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ORIGINAL ARTICLE

EFFECT OF DEXMEDITOMIDINE VS PLACEBO ON PROPOFOL INDUCTION & SEVOFLURANE MAINTENANCE REQUIREMENTS IN LAPAROSCOPIC CHOLECYSTECTOMIES USING BIS GUIDED GENERAL ANAESTHESIA

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ABSTRACT: BACKGROUND: Dexmedetomidine has been shown to blunt the stress response to surgery and anaesthesia. Hence our study was designed to evaluate the effect of intravenous (IV) Dexmedetomidine infusion on propofol & Sevoflurane requirements during general anesthesia for laparoscopic cholecystectomies without intra operative awareness. **MATERIALS AND METHODS:** 60 patients scheduled for laproscopic surgeries under general anesthesia were divided into Dexmedetomidine (D) group and Placebo (P) group of 30 each. Group D received a loading dose of Inj. Dexmedetomidine at 1 µg/kg diluted to 100 ml given over 15min, followed by maintenance with 0.5 µg/kg/h till the end of surgery. Group P received similar volume of IV normal saline (100 ml). Anesthesia was maintained with nitrous oxide in oxygen and Sevoflurane keeping BIS values between 40 to 60.Patients were monitored intraoperatively for haemodynamic variables, depth of anaesthesia propofol and sevoflurane consumption & postoperative pain. Results were analysed. **RESULTS:** 50% reduction (1 mg/kg) in the induction dose of propofol was observed along with a mean hourly Sevoflurane requirement of 15.54±2.8 in group D when compared to (2 mg/kg) propofol, 33.35±4.2 sevoflurane in group P to maintain adequate Depth of anaesthesia using BIS. In peri-operative period, the heart rate and blood pressures were significantly lower in Group D, when compared to placebo. Patients in Group D were better sedated and post-operative pain score was lower in Group D compared to Group P. **CONCLUSION:** Dexmedetomidine is an effective anesthetic adjuvant that reduces propofol & sevoflurane requirements without fear of intraoperative awareness.

KEYWORDS: Dexmedetomidine, Propofol induction, laparoscopic cholecystectomies, Bispectral index, awareness.

INTRODUCTION: Laparoscopic surgeries are routinely performed under general anesthesia & are associated with unique hemodynamic changes in the form of increased systemic vascular resistance, especially due to pneumoperitonium.[1] This may lead to hypertension, neccessating increasing the depth of anesthesia (DOA), and at times even requires the use of vasodilators.[2] We studied the use of Dexmedetomidine in laparoscopic surgeries and evaluated its effects on hemodynamics, anesthetic and analgesic requirement.[3] Administration of a drug known to decrease anesthetic requirement can lead to under-dosing of the anesthetic drugs, causing awareness under anesthesia. So we included BIS as a monitoring tool to study the depth of anaesthesia.[4]

BI SPECTRAL INDEX: The BIS index is an EEG parameter measured numerically so that the effects of anesthesia and sedation on brain can be studied.[4]

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DEXMEDETOMIDINE: Dexmedetomidine, the pharmacologically active d-isomer of medetomidine, is highly selective and specific α2-adrenoceptor agonist with sedative, analgesic and antianxiety properties.[5,6]

MATERIALS AND METHODS: A randomized, prospective, clinical study was formulated, and conducted at government general hospital Kakinada from January 2014 to October 2014.

After the approval of the Institutional Ethics Committee, 60 consented patients were randomly allocated into two groups as Group 'D' (Dexmedetomidine group) and Group 'P' (Placebo group) using computer generated random numbers.

Inclusion criteria: Patients belonging to ASA grade I and II; aged between 18 to 50 years; of either sex; scheduled for elective laproscopic surgeries.

Exclusion criteria: patients with ASA grade III/IV; and contraindication to the use of Dex e.g. liver, renal or cardiac disorder.

At the start of surgery, two intravenous (IV) lines were secured, one for anaesthetic purpose, One for study drug infusion. Baseline monitors like ECG, pulseoximetry, NIBP and BIS were attached and results were noted. All the patients were premedicated with glycopyrrolate 4mcg/kg, midazolam 0.03 mg/kg, ondansetron 4 mg intravenously (IV).All the patients received fentanyl in dose of 1.5 mcg/kg IV.

- Group D= Dexmedetomidine loading dose of 1μ/kg in 100ml saline over 15min followed by infusion @0.5μ/kg/hr in a 50ml syringe @10ml/hr.
- Group P=Normal saline loading dose 100ml/hr over 15min followed by infusion @ 10ml/hr.

After loading dose of study drug, anesthesia was induced with propofol 10 mg IV incremental doses to reach the BIS value 40-60, and at the same time the vocal response was checked. The dose of propofol needed to achieve BIS of 40-60 was considered as the induction dose. Succinylcholine 1.5 mg/kg was administered IV to facilitate intubation. Vasopressor response to laryngoscopy and intubation was documented by noting HR and BP.

All patients were intubated with appropriate sized cuffed endotracheal tube passed orally, and the placement was confirmed with auscultation and end-tidal carbon dioxide (EtCO2) recording. Anesthesia was maintained with nitrous oxide and oxygen mixture (60:40), and sevoflurane, using a closed circuit. Vecuronium was used to maintain intraoperative neuromuscular blockade. HR and BP response to pneumoperitoneum was documented and requirement of additional anesthetic/analgesic noted. Whenever required, anesthesia was deepened by increasing the sevoflurane concentration, followed by propofol top ups of 10 mg, if needed. Study drug infusion was continued until extubation.

Hemodynamic response to extubation was documented by observing the pulse and blood pressure. Intraoperative monitoring was documented during the preinduction, after the loading dose of study drug, at the induction of anesthesia, during laryngoscopy and intubation 0 3 5 10, and at pneumoperitoneum and then every 15 min till the end of surgery and continued during extubation and post operatively.

Side effects like hypotension, bradycardia, respiratory depression, postoperative nausea and vomiting were noted. Patients were observed for 6 hours in the recovery room, and then shifted to

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the ward. The time required for extubation and Ramsay sedation score (RSS) after extubation were also observed. The post-operative pain was assessed using visual analogue scale (VAS). The total and hourly Sevoflurane requirements were measured at the end of every hour.

The usage of Sevoflurane during anesthesia is calculated as follows:

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

Statistical Analysis: Data Analysis was done by unpaired 't' test using SPSS version 17. P value of less than 0.05 was considered as statistically significant.

RESULTS:

- A total of 60 patients were enrolled in our study. Mean HR on starting was 90±0.3 which fell to lowest mean of 61±0.16 (P = 0.0001) There was a transient yet significant fall in HR at beginning of the Dex infusion. HR was however sustained for the entire duration of infusion. Few Patients had sinus bradycardia (HR between 55- 60) at the start, however they did not require atropine administration.
- Mean systolic blood pressure (SBP) was comparable between both groups, and fell to 108±12.5 with loading dose of Dex compared to 115±12.0 in group P(P = 0.03). After that minimal fall was observed for entire duration of infusion. Similar observations were made at the time of creation of the pneumoperitoneum in group D patients.

Demographic parameters Mean diastolic blood pressure (DBP) fell from 80±10.3 to 76±11.2 which is statistically insignificant (p=0.15) in both groups. There was good control over the vasopressor response during laryngoscopy, and at creation of pneumoperitoneum.

Mean age in years	**43±12.6**	**44±12.8**
Gender	8: 12	9: 10
weight	52.5±6.01	50.6±7.03

Table 1

None of the 60 patients needed either metoprolol or nitroglycerine to counter the hypertension effect of pneumoperitoneum.

The mean dose of propofol required for induction was 57.5±10.1 mg. Intra-operatively, whenever propofol was required, it was given in 10 mg top ups depending on the BIS value.

We also studied the requirement of sevoflurane which was adjusted to maintain stable BP and BIS value. It was observed that the dial concentration of sevoflurane required was between 0.5 to 0.75 throughout the surgery; with peak requirement at the beginning and immediately after intubation, and then again during creation of pneumoperitoneum. With the loading dose of Dex itself, BIS value fell by 20% to reach a value 60 to 80, indicating good sedation (sedated but not unconscious, could be awakened by verbal commands). Intra-operatively BIS was maintained 40 - 60 for providing adequate DOA. BIS indicates anesthetic depth which was maintained with sevoflurane

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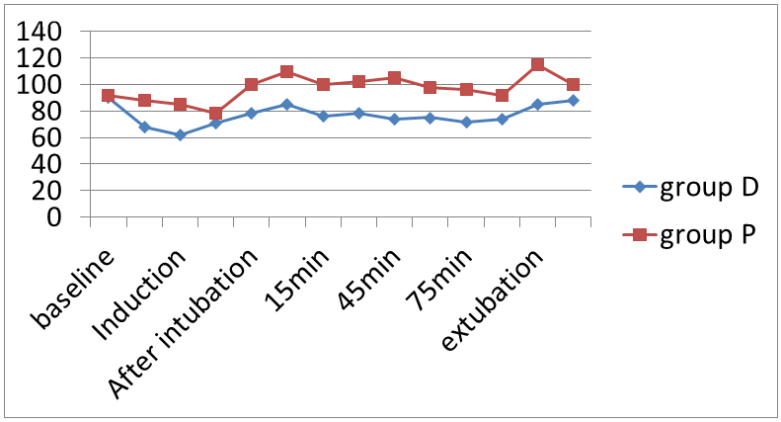
and if required propofol. We observed that BIS fell with induction to < 40 and rose to 60 with intubation when the gases were started (nitrous, oxygen and sevoflurane) after intubation, the BIS dropped to < 60 and remained so till the creation of pneumoperitoneum.

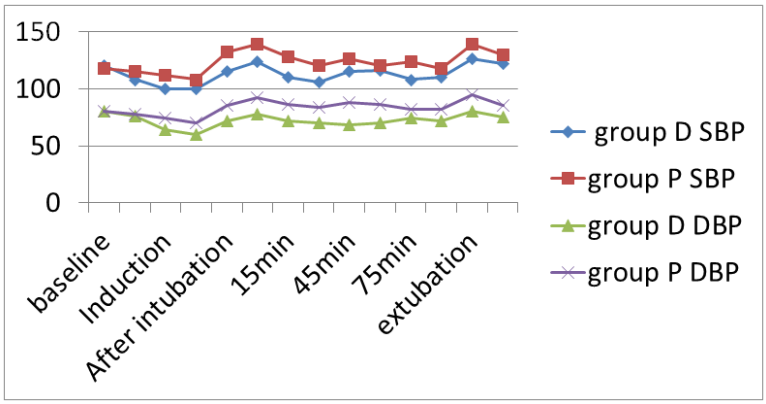
For rest of the period, BIS was well maintained. Extubation response was studied which appeared to be smooth in all patients of group D with minimal change in hemodynamics. Patients showed immediate eye opening and were responsive to verbal commands indicating no residual effects of Dex.

There was no difference in vecuronium requirement with the use of Dex. Patients were pain free in postoperative period. All patients were hemodynamically stable and comfortable in the recovery room. None of patients had postoperative nausea and vomiting (PONV), hypotension, bradycardia or episodes of respiratory depression, and were shifted to the ward after six hours.

- Ramsay sedation score was significantly higher at 2.8±0.65 in patients treated with Dexmedetomidine, while it was 1.28±0.41 in placebo group (P <0.0001) indicating arousable sedation.
- Pain assessed by visual analog scale at first hour of postoperative period was 2.15±0.79 in group D, which was significantly lower against 3.25 ± 0.5 in group P (P < 0.0001)



Comparision of heart rate in both groups



Comparision of blood pressure in both groups

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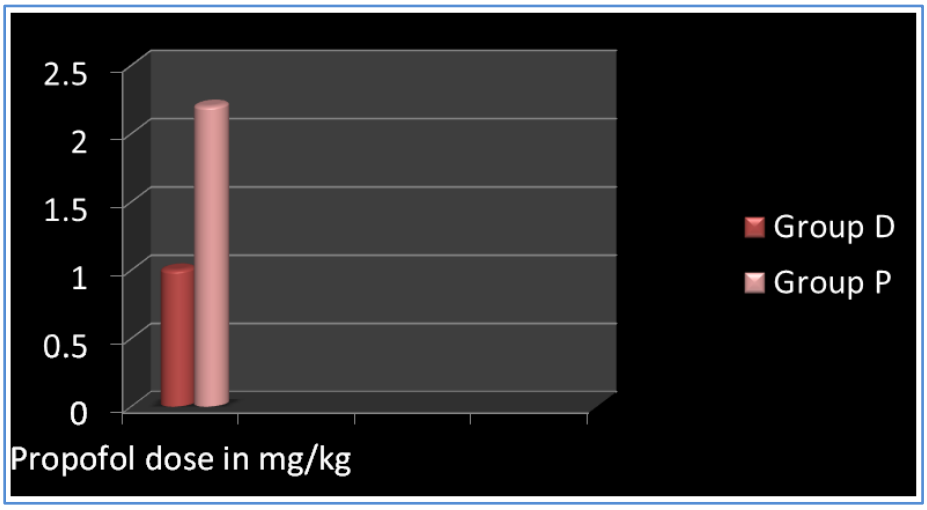
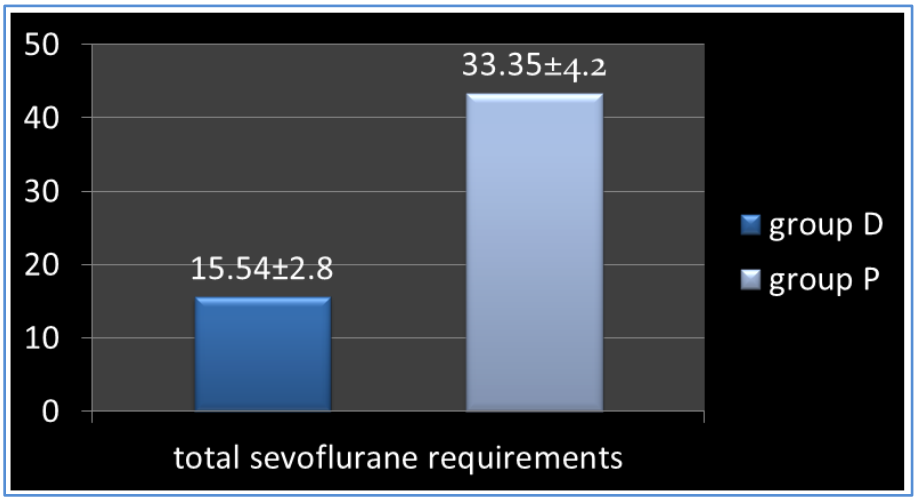


Effect of Dexmedetomidine on Propofol requirement



Effect of Dexmedetomidine on total sevoflurane requirements

DISCUSSION: Laparoscopic surgery leads to intraoperative stress during pneumoperitoneum by increasing the systemic vascular resistance and blood pressure at the same time producing nociception.[7]

Dexmedetomidine, shows specific and selective alpha2 adrenergic receptor agonism. The unique properties of Dexmedetomidine make it suitable for analgesia during the perioperative period.[8] The major sedative and antinociceptive effects of Dexmedetomidine are due to to its stimulation of alpha2A subtype located in locus coeruleus.[9]

Dexmedetomidine potentiates anesthetic effects of all intraoperative anesthetics. We observed that Dexmedetomidine significantly reduces induction dose of propofol. When compare to the routine induction dose of propofol (2 mg/kg), we observed a 50% reduction (1mg/ kg) with the use of Dexmedetomidine.

The BIS index is a numerically processed, clinically-validated EEG parameter that measures the effects of anesthesia and sedation on brain.[10] According to the manufacturer this monitoring may act as an additional vital sign that allows the clinicians to deliver anesthesia according to the patient need, and to assess and respond appropriately to a patient's clinical condition during surgery. Over all it may be helpful in maintaining adequate DOA. A study by Katoh et al.[11] examining the effect of increased age on the BIS index showed that the BIS index was a better predictor of depth of sedation than the end-tidal sevoflurane concentration.

Song and others observed that Bispectral Index Monitoring (BIS) during anesthesia helps in reducing Sevoflurane requirements and a faster emergence in patients undergoing tubal ligation procedures.[12] Dexmedetomidine also decreases the requirement of inhalational agents. Previous studies showed a 25% reduction of maintenance and concentration of isoflurane in patients who received Dexmedetomidine.[13] A 35-50% reduction of isoflurane requirement in patients treated with either low or high doses of isoflurane without premedication.[14] Our study also correlated with this, a 50 to 55% reduction in sevoflurane requirement were made in our study.

Dexmedetomidine has been shown to attenuate the sympathoadrenal stimulation during intubation effectively.[15,16] We observed that Dexmedetomidine effectively attenuates the vasopressor response of laryngoscopy, and intubation and the sympathoadrenal response occurring with pneumoperitoneum. Dexmedetomidine has been shown to provide good hemodynamic stability. It maintained HR and BP during perioperative period including during laryngoscopy and pneumoperitoneum.

At clinically effective doses, Dexmedetomidine has been shown to cause much less respiratory depression than any other sedatives. Dexmedetomidine use permits lower doses of anesthetics to be used thus resulting in a more rapid recovery from anesthesia. Patients are able to return to the baseline level of consciousness when stimulated. This feature was shown by Hall et al. using bispectral index (BIS) monitoring system and other psychometric tests.[17]

Studying Dexmedetomidine could invariably result in under-dosing the patient with anesthetics and analgesics, possibly resulting in inadequate DOA. Hence, we included BIS monitoring in our study.

CONCLUSION: Dexmeditomidine is a good anesthetic adjuvant that decreases the requirement of propofol and sevoflurane, maintains stable hemodynamics and adequate Depth of anaesthesia, and provides an excellent recovery profile during BIS guided general anesthesia for laparoscopic cholecystectomies.

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