**Original Research Article**

# A bispectral index guided study on the effect of dexmedetomidine on sevoflurane requirements during elective laparoscopic surgeries

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## Abstract

**Background:** General inhalational anaesthesia associated with adjuvant intravenous agents provides better sedation, hypnosis and analgesia. Drugs with such effects already established in the literature include benzodiazepines and opioids.

**Aim:** Aim of the study was to evaluate the effect of continuous infusion of Dexmedetomidine, on Sevoflurane requirement during general anesthesia with continuous monitoring of depth of anesthesia by BIS (Bispectral index) analysis in patients undergoing elective laparoscopic surgeries.

**Materials and methods:** 60 patients with ASA grade I and II, aged between 35-55 years, submitted to elective laparoscopic cholecystectomies under General Anesthesia were randomly divided into two groups of 30 each, one group received a loading dose of Dexmedetomidine at 1 mcg/kg for 10 min (10 minutes before starting the surgery), followed by maintenance dose of 0.5 mcg/kg/hour, till the end of surgery. The other group received similar volume of IV Normal Saline. MAP, HR, SpO2, EtCO2 and BIS were evaluated.

**Results:** There was no significant difference ($p>0.05$) between Dexmed and Saline groups with respect to mean age, weight, height, duration of anaesthesia and ASA grade. There was no significant difference ($p>0.05$) in the baseline heart rates and baseline mean arterial pressure between the two groups. There was a clinically and statistically significant reduction in HR and MAP in the Dexmed

group throughout intraoperative period compared to Saline group ($p < 0.05$). There was a statistically significant rise in HR and MAP in the Saline group during laryngoscopy and 15 minutes after the creation of pneumoperitoneum ($p<0.05$). Dexmed group had a stable hemodynamics during laryngoscopy and creation of pneumoperitoneum. No statistically significant difference was noted in the extubation time of both the groups. Mean RAMSAY Sedation score and Modified ALDRETE score was higher in Dexmed group. Usage of Sevoflurane (in ml) and usage of Sevoflurane /min was significantly low in Dexmed group.

**Conclusion:** Dexmedetomidine as a preanesthetic medication and intraoperative infusion was effective in blunting stress response to laryngoscopy and creation of pneumoperitoneum. It also decreased intraoperative anaesthetic requirement and had significant anaesthetic sparing property during BIS guided general anaesthesia providing a lighter sedation without the prolongation of extubation time or without any significant adverse effects.

## Key words

Bispectral index, Dexmedetomidine, Sevoflurane, Laparoscopic surgeries.

## Introduction

General inhalational anaesthesia associated with adjuvant intravenous agents provides better sedation, hypnosis and analgesia [1]. Drugs with such effects already established in the literature include benzodiazepines and opioids [1, 2]. New intravenous agents are being introduced in the clinical practice. α2- adrenergics have a promising potential in Anaesthesiology.

α2 receptors are a subgroup of noradrenergic receptors that mediate the function of the sympathetic nervous system. In addition to sedative effects, Dexmedetomidine has been labelled as "analgesia sparing" by the Food and Drug Administration (FDA). Dexmedetomidine when co administered with opioids, has no depressant effects on respiration, but its analgesic effects offer a significant advantage for patients at risk for respiratory decompensation. Dexmedetomidine promotes norepinephrine plasma levels decrease, analgesia, hemodynamic stability (decreased systemic blood pressure and heart rate), anti-sialogogue effect, decreased intraocular pressure without depressing breathing. Pharmacokinetic properties show 1.5 hours half-life, fast onset (less than 5 minutes) and peak effect in approximately 15 minutes [3].

Dexmedetomidine in anaesthesia has been related to preanesthetic medication, general anaesthesia adjuvant and postoperative medication [4]. As preanesthetic medication and general anaesthesia adjuvant, Dexmedetomidine decreases need for anaesthetics and analgesics administered for anaesthetic induction and maintenance, as well as attenuates adrenergic response to tracheal intubation.

Dexmedetomidine as general inhalational anaesthesia adjuvant provides a synergistic pharmacological interaction with the decreased inhalational anaesthetic concentration and, as a consequence, lowers the toxicity potential and better hemodynamic stability (via sympatholytic and analgesic effects), providing sedation, analgesia and minor respiratory depression at emergence.

Laparoscopic surgeries under general anaesthesia are associated with unique haemodynamic changes in the form of increased systemic vascular resistance, leading to hypertension, forcing the anaesthesiologist to increase the depth of anaesthesia (DOA), and at times, even require the use of vasodilators to tackle the rising blood pressure.

Several studies have indicated that administration of IV Dexmedetomidine during general anaesthesia can decrease the minimum alveolar anaesthetic concentration (MAC) of Sevoflurane.

Thus, a clinical study was conducted to assess the effect of Dexmedetomidine on Sevoflurane consumption.

This study aimed at evaluating the influence of Dexmedetomidine continuous infusion on Sevoflurane consumption during general anaesthesia, monitored by EEG Bispectral index (BIS).The study also aims at assessing the effect of intravenous Dexmedetomidine on perioperative hemodynamics and also postoperative recovery in elective laparoscopic surgeries with continuous monitoring of depth of anaesthesia guided by BIS analysis.

## Materials and methods

It was a randomized, controlled, single centred, double blinded, interventional and prospective study to evaluate the effect of continuous infusion of Dexmedetomidine, on Sevoflurane requirements during General Anaesthesia with continuous monitoring of depth of anaesthesia by BIS (Bispectral index) analysis. This study was conducted at Gandhi Hospital, Secunderabad after approval by the Institutional Ethical Committee, over a period of 12 months from July 2016 to June 2017.

**Inclusion criteria**

- Patients of either sex.
- Aged between 35 to 55 years.
- Patients belonging to ASA grade I and II.
- Normal BMI range from 18.5 to 24.9.

**Exclusion criteria**

- Patients planned for nasotracheal / fibreoptic /any other method of ET intubation, other than orotracheal intubation with conventional directlaryngoscopy.
- Contraindication/allergy to any of the agents/medicines being used in study.
- Patients with known kidney, liver and heart disorders. History of dementia and stroke or other organic brain disorders.
- Patients with psychiatric diseases.
- Patients on alpha-2 agonist/antagonist/ Beta blocker therapy.
- Patients with coronary artery disease and heart block.
- Patient with predicted difficult airway as assessed during pre op evaluation.

**Sample Size Selection**

The sample size was determined using the formula: N=Z2xPxQ/D2

Where Z was the confidence coefficient, P was the incidence rate in population, Q =1-P, D was the difference between the estimated value and true value in the population.

Taking P as 50% with 95% confidence level and with an error of estimate of D=16% the sample size worked out to be 38. Expecting some non-cooperation from the patient, attrition and 5 to 10% chances of the laparoscopic procedure being converted to open, the sample size fixed for the study was 60.

After the informed consent, 60 patients with physical status ASA I and II, aged between 35 and 55 years, submitted to elective laparoscopic cholecystectomy under General Anesthesia were randomly divided into two groups Dexmed and Saline of 30 each.

The total sample of 60 eligible, consenting patients was randomized into two study groups using computer software generated randomization method. Thus, 30 patients each were allocated to Dexmed and Saline groups and were assigned a serial code.

The Dexmedetomidine solution was prepared by diluting 2 mL of the original product presentation (100 mcg /ml) in 48 mL of 0.9% saline solution, with a final concentration of 4 mcg/ml.

Dexmed group received a loading dose of Inj. Dexmedetomidine at 1 mcg/kg for 10 min (10 minutes before starting of surgery), followed by maintenance with 0.5 mcg/kg/hour, till the end of surgery. Saline group received similar volume of

IV Normal Saline. Anesthetist who was blinded to the study group administered General Anaesthesia and primary investigator doing the study noted the variables.

**Preoperative evaluation**

A thorough pre-anesthetic check-up was carried out. Detailed history was taken and systems were examined. Pulse rate, blood pressure, height and body weight were noted. Routine investigations like Hemogram, Bleeding time, Clotting time, Prothrombin time, International normalized ratio (INR), LFT, RFT, and TSH were done in all the subjects and results confirmed to be within acceptable limits. After explaining the procedure, written informed consent was obtained from the patients.

**Preoperative Preparation**

All patients were kept fasting for six hours before surgery. After confirming nil per oral status, all the patients were premedicated with oral Alprazolam (0.5 mg) the day before surgery and in the morning on day of surgery. Patients were given Inj. Glycopyrrolate 4 mcg/kg, and Inj. Ondansetron 4 mg IV and Fentanyl 2 mcg/kg IV.

Patients were shifted to Operation Theatre and all standard monitors were connected. BIS sensor was attached to forehead and connected to BIS module and Sensor Quality Index (SQI) was ensured to be >50%. The baseline variables (HR, MAP, SpO2,) and baseline BIS values were noted. Dexmed group received a loading dose of Inj. Dexmedetomidine at 1 mcg/kg for 10 min (10 minutes before starting of surgery) and Saline group received similar volume of IV Normal Saline.

Mean arterial blood pressure (MAP), heart rate (HR), SpO2, EtCO2 and BIS were evaluated fifteen minutes before induction (MI), at induction (M0), during laryngoscopy and intubation, 15 min after creation of pneumoperitoneum (MP) and every 30 minutes after anaesthetic induction till the end of surgery (M30, M60, M90, M120 and M150 and M180) and continued during extubation, after extubation till the patient was shifted to PACU. Extubation time was measured from the time at which all anaesthetics were turned off.

If the surgical procedure was converted from laparoscopic to open, then the patient was excluded from the study. Any side effects like hypotension, bradycardia, post-operative nausea, vomiting and respiratory depression were noted.

At surgery completion (at the start of suturing of the laparoscopic ports), Sevoflurane, Dexmedetomidine infusion and Nitrous oxide was withdrawn. Residual neuromuscular blockade was reversed with Inj. Glycopyrrolate (0.01 mg/kg) and Neostigmine (0.05mg/kg).

The usage of Sevoflurane during anesthesia was calculated as follows:

Dion's Formula: Usage of volatile Anaesthetic (mL) = [Dialled concentration × Total fresh gas flow × Duration at that concentration × Molecular weight] / [2412 × Density].

Calculations:

Amount of liquid Sevoflurane used = PFTM/2412d

Where the variables represent

P=Vaporizer dial concentration in percent

F=Total fresh gas flow in lit/min

T=Time for which the concentration P was set in minutes M=Molecular mass of Sevoflurane in grams

D=Density of liquid sevoflurane in grams/ml

The fixed variables used were

F (total fresh gas flow) set at 3 L/min

M (molecular mass of sevoflurane) = 200.055 g

d (density of Sevoflurane at 21°C) = 1.52 g/ml

Substituting the fixed variables the equation can be re-written as: Amount of liquid Sevoflurane used = 0.00182 PT (where T is in seconds)

The time period for each concentration was labelled as T1, T2, T3 so on until T8 in seconds for concentration of 1%, 2%, 3% till 8%.

Total liquid Sevoflurane used was calculated as:

0.00182 (T1+ 2T2+ 3T3+ 4T4+ 5T5+ 6T6+ 7T7+ 8T8)

Where % and T represents dial setting and time for that setting respectively.

Data analysed using Students t test, Chi square test and Fisher Exact test. 5 patients each from Dexmed and Saline groups were excluded from study as laparoscopic procedure was converted to open. Sample size reduced to 50 i.e., 25 in Dexmed group and 25 in Saline group respectively. Data was analysed. p value<0.05 was taken as statistically significant.

## Results

The p-value was greater than the significance level 0.05 meaning the difference in age between Saline and Dexmed groups was not significant. So, the two groups were comparable with respect to age.

There was no significant difference between the mean height of the two groups (p>0.05). There was no significant difference between the mean weight of the two groups (p>0.05).

Both groups were comparable with respect to the distribution of ASA PS Grades (p>0.05). About 68.0% of the samples have ASA I and 32.0% had ASA II in Saline group. Almost 64.0% of the samples had ASA I and 36.0% had ASA II in Dexmed group (**Table – 1**).

**Table - 1:** Demographic distribution in two groups.

| Group | Mean | SD | t – value | Df | p - value |
|---|---|---|---|---|---|
| **Age (mean in years)** | | | | | |
| Saline | 44.72 | 4.138 | $0.137^{NS}$ | 48 | 0.891 |
| Dexmed | 44.88 | 4.096 | | | |
| **Mean height (in cm)** | | | | | |
| Saline | 160.4 | 5.099 | $0.679^{NS}$ | 48 | 0.500 |
| Dexmed | 161.4 | 5.315 | | | |
| **Mean weight in kg** | | | | | |
| Saline | 57.20 | 4.992 | $0.431^{NS}$ | 48 | 0.668 |
| Dexmed | 57.84 | 5.490 | | | |
| **Duration of Anesthesia** | | | | | |
| Saline | 180.5min | 17.12 | $0.107^{NS}$ | 48 | 0.915 |
| Dexmed | 180.0min | 17.25 | | | |

(NS - Difference is not significant.)

**Table - 2:** Comparison and analysis of baseline hemodynamic variables between the groups.

| Variables | Saline Group (Mean ±SD) | Dexmed Group (Mean±SD) | t-value | p-value |
|---|---|---|---|---|
| Heart Rate | 80.28 ± 8.404 | 77.24 ± 8.927 | 1.240 | p = 0.221 |
| Mean Arterial Pressure | 91.4 ± 8.5 | 92.1 ± 8.1 | 0.306 | |

Comparison of baseline heart rates in the two groups indicates that there was no significant difference (p>0.05) between the two groups. Similarly there was no significant difference between the groups with respect to baseline mean arterial pressure (**Table – 2**).

There was a statistically significant reduction in heart rate (HR) in Dexmed group throughout intraoperative period compared to Saline group (p < 0.05).

The percentage rise in mean heart rate from baseline to laryngoscopy HI to HL was

significantly higher in the Saline group ($p<0.05$). The percentage rise in mean heart rate from baseline to 15 min after pneumoperitoneum i.e., (HI) to (HP) was significantly higher in the Saline group ($p<0.05$). There was a statistically significant reduction in heart rate (HR) in Dexmed group throughout intraoperative period compared to Saline group ($P < 0.05$) as per **Figure - 1**.

**Figure - 1:** Comparison and analysis of baseline heart rate between the groups.

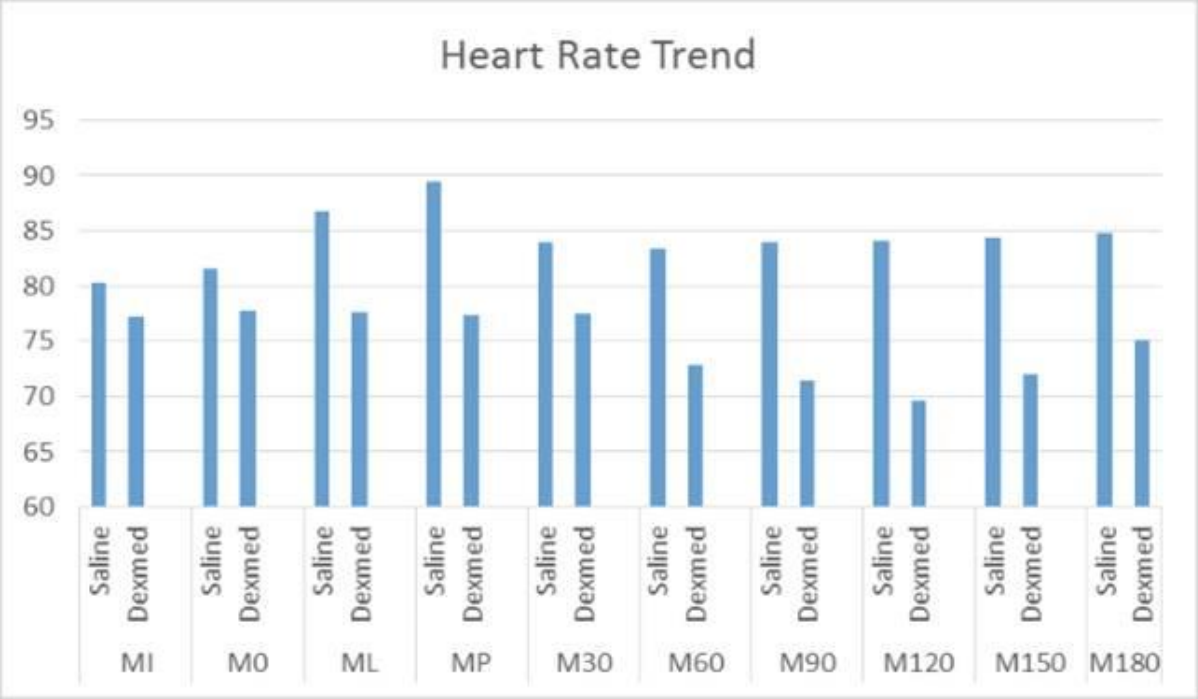



**Figure - 2:** Comparison and analysis of baseline mean arterial pressure between the groups.

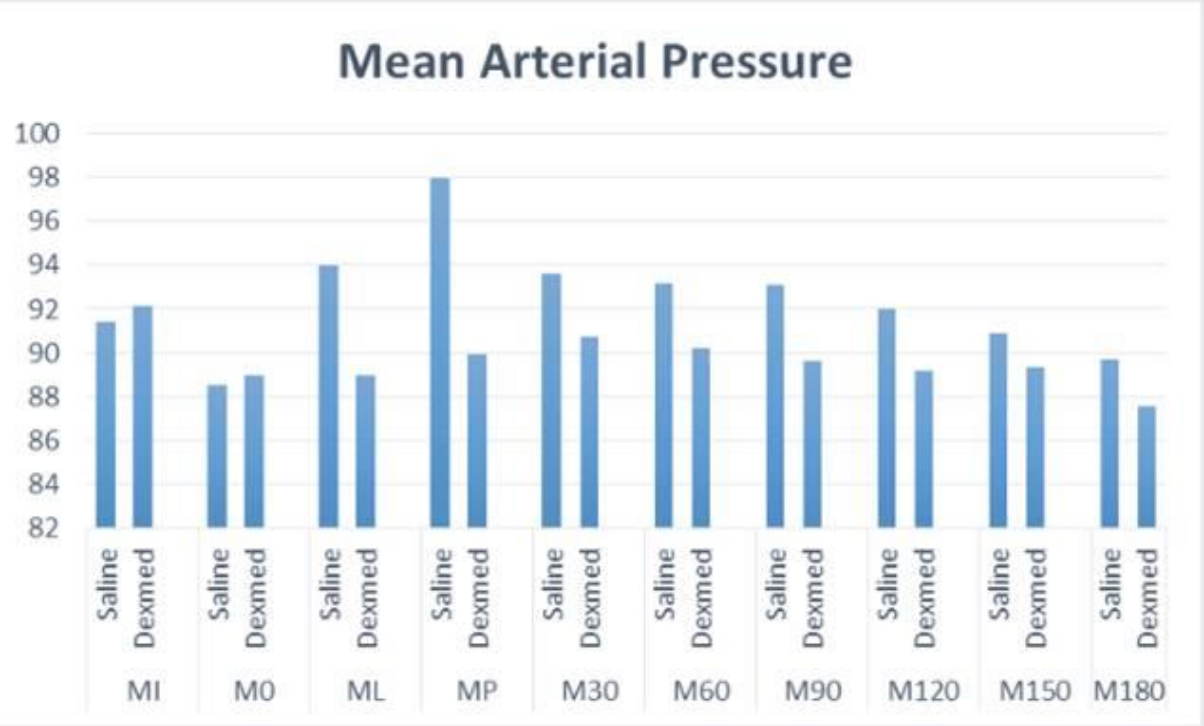


**Table - 3:** Comparison of between Saline and Dexmed groups.

| Group | Mean | SD | t – value | Df | p – value |
|---|---|---|---|---|---|
| **Extubation Time between Saline and Dexmed** | | | | | |
| Saline | 7.400 | 1.607 | $2.359^{NS}$ | 48 | 0.022 |
| Dexmed | 7.960 | 1.85 | | | |
| **Comparison of Usage in ml of Sevoflurane between Saline and Dexmed groups** | | | | | |
| Saline | 49.50 | 6.254 | 14.891** | 48 | 0 |
| Dexmed | 27.13 | 4.160 | | | |
| **Usage of Sevoflurane per minute between Saline and Dexmed groups** | | | | | |
| Saline | 0.275 | 0.025 | 16.540** | 48 | 0.000 |
| Dexmed | 0.152 | 0.027 | | | |

**Figure - 3:** Comparison of RAMSAY Sedation Score between Saline and Dexmed Groups.

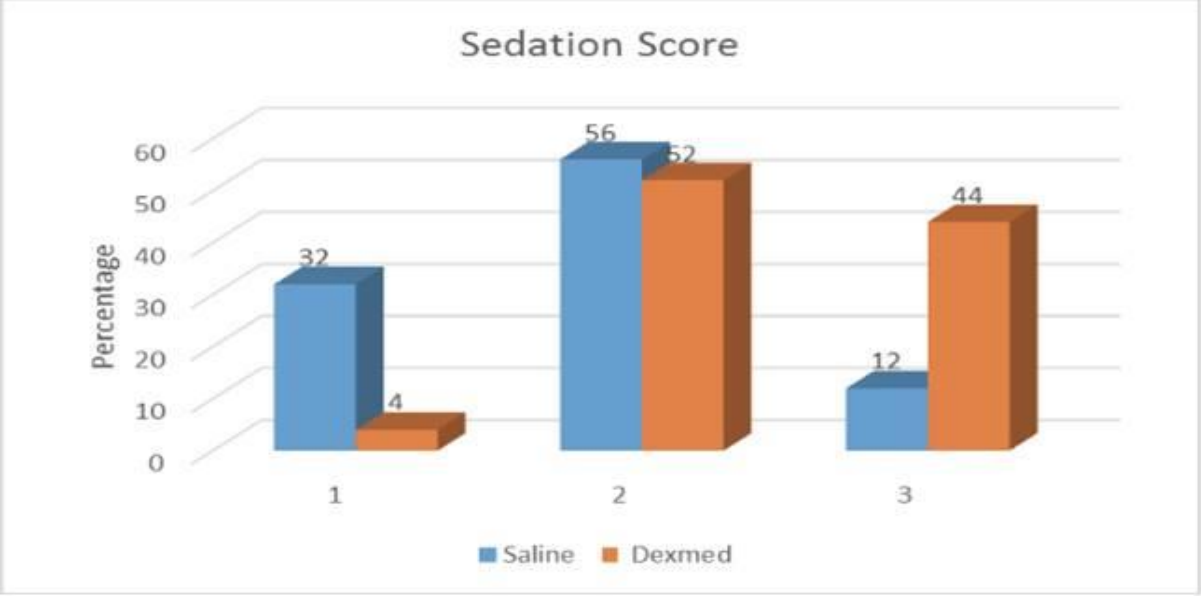
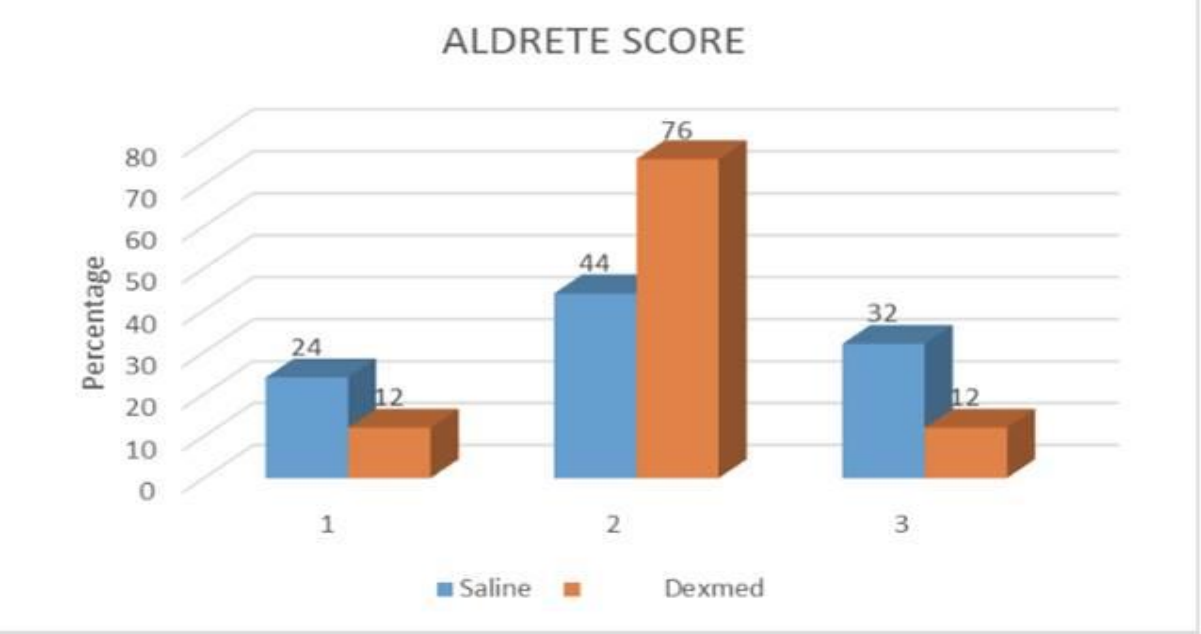



**Figure - 4:** Comparison of ALDRETE Score between Saline and Dexmed groups.



There was a statistically significant reduction in mean arterial pressure (MAP) in Dexmed group throughout the intraoperative period compared to Saline group ($p< 0.05$).

The percentage rise in mean arterial pressure from baseline to laryngoscopy MI to ML was significantly higher in the Saline group ($p<0.05$). The percentage rise in mean arterial pressure from baseline to 15 min after pneumoperitoneum i.e., MI to MP was significantly higher in the Saline group ($p<0.05$). There was a statistically significant reduction in mean arterial pressure (HR) in Dexmed group throughout intraoperative period compared to Saline group ($p< 0.05$) as per **Figure - 2**.

The p-value was greater than the significance level 0.05; the difference in extubation time between Saline and Dexmedetomidine was not significant. Extubation time was almost same in both Saline (7.400 ± 1.607) group and Dexmed (7.960 ± 1.859) group.

There was no statistically significant difference in extubation time between the 2 groups.

The difference in Sevoflurane usage between Saline and Dexmedetomidine is significant. **Table - 3** shows that the Sevoflurane usage was significantly high in Saline (49.50 ± 6.254) group compared to Dexmed (27.13 ± 4.160) group.

The p-value was less than the significance level 0.01; the difference in usage per minute between Saline and Dexmedetomidine was significant. **Table - 3** shows that the usage per minute was significantly high in Saline (0.275 ± 0.025) group compared to Dexmed (0.152 ± 0.027) group.
The p-value was less than the significance level 0.01 i.e., the difference in Sedation score between Saline and Dexmed groups was significant. About 32.0% of the samples had sedation score 1, 56.0% of the samples had sedation score 2 and 12.0% had sedation score 3 in Saline group. Almost 4.0% of the samples had sedation score 1, 52.0% of the samples had sedation score 2 and 44.0% had sedation score 3 in Dexmed group (**Figure – 3**).

The p-value was greater than the significance level 0.05 i.e., the difference in ALDRETE score between Saline and Dexmedetomidine was not significant. So, ALDRETE score was comparable. About 24.0% of the samples had ALDRET 8, 44.0% of the samples had ALDRETE 9 and 32.0% had ALDRETE 10 in Saline group. Almost 12.0% of the samples had ALDRETE 8, 76.0% of the samples had ALDRETE 9 and 12.0% had ALDRETE 10 in Dexmed group (**Figure – 4**).

## Discussion

### Demographic data

The demographic data collected was statistically analysed and it showed no statistically significant difference between the two groups with respect to the age, weight, height, ASA and duration of anaesthesia. The baseline heart rate and mean arterial pressure also showed no significant difference between the 2 groups. This analysis confirmed that both groups were comparable.

### Hemodynamic parameters

### Heart Rate

There was a clinically and statistically significant reduction in Heart Rate in Dexmed group throughout intraoperative period compared to Saline group ($p < 0.05$).

### Heart Rate at laryngoscopy

In Saline group, the Heart Rate increased from a baseline value of 80.28 ± 8.4 to 86.7 ± 9.7 beats per minute after laryngoscopy ($p<0.05$). In Dexmed group, the mean Heart Rate increased from a basal value of 77.24 ± 8.92 to 77.60 ± 8.40 beats per minute after laryngoscopy ($p>0.05$). Further in the study, the mean percentage rise in the Heart Rate from the baseline level to those immediately after the laryngoscopy in Saline group was 7.9 ± 4.9% and in Dexmed group was 0.56 ±1.71%.The mean difference was 7.4 % and the difference was found to be statistically significant ($p<0.05$).

This shows that the rise in heart rate was more with the Saline group than with the Dexmed group.

This finding corroborates with the study of Gourishankar Reddy Manne, et al. [5], who conducted study on the effects of Dexmedetomidine on hemodynamics in patients undergoing laparoscopic surgeries compared to Saline Placebo. They found that during laryngoscopy, heart rate increased from a basal value of 88.75 ± 5.71 to 106.25 ± 5.16 beats per minute in NS group, where as in Dexmed group, it increased from a baseline value of 91.90 ± 8.66 to 96.30 ± 4.66 beats per minute one minute post laryngoscopy.

Sulaiman S, et al. [6] had similarly shown that Dexmedetomidine effectively blunts the hemodynamic response to laryngoscopy and intubation compared to Saline placebo. In their study, the mean heart rate was 69.10 ± 10.7 beats per minute in the Dexmed group compared to 84.67 ± 11.3 beats per minute in the Placebo group at one minute post laryngoscopy.

Menda F, et al. [7] had found that Dexmedetomidine effectively blunted the haemodynamic responses to laryngoscopy and tracheal intubation compared to Placebo. They also noted that the haemodynamic parameters were lower at all times.

Bajwa SS, et al. [8] had shown that Dexmedetomidine was better in attenuating the sympatho-adrenal response to laryngoscopy and intubation when compared to Fentanyl. But in this study, they have administered Dexmedetomidine 1 mcg/kg along with 1 mcg/kg Fentanyl in one group and 2 mcg/kg Fentanyl in the other group compared to baseline values.

**Heart Rate after (15 min) pneumoperitoneum**

In laparoscopic surgery, CO2 is routinely used to create pneumoperitoneum and elevation of IAP with raised diaphragm causes various adverse effects on cardiovascular system. Plasma level of Catecholamines and Vasopressin increase immediately after pneumoperitoneum which activates the Renin-Angiotensin-Aldosterone system (RAAS) leading to characteristic haemodynamic alterations such as decreased cardiac output, elevated arterial pressure and increased systemic and pulmonary vascular resistance. Patients with compromised cardiac function may not be able to tolerate the haemodynamic changes. Various drugs have been used to attenuate above response during laparoscopic surgery. In spite of maintaining normocapnia and keeping intra- abdominal pressure below 14mm Hg, significant rise in heart rate, systolic blood pressure, diastolic blood pressure and mean arterial pressure was noticed in Saline group. In Saline group, the Heart Rate increased from a baseline value of 80.28 ± 8.4 to 89.36 ± 9.36 beats 15 min after the creation of pneumoperitoneum. In Dexmed group, the mean Heart Rate increased from a pre insertion value of 77.24 ± 8.92 to 77.4 ± 7 beats 15 minute after pneumoperitoneum. Further in the study, the mean percentage rise in Heart Rate from a baseline level to that 15 min after pneumoperitoneum in Saline group was 11.56 ± 5.8 % and in Dexmed group was 0.4 ± 3.24%.The mean difference was 11.1% and the difference was found to be statistically significant ($p<0.05$). This shows that the rise in Heart Rate was more with the Saline group than with the Dexmed group.

The above findings are similar to the study by Yogesh Chauhan, et al. [9] who studied the effect of Dexmedetomidine infusion on laparoscopic surgeries compared to Saline Placebo. They found that Heart Rate increased from a basal value of 84.16 ± 14.936 to 92.00 ± 22.94 beats in Saline group 15 minutes after the creation of pneumoperitoneum where as in Dexmed group, the heart rate decreased from a baseline value of 86.8 ± 4.13 to 79.08 ± 2.3 beats per minute. Gourishankar Reddy Manne, et al. [5] also found a significant rise in heart rate following pneumoperitoneum in NS group as compared to Dexmed group.

**Trends in Heart Rate**

There was a clinically and statistically significant reduction in Heart Rate in Dexmed group throughout intraoperative period compared to Saline group ($p< 0.05$). Bradycardia was noticed in 4 out of 25 patients in Dexmed group, which was treated with Inj. Atropine 0.6 mg IV. There was no incidence of bradycardia in Saline group.

In the study, after giving loading dose of Dexmedetomidine, there was a decrease in Heart Rate by 5.3%, decrease in mean arterial pressure by 1.3% from the baseline values. The incidence of hypotension and bradycardia may be related to the loading dose which on limiting to 0.4 mcg/kg will reduce their incidence.

Gourishankar Reddy Manne, et al. [5], who studied the effects of low dose Dexmedetomidine infusion on haemodynamic stress response, sedation and post-operative analgesia requirement in patients undergoing laparoscopic cholecystectomy also got similar results. Thus, infusion of sedative dose of Dexmedetomidine attenuates haemodynamic response to laryngoscopy and pneumoperitoneum with adequate depth of anaesthesia and maintains stable hemodynamics even with the creation of pneumoperitoneum.

**Mean arterial pressure**

In the study, the mean arterial pressure increased in both groups after insertion of ET-tube and after the creation of pneumoperitoneum. The increase in mean arterial pressure was noted to be more in the Saline group.

**Mean arterial pressure at Laryngoscopy**

In Saline group, the average MAP increased from a baseline value of 91.4 ± 8.5mm of Hg to 94.0 ± 7.789mm of Hg at laryngoscopy. In Dexmed group, the MAP decreased from a baseline value of 92.1 ± 8.1mmHg to 88.96 ± 7.541mm Hg at laryngoscopy. Further in the study, the mean percentage rise in MAP from baseline level to those immediately after laryngoscopy in Saline group was 2.9 ± 2.16 % and decrease in Dexmed group was 3.4 ± 3.12%. The mean difference was 6.3% and the difference was found to be statistically significant ($p<0.05$). This shows that the increase in MAP was more with Saline group than with Dexmed group.

The above findings are similar to the study by Gourishankar Reddy Manne, et al. [5], who studied on effects of low dose Dexmedetomidine infusion on hemodynamic stress response, sedation and post-operative analgesia requirement in patients undergoing laparoscopic cholecystectomy. They found that in NS group, significant haemodynamic stress response was seen following laryngoscopy, tracheal intubation, creation of pneumoperitoneum and extubation. In Dexmedetomidine group, the haemodynamic response was significantly attenuated. MAP increased from a baseline value of 98.65 ± 4.72 to 114.35 ± 13.12 mm of Hg during laryngoscopy in NS group, where as in Dexmed group, it decreased from a basal value of 101.50 ± 4.95 to 95.65 ± 6.59 mm of Hg.

Yogesh Chauhan, et al. [9] in his study found that mean value of MAP increased from a basal value of 95.10 ± 11.46 to 97.53 ± 16.05 mm of Hg during laryngoscopy in Saline group where as in Dexmed group, MAP decreased from a basal value of 87.26 ± 14.92 to 82.70 ± 14.92 mm of Hg.

**Mean arterial pressure at pneumoperitoneum**

In Saline group, average MAP increased from a pre intubation value of 91.4 ± 8.5mm of Hg to 97.96 ± 8.223 mm of Hg 15 min after the creation of pneumoperitoneum. In Dexmed group, the mean arterial pressure decreased from a base line value 92.1 ± 8.1 mmHg to 89.96 ± 7.14 mm Hg 15 min after the creation of pneumoperitoneum. Further in the study, the mean percentage rise in mean arterial pressure from baseline level to 15 min after the creation of pneumoperitoneum in saline group was 7.3 ± 2.68 % and in Dexmed group was 2.3 ± 2.126 %. The mean difference was 9.61% and the difference was found to be statistically significant ($p<0.05$). This shows that the increase

in mean arterial pressure was more with Saline group than with Dexmed group. Following intubation and creation of pneumoperitoneum, increase in arterial pressure was noticed in Dexmed group but it never crossed the base line value. Hence, Dexmed infusion was able to achieve haemodynamic stability during pneumoperitoneum.

The above findings are similar to the study by Gourishankar Reddy Manne, et al., who studied on effects of low dose Dexmedetomidine infusion on haemodynamic stress response, sedation and post-operative analgesia requirement in patients undergoing laparoscopic cholecystectomy. They found that in NS group, significant haemodynamic stress response was seen following laryngoscopy, tracheal intubation, creation of pneumoperitoneum and extubation. In Dexmedetomidine group, the haemodynamic response was significantly attenuated. MAP increased from a base line value of 98.65 ± 4.72 to 102.65 ± 9.97, 15 minutes after the creation of pneumoperitoneum in Saline group, where as in Dexmed group, it decreased from 99.30 ± 11.54 to 96.95 ± 10.28.

Yogesh Chauhan, et al. [9] in their study found that after the creation of pneumoperitoneum, mean value of MAP increased from a basal value of 95.10 ± 11.46 to 101.46 ± 19.21, 15 minutes after creation of pneumoperitoneum in Saline group where as in Dexmed group, MAP decreased from a basal value of 87.26 ± 14.92 to 84.53 ± 11.76 mm of Hg.

**Trends in mean arterial pressure**

There was a clinically and statistically significant reduction in mean arterial pressure in Dexmed group throughout intraoperative period compared to Saline group ($p< 0.05$). Following induction, a decrease in mean arterial pressure was noticed in Dexmed group and Saline group. Following intubation and pneumoperitoneum, increase in arterial pressure was noticed in Dexmed group from the induction values but it never crossed the baseline value. Hence, Dexmed infusion was able to achieve haemodynamic stability during pneumoperitoneum.

**Comparison of Sevoflurane Usage**

The usage of Sevoflurane during anaesthesia can be calculated as follows:

Dion's Formula: Usage of volatile Anaesthetic (mL) = [Dialed concentration × Total fresh gas flow × Duration at that concentration × Molecular weight]/[2412 × Density].

There was statistically significant (45.19%) reduction in the Sevoflurane usage, as suggested by 27.13 ± 4.16 mL in Dexmed group compared to 49.50 ± 6.254 ml usage in Saline group ($p< 0.001$).In order to get a better idea of the reduction in Sevoflurane usage, the usage of Sevoflurane/minute was calculated(by dividing total usage by anaesthesia time)and compared. The usage per minute is significantly high in Saline (0.275 ± 0.025) group compared to Dexmed (0.152 ± 0.027) group.

This result corroborates with studies of Harsoor S, et al. [10] where there was statistically significant (19.33%) reduction in the Sevoflurane usage, as suggested by 27.37 ± 2.76mL in Dexmed group compared to 33.93 ± 97 mL in Saline group ($p< 0.001$).

Use of Fentanyl reduces minimum alveolar concentration (MAC) of Sevoflurane significantly. Use of opioids along with Dexmedetomidine would confound its effect on requirement of inhalation agent. In the study, Fentanyl was administered in both groups, and a 45.19% decrease in the Sevoflurane usage was found in contrast to 19.33% reduction in the Sevoflurane usage in study done by Harsoor S, et al. [10] where Fentanyl was not used.

**Extubation Time**

The time from turning off of Sevoflurane to tracheal extubation was considered as time for extubation and it was 7.40 ± 1.6 min in Saline group, compared to 8.640 ± 2.07min in Dexmed group. Extubation time is higher in Dexmed (7.960 ± 1.85) group compared to Saline (7.400 ± 1.607) group but it is not statistically

significant.

This result corroborates with studies of Harsoor S, et al. [10] where it was 5.4 ± 1.35 min in the Control group, compared to 5.5 ± 1.82 min in Dexmed group.

Turan G, et al. [11] conducted a study on advantageous effects of Dexmedetomidine on haemodynamic and recovery responses during extubation for intracranial surgery and found that there was no statistically significant difference between Dexmedetomidine group and Control group regarding the duration of extubation and recovery (p>0.05).

C Afanador, et al. [12] studied the effect of intraoperative use of Dexmedetomidine on anaesthetic requirements and time to tracheal extubation in elective adult Heart surgery patients and they found that the time to tracheal extubation in DEX Cohort was shorter with respect to Control Cohort.

**Ramsay Sedation Score**

**30 minute after extubation**

**In Saline group:** About 32.0% of the samples had Sedation score 1, 56.0% of the samples had Sedation score 2 and 12.0% had Sedation score 3.

**In Dexmed group**: About 4.0% of the samples had Sedation score 1, 52.0% of the samples had Sedation score 2 and 44.0% have Sedation score 3.

Mean Ramsay Sedation score was significantly higher at 2.4 ± 0.57 in patients treated with Dexmedetomidine, while it was 1.80 ± 0.64 in Saline group (p< 0.001) indicating arousable sedation. None of the patients in Dexmedtomidine group had Ramsay score >3, i.e., none of the patients required intensive monitoring, but had arousable sedation.

These results corroborate with studies of Harsoor S, et al. [10] where Ramsay Sedation score was significantly higher at 2.6 ± 0.75 in patients treated with Dexmedetomidine, while it was 1.25 ± 0.44 in Placebo group (p< 0.001) .

**Modified ALDRETE Score (Recovery Score)**

In order to assess the quality of recovery, modified ALDRETE score was compared among the 2 groups.

**Saline group:** About 24.0% of the samples had ALDRET 8, 44.0% of the samples had ALDRETE 9 and 32.0% had ALDRETE 10.

**Dexmed group:** Almost 12.0**%** of the samples had ALDRETE 8, 76.0**%** of the samples had ALDRETE 9 and 12.0**%** had ALDRETE 10 in Dexmed group. Here, the p-value is greater than the significance level 0.05 i.e., the difference in modified ALDRETE score between Saline and Dexmed groups is not significant.

**Side Effects**

Patients were monitored for incidence of any side effects like Bradycardia, Hypotension, Vomiting, Respiratory depression, Laryngospasm, Bronchospasm, intraoperatively and post operatively (30 minutes after extubation).

Bradycardia was noticed in 4 out of 25 patients in Dexmed group, which was treated with Inj. Atropine 0.6 mg IV. There was no incidence of bradycardia in Saline group.

Post-operative vomiting was noticed in 3 patients in Saline group, but no patients in Dexmed group had post-operative vomiting. Dexmedetomidine is effective in controlling nausea, vomiting, pain of all patients of all age groups in the postoperative period. None of the patients in both groups had hypotension, bronchospasm, laryngospasm or respiratory depression after extubation. Thus, Dexmedetomidine as a preanaesthetic medication and intraoperative infusion was effective in blunting stress response to laryngoscopy and creation of pneumoperitoneum. It also decreased intraoperative anaesthetic requirement and had significant anaesthetic sparing property during BIS guided General Anaesthesia providing a lighter sedation without the prolongation of extubation time or without any significant adverse effects.

**Pharmaco-economics**

Inhalation agents account for significant cost of major long duration surgeries. The estimation of this cost to pre-calculate expected expenditure is not available in literature. As for intravenous agents, their relations to weight and other demographic parameters are also not well established. It can be easily assumed that the cost of Sevoflurane used during the procedure forms a major proportion of the economic variable during these procedures. However, the cost of inhalational agents used does not feature separately while calculating the total Anaesthesia-related expenditure. The retail price of Sevoflurane available in the Indian market is Rs. 7,350 per 250 ml bottle. So, the usage of Dexmedetomidine can cut down the cost of Sevoflurane by an average of Rs.370 for a 3 hour surgery (Rs 120/hour). Thus, a major observation in the study was that Dexmedetomidine infusion as an adjuvant in General Anaesthesia causes decreased requirements of Sevoflurane without compromising adequate depth of anaesthesia, thus it has anaesthetic-sparing property.

Plasma concentration of Cytokines and Interleukins as markers for stress response to surgery and effect of Dexmedetomidine on these stress markers. Studies on the effect of Dexmedetomidine infusion on newer inhalational agents like Desflurane can be tried. Different dose ranges of Dexmedetomidine can be compared to identify lowest dose requirement for stable hemodynamics. Study can be extrapolated Studies measuring Plasma concentration of Dexmedetomidine should be undertaken to establish the precise correlation between its dose and inhalational agent's requirements. Studies comparing other surgeries where pain component is higher. Studies measuring fraction of inspiratory Sevoflurane concentration and End tidal Sevoflurane concentration would improve the correlation between the Sevoflurane requirements with Dexmedetomidine use.

## Conclusion

To conclude, the continuous infusion of Dexmedetomidine, as an adjuvant in General Anaesthesia, significantly decreases the requirement of Sevoflurane for maintaining adequate depth of anaesthesia. Also, Dexmedetomidine infusion attenuates haemodynamic response to laryngoscopy and creation of pneumoperitoneum. Dexmedetomidine appears to have promising future applications with wide safety margin.

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