Research Article

Comparative evaluation of different doses of intravenous dexmedetomidine during laparoscopic cholecystectomy under general anesthesia

Pooja Singh, Avtar Singh Yadav, Sudhakar Dwivedi, Subhash K Agrawal

Department of Anesthesiology, Shyam Shah Medical College, Rewa, Madhya Pradesh, India

Correspondence to: Pooja Singh, E-mail: dr.pooja260887@gmail.com

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ABSTRACT

Background: Laparoscopy induces hemodynamic changes that lead to increased systemic vascular resistance, mean arterial pressure, heart rate, reduction in stroke volume, and cardiac output. Dexmedetomidine is a highly selective, potent, and specific alpha-2 agonist. It attenuates the hemodynamic changes associated with tracheal intubation, reduces plasma catecholamine concentration during anesthesia, and decreases perioperative requirements of inhaled anesthetics. **Objectives:** This study attempts to compare the effects of two different doses of dexmedetomidine in maintaining perioperative hemodynamic parameters during laparoscopic cholecystectomy. **Materials and Methods:** A total of 90 patients were randomly allocated to three groups, Group A (placebo), Group B (dexmedetomidine 0.5 μg/kg body weight), and Group C (dexmedetomidine 1 μg/kg body weight) of 30 patients each, undergoing elective laparoscopic cholecystectomy, under general anesthesia. The patients received preloaded study drug, 15 min before induction. The hemodynamic parameters were recorded before premedication, before induction, 1 min after intubation, 5 min after intubation before insufflation of CO_2, after insufflation of CO_2 at 1, 5, 10, 20, 30, 45, and 60 min, after release of CO_2, at 1 and 10 min after extubation. **Results:** The three groups were comparable for age, sex, weight as well as duration of surgery. Both doses maintained hemodynamic stability during laparoscopic cholecystectomy. However, lesser sedation was seen in the Group B as compared to Group C. **Conclusion:** Both doses of dexmedetomidine at doses were superior to placebo in terms of hamodynamic stability. Lesser sedation was seen with the 0.5 μg/kg body weight compared to dexmedetomidine 1 μg/kg body weight.

KEY WORDS: Dexmedetomidine; Pneumoperitoneum; Hemodynamic; Cholecystectomy

INTRODUCTION

The pneumoperitoneum and the patient positions required for laparoscopic surgeries induce pathophysiological changes that influence anesthetic management. Problems encountered during laparoscopic surgeries result from the physiological effects of pneumoperitoneum, patient positioning, and peritoneal absorption of the gas used for insufflation.[1]

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An understanding of the pathophysiological consequences of increased intra-abdominal pressure is important to prevent these changes and also to evaluate and prepare the patient pre-operatively in view of these disturbances.

Numerous agents have been used in an effort to minimize these hemodynamic effects during perioperative period, i.e., intraoperative propofol infusion, volatile agents, opioids, nitroglycerine infusion, and general anesthesia combined with epidural anesthesia and beta blockers but all have limited success.[2,3]

Alpha-2 agonists produce diverse responses, decrease central sympathetic outflow and reduce heart rate (HR), blood pressure and consequently total oxygen consumption during laryngoscopy, pneumoperitoneum, and perioperatively. These

effects may be beneficial in patients at risk of developing inadequate cardiac output or myocardial ischemia. At present, clonidine and dexmedetomidine are the two alpha-2 agonist commonly used in clinical practice.

Dexmedetomidine is a highly selective and potent alpha-2 agonist (alpha 2:alpha 1 = 1620:1) and is 7-10 times more specific for alpha-2 receptors compared to clonidine and has a shorter duration of action. Similar to clonidine, dexmedetomidine also attenuates the hemodynamic changes associated with tracheal intubation, reduces plasma catecholamine concentration during anesthesia and decreases perioperative requirements of inhaled anesthetic agents.[4]

The primary aim of this study is to evaluate and compare the effects of dexmedetomidine 0.5 μg/kg body weight and 1 μg/kg body weight on the hemodynamic response during pneumoperitoneum created during laparoscopic cholecystectomy.

MATERIALS AND METHODS

The present study was carried out at a tertiary care hospital in North India from August 2014 to July 2015. After approval from the Institutional Ethical Committee, the study was conducted on ninety patients of age 20-50 years and American Society of Anesthesiologists Grade I and II, posted for laparoscopic cholecystectomy under general anesthesia. Patients with known hypersensitivity to dexmedetomidine, ischemic heart disease, valvular heart disease, left ventricular failure, atrioventricular conduction block, uncontrolled hypertension, renal dysfunction, deranged liver function test, and endocrinological or neurological disorders were excluded from the study. A written informed consent was obtained from the patients.

Ninety patients were randomized to three groups of thirty patients each; Group A(100 ml 0.9% normal saline intravenous (IV) over 10, 15 min before induction), Group B (dexmedetomidine [Themis Medicare, India] 0.5 μg/kg body weight IV in 100 ml of 0.9% normal saline over 10, 15 min before induction), and Group C (dexmedetomidine [Themis Medicare, India] 1 μg/kg body weight IV in 100 ml of 0.9% normal saline over 10, 15 min before induction). The study drug was provided as coded identical syringes as per randomization protocol and was infused 15 min before induction. All patients were kept nil orally for at least 6 h before surgery. The premedication used was glycopyrrolate 0.2 mg, ranitidine 50 mg, ondansetron 4 mg, and pentazocine 30 mg (all administered intravenously. Pre-oxygenation was done with 100% oxygen for 3 min. All patients were induced with propofol 2 mg/kg body weight IV, and muscle relaxation was achieved with succinylcholine 1.5 mg/kg body weight. Patients were intubated using an appropriate size endotracheal tube and maintained on O_2:N_2O (30:70), sevoflurane and IV atracurium intermittently. HR, mean arterial pressure (MAP), systolic blood pressure (SBP), diastolic blood pressure (DBP), were recorded just before induction, 1 min after intubation, 5 min after intubation, before creation of pneumoperitoneum, 1, 5, 10, 20, 30, 45, and 60 min after creation of pneumoperitoneum, at the end of surgery and at 1, 10 min after extubation. More than 20% fall in MAP below baseline was considered as hypotension and was treated by decreasing sevoflurane and IV mephentermine 6 mg. HR <50 bpm was considered bradycardia and treated with atropine 0.6 mg intravenously. After surgery, reversal was achieved with glycopyrrolate 0.01 mg/kg and neostigmine 0.05 mg/kg. Patients were extubated and time to recovery was noted as defined as the time to vocalize after extubation.

Statistical Analysis

The sample size was calculated considering a projected difference of 20% in HR and 13% in MAP between the two doses to be significant, at 95% confidence limits, a Type 1 error of 0.05 and a power of 80%.[5] At the end of the study, the observations were tabulated and statistically analyzed using SPSS version 18. The data were reported as mean ± standard deviation. Chi-square test was used for categorical variables while continuous variables were compared using Student's *t*-test. For comparison, $P < 0.05$ was taken to be statistically significant.

RESULTS

A total of 124 patients were assessed for eligibility for this study, of which 25 refused to participate and nine did not meet the inclusion criteria. Therefore, 90 patients were randomized into three groups. All the 90 patients completed the study and were included in the final analysis (Figure 1). All the three groups under study were comparable to each other with respect to age, sex, weight, and duration of surgery (Table 1).

The baseline HR was comparable in all three groups. There was a significant increase in HR in Group A as compared to Groups B and C after laryngoscopy, intubation, as well as after creation of pneumoperitoneum. The HR was comparable among Group B and Group C at all these time points. Similar findings persisted at end of surgery and extubation with significantly higher HR in Group A compared to the

Table 1: Patient characteristics

Characteristics	Group A	Group B	Group C	*P* value
Age (years)	38.5±7.7	38.2±8.6	38.3±8.9	0.99
Weight (kg)	50.5±6.3	50.73±10.7	50.53±5.8	0.99
Sex				
Female	25	26	26	0.93
Male	5	4	4	
Duration of surgery (min)	78.1±12.4	83.5±27.7	79.5±19.9	0.59

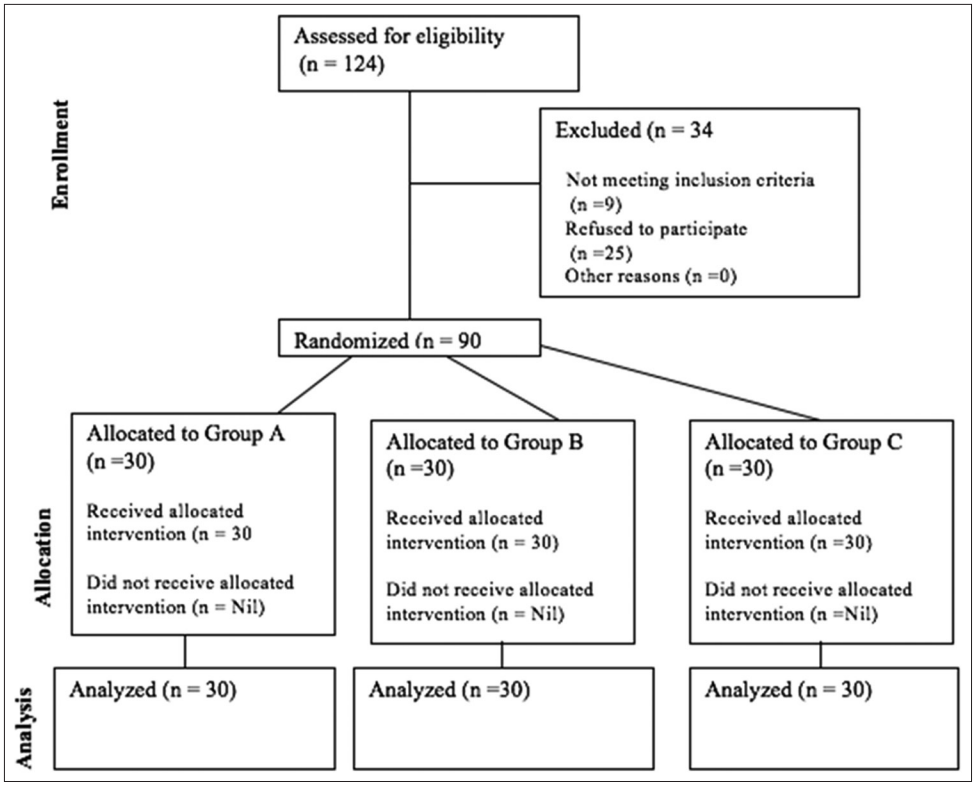

Figure 1: Consort flow chart

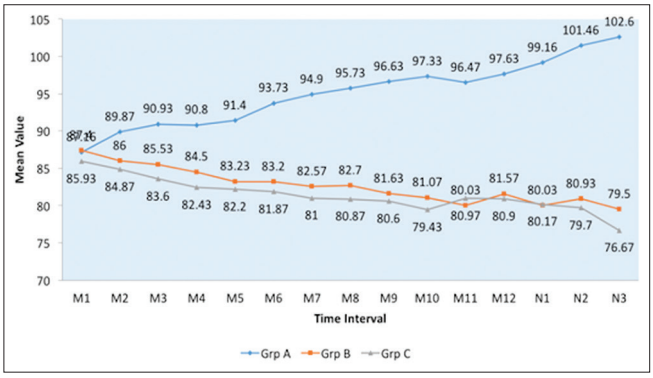

Figure 2: Heart rate in different groups

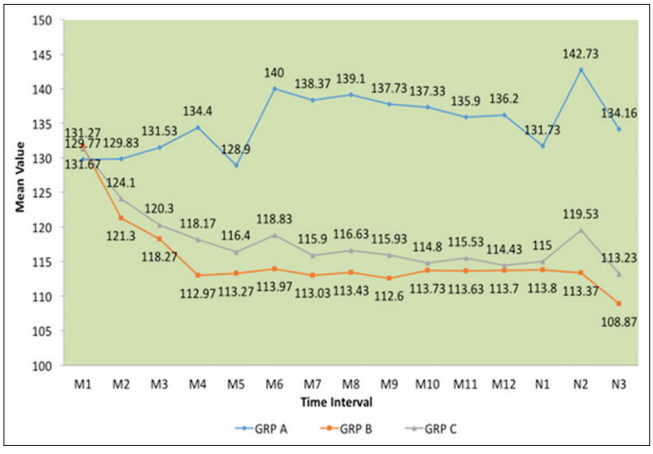

Figure 3: Systolic blood pressure in different groups

Groups B and C. again, the HR was comparable between Groups B and C (Figure 2).

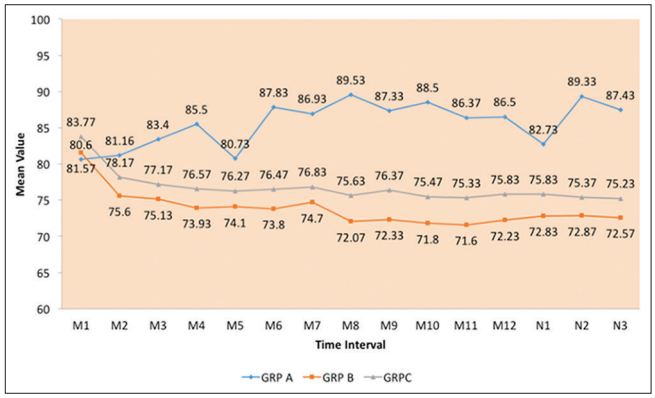

Figure 4: Diastolic blood pressure in different groups

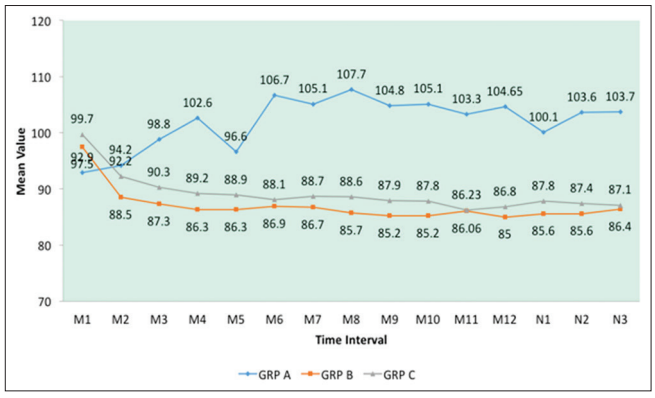

Figure 5: Mean arterial pressure in different groups

The baseline blood pressures (SBP, DBP, and MAP) were comparable in all the three groups. However, statistically significant increase in all parameters (SBP, DBP, and MAP)

was noted in Group A after infusion of the drugs, at 1 min after laryngoscopy and at intubation compared to Group B and Group C. The difference in BP was statistically insignificant between Group B and Group C. At 1 min, after the creation of pneumoperitoneum. SBP, DBP, and MAP were again higher in Group A compared to Groups B and C ($P < 0.05$) while these parameters were not significantly different between Groups B and C. The Group A maintained a significantly higher SBP, DBP, and MAP compared to Groups B and C throughout the pneumoperitoneum, at the end of surgery and 10 min after extubation. However, the difference in SBP, DBP and MAP at these time points in between Groups B and C was not significant (Figures 3-5).

The recovery time was significantly greater in Group C as compared to Groups A and B. The recovery time was not significantly greater in Group B as compared to Group A.

DISCUSSION

This study found that compared to placebo, the two doses of dexmedetomidine, given pre-operatively were associated with significantly lesser increases in HR after intubation, during creation of pneumoperitoneum as well as at extubation. Similarly, SBP and DBP were also lower in the dexmedetomidine groups as compared to placebo at all-time points after laryngoscopy. The two doses of dexmedetomidine had similar increases in HR and blood pressure. However, in the higher dose dexmedetomidine group the recovery time was significantly longer than other two groups.

Dexmedetomidine has been used in laparoscopic surgeries in several previous studies. A study compared dexmedetomidine to placebo in patients undergoing laparoscopic bariatric surgery and reported lower HR with dexmedetomidine.[6] Similar findings were reported in laparoscopic surgery in two other studies.[7,8] A study compared hemodynamic responses after dexmedetomidine and esmolol during laparoscopic cholecystectomy and found lower HR with dexmedetomidine.[9] Similar to our results, a previous study also reported that the intraoperative blood pressure values were significantly reduced in the dexmedetomidine 0.2, 0.4, and 0.8 mg groups compared with the control group.[6] The blood pressure in dexmedetomidine group was significantly lower after intubation, after reversal and post-operative recovery as compared to placebo group in another study.[7] The blood pressure values were significantly lower in the dexmedetomidine group compared to control group during pneumoperitoneum have been reported. There was no significant increase in blood pressure in dexmedetomidine group, compared to pre-operative levels during pneumoperitoneum, while it was a significant increase in control group during pneumoperitoneum period ($P < 0.05$).[9] Similarly, dexmedetomidine was superior to propofol in reducing HR and blood pressure during laparoscopic surgery.[8] A delay in recovery for first few hours post-extubation after using dexmedetomidine has been reported earlier.[10] However, we found that at doses of 0.5 μg/kg body weight, the delay in recovery was comparable to placebo. The sedative effect of dexmedetomidine is due to the hyperpolarization of noradrenergic neurons in the locus ceruleous of the brain stem.

While effects of dexmedetomidine on hemodynamic parameters have been described earlier, we have done a randomized control trial demonstrating these effects during laparoscopic surgeries (pneumoperitoneum). Further, we found that the sedative effects of dexmedetomidine are seen on the larger dose. Therefore the dose used in Group B can provide the hemodynamic benefits of dexmedetomidine without causing excess sedation. The limitations of the study include the small sample size, inclusion of patients with undergoing laparoscopic cholecystectomy only and similar age group of the patients. These points limit the generalizability of the findings to other patients. Further studies need to be conducted with an even larger sample size to corroborate the findings of this study, which may enlighten further the usefulness of different doses of dexmedetomidine in the anesthetic management of laparoscopic cholecystectomy.

CONCLUSION

From the present study, it can be concluded that dexmedetomidine in both doses (0.5 μg/kg body weight as well as 1 μg/kg body weight) is successful in attenuation of hemodynamic changes during intubation and pneumoperitoneum in laparoscopic cholecystectomy compared to placebo. However, dexmedetomidine in the dose of 0.5 μg/kg body weight does this with lesser sedation and hence this dose might be preferable for usage.

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