materials and Methods

### *Study Setting*

This was a single centre pragmatic randomised controlled open-label trial, performed over a period of 18 months from October 2016 to March 2018 in a the Department of Emergency Medicine of a tertiary care, medical college hospital in South India with an annual ED attendance of 30,000.

### *Method of Collection of Data*

Patient's data was captured on a pre-approved proforma which included demographic details, details of nature and mechanism of injuries, time and place of injury, on-scene-time, pre-hospital time, factors influencing the initial treatment.

We included all patients presenting to the emergency medicine department with age >55 years; radiologically confirmed fracture neck of femur or intertrochanteric fracture or both; pain numeric rating scale >/= 5; normal lower extremity neurovascular examinations and willing to participate in trial.

In patients shifted from other hospital for elective procedure and continued care; patients with altered pain perception – unconscious patients, patients with altered sensorium, severe head injury; known international normalized ratio > 3.0; prior femoral arteryvascular surgery on the same side as the fracture; patients with other significant trauma; hypoxia (pulse oximetry < 92%); hypotension (systolic blood pressure < 100 mm Hg); known hypersensitivity to local anaesthetics ormorphine were excluded from the study.

*Study Design*

After a valid consent, older adults with confirmed hip fractures satisfying both inclusion and exclusion criteria were randomized using an Internet based program into either of the two treatment arms:

1. Ultrasound guided three-in-one Femoral Nerve Block plus morphine (FNB group)

Or

2. Standard of Care (SC group) - Intravenous (IV) Morphine alone

The dose of the IV morphine was at the discretion of the treating physician with a target of 50% reduction in pain or per-patient request.

*Procedure of Femoral Nerve Block*

All the procedures were performed by 5 Emergency Physicians out of which 2 were in the consultant grade and the other 3 were ultrasonography-trained Emergency Medicine residents.

The participant was made to lie in a supine position on a standard ED trolley. The US used was Sonosite M-Turbo. The skin was painted with povidone iodine solution and draped. On the side of the affected hip, the US probe was be placed 1 cm distal to the inguinal ligament. The probe was adjusted to identify the femoral vessels and nerve in cross-section (Fig. 1). The nerve was identified as a hyperechoic structure approximately 1 cm lateral to the pulsatileartery. With a 27-gauge needle, a local skin wheal of 2% lignocaine is made 2 cm lateral to the US probe. An 18-gauge needle is used to deposit 2% lignocaine at the site of the skin wheal. At this puncture site, a 22-gauge Whitacre noncutting spinal needle is introduced at a 45-degree angle in plane to the US probe. The needle was visualized by US throughout the procedure to ensure that vascular puncture is avoided and 25 mL of 0.25% bupivacaine injected along the nerve sheath through this needle. The spread of local anaesthetic administered, is confirmed by an expanding hypoechoic area in the correct fascial plane. Immediately following the injection, manual pressure is held for 5 minutes 1 cm distal to the injection site.

Pain intensity (Numerical Rating Scale) and secondary outcome measures (Blood Pressure, Pulse Rate, Oxygen Saturation, Respiratory Rate, amount of rescue analgesia) was measured at time 0, 15 min, 30 min and 60 min post procedure/IV morphine.

*Assessment of Pain Relief*

We used patient reported pain scores to assess pain relief. Participants reported their pain using an 11-point numerical rating scale (NRS) which ranged from 0 (no pain) to 10 (worst pain imaginable). Baseline NRS scores were measured and repeat measurements were recorded at 15, 30 and 60 minutes post procedure. Summed Pain-Intensity Difference (SPID) over 1-hour study period was taken as the primary efficacy variable and was calculated using the Pain-Intensity Difference (PID).

*Statistical Analysis*

Data was entered into Microsoft excel data sheet and was analysed using IBM SPSS Statistics for Windows, version 22.0 (IBM Corp., Armonk, NY, USA). Categorical data was represented in the form of frequencies and proportions. Chi-square test was used as test of significance for qualitative data. Continuous data was represented as means, standard deviations, medians, ranges, and percentages as appropriate. Independent t test was used as test as significance to identify the mean difference between the two quantitative variables. MS excel and MS word were used to obtain various graphs.A p-value of $<0.05$ was considered as statistically significant after assuming all the rules of statistical tests.

**Results**

Eighty two patients were screened for the study. Twenty two were excluded; 12 suffered polytrauma due to RTAs; 5 had concurrent head injury with GCS<15; 3 did not give consent for the study; 2 haddistal neuro-vascular deficits. Sixty patients were included in the trial. Thirty patients in each arm completed the study (Fig. 2). The study population aged between 67 – 83 years with a mean age of 75 years. 70% (n=42) of the study population constituted of females. The most common mechanism of injury was accidental falls; 80% (n=48) as opposed to road traffic accidents; 20% (n=12). 76% (n=46) of the patients sustained inter-trochanteric fracture of which 11% (n=7) had comminuted fracture. The rest 24% (n=14) of the population sustained fracture neck of femur, of which 7% (n=4) had comminuted fractures of the neck. Only 12% (n=7) of the subjects had concurrent head injury but none with GCS less than 15. There was no significant difference between the treatment groups with respect to age, sex, mechanism of injury, vital signs (baseline and at 1 hour) and type of fracture. Baseline characteristics are represented

in Table 1. There was no significant difference in pre-intervention mean NRS scores between the two groups (p=0.855)(Table 2).

There was a significant decrease in pain intensityover time in the patients belonging to FNB group ($p < 0.001$). NRS (which represents the mean pain-intensity) and PID over 1 hour are displayed in Fig. 3 and 4. The primaryoutcome measure of our study, SPID over 1 hour was significantly greater in the FNB group (Table 2). All the individuals in

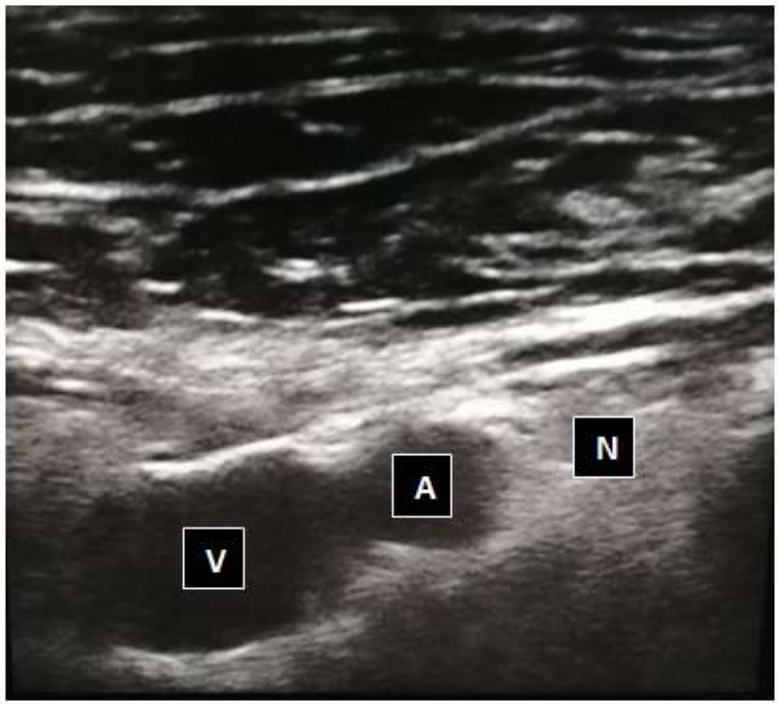


**Fig. 1:** Femoral Artery (A), Vein (V) and Nerve (N) as seen on ultrasonography

**Table 1:** Patient Characteristics and Vital Signs by Group Assignment

| Characteristics | FNB group | SC group |
|---|---|---|
| Age (yr) | 74 (55 – 88) | 77 (55 - 90) |
| Female sex, n (%) | 21 (70) | 21 (70) |
| Femoral neck fracture, | | |
| – Simple, n (%) | 4 (13) | 6 (20) |
| – Comminuted, n (%) | 3 (10) | 1 (3) |
| – Total, n (%) | 7 (23) | 7 (23) |
| Intertrochanteric fracture, | | |
| – Simple, n (%) | 19 (63) | 20 (67) |
| – Comminuted, n (%) | 4 (13) | 3 (10) |
| – Total, n (%) | 23 (77) | 23 23 (77) |
| Mechanism of injury | | |
| – Self-fall | 24 (80) | 25 (83) |
| – RTA | 6 (20) | 5 (17) |
| Vital signs | | |
| Initial SBP (mm Hg) | 153 (178 -134) | 156 (180 - 126) |
| Initial HR (beats/min) | 87 (72-114) | 91 (72-112) |
| Initial RR(cycles/min) | 17 (14-21) | 17 (14-20) |
| Initial $O_2$ sat (%) | 97 (91-100) | 95 (93-99) |
| 1 hour SBP (mm Hg) | 142 (126-170) | 147 (88-176) |
| 1 hour HR (beats/min) | 76 (62-103) | 84 (63-104) |
| 1 hour RR(cycles/min) | 15 (13-19) | 14 (6-19) |
| 1 hour $O_2$ sat (%) | 95 (81-100) | 92 (78-99) |

All data are represented as mean (range) unless otherwise specified.

FNB = Femoral nerve block; SC = Standard of Care; SBP = systolic blood pressure; HR = Heart rate; RR = Respiratory Rate; $O_2$ sat = Oxygen saturation.

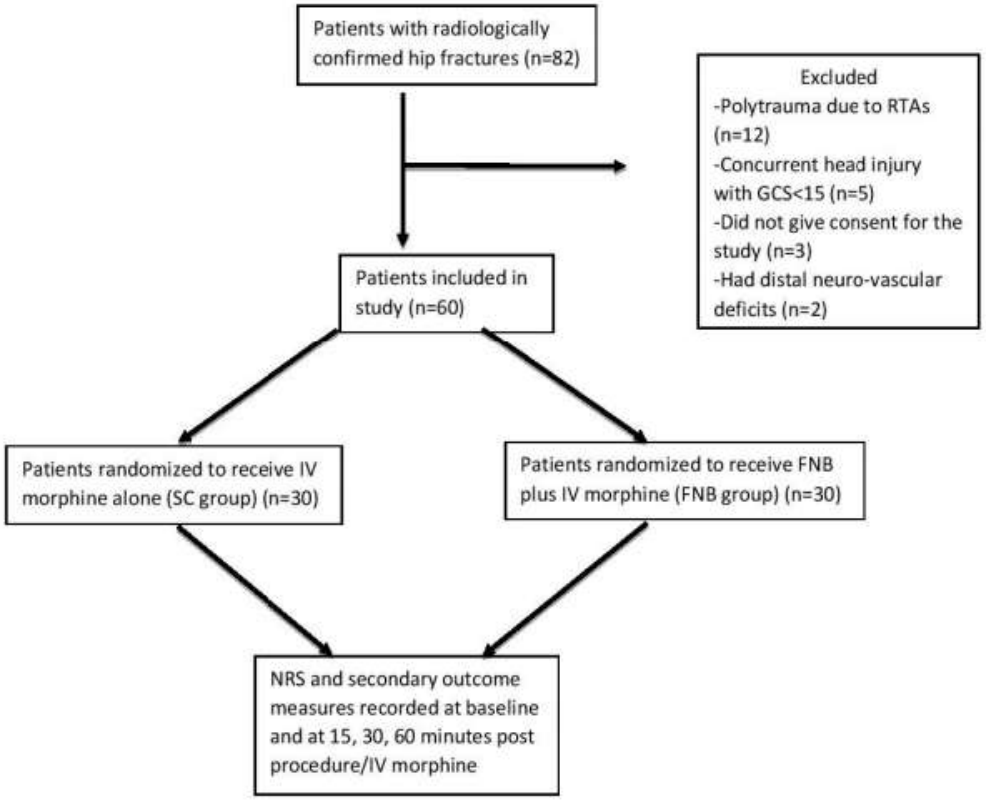


**Fig. 2:** Study flow diagram.

**Table 2:** Patient Outcomes by Group Assignment

| Outcome | FNB group | SC group | P value |
|---|---|---|---|
| Pain scores (NRS) | | | |
| – Baseline | 7.4 (6-9) | 7.4 (6-9) | 0.855 |
| – 1 hour | 2.0 (1-3) | 4.9 (3-7) | <0.001 |
| SPID | 292.0 (225-330) | 106.5 (45-195) | <0.001 |
| >33% SPID, n (%) | 30 (100) | 3 (10) | <0.001 |
| Parenteral analgesia | | | |
| – Pre-procedure morphine (mg) | 3.0 | 3.0 | |
| – Rescue morphine (mg) | 0.8 (0-6) | 9.5 (7-12) | <0.001 |
| Adverse events | | | |
| – Hypotension, n (%) | 0 | 4 (13) | 0.038 |
| – Respiratory depression, n (%) | 6 (20) | 10 (33) | 0.243 |
| – Nausea/vomiting, n (%) | 6 (20) | 9 (30) | 0.371 |

All data are represented as mean (range) unless specified otherwise.

FNB = femoral nerve block; SC = Standard of Care; NRS = numeric rating scale; SPID = summed pain-intensity difference.

Hypotension defined as systolic BP < 100 mm Hg; Respiratory depression defined as hypoxia (room air $O_2$ sat < 92%) or hypopnea (Respiratory Rate < 10 breaths/min) at any time during study period

*Statistically significant ($p < 0.05$).

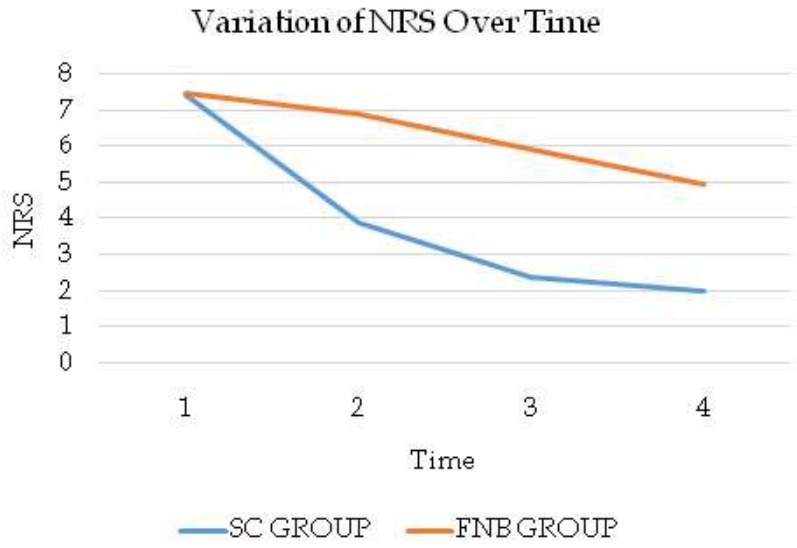


**Fig. 3:** Variation of Numeric Rating Scale (NRS) over time in FNB group and SC group

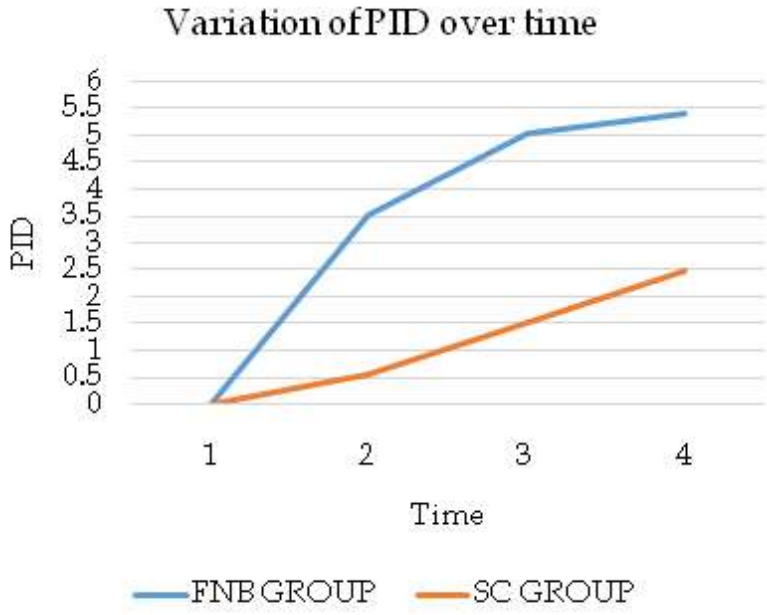


**Fig. 4:** Variation of Pain Intensity Difference (PID) over time in FNB group and SC group

the FNB group achieved at least 33% reduction in pain intensity over time; 93% (n=28) had at least 60% reduction. In the SC group, only 5% (n=3) individuals achieved a 33% reduction in pain.

With regard to our second outcome measure, parenteral opioid use, patients in the FNB group received significantly less parenteral opioid than those in the SC group (Table 2). Only 5 subjects in Femoral Nerve Block group received rescue analgesia over the study period as opposed to SC group, wherein all the subjects received additional doses of morphine. The range of rescue opioid doses ranged widely, between 7 to 12 mg in the SC group; 20% (n=6) of the participants received 7 mg, 50% (n= 15) received 9 mg and 30% (n=9) received 12mg of rescue dose of morphine. In the FNB group 10% (n=3) received 4 mg and 7% (n=2) received 6 mg of rescue dose of morphine.

However, in terms of occurrence of hypotension, the SC group had 13% (n=4) of participants who suffered hypotension at some stage of the study period which was statistically significant (p=0.038). With regard to occurrence of respiratory depression, and nausea/vomiting, there was no statistically significant difference between the two groups. No other adverse events occurred during the study period.

## Discussion

Several studies have used only Visual Analogue Scale (VAS), Numeric Rating Scale (NRS) and Pain-Intensity Difference (PID) for measurement of pain relief [21,22,30,31]. But Summed Pain-Intensity Difference (SPID) is a widely used variable to determine treatment response to analgesics over a relevant period of time and is a better tool as compared to PID. Hence, SPID over 1-hour study period was taken as the primary efficacy variable. It was calculated using the Pain-Intensity Difference (PID) at each time point. The PID was calculated as the change from baseline NRS for each measurement in time. SPID is the summation of the PID at each of the study time points and weighted using the amount of time since the prior assessment.

The benefit of using SPID is that it takes into account individual differences in baseline pain intensity, as well as time. SPID can also be reported as a percentage of maximum possible SPID (% SPID). Maximum possible SPID is the value that would be achieved if the patient were pain free (NRS = 0) for the entire study period. We were interested in the number of patients who achieved a % SPID of 33% [30]. A PID of 33% has been previously established to represent clinically important measurement in pain outcomes [32].

In our study there was a significant decrease in pain intensity over time in terms of decrease in NRS and increase in PID in the patients belonging to the FNB group ($p < 0.001$). Our primary outcome measure, the Summed Pain Intensity Difference over 1 hour was significantly greater in the FNB group ($p < 0.001$). The result of our study correlates with several similar studies done in the ED [21, 22, 30, 32].

Also patients in the FNB group received significantly less parenteral opioids ($p < 0.001$) than those in the SC group. All the patients in the SC group received several additional doses of morphine as compared to only five patients in the FNB group. Several similar studies also concluded that the amount of rescue analgesia received was more in the Standard of Care group as opposed to femoral nerve block group [30-35].

Among a few observed patients, the amount of intravenous opioid administered to the patients awaiting surgery increased as time to surgery increased. It was beyond the scope of the present study to examine the delays caused. However, it shows that FNBs were becoming in effective, long before most of the patients were being transferred to surgery. A better option would be to use a FNB infusion. Studies have identified several benefits of FNB infusions, including: patients being able to 'roll' onto their lateral side; continued use postoperatively for analgesia, allowing comfortable hip flexion; and improved respiratory function, as well as likely elevated mood [36].

With regard to occurrence of respiratory depression, nausea and vomiting, there was no statistically significant difference between the two groups which correlates with several other studies comparing the same secondary outcomes between the femoral nerve block and the Standard of Care groups [37-41]. Hypotension occurred in the standard care group which was statistically significant as compared to the FNB group. This was probably due to the repeated doses of intravenous opioids administered with an intention to achieve at least 50% reduction in pain. However, our study did not have enough power to detect differences in the adverse events. Further work is needed in this regard to characterize whether or not the use of FNBs affects the incidence of adverse events.

## Conclusion

Ultrasound-guided femoral nerve block as an adjunct to Standard of Care resulted in; 1) Significantly reduced pain intensity; 2) Decreased amount of rescue analgesia; 3) Significantly prevented the occurrence of hypotension when compared with SC group.

Hip fracture pain managed with intravenous opioids alone, proved to be inferior to femoral nerve block which as an adjunct to the standard care offered effective pain control in our study population,. Also, the femoral nerve block resulted in decreased quantity of the opioid received by the study group and hence had fewer chances of opioids related adverse effects. Hence, our data supports the routine use of femoral nerve block as an adjunct to morphine for pain management in the patients with hip fractures.

Future studies can examine additional outcomes with FNB like development of delirium, time taken for operative intervention, length of stay in the hospital. Subsequent studies can examine continuous (catheter based) femoral nerve block technique for a prolonged pain relief. There is also scope for studies on various other regional nerve blocks for injuries sustained by a patient with polytrauma.

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*Original Research Article*

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# A Comparative Evaluation of Respiratory Mechanics with I-Gel or ProSeal LMA as Airway Device in Laparoscopic Surgeries

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**Abstract**

*Objectives:* The study was designed to compare the respiratory mechanics of the patients with either I-Gel or ProSeal LMA as airway device during positive pressure ventilation while undergoing laparoscopic hernia repair surgeries. The other parameters compared are ease of insertion and airway trauma. *Methodology*: This randomized control study was conducted in our tertiary care hospital. 110 patients of ASA PS class 1-2 were randomly divided into 2 groups of 55 each. Premedication and anesthesia technique were standardized in both the groups. One group had PLMA as their airway device and the other group had I-gel as their airway device. We compared the respiratory mechanics (dynamic compliance, airway resistance and peak airway pressure) of these patients during positive pressure ventilation. The other parameters compared were ease of insertion and airway trauma. *Results*: I-Gel is a better device compared to PLMA in terms of dynamic compliance, peak airway pressure, airway resistance and ease of insertion was higher with PLMA. There was no significant difference in blood staining after removal of the device or trauma to lips, tongue and teeth between two groups. *Conclusion*: From our study, we concluded that I-Gel is a better device compared to PLMA in terms of dynamic compliance, peak airway pressure, airway resistance and ease of insertion. There was no significant difference in blood staining after removal of the device or trauma to lips, tongue and teeth between two groups.

**Keywords**: I-gel; Proseal LMA; Laparoscopic hernia repair; Compliance; Resistance; Peak airway pressure.

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## Introduction

With the advancement of technology compiled with availability of special instruments and high definition cameras, laparoscopic surgery has gained wide popularity among general population. It is also known as minimally invasive surgery and is the most important revolution in surgical techniques. Laparoscopic surgeries have been employed for procedures ranging across multiple

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surgical specialities. Its advantages compared to open procedures include less intraoperative pain and haemorrhage, fewer postoperative pulmonary complications and a shorter recovery time which allows a shorter hospital stay. Anaesthetic management of these cases poses special challenge due to creation of carbon dioxide pneumoperitoneum and extreme degrees of positioning with its own effect on cardiovascular system and respiratory system.

Laparoscopy is associated with problems such as increased risk for aspiration, endobronchial intubation, pneumothorax and gas embolism amongst many others. Endotracheal intubation and controlled mechanical ventilation were considered the gold standards in the anaesthetic management of laparoscopic procedures [1,2]. Hemodynamic response, chance of failed intubation, increased airway morbidity due to trauma are a few serious concerns with endotracheal tube (ETT). Introduction of supralaryngeal airway devices overcomes most of the above draw backs of ETT. Supraglottic airway devices have several advantages compared to endotracheal intubation, particularly avoidance of complications associated with endotracheal intubation, quick and easy placement of airway device itself, lesser requirement of neuromuscular blocking drugs as well as lower incidence of postoperative sore throat, dysphagia and dysphonia. Currently supralaryngeal airway devices (PLMA, I-gel) are increasingly being used instead of the tracheal tube for planned anaesthesia in laparoscopy.

Laryngeal Mask Airway ProSeal (PLMA) and I-Gel are supraglottic airway devices which produce high oropharyngeal seal pressure and have the facility for gastric decompression. I-Gel was developed in 2007 to overcome the limitations of PLMA. It utilizes a thermoplastic elastomer (Styrene butadiene styrene ethylene) which has a gel-like feel [3]. It was designed to create a non-inflatable anatomical seal of the pharyngeal, laryngeal and perilaryngeal structures while avoiding compression trauma. The shape, softness and contour accurately mirror the perilaryngeal anatomy to create the perfect fit so that compression and displacement trauma are significantly reduced. I-Gel also has a gastric drainage tube integrated to the upper tube for stomach decompression which reduces the risk of reflux and pulmonary aspiration. It has a semirigid stem to aid with insertion and prevents kinking. It has an intrinsic bite block to prevent compression of the airway tube, misplacement in the mouth and axial rotation. It is not necessary to insert fingers into the mouth of the patient for full insertion.

Pneumoperitoneum created during laparoscopic surgeries decreases thoracopulmonary compliance by 30% to 50% approximately. Reduction in functional residual capacity and development of atelectasis due to elevation of the diaphragm and changes in the distribution of pulmonary ventilation and perfusion from increased airway pressure can be expected. Decreased thoraco pulmonary compliance during pneumoperitoneum frequently results in increased airway pressures.

The study was designed to compare the respiratory mechanics of the patients with either I-Gel or ProSeal LMA as airway device during positive pressure ventilation while undergoing laparoscopic hernia repair surgeries. The other parameters compared are ease of insertion and airway trauma.

## Methodology

After obtaining ethical clearance and informed written consent, this randomized control study was conducted in 110 patients of ASA class I and II, aged 18-60 years, of both sexes scheduled for laparoscopic hernia repair at our hospital over a period of 2 years. Patients with anticipated difficult airway, mouth opening <2.5 cm, upper respiratory tract infections, BMI> 30 kg/$m^2$, risk of aspiration (full stomach, hiatushernia, GERD), restrictive/ obstructive lung disease, cervical spine deformity, cardiovascular diseases, neurological diseases were excluded from the study.

Each participant was randomly assigned either of the two groups.

Group 1-- ProSeal Laryngeal Mask Airway as the airway device.

Group 2 -- I-Gel as the airway device.

All participants in both groups were advised to fast overnight. Each of them was given Tab. Alprazolam 0.25 mg at bedtime on the day before surgery. Baseline vital signs (peripheral $O_2$ saturation, ECG, Pulse rate, Respiratory rate, Blood pressure) were noted before surgery. All patients were given Tab. Ranitidine 150 mg and Tab. Metoclopramide 10 mg 2 hrs before surgery. After preoxygenation, each of them was given Midazolam 1mg, Glycopyrrolate 0.2 mg and Fentanyl 1.5 mcg/kg intravenously. Anesthesia was induced with Propofol 2 mg/kg. Neuromuscular blockade was achieved with Vecuronium 0.1 mg/kg. Patients were ventilated using face mask with $N_2O$, $O_2$, Isoflurane before the insertion of the chosen airway device.

After mask ventilation appropriate sized airway device (Proseal LMA in Group 1 patients and I-gel in Group 2 patients) was inserted. Cuff of the Proseal LMA was inflated to 60 cm $H_2O$ and maintained at the same pressure throughout anaesthesia. In both groups the device was fixed by taping it to the chin.

An effective airway was confirmed by bilateral symmetrical chest movements, a square wave form of capnography and no audible leak of gases. If an effective airway could not be achieved the device was removed and reinserted and 3 attempts are allowed before failure of insertion is recorded.

*Ease of insertion* of the device was also recorded in both groups as easy/difficult/failure. Ease is defined as no resistance to insertion in the pharynx in a single manoeuvre. Difficult category includes those cases in which more than one attempt is needed for insertion/there is resistance to insertion in the pharynx. If more than 3 attempts were needed, the participant was excluded from the study.

For comparing *respiratory mechanics*, dynamic compliance, peak airway pressure and airway resistance were noted at different points of time—before pneumoperitoneum, 10mts after pneumoperitoneum, 30 mts after pneumoperitoneum and at the release of pneumoperitoneum.

*Compliance* of the lungs is defined as a change in lung volume per unit changein airway pressure ($\Delta V/\Delta P$). In mechanically ventilated patients dynamic compliance can be calculated as:

$C = V_t / (P_{peak} - PEEP)$

C = dynamic compliance; $V_t$– tidal volume; $P_{peak}$ –peak airway pressure; PEEP-positive end expiratory pressure.

*Airway resistance* is the pressure required to deliver a given flow of gas to the alveoli.It is expressed as change in pressure/flow.

$R = (P_{peak}-P_{plat}) /$Mean inspiratory flow rate.

After completion of the procedure anesthesia was discontinued. Blood staining of the device, tongue, lip and teeth trauma were noted.

## Observations and Results

*Statistical Analysis*

Quantitative variables were expressed in mean and standard deviation. Qualitative variables were expressed infrequency distribution. Between groups comparison of quantitative variables were analysedby 't' test and Chi-square test. A p value of 0.05 was taken as the level of significance. SPSS version 17.0 was used for statistical analysis.

Before pneumoperitoneum dynamic compliance was 44.20 ± 3.27 for PLMA and 50.67 ± 3.46 for I-Gel. 10 minutes after pneumoperitoneum, the value was 35.03 ± 2.93 for PLMA and for I-gel, it was 38.76 ± 2.77. 30 minutes after pneumoperitoneum, dynamic compliance was 36.81 ± 2.16 for PLMA and 40.87 ± 3.11 for I-gel. After release of pneumoperitoneum, dynamic compliance improved to 41.09 ± 2.61 for PLMA and 46.48 ± 3.67 for I-gel. Thus, dynamic compliance was found to be higher with I-gel at all points of study (before pneumoperitoneum, 10 mts after pneumoperitoneum, 30 mts after pneumoperitoneum and at the release of pneumoperitoneum) with a p value <0.001 (Table 1).

Airway resistance was slightly higher in PLMA group than I-gel group at all points of study, but was not statistically significant (Table 2).

Before pneumoperitoneum peak airway pressure was 20.38 ± 1.67 for PLMA and 18.58 ± 1.66 for I-gel. 10 minutes after pneumoperitoneum, the value was 24.20 ± 1.98 for PLMA and for I-gel, it was 22.76 ± 2.19. 30 minutes after pneumoperitoneum, peak airway pressure was 23.42 ± 1.77 for PLMA and 21.45 ± 2.12 for I-gel. After release of pneumoperitoneum, peak airway pressure was 21.51 ± 1.61 for PLMA and 19.75 ± 1.87 for I-gel. Peak airway pressure was significantly higher in PLMA group than I-gel group at all points of study with a p value <0.001 (before pneumoperitoneum, 10 mts after pneumoperitoneum, 30 mts after pneumoperitoneum and at the release of pneumoperitoneum) with a p value <0.001 (Table 3).

**Table 1:** Dynamic Compliance

| Dynamic Compliance | Proseal LMA (N=55) | | I-Gel (N=55) | | t | p |
|---|---|---|---|---|---|---|
| | mean | sd | Mean | Sd | | |
| Before pneumoperitoneum | 44.20 | 3.27 | 50.67 | 3.46 | -10.086 | <0.001 |
| 10 minutes after pneumoperitoneum | 35.03 | 2.93 | 38.75 | 2.77 | -6.841 | <0.001 |
| 30 minutes after pneumoperitoneum | 36.81 | 2.16 | 41.87 | 3.11 | -9.898 | <0.001 |
| After release of pneumoperitoneum | 41.09 | 2.61 | 46.48 | 3.67 | -8.882 | <0.001 |

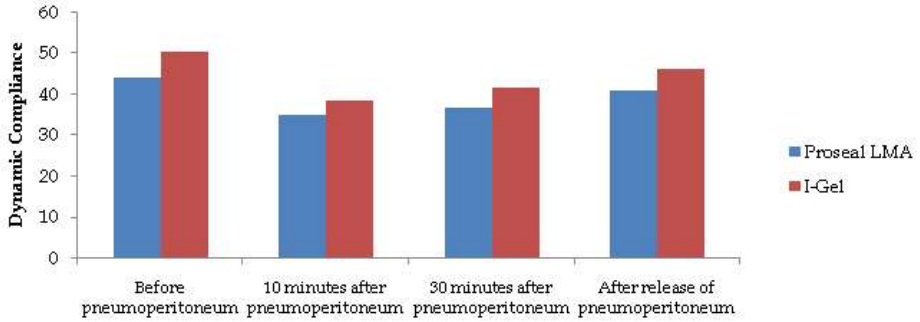


**Chart 1:** Dynamic compliance

**Table 2:** Airway Resistance

| Airway Resistance | Proseal LMA(N=55) | | I-Gel(N=55) | | t | p |
|---|---|---|---|---|---|---|
| | Mean | SD | Mean | SD | | |
| Before pneumoperitoneum | 10.48 | 1.93 | 10.58 | 6.04 | -.117 | .907 |
| 10 minutes after pneumoperitoneum | 15.32 | 1.82 | 14.63 | 3.99 | 1.161 | .248 |
| 30 minutes after pneumoperitoneum | 13.39 | 1.81 | 13.15 | 4.16 | .402 | .689 |
| After release of pneumoperitoneum | 11.08 | 1.74 | 10.60 | 5.14 | .659 | .511 |

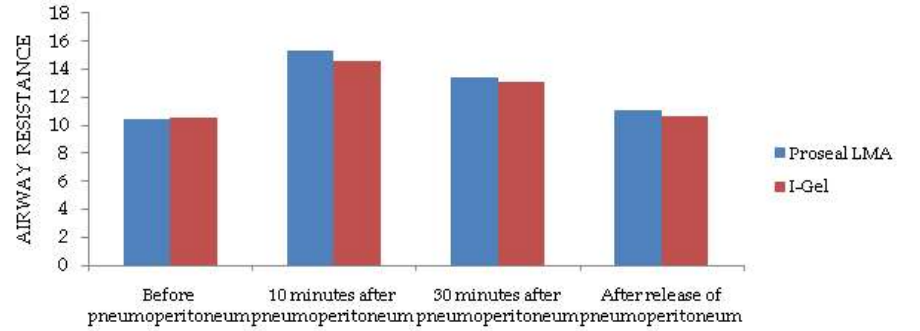


**Chart 2:** Airway Resistance

**Table 3:** Peak Airway Pressure

| Peak Airway Pressure | Proseal LMA (N=55) | | I-Gel (N=55) | | t | p |
|---|---|---|---|---|---|---|
| | Mean | SD | Mean | SD | | |
| Before pneumoperitoneum | 20.38 | 1.67 | 18.58 | 1.66 | 5.660 | <0.001 |
| 10 minutes after pneumoperitoneum | 24.40 | 1.98 | 22.76 | 2.19 | 4.109 | <0.001 |
| 30 minutes after pneumoperitoneum | 23.42 | 1.77 | 21.45 | 2.12 | 5.278 | <0.001 |
| After release of pneumoperitoneum | 21.51 | 1.61 | 19.75 | 1.83 | 5.371 | <0.001 |

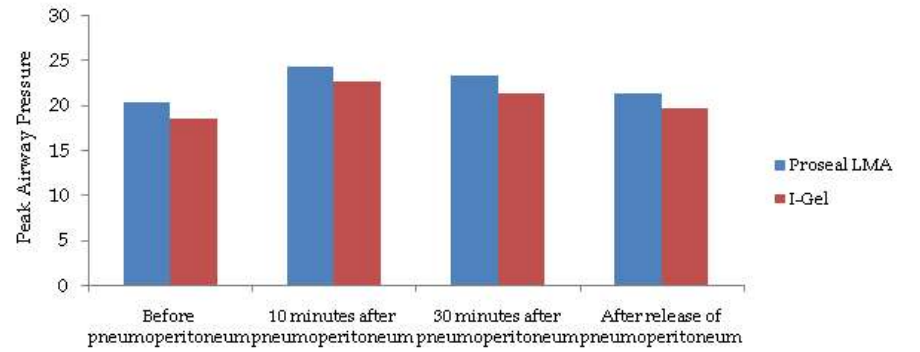


**Chart 3:** Peak Airway Pressure

**Table 4:** Grading of ease of insertion

| Ease of Insertion | Airway Device | | | | Total | | $\chi^2$ | df | p |
|---|---|---|---|---|---|---|---|---|---|
| | Proseal LMA | | I-GEL | | | | | | |
| | N | % | N | % | N | % | | | |
| Easy | 45 | 81.8 | 51 | 92.7 | 96 | 87.3 | 2.946 | 1 | 0.086 |
| Difficult | 10 | 18.2 | 4 | 7.3 | 14 | 12.7 | | | |
| Total | 55 | 100 | 55 | 100 | 110 | 100 | | | |

**Table 5:** Blood Staining

| Blood Staining | Airway Device | | | | Total | | $\chi^2$ | df | p |
|---|---|---|---|---|---|---|---|---|---|
| | Proseal LMA | | I-GEL | | | | | | |
| | N | % | N | % | N | % | | | |
| No | 48 | 87.3 | 52 | 94.5 | 100 | 90.9 | 1.760 | 1 | 0.185 |
| Yes | 7 | 12.7 | 3 | 5.5 | 10 | 9.1 | | | |
| Total | 55 | 100 | 55 | 100 | 110 | 100 | | | |

**Table 6:** Trauma Totongue, Lips, Teeth

| Trauma Totongue, Lips, Teeth | Airway Device | | | | Total | | $\chi^2$ | df | p |
|---|---|---|---|---|---|---|---|---|---|
| | Proseal LMA | | I-GEL | | | | | | |
| | N | % | N | % | N | % | | | |
| No | 52 | 94.5 | 52 | 94.5 | 104 | 94.5 | 0.000 | 1 | 1.000 |
| Yes | 3 | 5.5 | 3 | 5.5 | 6 | 5.5 | | | |
| Total | 55 | 100 | 55 | 100 | 110 | 100 | | | |

Ease of insertion was found to be higher in I-gel group, but was not statistically significant (Table 4).

There was no significant difference in blood staining after removal of the device or trauma tolips, tongue and teeth between two groups (Table 6).

## Discussion

Laparoscopy has several advantages compared to open procedures including less intraoperative pain and haemorrhage, fewer postoperative pulmonary complications and a shorter recovery time. Principal *respiratory complications [4]* during laparoscopic surgeries include $CO_2$ subcutaneous emphysema, Capnothorax, Capnomediastinum, Capnopericardium, Endobronchial intubation, Gas embolism and risk of aspiration. During laparoscopic surgeries, pulmonary compliance is decreased and resistance is increased leading to high airway pressures.

Supraglottic airway devices are nowadays a standard modality in airway management, filling a niche between the face mask and tracheal tube considering both anatomical position and degree of invasiveness. These devices are placed outside the trachea and provide a means of achieving a gas-tight airway. The laryngeal mask, as a new concept in airway management was first introduced by Archie Brain in 1983. Although it is an acceptable device in airway management, the issues with positive pressure ventilation (PPV), particularly in obese patients with decreased pulmonary compliance led to the design and development of the Pro Seal LMA (PLMA) in the late 1990's with modified cuff and drain tube, thereby offering protection against regurgitation of gastric contents and gastric insufflation and providing improved ventilatory characteristics.

Currently supralaryngeal airway devices (PLMA, I-Gel) are increasingly being used instead of the tracheal tube for planned anaesthesia in laparoscopy. Supra glottic airway devices have several advantages including lower incidence of sore throat, less hemodynamic upset during induction and maintenance of anesthesia and better oxygenation during emergence

The PLMA is the most complex of the specialized laryngeal mask devices. It was designed by Archie Brain in the late 1990s and released in 2000 [5]. The primary aim was to construct a supraglottic airway device with improved ventilatory characteristics that also offered protection against regurgitation and gastric insufflation. The major new features are a modified cuff and a drain tube.

I-Gel was developed in 2007 to overcome the limitations of PLMA. It utilizes a thermoplastic

elastomer (Styrene butadiene styrene ethylene) which has a gel-like feel. It creates a non inflatable anatomical seal of the pharyngeal, laryngeal and perilaryngeal structures while avoiding compression trauma.

PLMA and I-Gel have separate channels for gastric tube insertion and can be used for both spontaneous and controlled ventilation. There are certain differences in the fundamental design of thsetwo. I-gel is cuffless, made of a thermoplastic elastomer which creates an anatomical seal of pharyngeal laryngeal and perilaryngeal structures. The airway tube of I-Gel is bigger, where as PLMA hasa narrow reinforced airway tube with a large wedge shaped inflatable cuff and a larger drain tube. The cuff size and design influence the ease of insertion and oropharyngeal seal pressure, where as the diameter and length of airway tube determines its resistance. A cuffless supraglottic airway device offers some potential advantages with regards to ease of insertion and tissue compression. A supraglottic device with inflatable cuff absorbs anesthetic gases leading to increased mucosal pressure [6].

In our study, we tried to compare the respiratory mechanics (dynamic compliance, airway resistance, peak airway pressure) of patients undergoing laparoscopic hernia repair with I-Gel or ProSeal LMA as airway device. We also compared I-Gel and ProSeal LMA in terms of ease of insertion and airway trauma. 110 patients of ASA class 1-2 aged 18-60 yrs of both sexes scheduled to undergo laparoscopic hernia repair were included in the study. The study population was randomly divided into two groups with 55 patients in each. Premedication and anesthesia technique were standardized in both the groups. Group 1 had PLMA as their airway device and group 2 had I-gel as their airway device.

For comparing respiratory mechanics, we recorded tidal volume, peak airway pressure, plateau pressure and mean inspiratory flow rate at four points of time – before pneumoperitoneum, 10 minutes after pneumoperitoneum, 30 minutes after pneumoperitoneum and after release of pneumoperitoneum.

In mechanically ventilated patients dynamic compliance can be calculated as:

$C = V_t / (P_{peak} - PEEP)$

[C = dynamic compliance; Vt– tidal volume; $P_{peak}$ –Peak airway pressure; PEEP-Positive end expiratory pressure].

*Airway resistance* is expressed as change in pressure/flow

$R = (P_{peak} - P_{plat}) /$ Mean inspiratory flow rate

In our study using volume controlled ventilation, we found that dynamic compliance was significantly higher with I-gel at all 4 points of study ($p<0.001$). Peak airway pressure was significantly higher in PLMA group at all points of study. Airway resistance was slightly higher in PLMA group than I-gel group at all points of study, but was not statistically significant.

The inference from our study is that dynamic compliance is higher with I-gel and peak airway pressure was higher with PLMA. Airway resistance was lower with I-gel, though not statistically significant. I-gel was better when ease of insertion were compared.

*Limitations of the study*

Our study was not blinded since the researcher could not be blinded during airway management. Thus a question of observer bias can arise. Only ASA 1-2 patients with a BMI<30 $kg/m^2$ were included. So the data cannot be extrapolated to use of these devices in other groups. Also, we didn't perform fibreoptic evaluation to assess the positioning of the devices.

## Conclusion

From our study, we concluded that I-gel is a better device compared to PLMA in terms of dynamic compliance, peak airway pressure, airway resistance and ease of insertion. Therewas no significant difference in blood staining after removal of the device or trauma tolips, tongue and teeth between two groups.

*Conflict of interest:* None

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# Comparative Evaluation of Different Doses of Intravenous Clonidine in Attenuation of Haemodynamic Responses to Laryngoscopy and Intubation

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**Abstract**

*Background:* Now days, more and more patients with cardiovascular disorders are presenting themselves for surgery so anaesthesiologists are in search of safe and efficient drugs and techniques which can prevent cardiovascular responses due to laryngoscopy and intubation. Clonidine possesses beneficial effects on haemodynamics during stressful conditions like laryngoscopy and endotracheal intubation. We undertook this study to compare the effect of different doses of clonidine in attenuating the presser response to laryngoscopy and intubation in patients posted for elective surgery under general anaesthesia. *Materials and Methods:* This prospective randomized double blind controlled study was conducted on ASA Physical Status I and II patients in the age group of 20–60 years of either sex, scheduled for elective noncardiac surgeries under general anaesthesia requiring endotracheal intubation. Group A received 20 ml normal saline IV as infusion over 15 min whereas Group B, C and D received IV Clonidine 1, 2 and 3 µg/kg respectively, diluted to 20 ml with normal saline as infusion over 15 min. The parameters recorded were HR, SBP, DBP and MAP at 1,2,3,5,10 and 20 min after intubation. Postoperatively, heart rate, blood pressure, oxygen saturation ($SpO_2$) and sedation level were noted at 1 hour interval for 6 hours. Results were compiled and statistically analysed. *Results:* After laryngoscopy and intubation, the mean heart rate and blood pressure (SBP, DBP and MAP) showed a much lesser increase in clonidine treated groups B and C as compared to control group A and this was dose related. In clonidine treated group D, the mean pulse rate and blood pressure even did not show any rise despite the stimulus of laryngoscopy and intubation and remained near the basal value throughout the study period but this was clinically not worrisome and did not required any therapeutic intervention. The heart rate and blood pressure (SBP, DBP and MAP) returned to baseline values much earlier at 5 and 2 minutes in clonidine treated groups B and C respectively. Patients in all the three clonidine treated groups showed a dose related higher level of sedation as compared to control group. *Conclusion:* Clonidine at all the three different doses not only attenuated the intensity of haemodynamic responses to laryngoscopy and endotracheal intubation but also decreased the duration of the response. The effect of clonidine was clearly protective and was dose related.

**Keywords:** Clonidine; Haemodynamic response; Laryngoscopy; Endotracheal intubation.

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## Introduction

Endotracheal intubation is indeed one of the most remarkable contributions of anaesthesiologist to patient care. Laryngoscopy is a basic and essential step during tracheal intubation under general anaesthesia but both laryngoscopy and intubation are associated with haemodynamic changes which are transient and variable [1]. The hemodynamic response manifests as tachycardia and hypertension and it may have deleterious respiratory, neurological and cardiovascular effects such as cardiac arrhythmias, myocardial infarction, acute LVF, increased ICP and ruptured cerebral aneurysm [2,3].

As of today, more and more patients with cardiovascular disorders are presenting themselves for surgery so anaesthesiologists are also in search of safe and efficient drugs and techniques which can prevent cardiovascular responses due to laryngoscopy and intubation.

Several drugs have been used to attenuate haemodynamic changes such as lignocaine intravenous and topical) [4], calcium channel blockers like nicardipine [4], verapamil, nifedipine, diltiazem, beta blockers like esmolol [5], labetalol [5], metoprolol, atenolol, opiates like morphine, fentanyl [6], alfentanil, sufentanil, nalbuphine, nitroglycerine [7], gabapentin but administration of each is associated with related side effects.

Alpha-2 adrenoceptor agonists [8,9] have been used as premedication because of their beneficial properties in anaesthesia. Clonidine which is mainly used as an antihypertensive agent also possesses beneficial effects on haemodynamics during stressful conditions like laryngoscopy and endotracheal intubation. Clonidine reduces anaesthetic requirements, attenuates adrenergic, hormonal and haemodynamic stress responses to surgery, reduces anxiety and also causes sedation [10].

Studies on comparison of different doses of intravenous clonidine for this purpose are limited. Hence we undertook this study to compare the effect of different doses of clonidine in attenuating the presser response to laryngoscopy and intubation in patients posted for elective surgery under general anaesthesia.

## Material and Methods

After obtaining Institutional Ethical Committee clearance and written informed consent from participants, the study was conducted on ASA Physical Status I and II patients in the age group of 20–60 years of either sex, scheduled for elective noncardiac surgeries under general anaesthesia requiring endotracheal intubation.

Patients with known allergy to clonidine, substance abuse, base line heart rate < 60 beats/min, base line systolic BP <100 mm of Hg, neurologic illness, respiratory illness, cardiac illness, renal disease, hepatic disease, endocrinal disorders, anticipated difficult airway were excluded from the study.

Assuming a 10% difference of the percentage rise in HR or SBP between two groups, alpha = 0.05 and power of the study = 80%, the sample size, n = 24, in each group was required. So we had taken 25 patients in each group.

All patients were evaluated day before surgery. The patients who enrolled for study, received tablet ranitidine 150 mg and tablet alprazolam 0.25 mg orally at night before surgery and were kept nil by oral after midnight.

The patients were randomly allocated into four groups of twenty five patients each. Randomisation was done using computer-generated random number tables and sealed envelope technique. The procedure was double blinded, in which the anaesthesiologist administering the drug and the patients both were unaware of group allocation. Intravenous (IV) infusions were prepared by one anaesthesiologist who was not involved in further study. Another anaesthesiologist administered the infusion and recorded the parameters.

Group A received 20 ml normal saline IV as infusion over 15 min. Group B received IV Clonidine 1 μg/kg diluted to 20 ml with normal saline as infusion over 15 min. Group C received IV clonidine 2 μg/kg diluted to 20 ml with normal saline as infusion over 15 min. Group D received IV Clonidine 3 μg/kg diluted to 20 ml with normal saline as infusion over 15 min.

On arrival to operating room, all patients were monitored with electrocardiography, pulse oximetry and non-invasive blood pressure. An IV line was secured with 18 G intravenous cannula and Ringer's lactate infusion was started. Baseline heart rate (HR), systolic blood pressure (SBP), diastolic blood pressure (DBP), mean arterial blood pressure (MAP) and oxygen saturation ($SpO_2$) were measured. Inj glycopyrrolate 0.004 mg/kg, inj midazolam 0.03 mg/kg and inj fentanyl 2 μg/kg were given just before infusion of study drug. The study drug infusion was given over 15 min. Any

hypotension (SBP fall >20% from the baseline) was treated with increments of IV mephentermine 3 mg, and incidence of bradycardia (HR <50 beats) was treated with IV atropine 0.6 mg and such patients were excluded from further study.

After monitoring the haemodynamics for 10 min, the anaesthetic procedure was initiated. All the patients were pre-oxygenated for 3 min. General anaesthesia technique was standardised for all the four groups. All the patients were induced with IV propofol 2 mg/kg and IV succinylcholine 2 mg/kg body weight. Following laryngoscopy and endotracheal intubation, the parameters recorded were HR, SBP, DBP and MAP at 1, 2, 3, 5, 10 and 20 min after intubation. Anaesthesia was maintained with oxygen-nitrous oxide (40:60) and isoflurane. Muscle relaxation was maintained with Inj vecuronium 0.1 mg/kg loading then 0.02 mg/kg intermittent doses. Patients were monitored throughout intraoperative period with continuous ECG, $SpO_2$, heart rate and Blood pressure. After surgery, reversal was achieved with Inj neostigmine 0.05 mg/kg and Inj glycopyrrolate 0.01 mg/kg. After adequate recovery, patients were shifted to post-anaesthesia care unit.

Postoperatively, patients were monitored for 6 hours for heart rate, blood pressure, oxygen saturation ($SpO_2$) and sedation score [11] at 1 hour interval. Any complications like nausea, vomiting, bradycardia and hypotension were also recorded postoperatively for 6 hours. Level of sedation was assessed by using Ramsay sedation score [11].

Ramsay Sedation Score

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

Results were compiled and statistically analysed. One way analysis of variance (ANOVA), paired t-test and chi square test were applied where deemed appropriate. p-value ≤0.05 was considered as statistically significant.

## Results

All four groups were comparable with respect to their age, weight and gender distribution (Table 1)

The baseline mean heart rate was comparable among all the groups (Table 2). Just after study drug infusion, mean heart rate decreased by 0.047, 1.11, 2.27 and 4.70% in groups A,B,C and D respectively as compared to baseline values but the changes were statistically insignificant compared to preoperative values($p>0.05$) (Table 3). Before induction, the changes in heart rate in group A, B and C were statistically insignificant (0.47%, 4.77% and 4.45%; $p>0.05$) in groups A, B and C respectively whereas in group D, the decrease was statistically significant (8.13%, $p<0.05$). Statistically significant increases in mean heart rate with respect to basal value after laryngoscopy and endotracheal intubation were seen in groups A, B and C (58%, $p<0.001$;36.67%, $p<0.001$; 10.02%, $p<0.01$ respectively). However, a rise in mean heart rate was also observed in group D but this was statistically insignificant throughout the study period. The heart rate returned to baseline values at 10, 5 and 2 min in groups A, B and C respectively and thereafter remained near basal values till the study period.

The mean systolic blood pressure, mean diastolic blood pressure and mean arterial blood pressure were comparable among all the groups (Table 2). Just after study drug infusion, mean systolic blood pressure showed statistically insignificant changes in group A, B and C while it decreased significantly in group D but this was clinically not worrisome and did not require any therapeutic intervention (Table 4). Before induction, a statistically insignificant increase in mean systolic blood pressure was observed in group A. The decrease in mean systolic blood pressure in group B, C and D was statistically significant (6.10%, $p<0.05$, 8.37%, $p<0.01$ & 7.93%, $p<0.01$)) although none of the patients required any therapeutic intervention. After laryngoscopy and intubation, the mean systolic blood pressure showed a progressively

**Table 1:** Demographic profile

| Variables | Group A | Group B | Group C | Group D |
|---|---|---|---|---|
| Age (years) | 38 ± 14 | 39 ± 14 | 37 ± 12 | 38 ± 12 |
| Weight (kg) | 56 ± 6.8 | 57 ± 6.5 | 54 ± 7.2 | 57 ± 7.9 |
| Sex ratio (M:F) | 10:15 | 11:14 | 11:14 | 13:12 |

lesser increase in groups B and C as compared to group A but the increase was statistically significant in all three groups as compared to basal systolic blood pressure. In group D, the mean systolic blood pressure did not show any rise, infact it remained statistically significantly lower than baseline value throughout intraoperative period. The raised mean systolic blood pressure returned to baseline values at 10, 5 and 2 minutes in groups A, B and C respectively.

Just after study drug infusion, mean diastolic blood pressure decreased in all groups but that had no clinical significance (Table 2, 5). Before induction, the mean diastolic blood pressure decreased in all groups but no therapeutic intervention was needed in any patient. After laryngoscopy and intubation, the mean diastolic blood pressure showed a progressively lesser increase in groups B and C as compared to group A but the increase was statistically highly significant in all three groups. The mean diastolic blood pressure returned to baseline values at 5 and 2 minutes in groups B and C respectively but it remained high even till 10 minutes in control group A. While in group D, the mean diastolic blood pressure showed a significant fall than baseline diastolic blood pressure throughout the intraoperative period.

Just after study drug infusion, mean arterial blood pressure showed statistically insignificant increase in group A whereas there was decline noted in group B, C and D which was statistically significant only in group D (7.19%, $p<0.01$) (Table 6). Before induction, statistically insignificant increase in mean arterial blood pressure was observed in group A. The mean arterial blood pressure in all the clonidine treated groups (B, C and D) showed a decline which was statistically significant in all three groups but this needed no therapeutic intervention. After laryngoscopy and endotracheal intubation, mean arterial blood pressure increased in groups A, B and C to 129.20 ± 7.74, 114.17 ± 7.25 and 102.74 ± 9.33 mmHg respectively but it decreased in group D to 91.2 ± 8.90 mmHg (Table 2). The mean blood pressure remained at significantly higher level as compared to basal value till 10, 5 and 2 min in groups A, B and C respectively. In group D, the mean arterial blood pressure remained lower than the baseline value throughout the intraoperative period.

The mean sedation score observed at 0 hours postoperatively in groups A,B,C and D was 2.08 ± 0.27,3.16 ± 0.37, 3.28 ± 0.45 and 4.12 ± 0.33

**Table 2:** Haemodynamic parameters during induction and intubation

| Parameter | Baseline | Just after study drug | Before induction | After intubation at 0 min | at 1 min | at 2 min | at 3 min | at 5 min | at 10 min | at 20 min |
|---|---|---|---|---|---|---|---|---|---|---|
| **Heart Rate** | | | | | | | | | | |
| Group A | 83.96 ± 6.07 | 83.92 ± 5.28 | 84.36 ± 5.52 | 133 ± 8.13 | 126.68 ± 6.67 | 121.76 ± 8.70 | 110.28 ± 7.42 | 93.20 ± 5.99 | 85.92 ± 5.93 | 86.40 ± 4.87 |
| Group B | 82.88 ± 9.13 | 81.96 ± 7.86 | 78.92 ± 6.29 | 113.28 ± 8.67 | 110.84 ± 8.59 | 104.88 ± 7.23 | 88.72 ± 6.69 | 84.2 ± 4.36 | 82.56 ± 5.03 | 82 ± 6.04 |
| Group C | 82.6 ± 8.38 | 80.72 ± 5.59 | 78.02 ± 6.72 | 90.88 ± 4.63 | 90.92 ± 4.70 | 83.92 ± 4.37 | 83.68 ± 5.23 | 81.96 ± 5.09 | 81.64 ± 5.32 | 81.24 ± 5.15 |
| Group D | 85.04 ± 9.35 | 81.04 ± 6.66 | 78.12 ± 5.01 | 85.84 ± 5.12 | 84.84 ± 4.74 | 84.56 ± 8.37 | 82.68 ± 10.07 | 83.36 ± 7.08 | 84.32 ± 7.39 | 83.92 ± 8.39 |
| p value | 0.720 | 0.414 | .0005 | <0.00001 | <0.00001 | <0.00001 | <0.00001 | <0.00001 | 0.0631 | 0.0216 |
| **Systolic BP** | | | | | | | | | | |
| Group A | 124.96 ± 7.99 | 128.76 ± 6.83 | 126.88 ± 7.26 | 174.24 ± 8.49 | 167.40 ± 8.27 | 161.6 ± 8.68 | 152.56 ± 11.59 | 142.0 ± 9.02 | 125.64 ± 9.47 | 125.88 ± 6.14 |
| Group B | 125.16 ± 10.56 | 120.72 ± 10.28 | 117.52 ± 9.92 | 152.12 ± 9.46 | 143.66 ± 11.61 | 138.96 ± 12.65 | 134.88 ± 13.90 | 125.8 ± 13.49 | 119.2 ± 9.92 | 121.36 ± 10.36 |
| Group C | 124.96 ± 10.31 | 119.32 ± 10.85 | 114.68 ± 9.36 | 135.6 ± 9.99 | 132.84 ± 11.65 | 126.76 ± 10.19 | 116.96 ± 8.38 | 115.76 ± 9.47 | 116.76 ± 7.31 | 117.72 ± 7.64 |
| Group D | 125.96 ± 10.34 | 117.72 ± 7.34 | 115.96 ± 7.10 | 122.84 ± 7.38 | 116.6 ± 6.82 | 114.6 ± 6.68 | 115.64 ± 6.20 | 115.36 ± 6.86 | 117.48 ± 6.08 | 119.36 ± 6.29 |
| p value | 0.980 | 0.00015 | <0.00001 | <0.00001 | <0.00001 | <0.00001 | <0.00001 | <0.00001 | 0.00100 | 0.00249 |
| **Diastolic BP** | | | | | | | | | | |
| Group A | 78.72 ± 7.56 | 77.96 ± 6.56 | 77.92 ± 6.71 | 106.68 ± 11.39 | 108.44 ± 9.70 | 107.20 ± 9.18 | 102.96 ± 9.25 | 98.08 ± 10.14 | 81.12 ± 9.34 | 80.84 ± 7.69 |
| Group B | 79.88 ± 5.46 | 75.52 ± 6.15 | 73.92 ± 5.82 | 95.2 ± 7.48 | 90.96 ± 7.65 | 87.24 ± 7.60 | 84.72 ± 9.78 | 79.84 ± 8.60 | 80.44 ± 7.93 | 83.92 ± 9.67 |
| Group C | 78.8 ± 7.45 | 74.36 ± 6.60 | 72.76 ± 6.11 | 86.32 ± 9.86 | 84.96 ± 11.31 | 80.76 ± 7.46 | 73.28 ± 7.99 | 70.96 ± 8.85 | 72.68 ± 8.12 | 77.2 ± 7.02 |
| Group D | 82.08 ± 8.39 | 75.76 ± 6.28 | 74 ± 5.26 | 74.92 ± 9.39 | 72.56 ± 7.83 | 72.04 ± 8.89 | 76.16 ± 7.96 | 73.64 ± 8.22 | 76.2 ± 7.10 | 76 ± 5.73 |
| p value | 0.3436 | 0.2543 | 0.0180 | <0.00001 | <0.00001 | <0.00001 | <0.00001 | <0.00001 | 0.00015 | 0.00155 |
| **Mean BP** | | | | | | | | | | |
| Group A | 94.13 ± 7.23 | 94.89 ± 5.62 | 94.24 ± 5.72 | 129.20 ± 7.74 | 128.09 ± 7.61 | 125.33 ± 7.27 | 119.49 ± 9.02 | 112.72 ± 9.28 | 95.96 ± 5.57 | 95.85 ± 6.64 |
| Group B | 94.97 ± 6.41 | 90.58 ± 7.00 | 88.45 ± 6.41 | 114.17 ± 7.25 | 108.6 ± 5.84 | 104.48 ± 8.72 | 101.44 ± 10.98 | 95.16 ± 9.76 | 93.36 ± 6.86 | 96.4 ± 8.25 |
| Group C | 94.24 ± 7.88 | 89.34 ± 7.84 | 86.73 ± 7.01 | 102.74 ± 9.33 | 100.92 ± 11.08 | 96.09 ± 8.03 | 87.84 ± 7.95 | 85.89 ± 8.92 | 87.37 ± 7.42 | 90.70 ± 6.98 |
| Group D | 96.70 ± 8.85 | 89.74 ± 6.46 | 88.06 ± 5.40 | 91.2 ± 8.90 | 86.68 ± 6.71 | 87.8 ± 7.90 | 89.88 ± 7.33 | 88.84 ± 8.21 | 90.04 ± 6.39 | 90.88 ± 5.96 |
| p value | 0.6053 | 0.0178 | 0.00018 | <0.00001 | <0.00001 | <0.00001 | <0.00001 | <0.00001 | 0.00008 | 0.00299 |

respectively. It came to basal value at 1, 2,3 and 4 hours in groups A, B, C and D respectively (Fig 1). All the three clonidine treated groups showed a dose related higher sedation score as compared to the control group A and the difference was statistically highly significant( p<0.001). However it was noted that no hypoxic episode occurred in any patient included in the study during the postoperative period Two and four patients in group C and D respectively had episodes of bradycardia intraoperatively which was managed with intravenous injection atropine 0.6 mg. There were no episodes of hypotension in any of the patients in any of the groups.

**Table 3:** Percentage change in mean heart rate

| Observations | Group A Basal heart rate (per min) 83.96 ± 6.079 | | Group B Basal heart rate (per min) 82.88 ± 9.134 | | Group C Basal heart rate (per min) 82.6 ± 8.386 | | Group D Basal heart rate (per min) 85.04 ± 9.35 | |
|---|---|---|---|---|---|---|---|---|
| | % Change | p value | % Change | p value | % Change | p value | % Change | p value |
| Just after study drug infusion | -0.047 | >0.05 | -1.11 | >0.05 | -2.27 | >0.05 | -4.70 | >0.05 |
| Before induction | 0.47 | >0.05 | 4.77 | >0.05 | -4.45 | >0.05 | -8.13 | <0.05 |
| After intubation at 0 min | 58.00 | <0.001 | 36.67 | <0.001 | 10.02 | <0.01 | 9.40 | >0.05 |
| at 1 min | 50.88 | <0.001 | 33.73 | <0.001 | 10.07 | <0.01 | -0.23 | >0.05 |
| at 2 min | 45.00 | <0.001 | 26.54 | <0.001 | 1.59 | >0.05 | -0.56 | >0.05 |
| at 3 min | 31.34 | <0.001 | 7.04 | <0.05 | 1.30 | >0.05 | -2.77 | >0.05 |
| at 5 min | 11.00 | <0.001 | 1.59 | >0.05 | -0.77 | >0.05 | -1.97 | >0.05 |
| at 10 min | 2.33 | >0.05 | -0.38 | >0.05 | -1.16 | >0.05 | -0.84 | >0.05 |
| at 20 min | 2.90 | <0.05 | 1.06 | >0.05 | -1.64 | >0.05 | -1.31 | >0.05 |

**Table 4:** Percentage change in mean systolic blood pressure

| Observations | Group A Basal SBP (mmHg) 124.96 ± 7.99 | | Group B Basal SBP (mmHg) 125.16 ± 10.58 | | Group C Basal SBP (mmHg) 125.16 ± 10.53 | | Group D Basal SBP(mmHg) 125.96 ± 10.34 | |
|---|---|---|---|---|---|---|---|---|
| | % Change | p value | % Change | p value | % Change | p value | % Change | p value |
| Just after study drug infusion | 3.04 | >0.05 | -3.54 | >0.05 | -4.46 | >0.05 | -6.54 | <0.01 |
| Before induction | 1.53 | >0.05 | -6.10 | <0.05 | -8.37 | <0.01 | -7.93 | <0.01 |
| After intubation at 0 min | 39.43 | <0.001 | 21.54 | <0.001 | 8.34 | <0.001 | -2.47 | >0.05 |
| at 1 min | 33.96 | <0.001 | 14.95 | <0.001 | 6.13 | <0.05 | -7.43 | <0.001 |
| at 2 min | 29.32 | <0.001 | 11.02 | <0.001 | 1.27 | >0.05 | -9.01 | <0.01 |
| at 3 min | 22.08 | <0.001 | 7.76 | <0.01 | -6.55 | <0.05 | -8.19 | <0.001 |
| at 5 min | 13.63 | <0.001 | 0.51 | >0.05 | -7.51 | <0.01 | -8.41 | <0.01 |
| at 10 min | 0.54 | >0.05 | -4.76 | >0.05 | -6.71 | <0.05 | -6.73 | <0.01 |
| at 20 min | 0.73 | >0.05 | -3.03 | >0.05 | -5.94 | >0.05 | -5.23 | <0.05 |

**Table 5:** Percentage change in mean diastolic blood pressure

| Observations | Group A Basal DBP(mmHg) 78.72 ± 7.56 | | Group B Basal DBP (mmHg) 82.88 ± 9.13 | | Group C Basal DBP (mmHg) 78.88 ± 7.45 | | Group D Basal DBP (mmHg) 82.08 ± 8.39 | |
|---|---|---|---|---|---|---|---|---|
| | % Change | p value | % Change | p value | % Change | p value | % Change | p value |
| Just after study drug infusion | -0.96 | >0.05 | -5.45 | <0.05 | -5.73 | <0.05 | -7.69 | <0.01 |
| Before induction | -1.01 | >0.05 | -7.46 | <0.01 | -7.75 | <0.01 | -9.84 | <0.01 |
| After intubation at 0 min | 35.51 | <0.001 | 19.17 | <0.001 | 9.43 | <0.01 | -8.72 | <0.05 |
| at 1 min | 37.75 | <0.001 | 13.87 | <0.001 | 7.70 | <0.05 | -11.59 | <0.001 |
| at 2 min | 36.17 | <0.001 | 9.21 | <0.001 | 2.38 | <0.05 | -12.23 | <0.001 |
| at 3 min | 30.79 | <0.001 | 6.05 | <0.05 | -7.09 | <0.05 | -7.21 | <0.05 |
| at 5 min | 24.59 | <0.001 | -0.05 | >0.05 | -10.04 | <0.01 | -10.28 | <0.01 |
| at 10 min | 3.04 | >0.05 | 0.70 | >0.05 | -7.86 | >0.05 | -7.16 | <0.05 |
| at 20 min | 2.69 | >0.05 | 5.05 | >0.05 | -2.12 | >0.05 | -7.16 | <0.01 |

**Table 6:** Percentage change in mean of mean arterial blood pressure

| Observations | Group A Basal MBP (mmHg) 94.13 ± 7.23 | | Group B Basal MBP (mmHg) 94.97 ± 6.41 | | Group C Basal MBP (mmHg) 94.30 ± 8.02 | | Group D Basal MBP (mmHg) 96.70 ± 8.85 | |
|---|---|---|---|---|---|---|---|---|
| | % Change | p value | % Change | p value | % Change | p value | % Change | p value |
| Just after study drug infusion | 0.80 | >0.05 | -4.62 | >0.05 | -5.25 | >0.05 | -7.19 | <0.01 |
| Before induction | 0.11 | >0.05 | -6.86 | <0.05 | -8.02 | <0.01 | -8.93 | >0.001 |
| After intubation at 0 min | 37.25 | <0.001 | 20.21 | <0.001 | 8.95 | <0.01 | -5.68 | <0.05 |
| at 1 min | 36.07 | <0.001 | 14.35 | <0.001 | 7.02 | <0.05 | -10.36 | <0.001 |
| at 2 min | 33.14 | <0.001 | 10.01 | <0.001 | 1.89 | >0.05 | -9.20 | <0.001 |
| at 3 min | 26.94 | <0.001 | 6.81 | <0.05 | -6.85 | >0.05 | -7.05 | <0.01 |
| at 5 min | 19.74 | <0.001 | 0.20 | >0.05 | -8.91 | <0.01 | -8.12 | <0.01 |
| at 10 min | 1.94 | >0.05 | -1.16 | >0.05 | -7.34 | >0.05 | -6.88 | <0.01 |
| at 20 min | 1.82 | >0.05 | 1.51 | >0.05 | -3.81 | >0.05 | -6.07 | <0.01 |

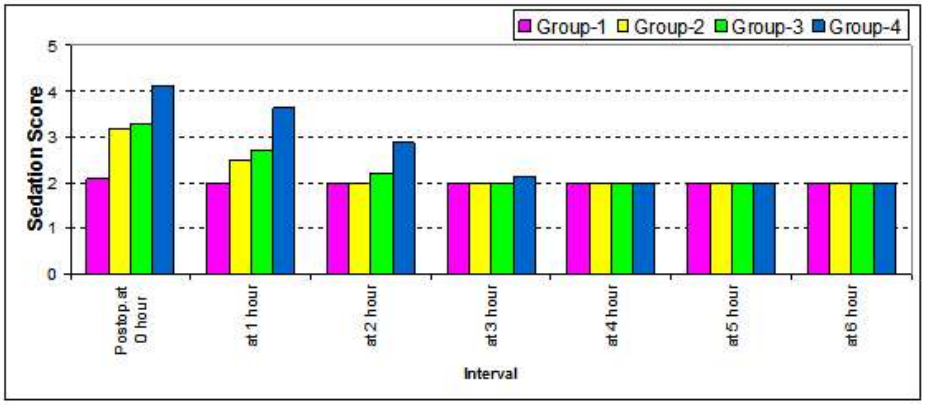


**Fig 1:** Sedation score

## Discussion

The sympathoadrenal response to laryngoscopy and intubation includes hypertension, tachycardia, predisposition to cardiac arrhythmia and increased myocardial oxygen consumption [12]. The sympathetic responses are associated with an acute increase in plasma concentration of epinephrine and norepinephrine [13]. Thus it is logical to select an agent which would prevent and minimize the laryngoscopy stimulation by the intubation process or an agent which would block the sympathetic activity associated with this stimulation. The measures for controlling haemodynamic responses aim to stabilize heart rate and blood pressure during laryngoscopy and intubation, in order to prevent any rise in myocardial work load and oxygen demand and hence, any complication thereof. Secondly, the aim to preserve perfusion of vital organs. At the same time, safety of such technique is also a prime concern. It is desirable to use a drug with least numerous, rapidly recognizable and easily treatable adverse effects. It is also desirable that the procedure should be simple so that it can be recommended as a routine measure.

Clonidine, α2 adrenergic receptor agonist, has been studied as a premedication in a dose of 1-3 µg/kg due to its beneficial effect on the hyperdynamic response to endotracheal intubation [14]. The haemodynamic effects of clonidine are both peripheral and central. Centrally it stimulates α2 adrenergic inhibitory neurons in the medullary vasomotor center [12]. As a result, there is a decrease in sympathetic nervous system outflow from central nervous system to peripheral tissues. Decreased sympathetic nervous system activity is manifested as peripheral vasodilatation and decrease in systemic blood pressure, HR and cardiac output [15]. Clonidine doses up to 4-5 µg/kg have been investigated frequently, though primarily for their anaesthetic-sparing effects in the intraoperative period and for their opioid-sparing effects in the postoperative period [16]. Oral premedication with clonidine 5 µg/kg has been used successfully to improve intraoperative haemodynamic stability and reduce anaesthetic and opioid requirements [17]. As bioavailability of clonidine after oral intake varies between 75% to 95%, so IV route of administration was chosen

to relate pharmacodynamic effects more precisely to a certain dose. Also, IV route produces a more immediate effect than oral route and is under direct clinical supervision of an anaesthesiologist who is able to respond to any adverse effects.

We selected 3 different doses of IV clonidine to find out optimal dose for attenuation of sympathoadrenal responses to laryngoscopy and intubation without side effects. We had compared 1 (Group B), 2 (Group C) and 3 (Group D) µg/kg IV clonidine with control group (Group A) and found that just after intubation, the rise in mean BP was 37.25% in group A, 20.21% in group B, 8.95% in group C and decreased 5.68% in group D and returned to baseline values at 5 min and 2 min in group B and C respectively but it remained significantly high even till 10 min in control group A. In group D mean BP remained significantly lower than baseline values throughout the intraoperative period. Heart rate just after intubation increased 58 % in group A, 36.67% in group B, 10.02% in group C and 9.40% in group D which returned to baseline values at 10, 5 and 2 min in group A, B, C respectively. Intraoperatively, none of the patients in group A and B had episodes of bradycardia whereas 8% patients in group C and 16% patients in group D had bradycardia.

Kulka PJ et al. [18] had noted that clonidine 2 µg/kg although decreased the rise in pulse rate after laryngoscopy and endotracheal intubation but this was not statistically significant. However, they noted that clonidine at doses of 4 µg/kg and 6 µg/kg equally attenuated the tachycardia seen after laryngoscopy and endotracheal intubation. However, Carabine et al. [19] demonstrated that clonidine at doses of 0.625 and 1.25 µg/kg administered IV 15 minutes prior to induction of anaesthesia attenuated the increase in pulse rate after laryngoscopy and endotracheal intubation. On the contrary, Wright et al. [20] noted, under almost identical conditions, that clonidine 1.25 µg/kg IV was not effective in preventing this response.

Sakshi Arora et al. 12 studied iv clonidine in a dose of 1 mcg/kg and 2 mcg/kg with iv fentanyl 2 mcg/kg and concluded that minimal dose of IV clonidine 1 µg/kg cause maximum attenuation of pressor response with minimal side effects. Kotak N et al. [21] and Sameenakousar et al. [22] used 2 mcg/kg safely to attenuate hemodynamic responses to laryngoscopy and intubation.

Ray M et al. 2010 [23] used 3 mcg/kg of clonidine IV over 15 min before induction and 1 mcg/kg/hr by continuous infusion during surgery and observed significance incidence of bradycardia and hypotension in their study. In contrast to our study, Ambrose C et al. [24] didn't found bradycardia with clonidine infusion (0.1-2 µg/kg) in critically ill children. However their study was conducted on paediatric population.

In our study, no patient showed any ECG signs of ischaemia. This might be due to fact that myocardial perfusion pressure was maintained as all the patients of this study belonged to ASA grade 1 and 2 and were free from any major systemic disorder. But the significant increase in haemodynamic parameters (Heart rate and Blood pressure) for a longer duration of period in the control group might have been deleterious in a hypertensive or patient with pre-existing IHD. Clonidine drug at the different doses used in this study definitely provides a benefit in this setting as it not only decreased the intensity of haemodynamic response to laryngoscopy and endotracheal intubation but it also decreased the time for which the haemodynamic parameters remained high after laryngoscopy and endotracheal intubation. Clonidine at dose of 3 µg/kg completely abolished any haemodynamic response to laryngoscopy and endotracheal intubation but had high incidences of bradycardia intraoperatively and more sedation postoperatively.

Although blood pressure remained less than the basal value in clonidine group D probably due to the higher dose (3 µg/kg) used but it did not require use of intravenous fluids or vasopressors. However, we feel that occurrence of hypotension with clonidine is not worrisome and it can be easily managed with proper administration of IV fluids during intraoperative as well as in postoperative period as the cause of hypotension after clonidine is usually hypovolaemia which is unmasked by clonidine induced decreased sympathetic outflow.

The mean systolic blood pressure was lower in clonidine groups C and D compared to other groups during the studied postoperative period. This can be explained by the higher drug dose used in these two groups. However, this decrease in blood pressure caused no concern and required no intervention. Similar observations were recorded for the mean diastolic blood pressure as well as the mean arterial blood pressure postoperatively during the first 6 hours. None of the patients in any of the groups had incidence of bradycardia postoperatively.

Sedation is a well known side effect of clonidine. In our study also, patients in all the three clonidine treated groups showed a higher level of sedation as compared to the control group. This is an advantageous situation as the patients were calm and comfortable throughout the studied

postoperative period and required no airway management in the clonidine groups which used lower doses (1 μg/kg and 2 μg/kg) indicating a well maintained airway and oxygenation. However in clonidine group D (3 μg/kg), 4 patients out of 25, required insertion of Guedel's airway and all these patients were comparatively elderly. Hence, caution must be exercised before administrating this higher dose of clonidine to elderly patients. In a study conducted by Ghignone M et al. [25], they observed that patients were better sedated in the clonidine group as compared to diazepam group. Similarly Rudra Segal et al. [26] found the sedative effect of clonidine better than in placebo group.

Clonidine though does not possess an antiemetic effect but this drug is supposed to non emetic. No difference in incidence of nausea and vomiting was noted between control group and clonidine groups in this study.

No incidence of rebound hypertension after clonidine withdrawal was seen in this study. Wing LMH [27] had noted similar finding and concluded that no evidence of an increased sympathetic nervous system activity was seen after single dose of clonidine. Rebound phenomenon after the sudden withdrawal of clonidine is seen only after treatment for 6-30 days.

*Limitation*

The present study was carried out in patients who were normotensive, not having hypertension or coronary artery disease. Hence our findings cannot be extrapolated in patients with hypertension and coronary artery disease. Further studied should consider this limitation.

## Conclusion

Clonidine at all the three different doses (1 μg/kg, 2 μg/kg and 3 μg/kg) not only attenuated the intensity of haemodynamic responses to laryngoscopy and endotracheal intubation but also decreased the duration of the response. The effect of clonidine was clearly protective and was dose related however caution must be exercised while using higher dose in elderly patients.

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*Conflict of interest:* None declared

*Ethical approval:* The study was approved by the Institutional Ethics Committee.

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# A Comparative Study: USG guided Adductor Canal Block Versus Femoral Nerve Block for Postoperative Analgesia for Knee Surgeries

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**Abstract**

In today's era, multimodal analgesia is the main strategy used for providing postoperative analgesia in patients undergoing knee surgeries yet 25-40% patients experience severe postoperative pain [1]. Intravenous opioids, epidural analgesia and non-steroidal anti-inflammatory drugs (NSAIDs) are commonly used analgesics but have many systemic side-effects [2]. Peripheral nerve blocks have minimal systemic side-effects and ultrasonography guided peripheral nerve block isa preferred method for providing pain relief. The femoral nerve block (FNB) was widely used for knee surgeries but it had the disadvantage of prolonged quadriceps muscle weakness which can be minimized by Adductor canal block (ACB). Therefore ACB has been introduced recently for knee surgeries. Thus, we decided to compare the efficacy of USG guided femoral nerve block and adductor canal block for postoperative analgesia in knee surgeries. Our study included adult patients undergoing knee surgeries. Fifty patients were randomly divided in two groups – group A: (n=25) received adductor canal block; group F: (n=25) received femoral nerve block, postoperatively. Both blocks were performed under USG guidance after complete wearing off of central neuraxial blockade. The average duration of sensory blockade for group F was 6.53 hours ± 4.64 while for group A was 5.77 hours ± 1.30 which was statistically not significant (p value >0.05). However, we found statistically significant difference in motor blockade in group A as compared to group F (p value <0.05). Thus we conclude that USG guided Adductor canal block effectively provides comparable postoperative analgesia to femoral nerve block while preserving the quadriceps muscle strength.

**Keywords:** Postoperative analgesia; Knee surgeries; Adductor canal block; Femoral nerve block.

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## Introduction

The aim of postoperative analgesia is to provide adequate pain relief with minimum side-effects. The benefits of an effective postoperative pain management include patient comfort and satisfaction, early ambulation, fewer cardio-respiratory complications, a decreased risk of deep vein thrombosis, faster recovery with less chances of development of neuropathic pain and reduced cost of care [1,2].

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The rising incidence of knee trauma and osteoarthritis has led to increase in number of knee surgeries. Recent consensus (2010) stated that about 14-28% of the cases operated for unilateral total knee arthroplasty (TKA) were not satisfied with regards to postoperative pain relief [3]. This intense pain often results in delayed mobilization, systemic side effects, increased in-hospital stay and expenditure for the patient [1-3].

Intravenous opioids were used to treat postoperative analgesia. They had some undesirable side-effects like sedation, respiratory depression, nausea, vomiting, hypotension, bradycardia, pruritus (37%) and inhibition of bowel function [1]. Non-steroidal anti-inflammatory drugs (NSAIDs) were mostly used to treat pain due to prostaglandins. However, they were associated with side effects like peptic ulcer disease, gastrointestinal bleeding, altered liver, platelets and renal functions [1].

Epidural analgesia has also been used for postoperative pain relief but the effect was found to be unpredictable due to the patchy action or possible dislodgement of the catheter. It also lead to retention of urine, hypotension and motor blockade. The motor blockade further hindered in mobilization [2].

Modern techniques for postoperative analgesia include the peripheral nerve blocks. Evidence based data has proved their efficacy in improving postoperative outcome and reducing the requirement of intra-venous (I.V.) opioids [1,2]. Among the peripheral nerve blocks, femoral nerve block (FNB) has been widely used to provide postoperative pain relief after knee surgeries. Despite being a successful block, it invariably decreases quadriceps muscle strength; thus delaying mobilization and increasing the risk of falling [2,4,5].

Adductor canal block (ACB) is a relatively new block with promising results. The local anaesthetic acts on saphenous nerve in the adductor canal. Being purely a sensory nerve, it not only provides adequate pain relief in postoperative phase but may also benefit by enabling the patients in early mobilization [2].

Thus taking in to consideration previously determined properties of both the blocks, we decided to do a comparative study to know the efficacy of USG guided femoral nerve block and adductor canal block for postoperative analgesia in all knee surgeries in our tertiary care centre.

## Materials and Methods

After the approval of the institutional ethical committee, this study was conducted at the attached tertiary care teaching hospital during the period from 2016 to 2018.

*Study design*: The study was an interventional prospective study.

Entire procedure was explained to the patients during pre-anaesthesia check-up and a written informed consent was taken from each patient preoperatively, in the language that he or she understood well.

*Sample size*: The study included 50 patients randomly divided in two groups of 25 each.

Group A(n=25) received USG guided Adductor canal block postoperatively.

Group F (n=25) received USG guided Femoral nerve block postoperatively.

*Inclusion criteria*: Patients belonging to ASA Grade I-II, who were 18 years and above and were posted for elective knee surgeries.

*Exclusion criteria*: Patients who were unwilling to participate in the study or who had infection at the site of the block or had coagulopathies.

All patients were kept nil by mouth for at least 6 hours prior to surgery. All patients received spinal anaesthesia (SA) under all septic precautions and standard monitoring, with Inj. Bupivacaine 0.5% heavy 0.3 mg/kg with 25G spinal needle, in $L_3$–$L_4$ space, after confirming free flow of cerebrospinal fluid. Patients were monitored for haemodynamic parameters throughout the intraoperative and postoperative period. After completion of the surgery and confirmation of complete regression of the central neuraxial blockade, peripheral nerve blocks (FNB or ACB) were administered under USG guidance. Image 1 shows the USG guided Right Adductor canal block.

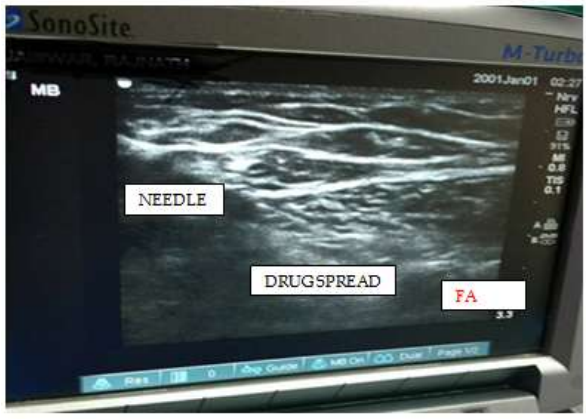


**Image 1:** USG image of needle position and the spread of drug while administration of Right Adductor canal block. FA- femoral artery.

Patients were monitored postoperatively for

1) The onset and duration of sensory blockade in both the groups by pin prick test.

2) The onset and duration of motor blockade in both the groups by leg raise test.

3) Pain scores using the visual analogue scale (VAS). VAS > 3/10 was considered to be significant and rescue analgesia was given.

4) Haemodynamic variability in both the groups.

5) Time taken for requirement of rescue analgesia in both the groups.

6) Occurrence of complications like infection, haematoma, vascular puncture and nerve injury, from the blocks in their respective groups.

Patients were monitored, starting from the time of administration of block (taken as 0 min) followed by intervals of 15 min, 0.5 hour, 1 hour and then at 2 hourly intervals till rescue analgesia was administered. Patients were observed for first 24 hours to know occurrence of any complication of the block administered.

## Observations and Results

The sample size for the study wasdetermined from previous studies. We had included 50 patients undergoing elective knee surgeries, randomly divided into two groups of 25 each. Postoperatively, after wearing off of the effect of spinal anaesthesia, Group A (n=25) received USG guided Adductor canal block, while Group F (n=25) received USG guided Femoral nerve block and were monitored for haemodynamic parameters, pain scores, time for requirement of rescue analgesia and complications for first 24 hours.

In the entire study, the p-value less than 0.05 were considered to be statistically significant. All the hypotheses were formulated using two tailed alternatives against each null hypothesis (hypothesis of no difference). The entire data is statistically analysed using Statistical Package for Social Sciences (SPSS version 21.0, IBM Corporation, USA) for MS Windows [6-8].

Table 1 shows that distribution of mean pain score at rest and on leg raise at 0-min, 15-min, 0.5-Hr, 1.0-Hr, 2.0-Hr, 4.0-Hr and 6.0-Hr did not differ significantly between two study groups (p-value > 0.05).

Figure 1 shows that the distribution of mean duration of sensory blockade for Group A was 5.77 hours ± 1.30 while for Group F was 6.53 hours ± 4.64 which did not differ significantly between two study groups (p-value = 0.438).

Figure 2 shows that the mean ± SD of time to rescue analgesia among the cases studied in Group F and Group A was 5.62 ± 2.75 Hours and 5.71 ± 1.25 Hours respectively which did not differ significantly between two study groups (P-value = 0.878).

The duration of motor blockade was significantly higher in Group F (5.92 hours ± 4.39) as compared to mean duration of motor blockade in Group A (no motor blockade was appreciated) (p-value = 0.001) as shown in Figure 3.

**Table 1:** Inter-group comparison of average (median) pain score in postoperative period.

| Pain Score (VAS) | | Group F (n=25) | | Group A (n=25) | | p-value |
|---|---|---|---|---|---|---|
| | | Median | Min – Max | Median | Min – Max | |
| At Rest | 0-Min | 1 | 1 – 2 | 1 | 1 – 2 | 0.389NS |
| | 15-Min | 0 | 0 – 1 | 0 | 0 – 2 | 0.188NS |
| | 0.5-Hr | 0 | 0 – 0 | 0 | 0 – 2 | 0.069NS |
| | 1.0-Hr | 0 | 0 – 1 | 0 | 0 – 1 | 0.641NS |
| | 2.0-Hr | 0 | 0 – 2 | 0 | 0 – 2 | 0.761NS |
| | 4.0-Hr | 2 | 0 – 3 | 2 | 0 – 3 | 0.435NS |
| | 6.0-Hr | 2 | 1 – 4 | 2 | 2 – 3 | 0.721NS |
| On Leg Raise | 0-Min | 2 | 1 – 3 | 2 | 1 – 3 | 0.881NS |
| | 15-Min | 1 | 0 – 2 | 1 | 0 – 3 | 0.923NS |
| | 0.5-Hr | 1 | 0 – 1 | 1 | 0 – 3 | 0.132NS |
| | 1.0-Hr | 1 | 0 – 2 | 1 | 0 – 2 | 0.661NS |
| | 2.0-Hr | 2 | 0 – 4 | 1 | 0 – 3 | 0.366NS |
| | 4.0-Hr | 3 | 0 – 5 | 3 | 1 – 5 | 0.187NS |
| | 6.0-Hr | 4 | 2 – 6 | 4 | 3 – 5 | 0.863NS |

Values are median and (Min – Max), P-values by Mann-Whitney U test. P-value<0.05 was considered to be statistically significant. NS-Statistically non-significant.

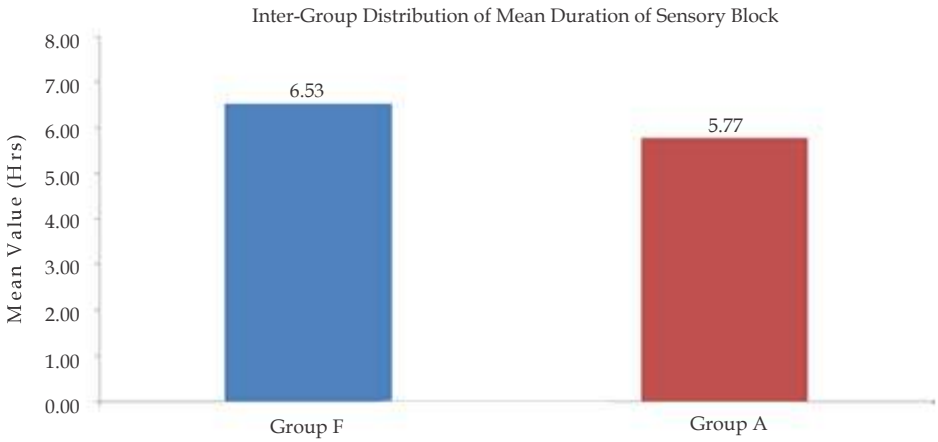


**Fig. 1:** Inter-group comparison of mean duration of sensory blockade.

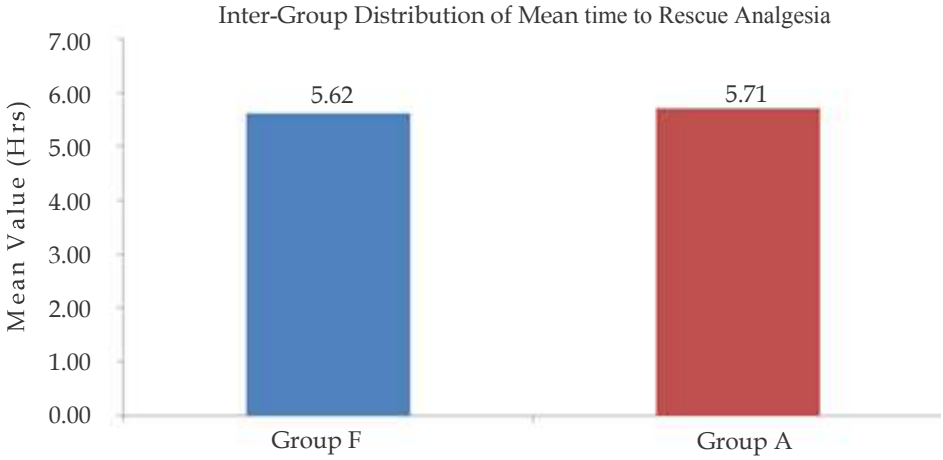


**Fig. 2:** Inter-group comparison of mean time to rescue analgesia.

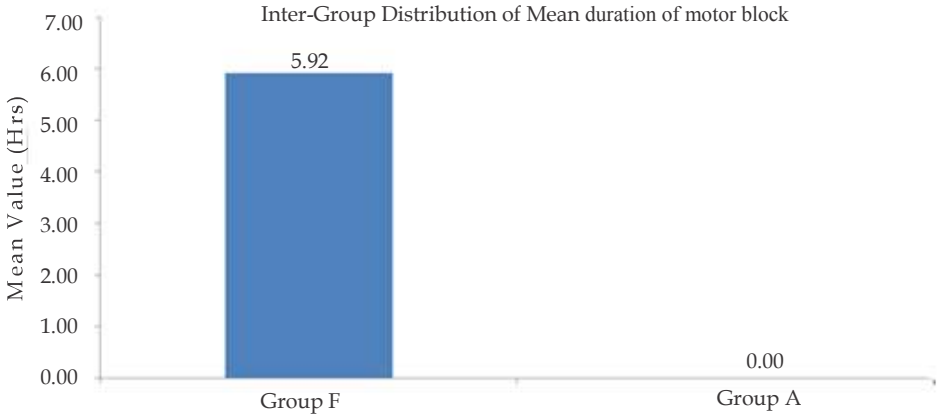


**Fig. 3:** Inter-group comparison of mean duration of motor blockade.

**Discussion and Conclusion**

Patients undergoing knee surgeries require adequate postoperative pain relief. It results in early recovery and rehabilitation thus improving overall outcome. The patients perceive maximum pain during the first 24 hours after surgery. We aimed to study the efficacy of USG guided Adductor canal block versus femoral nerve block for postoperative analgesia in knee surgeries. With the help of these blocks, we were able to keep these patients relatively pain free during immediate postoperative period.

The mean pain scores (Table 1) did not differ significantly at rest and on leg raise test, throughout the duration of the study till the time of administration of rescue analgesia between both the groups (p value >0.05 for all). The patients who received Adductor canal block were able to do an active leg raise test, while the patients who received femoral nerve block required assistance to do the leg raise test.

The duration of sensory blockade was comparable in both groups as shown in Figure 1. The mean duration of sensory blockade for patients in Group F was 6.53 hours ± 4.64, while for patients in Group A was 5.77 hours ± 1.30 with P value- 0.438. The time required for receipt of rescue analgesia did not differ significantly in both the groups with P value-0.878. (Figure 2)

Our results correlated well with results of the study by Stavros G. Memtsoudis et al. (2015). They compared ACB and FNB side to side on patients undergoing bilateral total knee replacement surgeries and concluded that FNB & ACB had equivalent analgesic potential; hence ACB could be an alternative to FNB [9]. Shu-Qing Jin et al. (2015) did a meta-analysis for effect of saphenous nerve block on knee surgeries and concluded that saphenous nerve block provided pain relief both during active flexion of the knee and at rest after knee surgery [10]. Similar findings were presented by Faraj W. Abdallah, M.D et al. (2016). They concluded that ACB provided non-inferior analgesia to FNB for patients undergoing anterior cruciate ligament surgeries [11].

In our study, patients who received USG guided femoral nerve block had significant motor blockade as compared to patients who received USG guided adductor canal block (p value-0.001). Also the duration of motor blockade was significantly higher in Group F as compared to Group A where we did not find any motor blockade (P value-0.001) as shown in Figure 3. These findings are supported by Sanjeev Sharma MD et al. (2009) wherein they had recognised quadriceps weakness as the major contributing factor (67%) in incidence of postoperative falls [4]. Similar study of **F**araj W. Abdallah M.D et al. (2016) concluded that ACB preserved quadriceps muscle function as compared to FNB in patients of anterior cruciate ligament reconstruction surgeries [11].

Recently, Duan Wang et al. (2017) did a meta-analysis and concluded that ACB is more beneficial to FNB regarding avoiding quadriceps muscle weakness and faster knee function recovery. It provided comparable pain relief to FNB and is associated with decreased risks of fall [12].

Adductor canal block also causes motor blockade if given proximally or if large volume of the local anaesthetic is used. This is because the local anaesthetic blocks the motor nerve to vastus medialis as it traverses the adductor canal. There have been studies reporting motor blockade post ACB (8%) but the blockade was not significant to cause any dysfunction [5]. In our study, we chose mid to lower 1/3$^{rd}$ part of adductor canal as the site of administration of the block and used 10cc volume of the local anaesthetic. Choosing a distal site for blockade spared the nerve to vastus medialis from being blocked and thus prevented motor weakness of the vastusmedialis. USG guidance helped us in accurate nerve location. It enhanced the success of the block and enabled us to use smaller volumes of the drug to achieve comparable analgesia.

Although there were no complications of the blocks, there were certain limitations to our study:

First of all, as per the protocol of Orthopaedic Department in our institute, mobilization of the patients undergoing knee surgeries starts after 48 hours postoperatively. Our study concluded at 24 hours postoperatively, hence we could not comment upon the mobilization of the patients and risk of falls in these patients. The second limitation was the small sample size. Further studies on large population groups are required to confirm whether the results of this study can be replicated.

Newer techniques are evolving day by day to help manage patients with severe postoperative pain. Among them, use of USG guided perineural catheters instead of single shot USG guided ACB or FNB, IPACK (Interspace between Popliteal Artery and posterior Capsule of the Knee) block and Cryoneurolysis have been introduced and comparative studies are on-going. The results of these studies can help in designing a comprehensive analgesic strategy for the postoperative period. It can benefit these patients and aid in their rehabilitation.

Thus from our study we conclude that USG guided adductor canal block can be used as an equivalent alternative to USG guided femoral nerve block for analgesia in postoperative period after knee surgeries. As Adductor canal block preserved quadriceps muscle strength, it may prove beneficial for early mobilization and rehabilitation of the patients.

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*Original Research Article*

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# Epidural 0.125% levobupivacaine with dexmedetomidine Versus Clonidine for Total Abdominal Hysterectomies: A Prospective Double Blind Randomized Trial

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**Abstract**

*Context:* Role of anesthesia for total abdominal hysterectomies is concerned with relieving pain during both intraoperative and the postoperative period. Several adjuvants are used to enhance the quality and duration of epidural anesthesia. *Aims:* We compared clonidine and dexmedetomidine as additives to levobupivacaine for epidural analgesia with emphasis on onset and duration of sensory block, duration of analgesia, and adverse effects. *Settings and design:* It is a randomized, double blind and prospective study conducted in tertiary care center. *Subject and Methods:* Sixty patients of American Society of Anesthesiologists (ASA) physical status Classes I and II who underwent total abdominal hysterectomies were randomly allocated into two equal groups. Group LC received 10 ml of 0.125% levobupivacaine + 1 $\mu g.kg^{-1}$ of clonidine and Group LD received 10 ml of 0.125% levobupivacaine + 1 $\mu g.kg^{-1}$ of dexmedetomidine through the epidural catheter. We evaluated onset of analgesia, time of peak effect, duration of analgesia, cardiorespiratory vitals, adverse effects, and need of rescue analgesics. *Statistical analysis:* Student's t-test and chi-square test. *Results:* Group LD demonstrated early onset, fast peak effect, prolonged postoperative analgesia, and stable cardiorespiratory vitals when compared with Group LC. There was a statistically significant reduction in analgesic requirement in group LD as compared to group LC. There were no major adverse effects in either group. *Conclusion:* As compared to clonidine, dexmedetomidine is a better neuraxial adjuvant to levobupivacaine, since it provides early onset, prolonged postoperative analgesia and stable cardiorespiratory vital parameters, without increasing adverse effects.

**Keywords:** Clonidine; Dexmedetomidine; Epidural analgesia; Levobupivacaine; Total abdominal hysterectomy.

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## Introduction

Administration of $\alpha_2$ agonists in epidural blocks, as adjuvants with local anesthetics in low doses offers new arena in the management of postoperative pain [1]. Levobupivacaine, S(−) enantiomer of bupivacaine, is known to have much safer pharmacological profile with reduced cardiac and neurological adverse effects because to its rapid protein binding rate [2,3]. Clonidine is a specific $\alpha_2$ adrenergic agonist having 200 fold selectivity for $\alpha_2$

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over $\alpha_1$ receptor. Dexmedetomidine, an imidazole compound has 8 times more specificity for $\alpha_2$ adrenergic receptors as compared to clonidine [4]. Dexmedetomidine is conferred with sedative, analgesic, and sympatholytic properties that blunt many of the cardiovascular stress responses that occurr during the perioperative period [5]. We conducted this study with the primary aim of comparing the duration of postoperative analgesia between epidural levobupivacaine 0.125% with clonidine and levobupivacaine 0.125% with dexmedetomidine for total abdominal hysterectomies. The secondary outcomes, such as onset of analgesia, hemodynamic variables, and adverse effects were evaluated in both the groups.

**Materials and Methods**

After obtaining hospital ethics committee approval and written informed consent was taken from each patient. Sixty adult female patients of American Society of Anesthesiologists (ASA) physical status Class I and II, between the age of 40 and 60 years undergoing total abdominal hysterectomy were enrolled for this study. The patients with coagulopathies, infection at injection site, mental retardation, second or thirddegree heart block, renal and hepatic insufficiency, uncontrolled hypertension and diabetes, and allergy to study drugs were excluded from the study. During preanesthetic visit, patients were meticulously examined clinically and routine investigations such as complete blood count, coagulation profile, serum creatinine, and electrocardiogram (ECG) were done. Entire procedure and 10 cm visual analog scale (VAS) (0, no pain and 10, worst pain imaginable) were explained during the preoperative visit. Patients were kept nil oral for 6 hours. Sixty patients were randomized using a computer generated randomization list [Fig. 1]. Patients were randomly allocated in to one of the two equal groups (30 patients in each group): group LD (dexmedetomidine group) and Group LC (clonidine group). After the patient entered the operation theater, an 18gauge intravenous (IV) cannula was secured, and intravenous fluid was started. And all standard monitors, namely blood pressure (BP), peripheral oxygen saturation by pulse oximetry ($SpO_2$), and ECG, were attached, and baseline vital parameters were recorded. With all aseptic precautions, back was painted and draped. At $L_3$-$L_4$ intervertebral space, local infiltration with 2% lidocaine was done and the epidural space was identified with an 18 gauge Tuohy needle (B. Braun, Melsungen, Germany) using the loss of resistance technique. None of our patients experienced accidental dural puncture. We placeda 20 gauge epidural catheter 4 cm into the epidural space and it was secured in place for postoperative analgesia. Intra vascular and intrathecal placement of epidural catheter was ruled out with a test dose of 3 ml epidural lignocaine 1.5% with adrenaline (1: 200,000). Subsequently, subarachnoid injection was given using a 25 gaugequincke spinal needle at L4–L5 intervertebral level and 15 mg 0.5% heavy bupivacaine was injected. The patient was laid back to the supine position. BP, Heart rateand $SpO_2$ were recorded every 3 minute for 15 min and every 5 min thereafter. The onset and level of sensory block was assessed using pin prick method and was recorded each minute until the start of surgery. Surgery was commenced only after the adequate level of sensory block was achieved. Once the surgery was completed, the patient was shifted to recovery room. The first dose of epidural injection was given when patient reported his VAS score is ≥3. Sixty patients were randomized into two equal groups: Group LD were injected with a 10 ml of levobupivacaine 0.125% with dexmedetomidine 1 $\mu g.kg^{-1}$, whereas Group LC were injected with a 10 ml of levobupivacaine 0.125% with clonidine 1 $\mu g.kg^{-1}$, through epidural catheter when the patient complains of pain (VAS ≥3). The epidural injection were given after negative aspiration test and post injection vitals were recorded. Pain was assessed using VAS scale of pain and sedation by Ramsay sedation score. BP, respiratory rate (RR), heart rate and $SpO_2$ were measured every 10 min until 30 min and thereafter every hour for 10 h.[8] We gave IVdiclofenac sodium 75 mg as rescue analgesic. After the epidural injection was given, the onset of analgesia (time from injection of the study medication to the first reduction in pain intensity to almost complete relief) and duration of analgesia (time from epidural injection to the time of the first request for rescue analgesic) were recorded in both groups. Any adverse effects such as nausea, vomiting, bradycardia,hypotension were looked for, recorded, and treated accordingly. Decrease in BP and HR by > 20% from the preoperative value was considered as hypotension or bradycardia, respectively, and was treated by intravenous fluid bolus, ephedrine, or atropine, as required. Nausea and vomiting were treated with IV ondansetron.

The data obtained from our study was tabulated and analyzed using the computer software (SPSS for Windows, Version 16.0. Chicago, SPSS Inc.). We used Student's t-test for numerical values and chi-square test for categorical values. The P value < 0.05 was considered as statistically significant.

## Results

The demographic profile of the patients and duration of the surgery in both groups were comparable.(Table 1) Group LD demonstrated an earlier onset (6.41 ± 0.85 min) of analgesia as compared to the addition of clonidine (7.67 ± 1 min). In addition to earlier onset, dexmedetomidine also helped in achieving the peak analgesic level in a shorter time (10.20 ± 7.85 min) compared with clonidine (12.23 ± 5.76 min). The duration of analgesia was significantly prolonged in dexmedetomidine group (445.33 ± 9.75 min) in comparision to clonidine group (324.17 ± 10.75 min). (Fig. 2) These analgesic characteristics were statistically highly significant ($p < 0.0001$) (Table 2). In comparison to Group LC (66.67%), less number of patients (46.67%) in Group LD required IV rescue analgesics.

In our study, we obsereved that during initial 240 min (baseline to 240 min), p value of VAS score being >0.05, it was statistically insignificant.(Fig. 3) VAS scores of two Groups LC and LD becomes statistically significant at 320–460 min time intervals ($p < 0.05$). Clonidine group demonstrated higher VAS score requiring rescue analgesia at 320

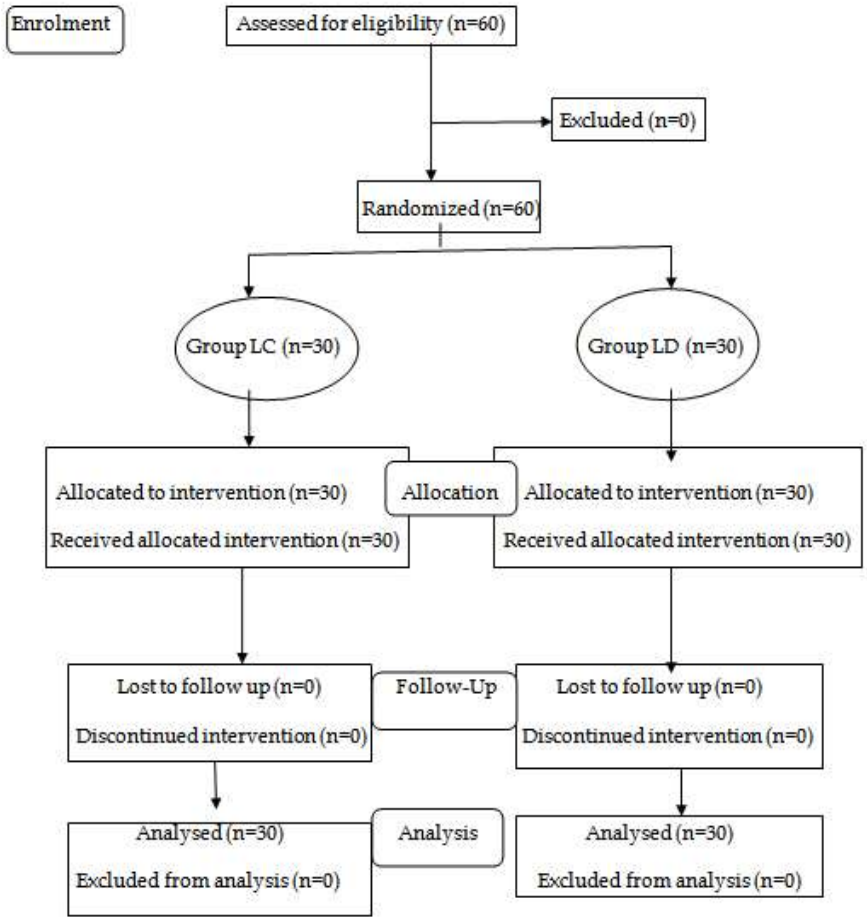


**Fig. 1:** Consort flow diagram

**Table 1:** Demographic profile of patients

| Character | Group LC (n=30) | Group LD (n=30) | p-value |
|---|---|---|---|
| Age (years) | 50.17 ± 7.90 | 49.83 ± 7.50 | 0.433 |
| Weight (kg) | 59 ± 6.94 | 58.83 ± 6.68 | 0.462 |
| Duration of surgery (min) | 106.83 ± 13.07 | 107.50 ± 12.52 | 0.420 |

Group LC – Levobupivacaine + Clonidine ; Group LD – Levobupivacaine + Dexmedetomidine, p value> 0.05; not significant.

**Table 2:** Comparison of analgesic characteristics between two groups

| Analgesic characteristics | Group LC (n=30) | Group LD (n=30) | p -value |
|---|---|---|---|
| Duration of analgesia (min) | 324.17 ± 10.75 | 445.33 ± 9.75 | <0.00001 |
| Time of onset of analgesia (min) | 7.67 ± 1 | 6.41 ± 0.85 | <0.00001 |
| Time of peak onset of analgesia | 12.23 ± 5.76 | 10.20 ± 7.85 | <0.00001 |
| Need of rescue analgesics n (%) | 20 (66.67) | 14 (46.67) | |

Group LC – Levobupivacaine + Clonidine; Group LD – Levobupivacaine + Dexmedetomidine, P value <0.001; higly significant.

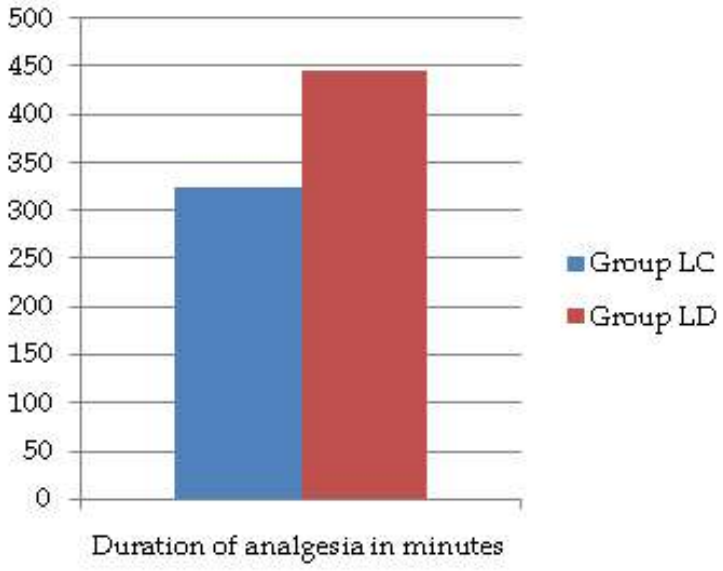


**Fig. 2:** Duration of Analgesia between two groups

Group LC – Levobupivacaine + Clonidine; Group LD – Levobupivacaine + Dexmedetomidine.

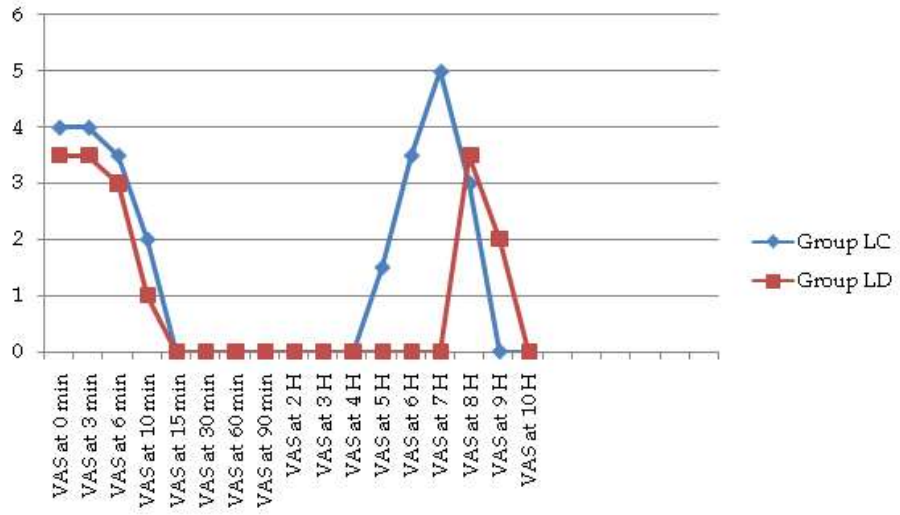


**Fig. 3:** Comparison of visual analog scale scores between groups

Group LC – Levobupivacaine + Clonidine; Group LD – Levobupivacaine + Dexmedetomidine.

min and peak VAS scores at 340–380 min, whereas in dexmedetomidine group VAS score begin to increase only after 390 min and reached maximum VAS scores at 460–490 min.The incidence of sedation, nausea, vomiting, and shivering were not statistically significant in either group. There were no episodes of hypotension, bradycardia, dizziness, and respiratory depression in either group.

## Discussion

The CSE technique is an effective modality for patients undergoing infra-umbilical surgeries who need effective and prolonged postoperative analgesia. CSE technique is a combination of the density, rapidity, and reliability of a subarachnoid block with the flexibility of epidural anesthesia to prolong the duration of analgesia [6]. Levobupivacaine, a long acting Senantiomer of bupivacaine is conferred with less cardiac and neural toxicity than bupivacaine. Levobupivacaine is found to be safe and effective for epidural and spinal anesthesia [7,9]. $\alpha_2$ agonists with anxiolysis, sedation, analgesic, and hypnotic properties are increasingly used as neuraxial adjuvants. $\alpha_2$ agonists are devoid of side effects such as nausea, vomiting, pruritus, and urinary retention as compared to opioids [10].

Dexmedetomidine is a highly specific $\alpha_2$ adrenergic agonist with 8 times greater affinity than clonidine and hence higher doses of it can be used with less α1 effect. When used neuraxially, clonidine enhances the action of local anesthetics, increases the intensity and duration of analgesia. It is conferred with sedative properties, and the adverse effects are hypotension and bradycardia [11].

In our study, we observed that addition of 1 $\mu g.kg^{-1}$ of dexmedetomidine to 0.125% levobupivacaine prolongs the duration of analgesia compared to addition of 1 $\mu g.kg^{-1}$ body weight of clonidine to 0.125% levobupivacaine in epidural block following total abdominal hysterectomies. In addition, dexmedetomidine achieved the faster onset of analgesia. Lesser patients (46.67%) in Group LD required diclofenac sodium injection as rescue analgesic than patients (66.67%) in Group LC.

There were no clinically significant variations in cardio-respiratory parameters throughout the study period, which proves the said effects of $\alpha_2$ agonists in maintaining a haemodynamically stable peri-operative, and post-operative period [12,13].

The safety profile of both these drugs was good as none of the patient in either group demonstrated deep sedation or respiratory depression which is in concordance with several other studies [14,15,16,17].

## Conclusion

Our results allow us to conclude that dexmedetomidine 1 $\mu g.kg^{-1}$ is a better neuraxial adjuvant to levobupivacaine 0.125% in comparison to clonidine 1 µg.kg-1 for providing early sensory onset and longer postoperative epidural analgesia without any major adverse effects in total abdominal hysterectomies.

*Key messages:*

In comparison to clonidine, dexmedetomidineis a safe and reliable neuraxial adjuvant to levobupivaine, as it provides early onset and prolonged postoperative anlagesia, without any side effects.

*Financial support and sponsorship:* Nil.

*Conflicts of interest:* There are no conflicts of interest.

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*Original Research Article*

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# Comparison between Butorphanol and Tramadol as an Anti-Shivering Agent in Patients Undergoing Spinal Anesthesia for Lower Limb Orthopedic Surgeries

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**Abstract**

*Introduction:* Shivering can be defined as a physiological response to core hypothermia. Occurrence of shivering is common in patients of regional anesthesia as well as general anesthesia. Shivering cause some serious health consequences so efforts should be taken to prevent or treat at earliest. *Aim:* To compare efficacy and safety of butorphanol over tramadol as anti-shivering agent under spinal anesthesia and to watch for any side effects. *Material and Methods:* A prospective randomized comparative study was conducted in 80 patients who developed shivering under spinal anesthesia posted for lower limb orthopedic surgeries. At onset of shivering, patients were randomly allocated in two study groups and study drug was given as slow intravenous injection. *Group B* - Injection butorphanol (1 mg) 1 ml slow iv. *Group T* - Injection tramadol (50 mg) 1 ml slow iv. Time taken to complete control of shivering, failure rate, recurrence rate, hemodynamic changes and side effects (nausea, vomiting, itching and sedation) were recorded during study period. Data were collected and analysed using statistical methods. *Result:* Response rate is similar in both groups. At 1 min post treatment, butorphanol group had more patients with complete control of shivering. There was significantly less chance of reccurence in butorphanol group. Hemodynamic parameters were comparable in both study groups through entire study. Butorphanol treated patients had mild to moderate degree of sedation than tramadol group. *Conclusion:* Both butorphanol and tramadol are effective in control of shivering under spinal anesthesia. Butorphanol has advantage of faster onset and lesser recurrence rate, only disadvantage being mild to moderate sedation which may warrant observation of respiration.

**Keywords:** Shivering; Butorphanol; Tramadol.

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## Introduction

Shivering is defined as involuntary repeated skeletal muscular activity in response to core hypothermia to augment metabolic heat production [1]. Spinal anesthesia is commonly used in various lower limb orthopedic surgical procedures. Shivering following spinal anesthesia is very common and incidence may varies from 40-60% [1,2]. Shivering can also occur in patients recovering from general anesthesia as well.

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Shivering following spinal anesthesia is due to impairment of thermoregulatory autonomic control under anesthesia. Spinal induced vasodilatation and decrease in shivering threshold by $0.5^0$C- $1^0$C cause redistribution heat from core to periphery [3]. Perioperative hypothermia is a major cause of shivering under spinal anethesia [4,5]. Other causes may include cold operating room atmosphere, cold intravenous fluids, drug reactions, transfusion reaction, high grade fever and septicemia.

Shivering under anesthesia may have serious consequences to patient. It can cause increase oxygen consumption, increase carbon dioxide production and hence lactic acidosis [5,6]. It can cause tachycardia and hypertension. Thus patient with cardiac disease or patients with low cardio pulmonary reserve, shivering may be detrimental [5,7]. Other problems are increase in intraocular pressure, increase in intracranial pressure and increase in minute ventilation [5,8,9]. Shivering is also undesirable to surgeon and anesthetist, besides stressful to patient.

Shivering under anesthesia has serious health consequences and various methods should be applied to prevent or control it. Various non pharmacological methods include ambient operating room temperature, iv fluid warmers, radiant heaters and space blankets [9,10]. Pharmacological drugs include two groups mainly, opioids (like morphine, pethidine, tramadol, butorphanol) and non opioids (like ketamine, magnesium sulphate, doxapram, granisetron, propofol).

Our study was carried out to compare butorphanol over conventional antishivering agent tramadol in control of shivering under spinal anesthesia in lower limb orthopedic surgical procedures. Our aim is to find more effective, safer and faster acting antishivering agent with minimal side effects.

## Materials and Methods

A prospective randomized double blind comparative study was conducted in our institute during June 2018 to Dec 2018. Total 80 patients with either gender between 20 to 40 years of age with ASA grade 1 or 2, posted for lower limb orthopedic surgery, who developed shivering under spinal anesthesia were included in our study.

*Exclusion criteria*

ASA grade 3 or 4

Patients with major systemic disease

History of allergy to study drugs

Head injury

Coagulation disorders

Patients with history of fever or sepsis

Informed written consent was taken from patients. Randomisation is done by sealed envelope technique. The cases were randomly allocated to two study groups, Group B (butorphanol) and Group T (tramadol).

All patients included in our study were evaluated pre operatively. After applying monitors, baseline vitals were recorded in operating room. The temperature of operation theatre was maintained between $22^0$C-$24^0$C in all cases. Baseline axillary temperature was recorded by mercury thermometer. All patients in our study received spinal anesthesia in sitting position. Spinal anesthesia was instituted in L2-L3 space with 23 G spinal needle.0.5% bupivacaine heavy was given 3 ml with aiming to achieve T10 dermatome sensory block. Surgery was permitted to start after achieving adequate level of spinal block.

When patient developed shivering grade 2 or 3 after giving spinal anesthesia, study drug was given as per study groups. All patients were given supplemental oxygen 6 liter / min via oxymask.

Group B - Inj. Butorphanol 1 mg (1 ml) iv diluted in 10 cc normal saline

Group T -Inj. Tramadol 50 mg (1 ml) iv diluted in 10 cc normal saline

Shivering is graded as follow

| | |
|---|---|
| Grade 0 | No shivering |
| Grade 1 | Mild fasciculations of head and neck |
| Grade 2 | Moderate / visible tremors involving more than one group of muscles |
| Grade 3 | Severe / gross muscular activity involving entire body |

Sedation score is graded as follow

| | |
|---|---|
| Grade 0 | Alert |
| Grade 1 | Arousable to verbal command |
| Grade 2 | Arousable to gentle tactile stimulation |
| Grade 3 | Arousable to vigourous tactile stimulation |
| Grade 4 | No awareness |

The study drug was given over 1 minute. Time taken for complete abolition of shivering (Grade 0) was noted from end of injection. Patients were monitored after giving study drug at 1 min, 3 min, 5 min, 10 min, 20 min, 45 min. Vitals (temperature, pulse, systolic BP, diastolic BP, $SpO_2$) were recorded during shivering and post treatment. If shivering

is not completely controlled (Grade 0) after 20 min of administering drug, it was considered as failure and patients were warmed by space blankets or heat warmers. Patients were closely monitored for recurrence of shivering, sedation and side effects (nausea vomiting, itching).

Recurrence of shivering within 20 min post treatment in any patient was actively treated by space blankets and heat warmers. Sedation score was assessed in both study groups. Any patient who developed nausea/vomiting was treated with iv injection ondansetron. Any patient who developed itching was treated with inj chlorpheniramine.

*Statistical Analysis*

All data were collected and analysed with SPSS 17 software. Statistical methods such as student's t test and chi square test were performed to find level of significance of our data values of both groups.

## Results

In our study, patients of both groups were comparable in regards to demographic characteristics, duration of surgery and ASA grade. (p value > 0.05, insignificant) (Table 1).

There was no significant difference among both groups in regards to axillary temperature (baseline and during shivering) and shivering grade at onset of shivering. There was slight fall in axillary temperature in both groups during shivering but difference is not statistically significant. Most of patients had grade 2 shivering at onset in both study groups.

Time taken to complete control of shivering at 1 min was significantly higher in group T compared to group B (p value<0.05). Complete cessation of shivering was 95% in group B compared to 85% in group T (p value >0.05). (Table 2 and 3).

Hemodynamic parameters were comparable in both groups during shivering and post treatment at 15 min. There is no statistically significance difference in both study groups (p value >0.05). There is rise in pulse rate during shivering in both study groups (Table 3,4).

Failure to control shivering (grade 0) within 20 min of injecting study drug was higher in tramadol group (15%) as compare to butorphanol group (5%), difference was statistically insignificant. Recurrence of shivering was observed significantly higher in tramadol group (35%) compared to butorphanol group (10%). Incidences of nausea / vomiting were found in both groups with no significant difference. Incidence of grade 1 and grade 2 sedation was

**Table 1:** Demographic characteristics (Mean ± SD and p value)

| | Group B | Group T | p value |
|---|---|---|---|
| Age (years) | 28.45 ± 8.56 | 30.36 ± 7.43 | 0.28 |
| Weight (kgs) | 50.32 ± 12.65 | 52.78 ± 10.54 | 0.34 |
| Gender (M:F) | 32/8 | 35/5 | 0.12 |
| ASA grade(1/2) | 36/4 | 38/2 | 0.39 |
| Duration of surgery(min) | 76.45 ± 12.88 | 74.34 ± 15.65 | 0.51 |

**Table 2:** Axillary temperature and shivering grade (Mean ± SD and p value)

| | | Group B | Group T | P value |
|---|---|---|---|---|
| Axillary temperature | Baseline | 36.48 ± 0.56 | 36.68 ± 0.42 | 0.07 |
| | During shivering | 35.25 ± 0.67 | 35.46 ± 0.42 | 0.09 |
| Shivering grade | Grade 2 | 35(92%) | 38(95%) | 0.58 |
| | Grade 3 | 5(8%) | 2(5%) | 0.58 |

**Table 3:** Response rate as anti-shivering agent

| Time to control shivering | Group B (n=40) | Group T (n=40) | p value |
|---|---|---|---|
| 1 min | 16 (40%) | 6 (15%) | 0.012 |
| 3 min | 10 (25%) | 8 (20%) | 0.59 |
| 5 min | 7 (17.5%) | 10 (25%) | 0.41 |
| 10 min | 4 (10%) | 7 (17.5%) | 0.33 |
| 20 min | 2 (5%) | 3 (7.5%) | 0.64 |
| 45 min | 2 (5%) | 6 (15%) | 0.13 |

**Table 4:** Hemodynamic parameters (Mean ± SD)

| Vitals | | Group B | Group T |
|---|---|---|---|
| Systolic blood pressure | Baseline | 116.65 ± 12.43 | 117.54 ± 11.67 |
| | During shivering | 114.43 ± 10.65 | 116 ± 13.76 |
| | Post treatment (20 min) | 117.12 ± 10.23 | 116.65 ± 10.87 |
| Diastolic blood pressure | Baseline | 70.54 ± 13.56 | 72 ± 11.34 |
| | During shivering | 70 ± 10.67 | 72.12 ± 12.63 |
| | Post treatment (20 min) | 72.12 ± 11.45 | 71.45 ± 10.37 |
| Heart rate | Baseline | 76.12 ± 14.56 | 78 ± 15.67 |
| | During shivering | 86.54 ± 12.67 | 86.57 ± 13.76 |
| | Post treatment (20 min) | 78.43 ± 12.45 | 82.34 ± 12.67 |

**Table 5:** Incidence of complications

| | Group B (n= 40) | Group T (n= 40) | p value |
|---|---|---|---|
| Failure | 2(5%) | 10(25%) | 0.0128 |
| Recurrence | 4(10%) | 14(35%) | 0.007 |
| Nausea / vomiting | 4(10%) | 6(15%) | 0.50 |
| Itching | 2(5%) | 1(2.5%) | 0.55 |
| Sedation (grade 1 or 2) | 10(25%) | 1(4%) | 0.008 |

significantly higher in butorphanol group (25% ) as compared to tramadol group (4%), difference being highly significant. Itching was observed only in two patients in group B and one patient in group T, difference was statistically insignificant.

## Discussion

Spinal anesthesia is commonly used in lower limb orthopedic surgeries. Shivering can occur in patients receiving spinal anesthesia as well as patients recovering from general anesthesia. Incidence of shivering under spinal anesthesia can range from 40-60% [1,2]. Shivering is body's compensatory mechanism to minimize heat loss and to increase metabolic heat production. Risk factors associated with shivering may include age, type and duration of surgery and level of spinal block [11].

Perioperative hypothermia is most common factor involve in incidence of shivering. Shivering under spinal anesthesia is due to sympathetic blockage induce vasodilatation and resultant heat loss below the level of block. Other contributing factors are rapid intravenous fluid infusions, cold operating room atmosphere and cold irrigating solutions [12].

Shivering is common perioperative problem encountered under spinal anesthesia, which has adverse health impacts on patients. Shivering causes tachycardia, hypertension, acidosis, increase oxygen consumption and increase carbon diaoxide production. Shivering can cause serious health consequences in patients with preexisting cardiac disease. Shivering can cause discomfort to patients besides interfering with baseline monitoring intraoperatively (blood pressure, oxygen saturation) [5]. So atmost care should be taken to prevent or control shivering as early as possible. Both nonpharmacological and pharmacological measures should be applied to effectively control shivering under spinal anesthesia.

Pharmacological methods by drugs like ketamine, propofol, granisetron, morphine, pethidine, tramadol, butorphanol and clonidine, shivering can be effectively controlled. Among them, opioids hold important place in a list of antishivering agents. Opioids acts as anti shivering agents by modulation of central thermoregulation (anterior hypothalamus, raphe nucleus and raphe magnus) [9]. In our study we compared efficacy of synthetic opioids (butorphanol and tramadol) in control of shivering. Tramadol exerts its anti shivering effect by its agonistic action on μ receptors thus preventing neuronal uptake of serotonin and noradrenaline. Butorphanol acts anti shivering agent by agonistic action on μ and ƙ receptors [13].

We compared tramadol and butorphanol as anti shivering agent in regards to their efficacy, onset of action and side effects (nausea, vomiting, itching and sedation).

In our study we had used axillary temperature by putting thermometer in axilla. Axillary temperature could be fairly good indicator of core temperature. Sessler et al. [2] had also revealed same findings in his study.

There were not any significant differences in baseline mean temperature preoperatively. Mean temperatures at onset of shivering were 35.25 ± 0.67$^0$C and 35.46 ± 0.42$^0$C. Difference in both study groups was not significant. Dhimar et al. [14] also found in their studies that mean temperature at onset of shivering was 36.2 ± 0.4$^0$C. Shivering was graded in our study on basis of Tsai and Chu scale (0-3 scale) [15].

In our study we found that butorphanol and tramadol both were effective in controlling shivering under spinal anesthesia. Butophanol and tramadol both had nearly similar results in regards to effective control of shivering. Our finding was accordance with findings of Bansal et al. [5] and Bhatanagar et al. [16]. In contrast to our findings, Mustak ali et al. [9] observed in their study that tramadol is more effective than butorphanol in control of shivering.

In our study we observed that response rate within 1 minute was more with butorphanol group compared to tramadol group, indicating butorphanol had more faster onset in control of shivering. Our findings were in correlation to findings of bansal et al. [5] and krithika et al. [11]. According to Bharat et al. [13], tramadol was faster in onset in control of shivering which was contradiction to our findings.

Our studies showed that there was lesser incidence of recurrence of shivering in butorphanol treated group compared to tramadol group. Butorphanol was highly effective to prevent recurrence. Our finding were similar to study done by Dhimar et al. [14] and Krithika et al. [11] who also demonstrate butorpanol had lesser chance of recurrence. In contrast to our study, Bharat et al. [13] who observed lower rate of recurrence in tramadol treated patients compared to butorphanol group.

There were no significant alterations in hemodynamic parameters during course of study in all patients both study groups. There was slight rise in pulse rate during shivering which was insignificant. Our findings were in correlation to studies of Dhimar et al. [14] and Mathews at al. [17] who also observed same.

We found no significant differences in regards to nausea, vomiting and itching in post treatment period in both study groups. Bansal et al. [5] also stated in their studies that incidences of nausea/ vomiting were comparable in butorphanol group and tramadol group. Sedation is assessed by using 4 point sedation scale. In our study, there was higher incidence of sedation in butorphanol group compared to tramadol group. Degree of sedation (grade 1/2) was significantly higher in butorphanol treated patients. Our findings were similar to study done by Joshi et al. [12] indicating that butorphanol treated patients had more sedation than tramadol treated group.

*Limitations*

There are a few the limitations of our study. Relatively small sample size is limitation of our study in regards to common perioperative problem. We have used axillary temperature as indicator of core temperature due to unacceptability of esophageal or rectal temperature probe.

## Conclusion

On basis of our study we can conclude that butorphanol and tramadol both are effective in control of shivering after spinal anesthesia. Butorphanol has added advantage of faster onset, lesser recurrence rate and mild to moderate sedation over conventional antishivering agent tramodol.

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

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*Original Research Article*

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# A Comparative Study of Intrathecal versus Epidural Tramadol for Post Operative Analgesia

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**Abstract**

*Back ground:* Pain is an integral part of all surgery and is the biggest cause of apprehension amongst patients. This apprehensive behavior creates a feeling of dissatisfaction with the pain relief methods used conventionally. Easy availability, ease administration and economical makes a method of analgesia successful (Lehmann et al.). Inj. Tramadol is a synthetic agonist opioid analgesic without any preference for any particular type of opioid receptor. Its presence in the central neuraxial system mediates the nociceptive action when given either intra thecally or epidurally. *Aim:* The present study was designated to compare postoperative analgesic efficacy and safety of epidural tramadol vs. intrathecal tramadol along with its physiological side effects. *Study Design:* Prospective, randomized-controlled, blinded trial. *Methodology:* 60 patients of either sex, ASA status I or II and posted for abdominal surgeries, gynecological surgeries, orthopedic surgeries were studied in two groups to receive either Inj. Tramadol intra thecally (Group II) along with spinal anesthesia or Epidurally (Group I) along with single shot epidural anesthesia. Duration and quality of analgesia (visual analog scale [VAS] scores), hemodynamic parameters, and adverse event were recorded and statistically analyzed using Chi square test and a p value of <0.05 was considered significant. *Results:* Mean duration of analgesia after epidural bolus of opioid tramadol was 9.86 ± 2.19 hours as compared to intrathecal tramadol which was significantly higher 14.23 ± 1.76. VAS score was always lower in Group I in comparison to other group during the study at various intervals. Hemodynamic parameter remained stable in both the groups. *Conclusion:* We conclude that tramadol 0.5 mg/kg with bupivacaine 0.5% intrathecally provides more effective and longer-duration analgesia than tramadol 1 mg/kg with bupivacaine 0.05% when given epidurally.

**Keywords:** Epidural analgesia; Postoperative pain; Tramadol.

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## Introduction

"For all pleasure mankind can get in not in happiness but from relief of pain." – *John Droden*

A patient posted for surgery is most apprehensive about the pain. They differ in their pain thresholds. It seems that most of the patients are dissatisfied with the techniques used for pain relief. The adequate treatment of pain has been an important yard stick for the quality care the hospital provides. Effective pain control is essential for optimum care

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of patient in the post operative period. If a method of analgesia is to be successful and available to a large number of patients it must be suitable for use even in a general ward and with ease of administration. (Lehmann et al., 1990) [5]. Tramadol a synthetic opioid, without the much dreaded side effects of Opioids, has recently found a place in the management of pain relief post operatively without the fear of respiratory depression. If used intrathecally its antinociceptive effect is known to be transmitted through opioid receptors present at the level of spinal cord. (Bernatzky et al. 1986) [2]. With this back ground we carried out this study (done in 1998) to study the effectiveness of opioids (Tramadol) when given intrathecally as compared to single shot epidural injection for providing pain relief in the post operative period along with the observation for its side effects if any.

## Material and Methods

This prospective randomized study was conducted after approval from institutional ethical committee and written informed consent of the patients. For the study 60 patients posted for elective genitourinary and lower limb surgeries of ASA grade I & II, aged 20-55 years of either sex were selected. They were divided in two groups randomly to receive either.

Group I Epidural Tramadol: Inj. Bupivacaine 0.5% 20 ml with Inj. Tramadol 50 mg.

Group II Intra thecal Tramadol: Inj. Bupivacaine 0.5% heavy 3 ml with Inj. Tramadol 25 mg.

After proper pre anesthetic checkup including the vital parameters, investigations, written informed consent patients were premedicated with Inj. Glycopyrrolate 0.2 mg, Inj. Midazolam 1 mg, Inj. Ondansetron 4 mg patients were randomly selected to receive either spinal or epidural anesthesia. No Analgesics were given pre or per operatively. Patients with failed block in whom general anesthesia was to be supplemented were excluded from the study. The Anesthesia procedure was performed under strict aseptic and antiseptic precautions either with 18 G Toughy needle (Group I) or 23 G spinal needle (Group II). Patients were observed for any change in the vital parameters per operatively and post operatively till 24 hours. For post operative pai assessment, Visual Analogue Scale (VAS 1-10) was used. Rescue analgesic of Inj. Diclofenac 75 mg was given when VAS was > 5. Any untoward event or complications were recorded.

## Results

The two groups were comparable in age, weight, sex, duration of surgery as showed in table 1. Table 2 shows the level of sensory block received after either of the procedure and table 3 shows the types of procedure selected in either group. Table 4 shows the mean duration of surgery in both the groups. All the observations were clinically and statistically comparable with no much significant change.

Per operative monitoring of Pulse, Blood pressure, $SpO_2$, respiration was done for both the groups. Graph 1 and Graph 2 show the changes in the mean pulse rate and mean arterial blood pressure in both the groups. The changes in the mean pulse rate were not much significant as compared with the pre operative value and also when compared statistically between both the groups. Even the mean Arterial pressure (MAP) did not show much change per operatively except at end of 2 hours in Group I which might be due to

**Table 1:** Demographic Variables

| Parameters | Group I (n=30) | Group II (n=30) | p value |
|---|---|---|---|
| Mean Age (years) | 37.43 ± 13.46 | 38.56 ± 14.1 | 0.946 |
| Sex Ratio (M:F) | 20:10 | 09:21 | |
| Weight (kg) | 56.93 ± 17.22 | 51.33 ± 8.78 | 0.562 |
| ASA grading (I/II) | 14:16 | 14:16 | 1 |

Values are Mean ± SD or numbers

**Table 2:** Sensory Block Level

| Level | Group I (n=30) | Group II (n=30) |
|---|---|---|
| T12 | 02 | 02 |
| T1 | 13 | 11 |
| T8 | 15 | 16 |
| T6 | 00 | 01 |
| Total | 30 | 30 |

pain in patient. The block level was not very high in either of the group and we did not observe any respiratory depression either due to technical snag or even the study drug used.

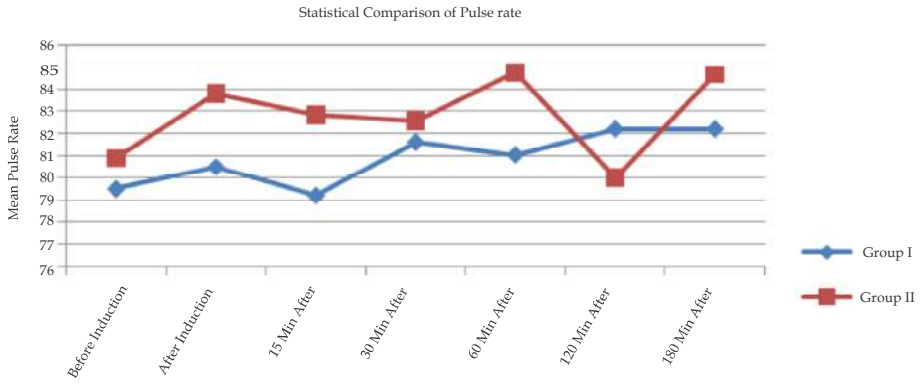
Post operative analgesia was noted for its duration and intensity using VAS. It was observed that 10 patients in group I had pain free period for 9 hours post surgery whereas it was 24 in Group II who were pain free even till 10-14 hours. 20 patients in Group I had pain free period of up to 14 hours and in Group II, 6 patients had pain free period up to 16 hours of surgery (Table 5). The need of rescue analgesia was more in Group I than in Group II. The mean VAS was 3.8 in group I and 3 in group II at the end of 12 hours which was still around 3.2 at the end of 24 hours in group I which was around 5.5 in group II (Table 6).

The duration of recovery from the anesthetic effect in both the group i.e., the recovery from sensory block and motor block (Modified Bromage Scale) were observed (Table 8 and Table 7 respectively).

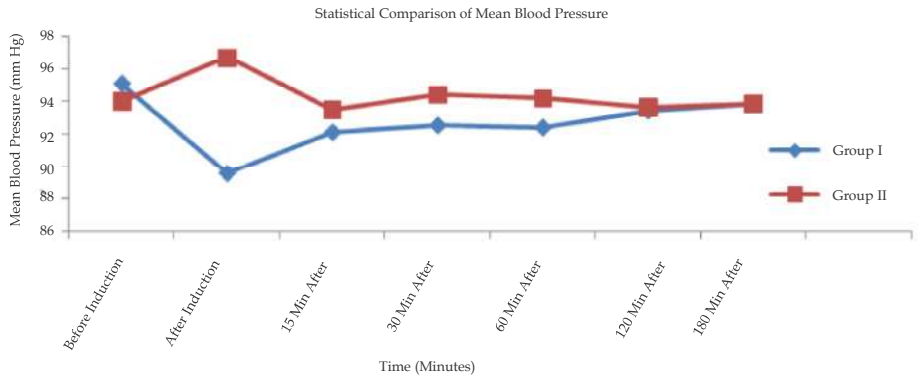
Anticipated complications like hypotension, bradycardia, nausea, vomiting, itching, urinary retention and drowsiness were not seen in any patients in either group except for two patients who had backache 24 hours of procedure in Group I.

**Table 3:** Types of Surgery

| No. | Surgery | Group I | Group II |
|---|---|---|---|
| 1 | Abdominal Hysterectomy | 6 | 5 |
| | Inguinal Hernioplasty | 10 | 12 |
| 3 | Vaginal Hysterectomy | 5 | 2 |
| 4 | Haemorrhoidectomy | 3 | 3 |
| 5 | DHS for # hip | 6 | 8 |




**Graph 1:**




**Graph 2:**

**Table 4:** Showing the Mean Duration of Surgery

| Duration of Surgery In Minutes | Group I | Group II |
|---|---|---|
| 30-40 | 01 | 00 |
| 41-50 | 00 | 02 |
| 51-70 | 05 | 06 |
| 71-90 | 10 | 10 |
| 91-100 | 11 | 12 |
| 101-140 | 03 | 00 |
| Mean ± SD | 76.36 ± 26.62 | 74.52 ± 23.53 |

**Table 5:** Showing the Mean Duration of Analgesia in Both Groups

| Duration (Hours) | Number of Patients | |
|---|---|---|
| | Group I | Group II |
| 5-9 | 11 | 00 |
| 10-14 | 19 | 24 |
| 15-16 | 00 | 06 |
| 20-25 | 00 | 00 |
| MEAN ± SD | 9.86 ± 2.19 | 14.23 ± 1.76 |
| p value | <0.01 = Highly significant | |

**Table 6:** Showing Comparison of Pain Score (VAS) at Different Intervals

| Duration (Hrs) | Visual Analogue Scale | | T Value | p Value | Inference |
|---|---|---|---|---|---|
| | Group I | Group II | | | |
| 1 | 0.5 ± 0.67 | 0.1 ± 0.33 | 0.34 | >0.05 | NS |
| 2 | 1.1 ± 0.83 | ± 0.44 | 0.23 | >0.05 | NS |
| 4 | 1.7 ± 1.05 | 1.5 ± 0.5 | 0.95 | >0.05 | NS |
| 8 | 3.9 ± 0.92 | 2.2 ± 0.55 | 8.71 | >0.01 | HS |
| 12 | 5.1 ± 0.56 | 4.1 ± 0.58 | 6.8 | >0.01 | HS |
| 24 | 5.5 ± 0.49 | 4.6 ± 0.47 | 7.5 | >0.01 | HS |

**Table 7:** Showing Time to Recover from Motor Block (Bromage Scale)

| Time (Hours) | Group I | Group II |
|---|---|---|
| 2-4 | 20 | 08 |
| 4-6 | 10 | 19 |
| 6-8 | 00 | 03 |
| 8-10 | 00 | 00 |
| Mean ± SD | 3.32 ± 1.01 | 4.15 ± 0.98 |

**Table 8:** Showing Time to Recover from Sensory Block by Pin Prick Method Below T 12 Levels

| Time (Hours) | Group I | Group II |
|---|---|---|
| 2-4 | 20 | 12 |
| 4-6 | 09 | 18 |
| 6-8 | 01 | 00 |
| 8-10 | 00 | 00 |
| MEAN ± SD | 3.96 ± 1.18 | 4.36 ± 1.25 |

**Table 9:** Showing Post Operative Complications

| Complications | Group I | Group II |
|---|---|---|
| Nausea | 02 | 00 |
| Vomiting | 00 | 00 |
| Hypotension | 00 | 00 |
| Bradycardia | 00 | 00 |
| Urinary retention | 00 | 00 |
| Drowsiness | 00 | 00 |
| Itching | 00 | 00 |
| Backache | 02 | 00 |

## Discussion

Post operative pain is a self limiting phenomenon and most severe during first day following surgery. Various factors are attributed as the cause of post operative pain like type of surgery and its incision, subjective threshold of the patients, surgical complications, anesthetic management and quality of post operative care. Narcotics have established their role for the relief of post operative pain where it is used either orally, systemically, as infusions or dermally. Use of opioids in central neuraxial block was first done in 1979 after the discovery of opiates receptor in spinal cord. Whether given intra thecally or epidurally the effect of opioids is caused after crossing the meningeal layers and covering the whole cord through CSF where it causes its action by acting on opioid receptors [1]. The known side effects of opioids also occur after administration by spinal or epidural route as they get absorbed in the systemic circulation.

Tramadol a synthetic opioid when used in central neuraxial blockade causes its effect by acting on spinal as well as supra spinal opioid receptors in the CNS (Karl et al., 1976). The anti nociceptive action is mediated by its acting on μ receptors (Shank et al., 1992) [8]. Moreover it was also observed that the effect of Tramadol was not antagonized by Naloxone totally suggesting its non opioid mechanism of its anti nociceptive property (shown by inhibition of non amine uptake).

In this present study done in 1998 where Tramadol was administered through either epidural or intrathecal route for relief of post operative pain in patients under going various types of surgeries as shown in table 3. Monitoring of patients for pulse, blood pressure, $SpO_2$, respiration and comparing at various intervals showed that vitally patient stayed stable all through out the surgery when compared to pre operative values as well as between two groups. A good pre loading and not allowing the sensory effect to rise high above causing sympathetic block can be the reason for this stability (Graph 1 and Graph 2).

There was no respiratory depression in either group either due to high level of sensory block or the study drug. This implies that Tramadol 25 mg intra thecally or 50 mg epidurally is safe enough to have any adverse effect on respiration or cardio vascular system.

Our main concern of postoperative analgesia was observed by Visual Analogue Scale (VAS) and it revealed that patients receiving tramadol through epidural route experience pain earlier (10 patients had pain free period of around 9 hours, 20 patients had pain relief up to 15 hours) as compared to intra thecal route (24 patients had pain free period up to 14 hours, rest 6 had pain relief up to 16 hours). Rudra A et al. [7] observed that when tramadol used alone in epidural route produces analgesia for up to 10 hours post operatively when compared to local anesthetic alone which advocates the use of opioids in central neuraxial block for pain relief. Because of shorter duration of analgesia in Group I as compared to Group II, the use of rescue analgesia was early and evens more in Group I suggesting good quality of analgesia with intra thecal route Table 5 and Table 6.

Few patients do develop nausea and vomiting when Tramadol is used systemically. After its use in central neuraxial block, the rate of complications was found to be quite less in our study (Table 9).

## Conclusion

Intrathecally administered tramadol 25 mg has longer duration of post operative analgesia than the epidurally administered tramadol 50 mg with substantial patient safety as there was no respiratory depression and minimal incidence of the anticipated complications like nausea, vomiting, allergic reaction, and hypotension. With advent of newer receptor specific opioids there is a scope for further evaluation of this route of administration of opioids for post operative pain relief.

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# A Comparative Study of Lignocaine Nebulization with Intravenous Lignocaine in Attenuation of Pressor Response to Laryngoscopy and Intubation

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**Abstract**

*Background:* Laryngoscopy and endotracheal intubation is often associated with hypertension and tachycardia because of sympatho-adrenal stimulation which is usually transient. In patients with cardiovascular and cerebrovascular diseases, the sudden hemodynamic response can produce deleterious effects in the form of myocardial ischaemia or infarction, arrhythmias, cardiac failure, raised ICP and cerebral haemorrhage. In view of this, the present study was undertaken to evaluate and compare the effects of 2% Lignocaine 2 mg/kg nebulization given 10 minutes and 2% Lignocaine 2 mg/kg iv given 90 seconds before induction for attenuation of intubation response. *Materials & methods:* Sixty ASA Grade I & II patients in the age group 20-60 years of either sex scheduled for elective surgeries under general anaesthesia were allocated into Group A and Group B with the sample size of 30 in each. Group A received nebulization with 2% lignocaine 2 mg/kg 10 minutes and Group B received 2% lignocaine 2 mg/kg intravenous 90 sec before induction. Heart rate, systolic and diastolic blood pressure and mean arterial pressure and $SpO_2$ were recorded, basal values and subsequently at 1st, 3rd, 5th, 7th and 10th minute after intubation. *Results:* It was noted that, Group A, the rise of HR, SBP, DBP, MAP at 1 min after intubation were found to be 24.86 bpm, 9.6 mm Hg, 20.44 mm Hg, 22.30 mm Hg respectively. In Group B, the rise of HR, SBP, DBP, MAP were found to be 11.7 bpm, 3 mm Hg, 2.61 mm Hg, 4.77 mm Hg respectively. *Conclusion:* It was seen that use of lignocaine has suppressed heart rate and blood pressure changes to laryngoscopy and endotracheal intubation. In fact intravenous lignocaine has better suppressing property than nebulization of lignocaine.

**Keywords:** Laryngoscopy; Endotracheal intubation; Cardiovascular response.

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## Introduction

The major responsibility of an anaesthesiologist is to secure airway to provide adequate ventilation to the patient during general anaesthesia. Endotracheal intubation is the gold standard of securing the airway. However, endotracheal intubation requires time, a skilled anaesthesiologist, appropriate instruments and adequate circumstances with respect to space and illumination.

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Laryngoscopy and endotracheal intubation is associated with intense sympatho-adrenal stimulation resulting in increase in heart rate (HR) and blood pressure (BP) consequent to the release of catecholamines [1,2]. The cardiovascular response is a reflex phenomenon. This is mediated by Vagus and Glossopharyngeal cranial nerves. They carry the afferent stimulus from epiglottis and infraepiglottic region activating vasomotor centre to cause a peripheral sympathetic adrenal response resulting in hypertension, tachycardia and arrhythmias [3,4,5].

The hemodynamic response, being transient in nature may not be of much clinical significance in normal healthy individuals [6]. However, in patients with limited myocardial reserve, with raised intracranial pressures (ICP) or intraocular pressures (IOP), the laryngoscopic reaction may predispose to development of pulmonary edema [7], myocardial insufficiency [8] and cerebrovascular accidents [9]. Thus, there is necessity to blunt these harmful laryngoscopic reactions.

Attenuation of stress response to laryngoscopy and intubation has been practiced either by non-pharmacological or pharmacological methods.

The non-pharmacological methods used are smooth and gentle intubation with a shorter duration of laryngoscopy, insertion of Laryngeal Mask Airway (LMA) [10,11] or advanced airways [12] and blocking glossopharyngeal & superior laryngeal nerves. [13]. Pharmacological methods like topical or intravenous lignocaine, high dose of opioids [14], α & β adrenergic blockers [15,16], calcium channel antagonists [17] like diltiazem, verapamil, vasodilators like nitroglycerine [18] and α2 agonists like clonidine [19] & dexmedetomidine [20,21] are used.

Topical anaesthesia with lignocaine in forms of viscous gargles [22], lignocaine aerosols [23] or oropharyngeal sprays [24] remains a popular method alone or in combination with others to attenuate the stress response.

Intravenous lignocaine has been used to suppress cough during tracheal intubation [25], laryngospasm and cough during extubation [26]. It has also been used to suppress airway hyperactivity and mitigate bronchoconstriction [27]. Intravenous lignocaine with its well established centrally depressant and anti-arrhythmic effects is found to be more suitable alternative to attenuate the stress response as compared to other forms of lignocaine [28,29,30]. The purpose of our study is to compare the effect of nebulization of lignocaine with intravenous lignocaine on blunting the hemodynamic response to laryngoscopy and tracheal intubation.

The study will also help us standardize minimal safe dose of lignocaine to attenuate the stress response which can be safely practiced prior to induction making it simple, practical, effective and economical prophylactic method.

## Material and Methods

After obtaining approval from ethics committee and informed consent from patients, 60 Patients with ASA grade I and II in the age group of 20 to 60 years of either sex posted for elective surgery to be done under general anaesthesia were divided into two groups randomly as,

**Group A** - received Lignocaine (2%) nebulization 2 mg/kg 10 minutes prior to induction, N- 30.

**Group B** - received intravenous Lignocaine (2%) 2 mg/kg 90 seconds prior to induction, N- 30.

A detailed pre-anaesthetic evaluation including history of previous illness, previous surgeries, general physical examination and systemic examination was done. Baseline investigations were carried out. A written informed and valid consent was taken after explaining the anaesthetic procedure in detail. Patient arrived to the preoperative room 30 minutes before surgery and preoperative basal heart rate, non-invasive blood pressure readings, $SpO_2$, cardiac rate and rhythm were also monitored from a continuous visual display of electrocardiogram from lead II were recorded. The patient in Group A received Lignocaine (2%) nebulization 2 mg/kg undiluted using a simple fitting face mask with Compressor Nebulizer (DeVilbiss-3655I) 10 min before induction. Patient was taken inside Operation Theatre and standard monitors such as Electrocardiogram (ECG), pulse oximeter ($SpO_2$) and Non-invasive sphygmomanometer (NIBP) cuff were attached. All patients were pre-oxygenated with 100% oxygen for 3 minutes by a face mask. All patients were pre-medicated with Inj. Midazolam 1mg, Inj. Fentanyl 2 µg/kg iv.

The patient in Group B received 2% lignocaine 2 mg/kg body weight 90 sec before induction.

Anaesthesia was induced with inj. propofol 2 mg/kg iv as 1% solution, after loss of consciousness and confirmation of adequacy of mask ventilation endotracheal intubation was facilitated with succinylcholine 1.5 mg/kg iv. Laryngoscopy was performed using Macintosh laryngoscope,

under visualization of vocal cords a lubricated (2% lignocaine jelly) cuffed endotracheal tube of appropriate size was passed. After confirming bilaterally equal air entry, the endotracheal tube was secured. Anaesthesia was maintained using 50% nitrous oxide and 50% of oxygen and 1% sevoflurane. After the patients recovered from succinylcholine further neuromuscular blockade was maintained with non-depolarizing muscle relaxant atracurium 0.5 mg/kg iv.

Heart rate (HR), Systoloic Blood Pressure (SBP), Diastolic Blood Pressure (DBP), Mean Arterial Pressure (MAP) were noted as below-

1. Basal before giving any study drugs and premedication
2. at 1, 3, 5, 7 and 10 minutes after laryngoscopy and intubation

At the end of the procedure patients were reversed with Neostigmine 0.05 mg/kg iv and glycopyrrolate 0.01 mg/kg iv and extubated after recovery of adequate muscle power and consciousness.

## Results

*Statistical methods:*

The collected data was compiled in EXCEL sheet and Master sheet was prepared. Data was presented by visual impression like Bar-Diagram, Histogram. Qualitative was represented in form values & percentages. Chi-square test was used for qualitative data. For comparison of Quantitative variables of two groups unpaired t-test was used.

p- Value < 0.05 – Statistically significant (S)

p- Value > 0.05 – Not significant (NS)

Samples are age matched (Group A mean 38.20 ± 10.63, Group B mean 39.80 ± 12.45) with t = 1.68 and p = 0.098**.** Samples are weight matched (Group A mean 57.00 ± 10.35, Group B mean 60.63 ± 9.92) with t = 1.08 and p = 0.248. There was no significant difference in age, gender and weight distribution in the two groups.

**Table 1:** Table showing changes in Mean Heart Rate

| HR | Group A Mean ± SD | Group B Mean ± SD | t-value | P-value |
|---|---|---|---|---|
| Basal | 86.97 ± 11.23 | 87.30 ± 13.09 | 0.145 | P=0.928 NS |
| Post-intubation | | | | |
| 1 Minute | 111.83 ± 15.91 | 99.00 ± 12.25 | 3.50 | P=0.001 S |
| 3 Minute | 105.87 ± 16.46 | 96.90 ± 15.01 | 2.41 | P=0.031 S |
| 5 Minute | 95.33 ± 14.81 | 93.36 ± 12.91 | 0.743 | P=0.477 NS |
| 7 Minute | 92.30 ± 14.93 | 89.73 ± 12.79 | 0.715 | P=0.467 NS |
| 10 Minute | 88.33 ± 12.56 | 87.93 ± 12.41 | 0.124 | P=0.902 NS |

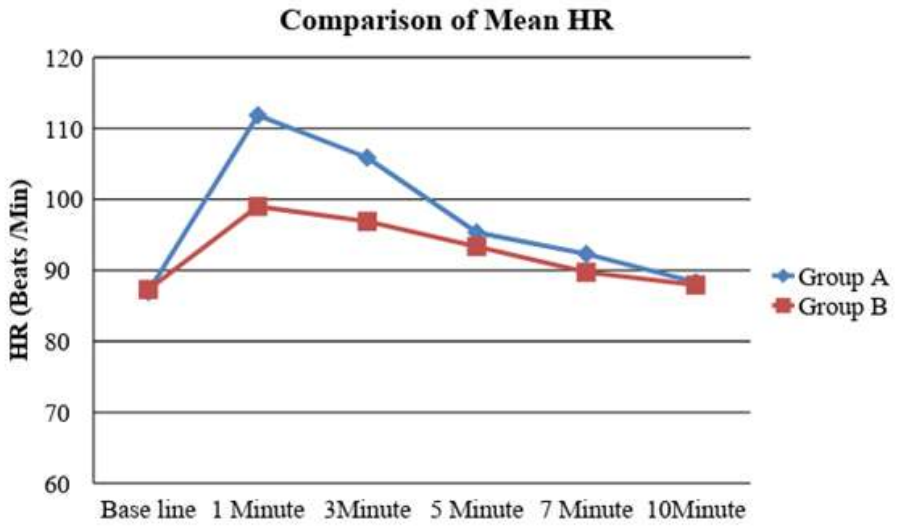


**Fig. 1:** Graph showing changes in Mean Heart Rate (HR)

**Table 2:** Table showing changes in Mean Systolic Blood Pressure (SBP)

| | Group A Mean ± SD | Group B Mean ± SD | t-value | P-value |
|---|---|---|---|---|
| Base Line | 130.17 ± 11.13 | 132.10 ± 15.18 | 0.247 | P=0.629 NS |
| Post-intubation | | | | |
| 1 Minute | 139.77 ± 13.39 | 135.10 ± 14.68 | 2.09 | P=0.039 S |
| 3Minute | 130.13 ± 19.53 | 121.97 ± 17.85 | 1.98 | P=0.031 S |
| 5 Minute | 125.73 ± 18.84 | 114.23 ± 17.08 | 2.44 | P=0.016 S |
| 7 Minute | 119.53 ± 15.25 | 113.10 ± 18.46 | 3.07 | P=0. 003 S |
| 10 Minute | 116.66 ± 11.56 | 113.73 ± 17.35 | 1.26 | P=0.102 NS |

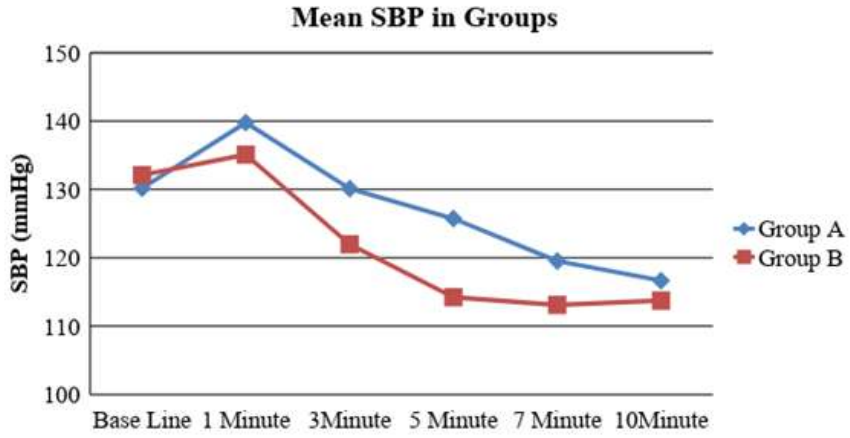


**Fig. 2:** Graph showing changes in Mean Systolic Blood Pressure (SBP)

**Table 3:** Table showing changes in Mean Diastolic Blood Pressure (DBP)

| DBP | Group A Mean ± SD | Group B Mean ± SD | t-value | P-value |
|---|---|---|---|---|
| Base Line | 83.26 ± 7.83 | 84.46 ± 8.92 | 0.553 | P=0.582 NS |
| Post-intubation | | | | |
| 1 Minute | 103.70 ± 11.20 | 87.07 ± 18.69 | 4.18 | P=0.000 S |
| 3 Minute | 89.90 ± 10.79 | 80.26 ± 11.32 | 3.37 | P=0.001 S |
| 5 Minute | 81.90 ± 11.27 | 75.80 ± 12.04 | 2.25 | P=0.028 S |
| 7 Minute | 79.80 ± 8.05 | 76.30 ± 12.47 | 1.29 | P=0. 202 NS |
| 10 Minute | 78.93 ± 5.36 | 75.17 ± 10.85 | 1.70 | P=0.094 NS |

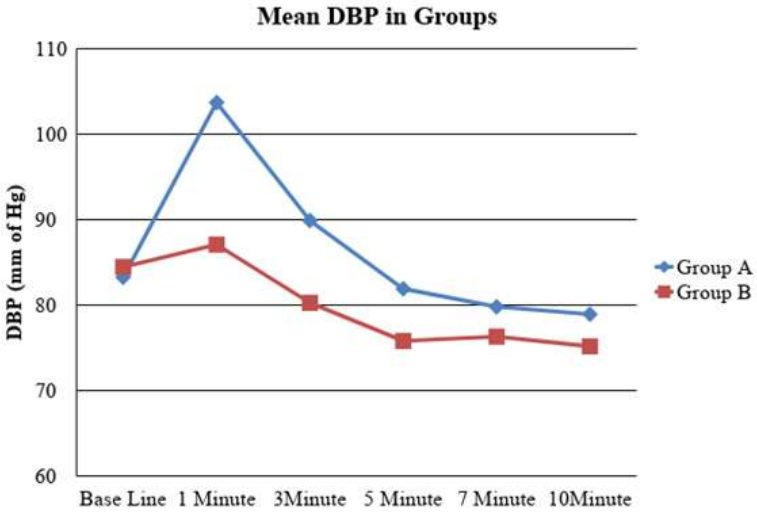


**Fig. 3:** Graph showing changes in Mean Diastolic Blood Pressure (DBP)

**Table 4:** Table showing changes in Mean Arterial Pressure (MAP)

| MAP | Group A Mean ± SD | Group B Mean ± SD | t-value | p-value |
|---|---|---|---|---|
| Base Line | 98.63 ± 7.83 | 100.23 ± 10.05 | 0.763 | p=0.642 NS |
| Post-intubation | | | | |
| 1 Minute | 120.93 ± 11.64 | 105.00 ± 11.01 | 5.44 | p=0.000 S |
| 3 Minute | 105.86 ± 12.44 | 94.23 ± 12.23 | 3.65 | p=0.001 S |
| 5 Minute | 95.90 ± 12.43 | 88.16 ± 12.77 | 3.29 | p=0.001 S |
| 7 Minute | 92.03 ± 10.39 | 88.83 ± 13.42 | 1.43 | p=0. 104 NS |
| 10 Minute | 90.86 ± 7.90 | 87.96 ± 12.38 | 1.12 | p=0.128 NS |

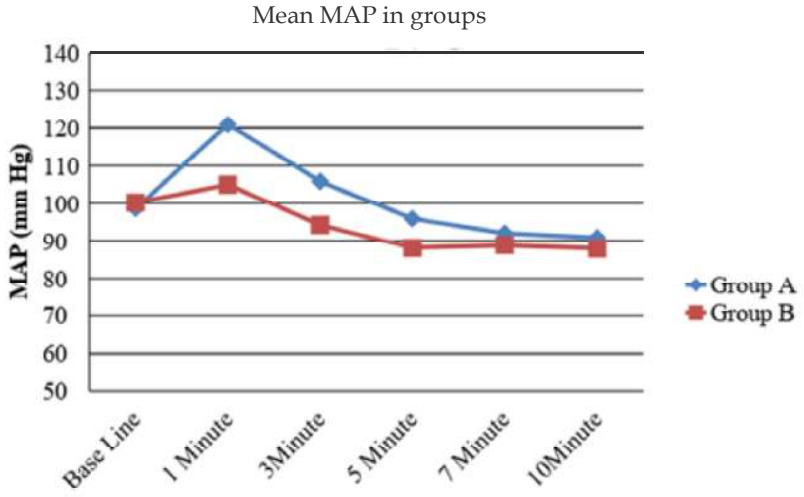


**Fig. 4:** Graph showing changes in Mean Arterial Pressure (MAP)

## Discussion

Local anaesthetic like lignocaine has been the most common agent used for blunting the hemodynamic responses to laryngoscopy and tracheal intubation. Lignocaine has been used by the following routes to blunt the hemodynamic responses to intubation:

- As lignocaine gargle for oropharyngeal analgesia [22]
- As lignocaine aerosol for intratracheal analgesia [23]
- As intravenous infusion for analgesia [31]
- As a topical spray [24]

Lignocaine has been successfully used to blunt the hemodynamic responses to intubation. The mechanisms explained for this action of lignocaine and desirable properties are as follows:

1. Suppression of airway reflexes elicited by irritation of epipharyngeal and laryngopharyngeal mucosa [32].
2. Effectively prevents and treats laryngospasm [26].
3. Excellent cough suppressant [25].
4. Myocardial depression [23].
5. Peripheral vasodilatation [23].
6. Antiarrhythmic properties [33].
7. Increasing depth of general anaesthesia, reduction in anaesthetic requirements of nitrous oxide and halothane [34].
8. Depression of autonomic nervous system [35].
9. Analgesic properties when given intravenously [31].

Gianelly et al. [36] concluded that the concentration of lignocaine in the blood following intravenous administration was directly related to the dose given. They also concluded that an effective safe blood level of 2 to 5 µg/ml is obtained by intravenous bolus of 1 to 2 mg/kg and major side effects may occur with blood levels 9 µg/ml. Adriani [37] asserts that the topical anaesthetic agents applied to the larynx and trachea are readily absorbed from the pulmonary alveoli.

The blood levels achieved after oropharyngeal anaesthesia with viscous lignocaine (25 ml of 2% as mouth wash and gargle 15 min before laryngoscopy) was found to be 0.5 µg/ml at the time of laryngoscopy [20]. The average lignocaine level following aerosol anaesthesia of the upper airway (6-8 ml of a mixture of 1/3 of 2% viscous lignocaine and 2/3 of 4% aqueous lignocaine) was 1.2 µg/ml at 1 minute and 1.4 µg/ml at 2 minutes did prevent PVC [23] in the treated patients even though minimum blood levels effective in suppression of premature ventricular contractions range from 0.6 – 2 µg/ml.

Inhalation of lignocaine aerosol is a safe, simple, effective and generally accepted method. Obvious limitations are small children, uncooperative patients, patients in whom there is danger due to regurgitation and vomiting and lack of time is another limitation. With all the advantages and ease of administration of lignocaine and minimal side effects the present study was carried out to evaluate the efficacy of lignocaine in blunting the hemodynamic response to laryngoscopy and endotracheal intubation using two different routes of administration at similar dosage and look for any side effects.

Mounir Abou-Madi et al. [28] compared two doses of 2% lignocaine when given intravenously for suppression of pressor response and suggested 1.5 mg/ kg provided better control of pressor response compared to 0.75 mg/ kg when given 2 to 3 min before laryngoscopy. Stanlay Tarn et al. [29] observed that intravenous lignocaine at a dose of 1.5 mg/kg attenuated the increase in Heart rate (HR) and Arterial Blood Pressure (ABP), only when given 3 min, before intubation and did not give any protection when given at 1 min, 2 min and 5 min before intubation. Mohan K, Mohana Rupa L [38] stated that Intravenous lignocaine 2% in the dose of 1.5 mg/kg given 3 minutes before laryngoscopy and intubation is helpful in attenuating the cardiovascular response to intubation. Gulabani M et al. [39] said that lignocaine in a dose of 1.5 mg/kg given 3 min before laryngoscopy and intubation was more effective than dexmedetomidine 0.5 µg/kg in attenuating the increase in systolic and DBP at 3 min and 5 min after endotracheal intubation. We used 2 mg/ kg of 2% lignocaine intravenous for attenuation of pressor response and preferred to give 90 sec before induction and intubation was done 90 sec after induction as we used succinylcholine; thus duration between iv lignocaine and intubation was 3 minutes.

Bahaman Venus [40] studied the effects of nebulization of 6ml of 4% lignocaine on cardiovascular response to laryngoscopy and intubation 5 min before induction compared to control with saline nebulization. The pressor response and tachycardia was successfully prevented by the aerosol group than the control. Ahmed M. et al. [41] used Lidocaine 2% (2 mg/kg) in 5 ml saline was added to a standard nebulizer with a full face mask attached with $O_2$ flow at 3 L/min., then the patient was asked to inhale the local anesthetic vapor deeply for 15 minutes. Patient's tolerance to endotracheal tube in the study group showed a highly significant increase in numbers of patients in grade 0 and highly significant decrease in numbers in grades 1 and 2 in comparison with the control group.

***Data Analysis***

*Heart rate changes* (as shown in Table 1 and Figure 1)

In Group A, where nebulization of 2% Inj. Lignocaine 2 mg/kg 10 minutes before laryngoscopy and intubation was used to blunt the pressor response, the base line value of Heart rate (HR) was 86.97 bpm. One minute following laryngoscopy and intubation, the heart rate (HR) increased to 111.83 bpm, representing a rise of 24.86 bpm above the baseline value. Thus the maximal rise in heart rate (HR) seen was by an average of 24.86 bpm. It was seen that the elevated heart rate (HR) started settling down towards base line value by 10 min. In Group B, where 2% Inj. Lignocaine 2mg/kg iv was administered to attenuate the hemodynamic response to laryngoscopy and intubation, the baseline value of Heart rate (HR) was 87.30 bpm. One minute following laryngoscopy and intubation, the heart rate (HR) increased to 99 bpm, representing a rise of 11.70 bpm above the baseline value. Thus the maximal rise of Heart rate (HR) seen in the Group B was by an average of 11.70 bpm. It was seen that the elevated Heart rate (HR) started settling down towards the baseline value by 7 min. The maximum rise in heart rate was noted at 1 min following intubation in both the groups which concurs well with mentioned studies above. The mean rise in Heart rate at 1 min in Group A was 24.86 bpm compared to 11.70 bpm in Group B. The mean rise in the heart rate was comparatively lesser in the intravenous group and statistically significant when compared to the Group A.

*Blood Pressure Changes* (as shown in table 2, 3, 4 and figure 2, 3, 4)

In Group A, where nebulization of 2% Lignocaine 2 mg/kg 10 min before laryngoscopy and intubation

to blunt the pressor response, the maximal increase in the SBP, DBP and MAP was found to be 9.60 mm Hg, 20.4 4 mm Hg and 22.30 mm Hg respectively.

In Group B, where 2% Lignocaine 2 mg/kg iv was employed 90 sec before laryngoscopy and intubation to blunt the pressor response, the maximal increase in the SBP, DBP and MAP was found to be 3.0 mm Hg, 2.41 mm Hg and 4.77 mm Hg respectively. The attenuation of pressor response was highly significant in the Intravenous group

## Conclusion

Lignocaine in both routes is easy, safe and effective method to blunt hemodynamic response to laryngoscopy and intubation. Intravenous lignocaine 2% in the dose of 2 mg/kg 90 sec before induction effectively controlled the hemodynamic response to laryngoscopy and endotracheal intubation. Nebulized lignocaine 2% in the dose of 2 mg/kg was less effective in controlling the hemodynamic changes as compared to intravenous lignocaine 2%.

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# Dexmedetomidine Infusion to Reduce Emergence Agitation Post Operatively

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**Abstract**

*Background*: Emergence Agitation is a very common phenomenon seen after nasal surgeries, can be due to the nasal packing done and feeling of shortness of breath. We did this study to investigate the efficacy of Inj. Dexmedetomidine infusion to reduce the incidence of emergence agitation in adults undergoing nasal surgeries. *Methods*: 60 adult patients undergoing nasal surgeries were randomized into two groups. The Group-D (n=30) receive dexmedetomidine infusion at rate of 0.5 mcg/kg/hour from starting of induction of anesthesia and stopped before extubation while Group-P (n=30) received normal saline infusion as placebo. Induction of anesthesia was done with Inj. Propofol (2-2.5 mg/kg) & fentanyl (1 mcg/kg) and sevofluarane used for maintainance of anesthesia. The incidence of Emergence Agitation (EA) evaluated by Ricker's Agitation sedation scale (RSAS) and intraoperative haemodynamic stability were evaluated in study. *Results*: Incidence of Emergence agitation was lower in Group-D than Group-P. Mean arterial blood pressure & heart rate were stable intra operatively and during emergence agitation in Group-D as compared to Group-P. There was no delay in extubation observed with no residual sedation in group D. *Conclusion*: Emergence agitation in the early post extubation phase following general anesthesia is a prevelantphenomenon seen during nasal surgery patients in adults. Intra operative dexmedetomidine infusion reduces postoperative Emergence Agitation (EA) and provides good intra operative haemodynamic stability in adults undergoing nasal surgeries without any respiratory depression and delayed extubation.

**Keyword:** Emergence Agitation; Dexmedetomidine; Ricker's Agitation Sedation Scale (RSAS).

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## Introduction

Emergence agitation phenomenon that develops in the early phase of recovery from general anesthesia, and is characterized by agitation, confusion, disorientation, and possible violent behavior. EA is a mental state in which there is a lack of connection between consciousness and the patients' behavior, which is characterized by excitement, irritability, disorientation and inappropriate behavior. EA is transient but quite disturbing for patients and OR staff and can cause

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injury, hemorrhage, and self extubation. Various causes can be attributed for this agitated behavior like history of smoking, alcohol, obesity, duration of surgery, type of anesthetic agent used.

Dexmedetomidine is a highly selective alpha 2-adrenergic receptor agonist used widely in intensive care unit for its sedative, analgesic and anxiolytic effects without causing respiratory depression. When used per operatively, it shows better intraoperative haemodynamic stability and minimizes the response to surgical stimuli. Its use can be synergistic, reducing requirement of other anaesthetic agents.

The aim of the present study was to determine efficacy of dexmedetomidine in prevention of postoperative EA providing good haemodynamic stability per operatively in adults undergoing nasal surgeries.

**Methodology**

After approval from he hospital ethical committee, a prospective study was carried out in adult patients under going nasal surgeries for various indications at our hospital, from January 2018 to December 2018. Patients of age group 18-50 years of ASA I and II were included. Exclusion criteria were Grade III and IV, patients with co morbid conditions and systemic disease like diabetes, renal involvement, and liver abnormalities. A written, informed consent was obtained from all patients after full explanation of the study.

After proper premedication with inj. glycopyrolate 0.2 mg, inj.midazolam 1 mg, inj. ondansetron 8 mg/kg, inj. fentanyl 1 µg/kg., securing a large bore intravenous cannula, General anesthesia was administered to all the patients with inj.propofol (2-2.5 mg/kg) till loss of eyeless reflex and inj.succinylscoline (2 mg/kg) and inj.atracurium (0.5 mg/kg). The patients were divided into two groups. Group-D to receive Dexmedetomidine 0.5 mcg/kg/hour in an infusion immediately after the induction of anaesthesia while Group-P to receive normal saline as placebo. All other personnel and observers were blinded to the study grouping. The dexmedetomidine infusion was prepared by an attending anaesthesiologist and started immediately after intubating the patient. Anesthesia was maintained with oxygen and nitrous oxide in ratio of 50:50, inhalational agent sevoflurane at the concentration of 1.5–2% to maintain the desired MAC and Muscle relaxation was maintained by IV atracurium as per body weight at regular intervals. Per operatively the Patients were monitored all through out for Pulse, Blood Pressure, $SpO_2$, $EtCO_2$, and Temperature. Observations of Mean Arterial Blood Pressure, Heart rate was made preoperatively, and then 10, 30, 45 minutes for every fifteen minutes till the end of surgery. The dexmedetomidine infusion was stopped before extubation and any stimulation of patients was avoided except verbal command to open eyes. The Operating ENT surgeonon completion of surgery performed nasal packing anticipating postoperative hemorrhage. For nasal packing, gauze or saline-soaked Merocel was applied.

Patients were observed immediately after extubation for any emergence phenomenon. Post operative Emergenceis usually considered in between time interval from'time zero' to 2 min after extubation. Emergence agitation (EA) was evaluated by Riker sedation agitated scale [7,8] (RSAS, table1); this scale is usually used for agitated behavior in Intensive Care Units. It is a scale which scales the agitated behavior through various parameters and is scaled from score of 7 maximum (dangerous EA) to 1 as minimum. RSAS was measured at 2 min, 5 min & 10 min interval after extubation. The maximum RSAS scale noted was recorded, A score of ≥ 5 at any time was considered as emergence agitation (EA) A Scale of 7 was considered as dangerous EA. The presence of adverse side effects like sedation, delayed extubation & vomiting also evaluated.

Guidelines for RSAS Assessment

1. Agitated patients are scored by their most severe degree of agitation as described

2. If patient is awake or awakens easily to voice ("awaken" means responds with voice or head shaking to a question or follows commands), that's a RSAS 4 (same as calm and appropriate – might even be napping).

3. If more stimuli such as shaking is required but patient eventually does awaken, that's RSAS 3.

4. If patient arouses to stronger physical stimuli (may be noxious) but never awakens to the point of responding yes/no or following commands, that's a RSAS 2.

5. Little or no response to noxious physical stimuli represents a RSAS 1. This helps separate sedated patients into those you can eventually wake up (RSAS 3), those you can't awaken but can arouse (RSAS 2), and those you can't arouse (RSAS 1).

## Results

A total of 60 patients were considered for the study. After randomization patients were divided in two groups. Group D to receive dexmedetomidine infusion (0.5 μg/kg/hour) and Group P to receive normal saline infusion during surgery. The infusion was stopped before surgery and the patients were observed for any emergence phenomenon after extubation. The time from extubation (time '0') to two minutes was considered for emergence agitation behavior if any.

Demographically there was no difference between the groups as far as age, sex and weight of the patient was concerned (Table 2).

Patients undergoing surgeries like Septoplasty for Deviated Nasal septum, FESS for nasal polyps, endoscopic DCRs were included for our study. Types of surgery and duration of surgery in both the groups were also comparable (Table 2).

Sevoflurane was maintained at 2% dial concentration initially at the start of surgery in both the groups and then adjusted as per the desired MAC of approximately 1. (the value reduces by around 50% when $N_2O$ is used simultaneously). MAC value was 0.9 ± 0.2 in group D and was 1 ± 0.3 in group P and this was clinically not significant.

At the end of surgery patients were observed for the arousal state. The time from discontinuation of sevoflurane to time to verbal response was slightly longer in group D (8.2) as compared with group P (7.5) was noted. The mean time from discontinuation of inhalation anesthetic agent to extubation was 9 min in group D as compared to 8.8 min in group P. This difference was not of much clinical significance. There was no respiratory depression observed in either group (decrease in tidal volume or holding of breath) (Table 3).

The incidence of emergence agitation (EA) as observed by RSAS score was lower in Group D (20%) than in group P (50%),while no patients were dangerously agitated in either group in our study as shown in table 4 and graph 1. This agitated behavior subsided in 15 minutes of extubation in all patients. Airway reflexes, coughing and swallowing were well preserved in both the groups. The time at which rescue analgesic was given was noted. When compared the difference was not of much clinical significance. Trickling of blood, secretions from posterior nasopharynx can cause vomiting, but the use of anti emetics also was not much in either group (Table 4).

Hemodynamic monitoring of the patients in both the groups was done and pulse, Blood pressure

**Table 1:** Riker Sedation-Agitated Scale

| | | |
|---|---|---|
| 7 | Agitated dangerous agitation | Pulling of ET tube, trying to remove catheter, climbing over bed rail, striking at staff, thrashing side to side |
| 6 | Very agitated | Does not calm, despite frequent verbal reminding of limits, requires physical restraints, biting ET tube |
| 5 | Agitated | Anxious or mildly agitated, attempting to sit up, calm down to verbal instruction |
| 4 | Non agitated, calm & cooperative | Calm, awake and easily, follows commands |
| 3 | sedated | Difficult to arouse, awakens to verbal stimuli or gentle shaking but drifts off again, follows simple command |
| 2 | Very sedated | Arouses to physical stimuli but does not communicate or follow command, may move spontaneously |
| 1 | Unarousable | Minimal or no response to noxious stimuli |

**Table 2:** Demographic Distributions

| | Group D (N=30) | Group P (N=30) | p Value |
|---|---|---|---|
| Age (avg) | 39.6 | 38.5 | >0.05 |
| Gender Male/Female | 18/12 | 17/13 | >0.05 |
| Weight (avg) | 55.3 | 53.7 | >0.05 |
| Duration of surgery (min) | 94 | 98 | >0.05 |

**Table 3:**

| | Group D | Group P | p Value |
|---|---|---|---|
| Time to verbal response (min) | 8.2 | 7.5 | <0.05 |
| Time to extubation (min) | 9 | 8.8 | >0.05 |

were noted before induction, after induction, 10, 30, 45 minutes after induction till the end of surgery. Post operatively also the patients were monitored for the vitals in the recovery room. Looking to the type of patients studied the mode of anesthesia and drugs used, not much gross changes were noted in the vital parameters of the patients. Comparing it within the group and with either group these changes were not of much clinical significance (Table 5 and 6). More so over it was found that patients receiving dexmedetomidine infusion were more stable as far as vitals were taken in consideration to that of pre operative values.

Other side effects related to anesthesia, surgery like vomiting, bradycardias, vomiting, bleeding, were not observed.

**Table 4:** Showing the Emergence Agitation (EA)

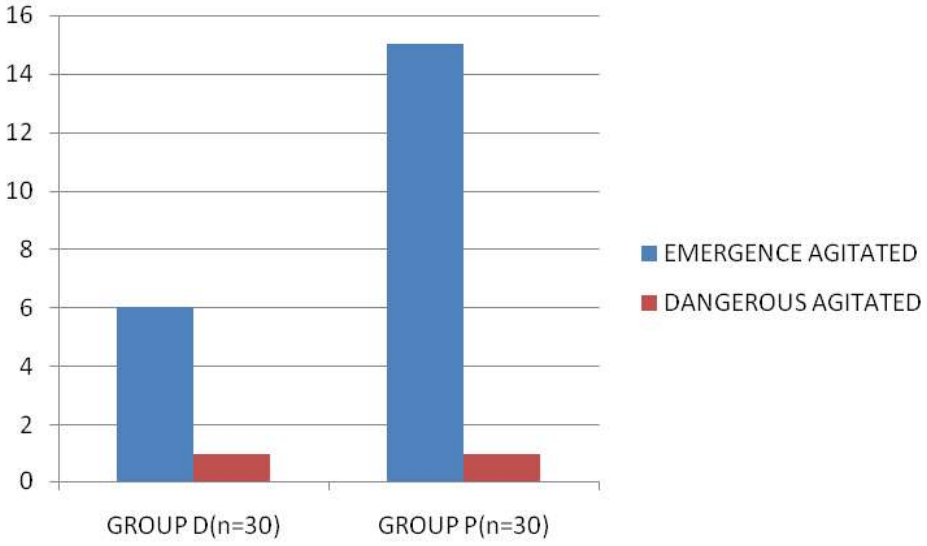
| | Group D (N=30) | Group P (N=30) | p Value |
|---|---|---|---|
| Emergence Agitated | 6 | 15 | <0.001 |
| Dangerous Agitated | 1 | 1 | >0.05 |

**Table 5:** Changes in Heart Rate

| | Group D | Group P |
|---|---|---|
| Before induction | 90.2 ± 7.94 | 89.4 ± 7.64 |
| After 10 min | 82.4 ± 7.38 | 82.2 ± 7.37 |
| After 30 min | 76.3 ± 6.58 | 84.3 ± 7.57 |
| After 45 min | 74.7 ± 6.23 | 86.5 ± 7.81 |
| At extubation | 92.6 ± 8.52 | 102 ± -9.37 |
| 2 min after extubation | 84.9 ± 7.61 | 100 ± 9.12 |

**Table 6:** Changes in Mean Arterial Blood Pressure (MAP) (Avg ± SD)

| | Group D | Group P |
|---|---|---|
| Before induction | 88.9 ± 7.81 | 88.6 ± 7.72 |
| After 10 min | 79.6 ± 7.52 | 79.4 ± 7.38 |
| After 30 min | 77 ± 6.60 | 84.6 ± 7.54 |
| After 45 min | 78.3 ± 6.63 | 86.2 ± -7.85 |
| At extubation | 90.9 ± 8.07 | 98.5 ± 8.43 |
| 2 min after extubation | 88.86 ± 7.56 | 94.3 ± 8.12 |




**Graph 1:** Showing the Emergence Agitation (EA)

## Discussion

The results of this prospective randomized prospective study suggest that dexmedetomidine infusion at rate of 0.5 mcg/kg/hour intraoperatively from the starting of induction of anesthesia till extubation in adults patients undergoing nasal surgeries was effective in reducing postoperative emergence agitation and it provides more stable haemodynamics environment without any respiratory depression or delayed extubation and with bare minimum complication & side effect.

Intraoperative dexmedetomidine infusion helps in stable haemodynamic picture during surgery and during emergence. Emergence Agitation (EA) is common after nasal surgeries due to postoperative bilaterally nasal packing which causes a sense of suffocation. The mainstay for management of emergence agitation is elimination of preventable causes, especially in at-risk patients. Other factors being smoking, obesity, alcoholism, use of benzodiazepines, inhalational agents and the feeling of tracheal tube [9,10]. It is the nonuniform recovery of different parts of the central nervous system that has been postulated as the main mechanism of emergence agitation. We only included patients undergoing nasal surgeries expected to have higher risk of emergence agitation as they required nasal packing bilaterally [10], (though the patients undergoing nasal surgeries for various reasons are habituated with the nasal obstruction – habituated mouth breathers) Dexmedetomidine provides sedation and analgesia without any respiratory depression postoperatively [3], and this helps to reduce the emergence reaction which usually arises during the non uniform awakening of different parts of central nervous system. So the use of dexmedetomidine infusion for preventing emergence agitation in our study is advocated. As expected result of our study were similar to previous study (S.Y. Kim, J.M. Kim et al.) [1] in which incidence of emergence agitation was 52% in group P as compared to group D in which incidence of EA was 28%.

In another study done by Akanksha Garg, Manoj Kamal et al. [11], they studied the reduction in incidence of emergence phenomenon occurring postoperatively in nasal surgeries in which they used Inj. Dexmedetomidine 1 μg/kg bolus followed by infusion of 0.4 μg/kg/hr intravenously. They concluded that the incidence is highly reduced but there is delayed extubation with post operative sedation seen in many study cases.

Yingging Sun, Yuanhai li et al. [12] studied different infusion doses of Inj. Dexmedetomidine of 0.25, 0.5 and 1 μg/kg to study the incidence of post operative emergence phenomenon and concluded that 0.5 μg/kg/hr has better effect than 0.25 μg/kg/hr. Moreover, a dose of 1 μg/kg/hr did not have any added advantage over 0.5 μg/kg/hr infusion.

In a similar study it was seen that intraoperative infusion of dexmedetomidine reduces the incidence of emergence agitation in paediatric patients by 50-70% [2].

As observed by RSAS score, The time to verbal response after discontinuation of the infusion was slightly longer in group D as compared to group P. this can be attributed to more sedation caused by dexmedetomidine but when compared to group P this time duration was not of much clinical significance. Residual effects like sedation or agitation in the recovery room was not seen in any of our cases from both groups.

The use of Dexmedetomidine at the dose of 0.5 μg/kg/hr does not reduce the requirement of sevoflurane which was seen in other studies, [11] where they used more concentration of the dexmedetomidine (1 μg/kg bolus followed by the infusion of 0.4 μg/kg/hr). We tried to maintain the MAC around 1 in both our groups. In similar study [1] there was no reduction of inhalational agent where they used Inj. Dexmedetomidine in the concentration of 0.4 μg/kg/hr.

Dexmedetomidine can cause haemodynamic changes specially bradycardia and hypotension specially when given in loading doses. A loading dose of 1 mcg/kg followed by 0.5 mcg/kg/ hour infusion intraoperatively, can cause delayed extubation and residual sedation in PACU. While use of dexmedetomidine only in infusion form with dose of 0.2–0.5 mcg/kg/hour infusion intraoperatively more haemodynamic stability [5]. We administered continuous infusion of dexmedetomidine 0.5 mcg/kg/hour during intraoperatively period to reduce postoperative emergence agitation and maintaining intraoperative haemodynamic stability [4]. With this dose the occurrence of hypotension and bradycardia were not seen to that extent requiring treatment. None of the patient had postoperative nausea vomiting in both groups. The mainstay for management of emergence agitation is elimination of preventable causes, especially in at-risk patients. The following are the main strategies to reduce the occurrence and consequences of emergence agitation episodes: encouraging patients to quit smoking at least 1 week before surgery, providing adequate postoperative

analgesia, removing tracheal tubes and urinary catheters as early as possible following surgery, and more vigilant monitoring for emergence agitation in younger patients. Some limitations can be pointed to the present study, like subjective or objective preoperative data on patients' nasal obstruction were absent, the impact of different nasal packing types on breathing difficulty could not be individually evaluated.

## Conclusion

Inj. Dexmedetomidine infusion used intraoperatively at rate of 0.5 µg/kg/hour till extubation reduces the incidence of postoperative emergence agitation and maintain stable haemodynamics changes during intraoperative period and during emergence without delayed extubation & residual sedation in nasal surgeries.

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[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/HSQ20.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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