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An observational study to compare the efficacy of dexmedetomidine versus butorphanol for balanced anaesthesia and postoperative analgesia in patients undergoing laparoscopic surgery

Dr.Sara Mary Thomas
Professor, Department of Anaesthesiology, Shrimati Bhikhiben Kanjibhai Shah Medical Institute | Research Centre, Sumandeep Vidyapeeth (An Institute Deemed to be University), Piparia, Vadodara, Gujarat, India

Dr.Richa Tailor
Assistant Professor, Department of Anaesthesiology, Shrimati Bhikhiben Kanjibhai Shah Medical Institute | Research Centre, Sumandeep Vidyapeeth (An Institute Deemed to be University), Piparia, Vadodara, Gujarat, India

Dr.Pranav Kanabar
3rd year MD resident, Department of Anesthesiology, Shrimati Bhikhiben Kanjibhai Shah, Medical Institute &Research Centre, Sumandeep Vidyapeeth (An Institute Deemed to be University) Piparia, Vadodara, Gujarat, India

Dr.Dinesh Chauhan
Professor & HOD, Department of Anaesthesiology, Shrimati Bhikhiben Kanjibhai Shah Medical Institute | Research Centre, Sumandeep Vidyapeeth (An Institute Deemed to be University), Piparia, Vadodara, Gujarat, India

Dr.Arpit Shah
Senior Resident, Department of Anaesthesiology, Shrimati Bhikhiben Kanjibhai Shah Medical Institute | Research Centre, Sumandeep Vidyapeeth (An Institute Deemed to be University), Piparia, Vadodara, Gujarat, India

***Abstract*---**To compare efficacy of intravenous dexmedetomidine versus butorphanol for balanced anaesthesia and postoperative analgesia in patients undergoing laparoscopic surgery under general anaesthesia. After obtaining institutional ethical committee approval & written informed consent 54 adults of either gender aged 18-60 years, of grade I & II ASA were divided into two equal groups; Group D

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***Corresponding author**: Kanabar, P.; Email: pranav.kanabar@gmail.com*
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received Inj. Dexmedetomidine 1 μg/kg i.v. & Group B, Inj. Butorphanol 10 μg/kg i.v., in 100ml NS over 10 minutes before induction. Standard general anaesthesia technique including propofol, succinylcholine/Atracurium, IPPV & Isoflurane/N20 was administered. Heart rate (HR), systolic blood pressure (SBP), diastolic blood pressure (DBP), mean arterial pressure (MAP) & SPO2 were recorded at - baseline, after-drug administration, induction, at intubation & 1, 3 & 5 minutes after intubation, at pneumoperitoneum & 15 minutes intervals upto 30 minutes after extubation. Postoperative Visual Analog Scale (VAS) Scores & Ramsay Sedation Score (RSS) were evaluated half hourly till score of >4 & <2 were recorded, respectively. HR, SBP, DBP & MAP were found to be lower from baseline in Group D & Group B after intubation, pneumoperitoneum & extubation but the reduction in Group B was significant ($p<0.05$) as compared to Group D. VAS scores were found to be significantly lower in Group B than in Group D ($p<0.05$) for up to 240 minutes. Ramsay Sedation Scores were significantly higher ($p<0.05$) in Group B than in Group D upto 120 minutes. A single dose of intravenous Butorphanol (10 μg/kg) preoperatively effectively attenuates sympatho-adrenal stress responses of laparoscopic surgeries maintaining better hemodynamics along with improved postoperative analgesia. Dexmedetomidine causes less post-operative sedation in comparison to Butorphanol.

***Keywords*---**laparoscopic surgery, dexmedetomidine, α2- adrenoceptor agonist, butorphanol, opioids, stress response.

Introduction

First laparoscopic surgery was successfully performed by Phillipe Mouret in 1987, since then laparoscopic surgeries have become the gold standard attributed to benefits such as minimal - incision, disturbance of homeostasis, morbidity, mortality, recovery time and hospital stay along with consequent reductions in healthcare costs.[1,2]. Albeit laparoscopic surgeries pose significant challenges to their successful anaesthetic management, mainly due the combined effects of pneumoperitoneum, patient position, anaesthesia, and hypercapnia from the absorbed CO2 that is used to produce pneumoperitoneum. Pneumoperitoneum creation leads activation of renin–angiotensin–aldosterone system resulting in increase in renin activity and increase in plasma levels of norepinephrine and epinephrine leading to an elevated arterial pressure, increased systemic and pulmonary vascular resistance, and decreased cardiac output.[3,4]

Balanced anaesthesia is the technique in which a number of agents are combined to produce desired effect.[5] Dexmedetomidine is a newer active dextroisomer of medetomidine, specific and highly selective alpha-2-adrenergic agonist causing dose dependent reduction in anaesthetic and analgesic requirements, promote perioperative hemodynamic stability, reduce myocardial ischemia, improve renal function, provide sedation and anxiolysis, and attenuate neuro-humoral “stress response” of major surgery without causing respiratory depression and is 7 to 10

times more potent than clonidine.[11] It inhibits norepinephrine release and produces predictable dose–dependent reduction in arterial blood pressure (BP) and heart rate (HR).[12]

Butorphanol tartrate is a synthetic intermediate acting opioid, having partial agonist-antagonist activity at μ and agonist activity at the κ opioid receptor with analgesic potency greater than morphine and pethidine. Combining opioids with sedative-hypnotics and/or volatile anaesthetics leads to reduction in preoperative pain and anxiety, decrease somatic and autonomic responses to airway manipulations, improve hemodynamic stability, lower requirements for inhaled anaesthetics, and provide immediate postoperative analgesia.[13,14] Butorphanol has been known to produce prolonged analgesia and amnesia, stable haemodynamic parameters, no postoperative respiratory depression and no prolongation of the recovery room stay.[16,17]. Hence, in this study we evaluate and compare the efficacy of Dexmedetomidine or Butorphanol for balanced anaesthesia and post-operative analgesia in patients undergoing Laproscopic Surgery.

Material and Methodology

After obtaining approval of the institutional ethics committee (Ref.: SVIEC/ON/MEDI/BVPG/D19199) and written informed consent from all patients, a prospective observational study was conducted on 54 patients posted for laparoscopic surgeries under general anaesthesia. Patients belonging to ASA Grade I and II, aged between 18-60 years, and of either sex were included in the study. Pregnant and lactating women, patient with acute and chronic renal failure, compromised cardiovascular function including bradyarrhythmia or heart blocks, severe deranged liver function, patients on beta blocker & surgeries lasting for more than 3 hours were excluded from the study. After preanaesthetic check up, patients were kept nil by mouth for 6 hours prior to surgery; they were also familiarised with Visual Analogue Scale(VAS). After arrival in operation theatre, patient was connected to multichannel monitor which records heart rate (HR), non-invasive measurements of systolic, diastolic and mean arterial pressure (SBP, DBP, MAP), continuous ECG monitoring, oxygen saturation by pulse oximeter (SPO2) and end tidal carbon dioxide (EtCO2). An 18 gauge venous cannula was secured and intravenous fluid namely Ringer lactate was started. Patient was premedicated with Inj. Glycopyrrolate 0.004mg/kg i.v., Inj. Ondansetron 0.1mg/kg i.v. & Inj. Ranitidine 50 mg i.v. A consultant anaesthesiologist administerd the test drugs 10 minutes before induction of anaesthesia as an infusion. Group D was given Inj. Dexmedetomidine 1 μg/kg i.v. as an infusion in 100 Normal Saline over 10 minutes & Group B was given Inj. Butorphanol 10 μg/kg i.v. as an infusion in 100ml Normal Saline over 10 minutes. Patient was pre-oxygenated with 100% oxygen for 3 minutes and induced with Inj. Propofol 1-2mg/kg i.v. and Inj. Succinylcholine 1.5-2mg/kg i.v. was given to facilitate intubation. Trachea was intubated with cuffed endotracheal tube of appropriate size, bilateral air entry checked and tube was secured. End tidal carbon dioxide (EtCo2) was monitored. Anaesthesia was be maintained with O2, N2O at 1:1 ratio and Isoflurane using circle system. Inj. Atracurium loading dose 0.5mg/kg i.v. followed by maintenance with 0.1 mg/kg i.v. was administered. Patient was mechanically ventilated on Volume Control mode and

settings were adjusted to maintain EtCo2 between 35 to 45 mmHg. Intra-abdominal pressure was maintained between 12-14 mmHg. Monitoring of parameters i.e. HR, SBP, DBP, MAP, SPO2 were noted at predetermined time intervals as follows:

Time Interval	T
Baseline	T0
After Drug Infusion	T1
After Induction	T2
At intubation	T3
1 minute after intubation	T4
3 minutes after intubation	T5
5 minutes after intubation	T6
15 minutes after intubation	T7
After pneumoperitoneum	T8
5 minutes after pneumoperitoneum	T9
10 minutes after pneumoperitoneum	T10
15 minutes after pneumoperitoneum	T11
30 minutes after pneumoperitoneum	T12
45 minutes after pneumoperitoneum	T13
60 minutes after pneumoperitoneum	T14
90 minutes after pneumoperitoneum	T15
120 minutes after pneumoperitoneum	T16
Release of pneumoperitoneum	T17
Extubation	T18
1 minute after extubation	T19
5 minutes after extubation	T20
10 minutes after extubation	T21
15 minutes after extubation	T22
30 minutes after extubation	T23
60 minutes after extubation	T24

Fall in HR < 50/min was considered as Bradycardia and was treated with Inj. Atropine 0.6mg i.v. Fall in SBP < 80 mmHg was considered as hypotension and initially treated with 200 ml of bolus Ringer Lactate fluid and incremental doses of 6mg Inj. Mephentermine i.v. was given if there was no improvement with fluid trial. After completion of surgery, neuromuscular blockade was reversed with Inj. Neostigmine (0.05mg/kg) i.v. and Inj. Glycopyrrolate (0.008mg/kg) i.v. Extubation was carried out after fulfilling the extubation criteria. Mean duration of surgery i.e. from time of incision to closure was noted. Post operatively sedation was assessed half hourly by RAMSAY Sedation Score[39] (RSS) till score of < 3 was achieved. Post-operative analgesia was assessed half hourly by VAS score till VAS >=4 was reached and as Inj. Tramadol 1-2mg/kg i.v. was given as rescue analgesia. Duration of post-operative analgesia was defined as time required for VAS to reach >= 4 post operatively and was noted. Post-operative complications like nausea, vomiting, respiratory depression, dryness of mouth or any other complication arising were noted.

Results

54 patients were enrolled in this study and were randomised into two groups of 27 patients each. Demographic profile like age, sex, weight, ASA physical status, duration of anaesthesia were comparable between the groups as presented in Table1.

Table 1
Demographic Profile

Parameters	Group-B	Group-D	p-value
	Mean ± SD	Mean ± SD	
Age (in years)	45.59 ±9.78	40.44 ±11.14	0.0768
Weight (in Kg)	58.33 ±8.22	60 ±7.33	0.0814

Haemodynamic parameters including mean HR, SBP, DBP & MAP were comparable at baseline, after drug administration and after induction among the two groups. At intubation (T3) there was 12% rise in HR, 12% rise in SBP, 12% rise in DBP and 10% rise in MAP from baseline value in Group B as compared to 24% rise in HR, 27% rise in SBP, 26% rise in DBP and 25% rise in MAP in Group D with $p<0.05$. Similarly, 1 minute after intubation (T4) there was 14% rise in HR, 14% rise in SBP, 13% rise in DBP and 11% rise in MAP from baseline value in Group B as compared to 21% rise in HR, 29% rise in SBP, 27% rise in DBP and 24% rise in MAP in Group D with $p<0.05$ [Figure: 1,2,3,4]. As seen, the rise in HR, SBP, DBP, MAP at intubation and 1 minute after intubation was more in group D as compared to Group B, p - value<0.05.

Subsequently there was fall in HR, SBP, DBP and MAP 3 minutes after intubation and onwards (T5 onwards) in both the groups but on comparing the difference in decrease of these parameters between the groups it was found that in group B the decrease in HR, SBP, DBP, MAP was more than 17% ,19%, 18%, 16% respectively as compared to the fall in HR, SBP, DBP, MAP in group D ($p < 0.05$). Throughout the remaining intraoperative period the mean HR, SBP, DBP and MAP in group B remained low including during pneumoperitoneum creation (T8) & extubation (T18) as compared to group D and the difference remained statistically significant ($p<0.05$) till T19. [Figure: 1,2,3,4].

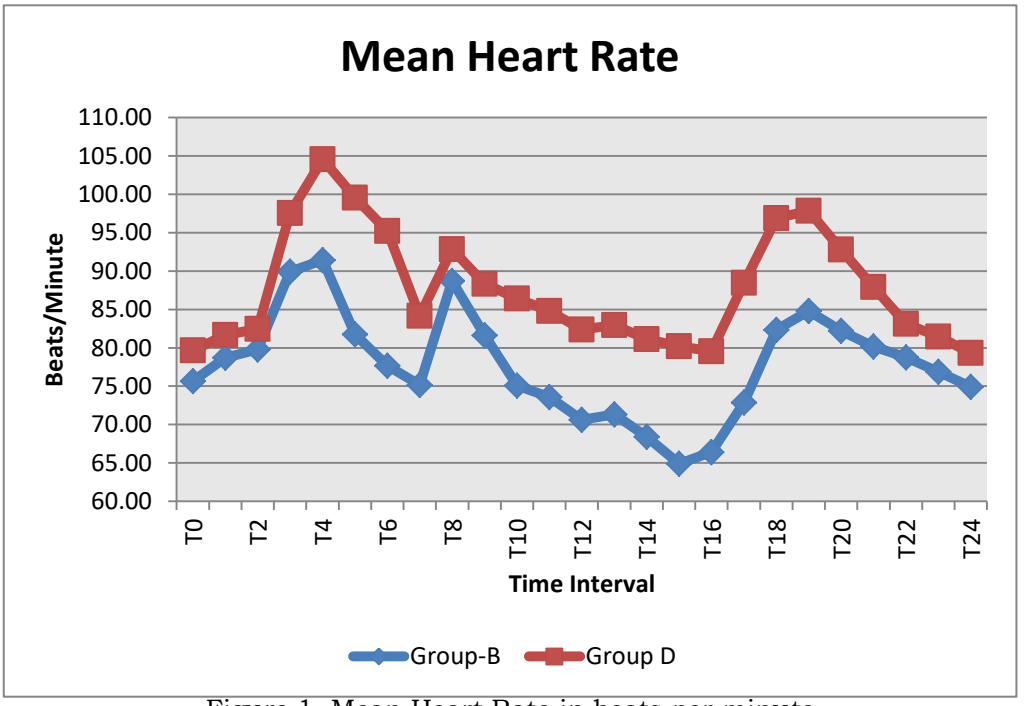

Figure 1. Mean Heart Rate in beats per minute

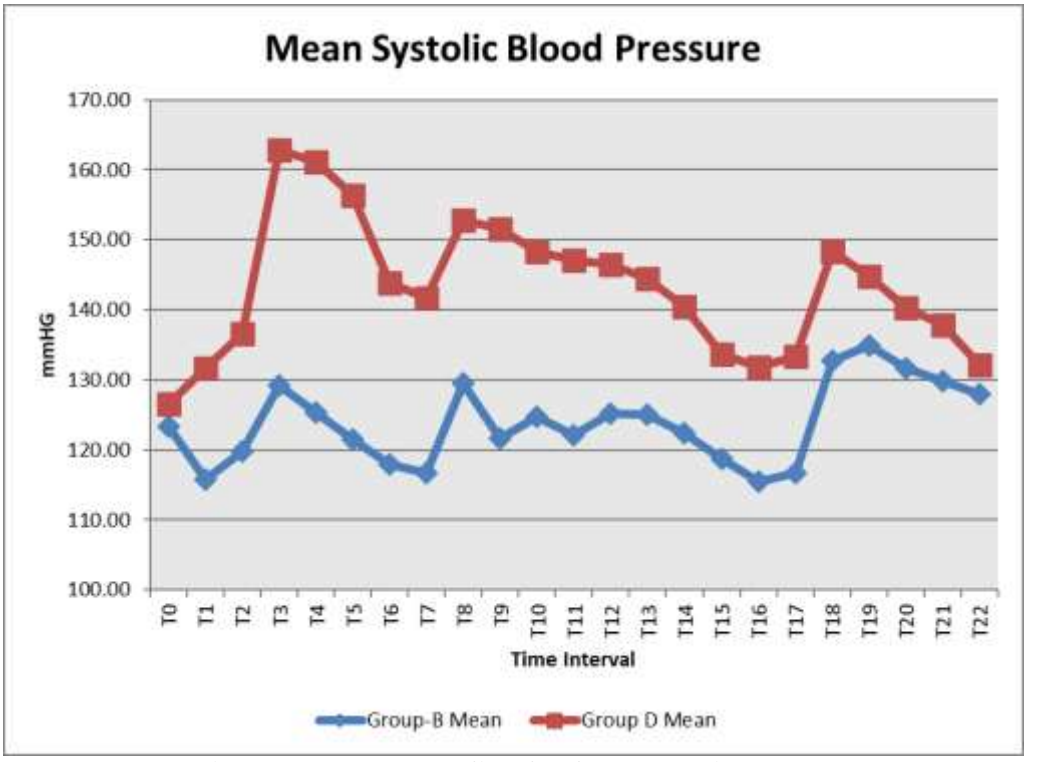

Figure 2. Mean Systolic Blood Pressure in mmHg

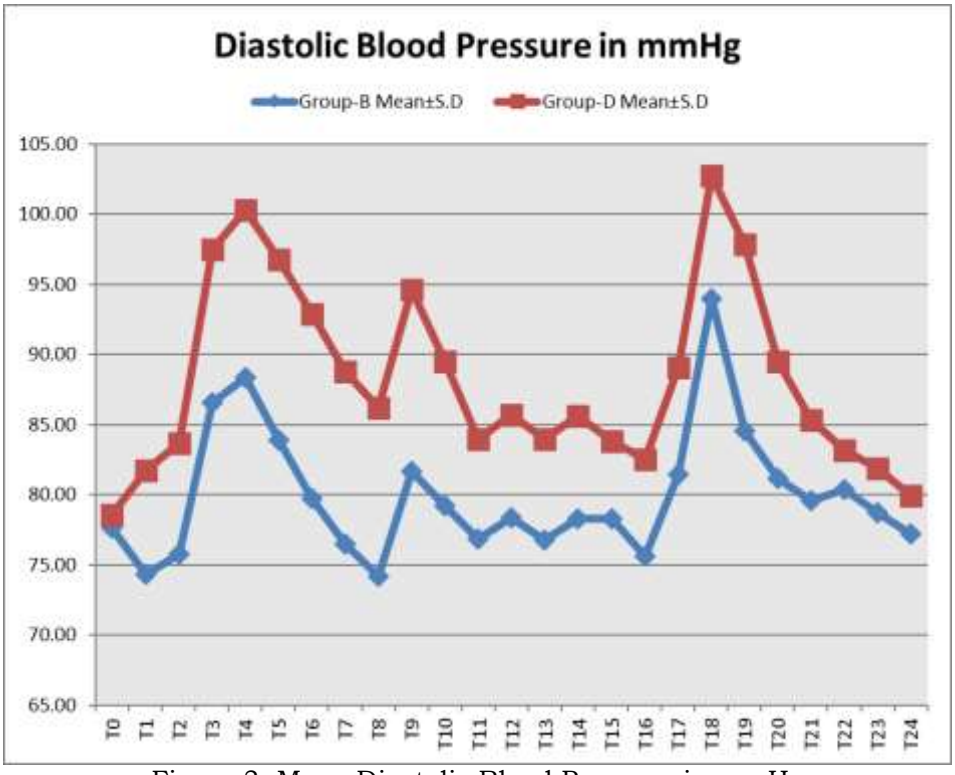

Figure 3. Mean Diastolic Blood Pressure in mmHg

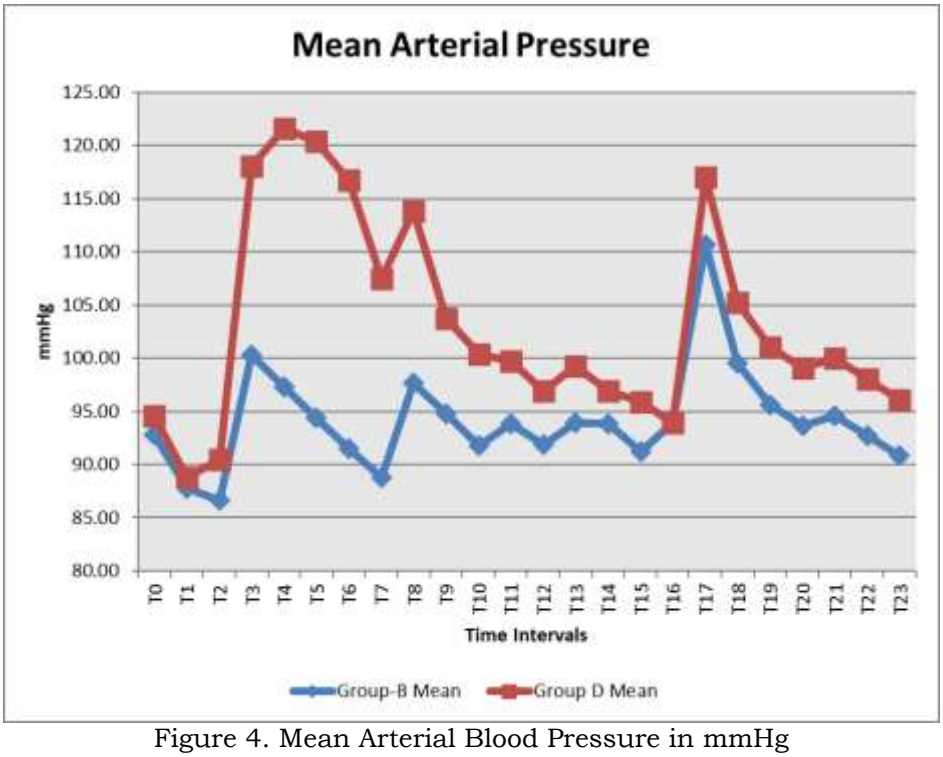

Figure 4. Mean Arterial Blood Pressure in mmHg

Postoperatively, majority of patients required rescue analgesia by up to 240 minutes in butorphanol group as compared to 30 minutes in group D, ($p<0.05$) as shown in Figure 5.

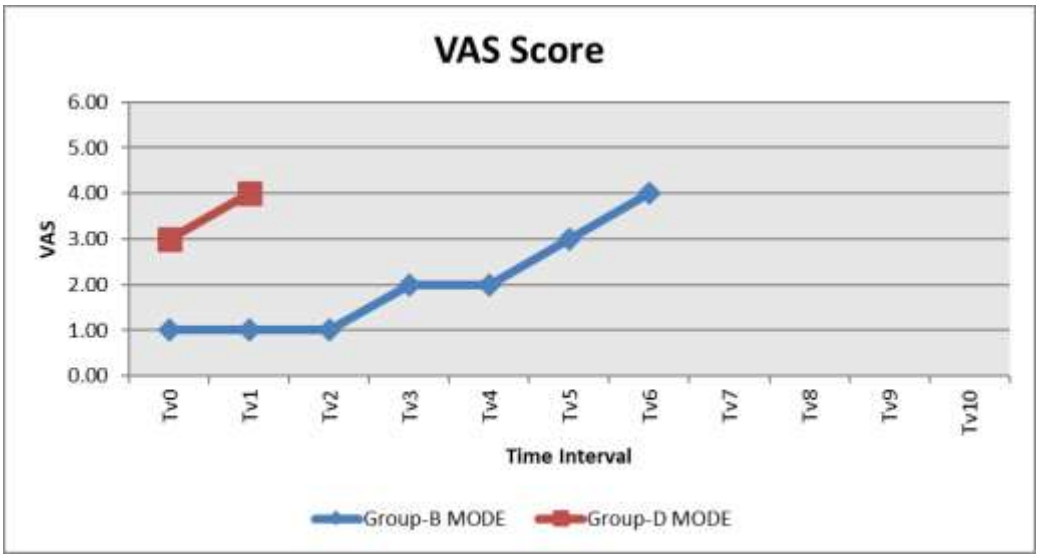

Figure 5. Visual analog scale score

It was observed that majority of patients in Group B had significantly higher levels of sedation (RSS 4) at extubation in comparison to Group D (RSS 3) and most of the patients in Group B attained Ramsay sedation score of 2 by 120 minutes as compared to 30 minutes in group D ($p<0.05$) as shown in Figure 6.

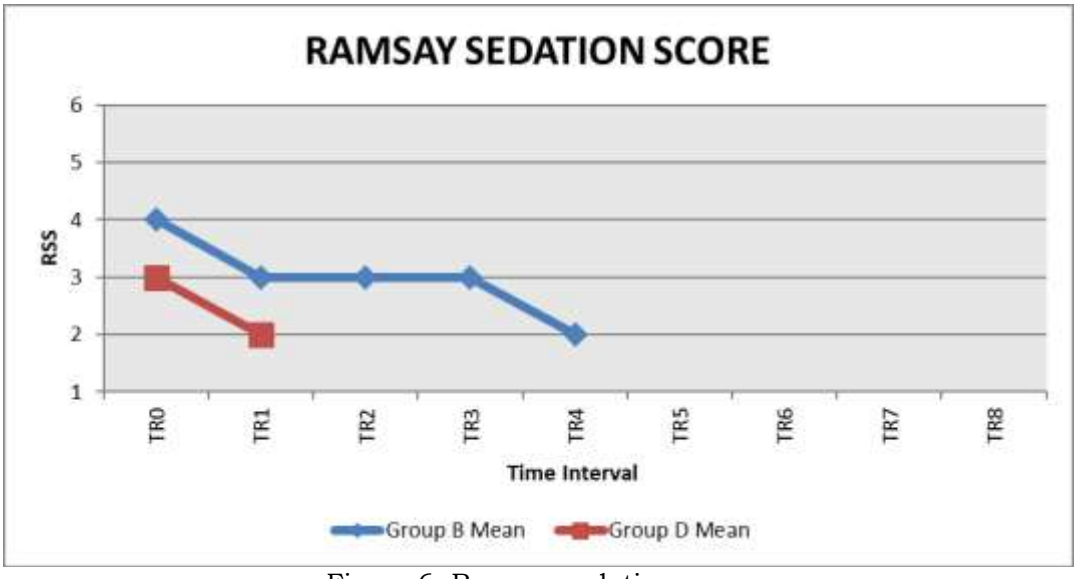

Figure 6. Ramsay sedation score

No adverse effects were seen in either of the groups.

Discussion

Pneumoperitoneum during laproscopic surgeries leads to raised systemic vascular resistance (SVR), mean arterial pressure (MAP), cardiac filling pressure and reduced cardiac index (CI). Carbon dioxide insufflation and its resultant peritoneal uptake causes hypercarbia, leading to sympathetic nervous system stimulation thereby causing raised heart rate, blood pressure and risk of arrhythmia. Myocardial contractility and reduction in arrhythmia threshold are caused by hypercapnia [3,4]. Endotracheal intubation and laryngoscopy often leads to hypertension and tachycardia and cardiac dysarrythmias. This is due to reflex sympathetic discharge which occurs as a result of pharyngeal and laryngeal stimulation. Such stimulation is more often associated with increase in plasma epinephrine concentration.[5]

A very limited numbers of trials have been conducted comparing the efficacy of intravenous dexmedetomidine versus intravenous butorphanol as premedication on peri-operative haemodynamics and for balanced anesthesia in laparoscopic surgery. Dexmedetomidine is a newer, potent α2 receptor agonist with high ratio of specificity (α2/α1 - 1620:1) having sympatholytic, analgesic, anxiolytic and sedative property with minimal depression of respiratory function. Its action on catecholamines inhibiting their uptake leads to titrable reduction in blood pressure and heart rate. [11,12] Ahmad Waqar Khan, Dheeraj Saxena et al. & P Indira, Rajola Raghu et al. in their respective studies used 1 ug/kg of dexmedetomidine prior to induction of anesthesia to evalute its response to laryngoscopy and intubation and observed that 1 µg/kg of dexmedetomidine did not cause any unwanted side effects such as severe hypotension, bradycardia, seavere nausea and vomiting.[29,33,40] Hence in our study we used dexmedetomidine in a similar dose as at 1 µg/kg prior to induction.

While administering balanced anaesthesia, an ideal opiod should allow for rapid onset with titrable effect, while competently preventing responses to various unwanted stimuli. It should very rarely require supplementation and should cause limited depression of cardiovascular and respiratory system allowing return of satisfactory spontaneous ventilation in acceptable time frame along with producing lasting post operative analgesia with very little side effects. Butorphanol being a competent partial agonist-antagonist at µ opioid receptor and agonist at κ opioid receptor with limited respiratory depression is one such agent.[16] Anuja Agrawal, Jitendra Chauhan et al. conducted a study comparing dexmedetomidine (1 µg/kg i.v. loading dose followed by 0.7 µg/kg/hr infusion) and butorphanol (10 µg/kg i.v. loading dose and 2 µg/kg/hr infusion) and found no significant adverse events associated.[28] Hence in our study we used butorphanol in a similar dose as at 10 µg/kg prior to induction to evaluate its efficacy in reducing pressor responses to laryngoscopy and intubation.[19]

With respect to demographic profile of the subjects of this study, Group D (dexmedetomidine) and Group B (butorphanol) were statistically comparable in terms of number of patients, age, weight, gender, ASA status and duration of surgery. ($p>0.05$) The observed demographic data of this study was similar to the findings of study carried out by Ahmad Waqar Khan, Dheeraj Saxena et al. who evaluated intravenous dexmedetomidine (1 µg/kg IV) versus butorphanol (30

μg/kg IV).[33]. Regarding mean heart rate (HR), SBP, DBP & MAP in the present study we observed that butorphanol group had reduction in HR, SBP, DBP & MAP in comparison to dexmedetomidine group after intubation, pneumoperitoneum and even after extubation ($p<0.05$). Our findings were consistent with study done by Beverly K. Philip, Dubravka Freiberger et al. who compared intravenous butorphanol (20 μg/kg i.v.) with fentanyl (1 μg/kg i.v.) in laproscopic surgeries and found that butorphanol was better at controlling HR, SBP, DBP & MAP than fentanyl after intubation and pneumoperitoneum.[18]

Dr. Bhavna H.Sojitra, Dr. Deepali L Patel et al. in their study of comparing intravenous butorphanol (25 μg/kg i.v.) with fentanyl (2 μg/kg i.v.) in patients undergoing laproscopic surgeries observed that the mean intra-operative HR, SBP, DBP & MAP remained lower in butorphanol group ($p<0.05$) as compared to fentanyl, findings of the present study also corroborate the same.[30]. M. Hanumantha Rao, V. Satyanarayana et al. studied butorphanol (40 μg/kg i.v.) and fentanyl (2 μg/kg i.v.) for balanced anesthesia in patients undergoing laproscopic surgeries and found that a significant fall in HR, SBP, DBP & MAP was noted in butorphanol group post intubation ($p<0.005$) in comparison to fentanyl.[22]

Our observations were in contrast to the study by Jayshree P Vaswani, Debasis Debata et al. in which they observed the dexmedetomidine administered in bolus followed by continuous infusion intraoperatively was superior to fentanyl bolus followed by continuous infusion in attenuating stress response to intubation, pneumoperitoneum and extubation.[25] But the study done by Beverly K. Philip, Dubravka Freiberger et al., Dr. Bhavna H.Sojitra, Dr. Deepali L Patel et al. & M. Hanumantha Rao, V. Satyanarayana et al. have found butorphanol significantly more potent than fentanyl in blunting hemodynamic stress response to intubation and pneumoperitoneum creation during laproscopic surgeries [18,22,30]. Limited studies are available comparing single dose intravenous Dexmedetomidine versus intravenous Butorphanol as adjuvants to general anaesthesia in laproscopic surgeries but there are adequate studies showing intravenous Butorphanol as a better adjuvant than Fentanyl for the same. Hence further studies are needed to validate the findings of the present study demonstrating intravenous Butorphanol more efficient than intravenous Dexmedetomidine as a premedication in general anaesthesia for laproscopic surgeries.

Our study found that butorphanol group also had favorable post-operative pain profile as the patients remained relatively pain-free up to 240 minutes after extubation in comparison to dexmedetomidine group which required rescue analgesia with in 30 minutes of extubation. ($p<0.05$). Our findings were consistant with Shital S. Ahire, Shweta Mhambrey et al who also found butorphanol (20 μg/kg) better than fentanyl (2 μg/kg) in providing postoperative analgesia. [17]. However, sedation scores as assessed by Ramsay Sedation Scores in this study remained significantly higher in butorphanol group in comparison to dexmedetomidine group up to 120 minutes post-operatively($p<0.05$). Our findings were similar to observations by Vidhya N, Prakash V et al. who found sedation scores to be higher in butorphanol (20 μg/kg) group when comparing with nalbuphine (100 μg/kg). [29]. During the course of the present study, no adverse events were noted in any patient.

Conclusion

To conclude, butorphanol, when administered as premedication as part of general anesthesia in patients undergoing elective laproscopic surgeries, causes greater attenuation of stress response to tracheal intubation, pressor changes of pneumoperitoneum and provides better post-operative analgesia in comparison to dexmedetomidine without much adverse effects. Hence, intravenous butorphanol in dose of 10 μg/kg as loading dose over 10 minutes prior to induction of general anaesthesia in laparoscopic surgeries may be recommended for better haemodynamic stability with adequate intra and post operative analgesia.

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