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Original Research Article

To Study the Efficacy of Dexmedetomidine for Attenuation of Haemodynamic Responses in Patients Undergoing Laparoscopic Surgeries

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Abstract: ***Background:*** Laparoscopic surgery is among the routinely performed surgeries. However, it leads to hemodynamic instability with potentially harmful consequences. Dexmedetomidine is found to provide good hemodynamic stability required during laparoscopy when performed under general anesthesia. The aim of the study was to assess the efficacy of dexmedetomidine in attenuation of hemodynamic responses. ***Method:*** A prospective comparative study was conducted at a tertiary care center, Kolhapur including a total of 60 patients between 18-60 years and belonging to Grade I and II as per American society of Anesthesiologists (ASA) who underwent laparoscopic surgeries under general anesthesia. All the patients were equally randomized and infused with either dexmedetomidine (Group D) or 0.9% saline (Group S) and baseline hemodynamics were recorded prior to the administration of general anesthesia. Post-operative requirement of analgesia (within 24 hours) and the recovery time were recorded. Outcomes of both the groups were compared by Chi square and a P-value <0.05 was considered significant. ***Result*:** No significant difference was found in preoperative heart rate and Mean Arterial Pressure (MAP) in both the groups (P= 0.8994; P= 0.5643, respectively). Post intubation, heart rate and MAP were significantly lower throughout the surgery, in group D (P<0.05). Requirement of isoflurane and incidence of hypertension were significantly higher in group S (P= 0.0031) whereas the requirement of post-operative analgesia were significantly less group D (P=0.0015; P=1.51e^{-08} respectively). ***Conclusion****:* Perioperative IV dexmedetomidine is very useful in stabilizing haemodynamics in patients undergoing laparoscopic surgeries under general anesthesia.

Keywords: Laprascopy, pneumoperitonium, hypertension,dexmeditomidine, postop-pain management.

INTRODUCTION

In laparoscopic surgeries, carbon dioxide (CO_2) is insufflated in peritoneal cavity to create pneumoperitoneum (PNP) [1, 2]. Post PNP, plasma levels of norepinephrine, epinephrine and plasma rennin activity increases [3]. The combined changes contribute to elevated arterial pressure, increased systemic and pulmonary vascular resistance and reduced cardiac output. Furthermore, CO2 insufflation may cause respiratory acidosis leading to cardiac arrhythmias [4]. Dexmedetomidine, a class of central alpha-2 adrenergic agonists, imparts several beneficial actions such as improved hemodynamic stability in response to endotracheal intubation and surgical stress, reduced anesthetic and opioid requirements, speedy recovery improved sedation, anxiolysis and analgesia [5-10]. The aim of the present study is to therefore evaluate the efficacy of dexmedetomidine in blunting the neuro-endocrine response and subsequent hemodynamic changes that occur during critical incidences such as laryngoscopy, endotracheal intubation, creation of PNP and extubation in patients undergoing laparoscopic surgeries.

MATERIALS AND METHODS

A prospective comparative study was conducted in the anesthesia department at a tertiary care centre in Kolhapur. The study was approved by the institutional ethical committee. American society of Anesthesiologists' (ASA) Grade I and II patients of

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either sex between 18 to 60 years of age undergoing laparoscopic surgeries under general anesthesia who gave informed consent were included in the study. Patients with an anticipated difficult airway, oropharyngeal pathology, patients on beta blockers, with conduction defects of the heart (heart blocks), with known allergy to the drug and morbidly obese patients (BMI > 35 kg/m^2) were not considered for the study.

Patients were randomized according to the computer-generated randomization procedure into two groups of 30 each (computed according to power calculations), Group D – Dexmedetomidine group and Group S – placebo group. The study drug was provided as prefilled and coded identical 1 mL syringes for the loading dose and 50 mL syringes for the infusion dose, containing study drugs, as per the randomization protocol, in dilutions of: For loading dose: Dexmedetomidine – 1 ml (100 mcg/ml) Saline 0.9% - 1 ml. For infusion: Dexmedetomidine – 50 ml (1 mcg/ml) Saline 0.9 % - 50 ml.

In the operation theatre, baseline monitors such as electrocardiogram (ECG), Pulse Oximeter, and Non – Invasive Blood Pressure (NIBP) were attached. Baseline values of Heart rate (HR), Oxygen Saturation (SpO_2), Systolic Blood Pressure (SBP), Diastolic Blood Pressure (DBP) and Mean Arterial Pressure (MAP) were noted. The study drug was started 20 minutes prior to induction of general anesthesia. Patients belonging to group D received a loading dose of dexmedetomidine at 1mcg/kg over 20 mins, followed by maintenance infusion of dexmedetomidine at the rate of 0.4 mcg/kg/hour. Patients belonging to the Group S received Saline 0.9 % at a similar rate as dexmedetomidine infusion. All patients received inj. Fentanyl 1.5 mcg/kg 5 mins prior to induction of general anesthesia. General anesthesia (GA) was induced with inj. Propofol 2 mg/kg. Endotracheal intubation was facilitated with inj. Succinylcholine 2 mg/kg. End – Tidal Carbon dioxide ($ETCO_2$) was monitored throughout the surgery and maintained between 35-40 mm of Hg. General anesthesia was maintained on O_2, N_2O, Isoflurane and inj. Vecuronium bromide. Intra-Abdominal Pressure (IAP) was maintained between 12 – 14 mm of Hg. Intraoperative hypertension was managed by nitroglycerin (NTG) infusion. Intraoperative bradycardia was treated with inj. Atropine Sulphate. On completion of surgery patients' neuromuscular blockade was reversed using inj. Neostigmine 0.05 mg/kg and inj. Glycopyrrolate 0.008 mg/kg. Patients were extubated and transferred to post-operative recovery room and observed for the next one hour for any evidence of complications or adverse events. Hemodynamic Parameters were noted before starting the study drug (M1), 10 minutes after starting the study drug (M2), after induction (M3), during intubation (M4), before creation of PNP (M5), 10 (M6), 20 (M7) and 30 (M8) minutes after creation of PNP, at the end of PNP (M9), 10 minutes after extubation (N1) and 30 minutes after extubation (N2). Study Drug infusion was stopped after extubation. Post-operative requirements of analgesics, inj. Diclofenac sodium (DS), in the first 24 hours were assessed.

Data analysis was performed on R v1.2.5001. Students' unpaired "t" test was used to compare quantitative variables in both groups. The categorical data was compared using chi square test. $P \leq 0.05$ was considered to be statistically significant.

RESULTS

No significant difference between group D and S was observed and distribution of demographic characteristics was comparable ($P>0.05$) (Table 1).

There was no significant difference in the preoperative heart rate between the two groups ($P=0.8994$). However, heart rate was significantly lower and closer to the baseline in group D as compared to group S, post intubation and during PNP. Heart rate in group D remained lower throughout the period of PNP on paired t-test at 5 % CI ($P<0.05$) (Table 2).

There was no significant difference in the preoperative MAP between the two groups ($P=0.5643$). Post-intubation, MAP was lower in group D and closer to the baseline as compared to group S; and likewise, PNP also remained lower throughout the study ($P<0.05$) (Table 3).

Two patients from Group D suffered from bradycardia (HR <50 bpm) requiring inj. Atropine intraoperatively. Requirement of isoflurane and incidence of hypertension in both groups is presented in (Table 4).

Mean recovery time post extubation as indicated by the ability to vocalize. This was significantly prolonged in Group S (6.23 ± 2.20 minutes) when compared to Group D (2.36±1.12 minutes) ($P=1.51e^{-08}$). Group D required a significantly lower total dosage of inj. Diclofenac sodium (115±47.16 mg) within the first 24 hours, post-operatively as compared to patients of group S (160±61.44 mg) ($P=0.001502$).

Table-1: Demographic and surgical distribution of the groups

Details	Group D	Group S	P value
Age (Years)	33.96 ± 8.41	36.06 ± 10.62	0.393
Sex (F:M)	18:12	14:16	0.437
Weight (Kg)	49.77 ± 7.61	50.4 ± 8.73	0.762
ASA Class (I:II)	26:4	23:7	0.504
Type of Surgery (LA:LC)	6:24	7:23	0.754
Duration of Surgery	88.77 ± 25.55	85.4 ± 20.9	0.578
Duration of PNP	58.5 ± 24.26	53.57 ± 19.86	0.392

*P significant at <0.05

Table-2: Changes in heart rate (beats per minute) between group D and S

Time	Group D	Group S	P value
M1	82.13 ± 12.61	81.70 ± 13.61	0.8994
M2	81.17 ± 13.94	82.93 ± 12.52	0.6089
M3	79.00 ± 13.67	85.06 ± 13.10	0.00385*
M4	83.23 ± 12.57	102.73 ± 15.53	1.79E-07*
M5	74.80 ± 14.23	88.96 ± 14.07	6.82E-05*
M6	71.67 ± 12.00	95.60 ± 13.25	2.95E-11*
M7	71.16 ± 11.46	96.50 ± 9.99	3.45E-11*
M8	69.56 ± 10.41	95.73 ± 12.48	9.54E-06*
M9	69.10 ± 10.68	87.96 ± 11.08	6.70E-08*
N1	70.93 ± 11.64	96.36 ± 16.62	2.2E-16*
N2	77.70 ± 10.19	91.23 ± 9.47	7.18E-05*

*P significant ≤0.05

Table-3: Changes in MAP (mm of Hg), presented in terms of mean ± SD, (n=60, 30 in each group)

Time	Group D	Group S	P value
M1	94.93 ± 8.85	92.76 ± 18.49	0.5643
M2	94.46 ± 8.66	96.93 ± 9.31	0.2917
M3	83.97 ± 10.54	92.03 ± 11.50	0.0064*
M4	91.06 ± 11.94	110.83 ± 14.11	5.77E-07*
M5	84.63 ± 10.25	101.2 ± 11.88	1.40E-06*
M6	90.36 ± 9.45	110 ± 8.93	3.72E-10*
M7	88.93 ± 10.04	106.83 ± 7.50	1.22E-08*
M8	87.24 ± 8.52	106.2 ± 6.95	1.02E-05*
M9	86.36 ± 9.16	100.87 ± 7.86	1.49E-06*
N1	90.57 ± 9.13	104.1 ± 8.22	5.35E-06*
N2	90.90 ± 7.40	99.23 ± 7.95	0.002938*

*P significant at <0.05

Table-4: Patient distribution according to adverse effects

Adverse effects	Group D	Group S	P value
Bradycardia	2	0	0.1529
Hypertension	0	8	0.0031*
Isoflurane (1-5%)	7	30	0

*P significant at <0.05

DISCUSSION

Laparoscopic surgery induces intraoperative stress during PNP by increasing the systemic vascular resistance and blood pressure at the same time producing nociception. These pathophysiological changes are due to the combined effects of mechanical and neurohumoral factors. Dexmedetomidine belongs to the imidazole subclass of alpha-2 receptor agonist. It is the S-enantiomer of medetomidine, which has been used since many years in veterinary practice for its hypnotic, sedative and analgesic effects. Intravenous alpha-2 adrenoreceptor agonist administration leads to a decrease in heart rate and a transient increase in arterial blood pressure and systemic vascular resistance, however there is a decrease in cardiac output due to the activation of postjunctional vascular alpha-2 adrenoceptors. The initial increase in arterial blood pressure is probably caused by the vasoconstrictive effects of dexmedetomidine when stimulating peripheral alpha-2 receptors. This is followed by a longer lasting decrease

in heart rate and blood pressure due to a centrally mediated decrease in sympathetic tone and an increase in vagal activity. Increase in blood pressure and heart rate occurs most commonly from reflex sympathetic discharge in response to laryngotracheal stimulation, which in turn leads to increased plasma norepinephrine concentration. These changes may be fatal in patients with heart disease and high blood pressure [7]. Critical incidences such as laryngoscopy and intubation, PNP and extubation increases the HR and MAP in patients undergoing laparoscopic surgeries as evident here. However, dexmedetomidine attenuated this sympathoadrenal response and provided hemodynamic stability similar to previous studies [9, 11, 15].

Dexmedetomidine potentiates anesthetic effects of all intraoperative anesthetics. The first report of reduced requirement of isoflurane with dexmedetomidine in humans was published in 1991 which showed a 25 % reduction of maintenance and concentration of isoflurane in patients who received dexmedetomidine [12]. The end-tidal concentrations of isoflurane as compared to the traditional requirement during laparoscopic surgeries was observed to be 30 % less with dexmedetomidine [13].

Moreover, dexmedetomidine has been found to reduce the intra and post-operative requirements of opioids [11, 14]. This effect of dexmedetomidine is classically described as opioid sparing effect. The same was confirmed here in terms of the decreased total analgesic requirement in first 24 h postoperative period with perioperative dexmedetomidine.

Dexmedetomidine also has significant effect on the recovery time; this can be attributed to dexmedetomidine's ability to provide sedation without affecting the function of respiratory system and also to reduce requirement of propofol to some extent [10]. However, such an expeditious recovery has not been reported in previous studies.

CONCLUSION

Perioperative IV dexmedetomidine serves as a very useful anesthetic adjuvant to control hemodynamic stress responses to intubation, pneumoperitonium and extubation in patients undergoing laparoscopic surgeries. It helps in expeditious recovery and reduces the post-operative analgesic requirements without any significant adverse effects.

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