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Original Research Article

Evaluation of efficacy of dexmedetomidine in providing haemodynamic stability during perioperative period in patients undergoing laparoscopic Cholecystectomy

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Abstract

Background: In the present era, one of the most commonly practiced surgeries for gall bladder diseases is Laparoscopic cholecystectomy. Pneumoperitoneum essential for laparoscopic surgery and is produced by administration of carbon dioxide during laparoscopic surgical procedures results in multiple haemodynamic changes. These changes can be attenuated by various drugs. The present study was envisaged to evaluate the effectiveness of dexmedetomidine to offer perioperative hemodynamic stability in patients experiencing laparoscopic cholecystectomy.
Method: The present prospective, double blind, randomized controlled study, enrolled total 60ASA class I/II patients having 18-65 years age and randomly assigned in two groups of 30 patients in each. Dexmedetomidine IV infusion at 0.2μg/kg/hr has given to Dexmedetomidine group while control group received normal saline 0.9% IV infusion at 0.2μg/kg/hr. The infusions were started 5 minutes before anaesthesia induction and in both groups haemodynamic changes were assessed throughout the perioperative period and compared between two groups.
Results: The result of present study suggested that dexmedetomidine group significantly lower the elevated heart rate, systolic and diastolic blood pressure as well as mean arterial pressure than the control group. In both the groups, there was no difference in emergence from anaesthesia. In control group 4 (13.3%) patients had nausea/vomiting whereas not a single patient had any complications in dexmedetomidine group.
Conclusion: During laparoscopic cholecystectomy, dexmedetomidine infusion of 0.2μg/kg/hr provides perioperative haemodynamic stability in ASA I/II class patients and facilitate smooth emergence from anaesthesia with reduction in post-operative complications.
Keywords: Laparoscopy, Cholecystectomy, Pneumoperitoneum, Carbon dioxide, Haemodynamic stability, Dexmedetomidine, Anaesthesia, Perioperative complication.

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1. Introduction

Laparoscopic surgery is a modern surgical technique involving insufflations of gas (usually CO_2) into the peritoneal cavity under pressure to separate the organs from the abdominal cavity. [1] Laparoscopic cholecystectomy has revolutionised gall bladder surgeries and now became the gold standard for the treatment of cholelithiasis. For laparoscopic surgery, Pneumoperitoneumis required which produced by administration of carbon dioxide during laparoscopic surgical procedures.[2,3] Both pneumoperitoneum and CO_2 causes adverse cardiovascular effects.[4] All these changes contribute to increased systemic and pulmonary vascular resistance, elevated arterial pressure and reduced cardiac output.[5] Generally these hemodynamic changes are due to increased release of catecholamines and vasopressin or both.[6]

Laparoscopic cholecystectomy is performed in reverse Trendelenburg position which leads to reduced venous return and there by further reduced cardiac output. Hypercapnia is a condition due to CO_2 pneumoperitoneum which activates sympathetic nervous system leading to an increase in heart rate, blood pressure, arrhythmias and myocardial contractibility. Similarly it sensitizes the myocardium to catecholamines when volatile anaesthetic agents are used. [7]

Attenuation of adverse hemodynamic response to pneumoperitoneum is usually done by opioids [8], vasodilators [9], and α_2 adrenergic agonists.[10] Dexmedetomidine is a highly selective α_2 adrenergic agonist possesses analgesic, anxiolytic, hypnotic, sedative, sympatholytic properties without producing significant respiratory depression.[11] When these receptors gets activated in brain and spinal cord inhibits neuronal firing, thereby initiating bradycardia, hypotension, sedation and analgesia. Normally presynaptic activation of α_2 adrenergic receptors prevents the release of norepinephrine while postsynaptic activation of α_2 adrenergic receptors in CNS inhibits sympathetic activity and therefore can decrease heart rate and blood pressure. [12] Hence the current study was undertaken with an aim to estimate the effectiveness of dexmedetomidine to offer intraoperative and post-operative haemodynamic stability in patients undergoing laparoscopic cholecystectomy.

2. Materials and Methods

The prospective, randomized, double blind, clinical study was conducted after obtaining Institutional Ethical Committee approval and written informed consent from 60 patients of either sex of 18-65 years age, 40-80 kg weight, ASA grade I/II who scheduled for elective laparoscopic cholecystectomy under general anaesthesia. Patients with age <18 or > 65 years, ASA III and above, breastfeeding mothers, pregnancy, morbid obesity, severe hepatic/ renal/ endocrine and cardiac dysfunction, allergic to α_2 adrenergic agonist/sulfa drugs, bradycardia (heart rate < 60/min), hypertensive (on β Blocker & Calcium channel blockers) and those unwilling for consent were excluded from the study.

One day prior to surgery, a careful history and a thorough general and systemic examination were carried out and patient's preliminary data with all relevant investigation were recorded. All the included patients were randomly allocated in two equal groups using computer generated randomized chart. Dexmedetomidine group received Dexmedetomidine IV infusion at 0.2μg/kg/hr and control group received normal saline 0.9% IV infusion at 0.2μg/kg/hr.

On the day of surgery, in the preoperative holding region, patients were re-evaluated, nil-by-mouth status was confirmed and baseline vital parameters were measured. All patients were taken in the operation theatre on scheduled time and monitors were attached (ECG, SpO_2 and NIBP) to record vital parameters such as Heart rate (HR), Diastolic blood pressure (DBP), Systolic blood pressure (SBP), SpO_2 and Mean arterial pressure (MAP). An IV line was taken and IV fluid was started at 4-5 ml/kg/hr. All the patients were pre-medicated with intravenous injection of Atropine 0.01mg/kg in Ringer lactate pint, Midazolam 0.02 mg/kg, Ranitidine 1 mg/kg and Ondansetron 0.08 mg/kg. All patients received 6 litres of Oxygen for 5 minutes after premedication by Hudson's mask.

An infusion of the study drug was started 5 minutes prior to anaesthesia induction. Patients were pre-oxygenated with 100% oxygen and then induction was carried with Inj. Propofol 2-2.5mg/kg and Inj. fentanyl 2μg/kg IV in graded doses till unconsciousness. Inj. Succinylcholine 1.5mg/kg was administered after confirming adequacy of ventilation and after 60 seconds of IPPV, laryngoscopy was performed by an experienced anaesthesiologist (II year resident) and appropriate sized PVC cuffed endotracheal tube was inserted. A well lubricated nasogastric tube was inserted in all patients after tracheal intubation. Anaesthesia was maintained with 0.8% isoflurane and with 40:60 proportion of O_2:N_2O and muscle relaxation was maintained by Inj. Vecuronium bromide at 0.1mg/kg as loading dose and intermittent top-ups of 0.02 mg/kg when required. Patients were ventilated with an initial tidal volume of 6-8 ml/kg and 14 breaths/min of respiratory rate, which was later adjusted to have the $EtC0_2$ within 35-40 mmHg. The top ups of Fentanyl (0.5μg/kg) were given to maintain the mean arterial pressure within 20% of baseline. Intra-abdominal pressure was kept below 14mmHg. Intra-operatively all the patients received inj. diclofenac 75mg IV as analgesia. Whole reversal of neuromuscular blockade was attained with Inj. Glycopyrrolate 0.008 mg/kg & Inj. Neostigmine 0.06 mg/kg at the end of surgery and patients were extubated after establishment of spontaneous, adequate and regular respiration and appropriate response to verbal commands with good muscle power. The nasogastric tube was kept *in situ*.

Intra-operative: HR, SBP, DBP, MAP, SpO_2, End tidal CO_2, Intraabdominal pressure (after pneumoperitoneum) and adverse events (bradycardia, tachycardia, hypotension and hypertension) were recorded every 15 minutes till the end of surgery. The Patients with fluctuations in BP and HR > 20% of baseline value were recorded and treated accordingly. All parameters were monitored every 15 mins after pneumoperitoneum till the end of surgery by a blinded observer who unaware of the drug administered. The infusions of isoflurane and study drug were stopped at the end of pneumoperitoneum and recorded number of patients requiring total fentanyl top-ups. After the stoppage of infusion, the time interval of tracheal extubation and respond to verbal command was recorded.

Post operatively, the parameters like HR, DBP, SBP, MAP and SpO_2 were noted every 15 min thereafter for 2hrs of the patient received oxygen under Hudson's mask and IV fluids. Post-operative complications such as nausea-vomiting was noted as Yes or No and if present was treated with Inj. Ondansetron 0.1mg/kg IV. A provision was made for recording and treatment of following side effects.

Hypotension: Was defined as reduction in blood pressure by <20% MAP & was to be treated with fluid challenge in aliquots of 5-10ml/kg of Ringer's lactate & if there is no response to it, then Inj. Ephedrine 0.12mg/kg IV to be given & if still no response to it, then vasopressor like dopamine 5-10 µg/kg/min IV.

Hypertension: Was diagnosed if there is >20% rise in MAP of baseline on 2 or more readings in 2-3 mins & would be tackled by deepening the level of anaesthesia, maintaining $ETCO_2$, SPO_2 and by NTG infusion if required.

Bradycardia: Was defined as reduction in heart rate by >20% & was to be treated with Inj. Atropine 0.01mg/kg IV.

2.1 Statistical analysis

Demographic data was analyzed by Pearson's chi-square test. Changes in the HR, DBP and SBP were analyzed using unpaired't' test. 'P' value less than 0.05 was considered significant.

3. Observations and Results

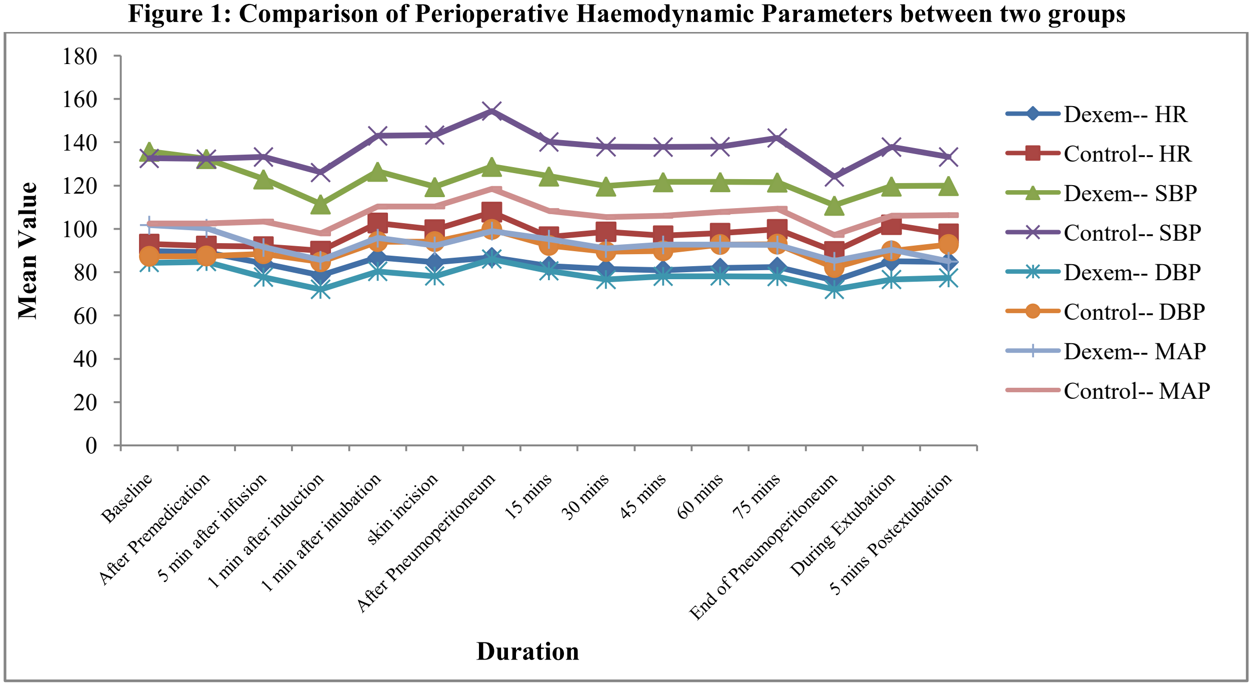
A total of 60 patients were enrolled for the study that underwent elective laparoscopic cholecystectomy under general anaesthesia and were randomly assigned into two groups of 30 patients each. The demographic profiles of the patients, duration of anaesthesia and duration of surgery were comparable between two groups and difference was statistically not significant, (Table 1).

Table 1: Demographic profile of the patients, duration of surgery and anaesthesia

Parameters	Dexem Group	Control Group	P value
Age (years)	40.70 ± 8.53	38.23±8.61	0.269
Weight (kg)	59.67±9.45	60.57±10.49	0.728
Sex (M/F)	12/18	17/13	0.196
ASA class (I/II)	23/7	21/9	0.559
Duration of Surgery (mins)	69.93±4.09	67.90±4.51	0.072
Duration of Anaesthesia(mins)	79.63±4.0	77.77±5.17	0.123

It has been found that there was no statistically significant difference in the baseline haemodynamic parameters (HR, DBP, SBP and MAP) and haemodynamic parameters after premedication between two groups, (P>0.05).Hence both the groups were comparable. In dexmedetomidine group, there was statistically significant decrease in HR, SBP, DBP and MAP after 5 minutes of infusion, after intubation, after pneumoperitoneum and throughout the observation period till extubation as compared to baseline values. While in control group, there was statistically significant increase in all haemodynamic parameters after infusion, after intubation, after pneumoperitoneum and throughout the observation period till extubation as compared to baseline values (Figure 1).

Figure 1: Comparison of Perioperative Haemodynamic Parameters between two groups



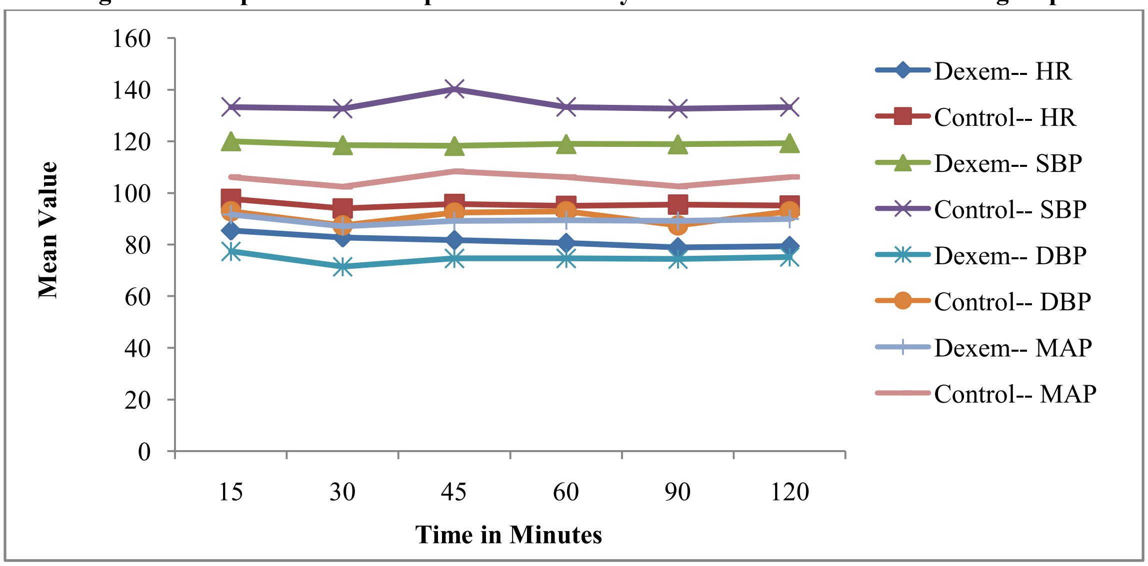
The mean duration of extubation time in Dexem group was 7.1 ± 0.58/mins and in control group it was 6.74±0.73 /mins. In Dexem group the mean duration of response to oral commands was 8.78±0.72/mins and in control group it was found 8.66 ± 0.73 /mins. There was no statistically significant difference found in the response to oral commands and extubation time (P>0.05).More number of fentanyl top ups were required for control group as compared to dexmedetomidine group, (P<0.05), (Table 2).

Table2: Required Number of Fentanyl Top Ups [0.5 µg/Kg]

No of Top Ups	Dexem group	Control group
	Number of cases (%)	Number of cases (%)
0	24 (80)	05 (16.67)
1	06 (20)	07 (23.33)
2	00 (00)	18 (60.00)

Postoperative haemodynamic parameters (HR, DBP, SBP and MAP) were lower in dexem group than control group which was statistically significant when compared in both the groups (P<0.05), (Figure 2). In both the groups, there was no fall in oxygen saturation and the data was statistically not significant (P>0.05). In control group 4 (13.3%) patients had nausea / vomiting while in dexmedetomidine group not a single patient had any complications.

Figure 2: Comparison of Postoperative Haemodynamic Parameters between two groups



4. Discussion

Dexmedetomidine is a greatly selective α_2 adrenergic agonist and possess various pharmacological activities like analgesia, sedation, anxiolysis and sympatholysis. Looking at these pharmacological properties, it has been evaluated in the past to assess its effect on haemodynamic responses in patients undergoing laparoscopic surgeries. [13] The molecule has been used in infusion form with or without bolus dose. In numerous studies, it has been found that dexmedetomidine infusion rates ranging from 0.1 to 10 µg/kg/hr have been used. [14,15] The studies with higher infusion rates had more rates of adverse effects such as bradycardia and hypotension. Tufanogullari and coworkers [16] reported that doses of 0.2, 0.4, 0.6 µg/kg/hr of dexmedetomidine in 80 morbidly obese patients for laparoscopic bariatric surgery. The author suggested that 0.2 µg/kg/hr produced lesser occurrence of cardiovascular complications (bradycardia and hypotension). Therefore infusion rate of 0.2µg/kg/hr of dexmedetomidine is used in the present study.

The increase in heart rate, diastolic and systolic blood pressure and mean arterial pressure was significantly decreased in the dexmedetomidine group as compared to control group. Thus, dexmedetomidine infusion in the perioperative period in laparoscopic cholecystectomy provides better haemodynamic stability, and this finding is comparable with the previous studies.[17-20] Joris *et al*[21] observed that Peritoneal insufflations caused a significant increase (±35%) of mean arterial pressure, a significant reduction (±20%) of Cardiac index, and a significant increase of systemic (±65%) and pulmonary

(±90%)vascular resistances. Similarly in present study, there was increase in HR, SBP, DBP and MAP after pneumoperitoneum in either groups, but rise was lesser in dexmedetomidine group when compared to placebo group.

A significant drop in cardiac output at 16 mmHg of intra-abdominal pressure was reported by Ishizaki *et al*[22]. But at 12 mm Hg of intra-abdominal pressure, haemodynamic alterations were not observed. Based on all these observations the current recommendation is to monitor intraabdominal pressure and to keep it as low as possible. In current study, following pneumoperitoneum with carbon dioxide, minute ventilation was adjusted so as to maintain normocapnia, Intraabdominal pressure (IAP) was monitored throughout the surgery and maintained below 14 mm Hg. Inspite of maintaining end tidal carbon dioxide (CO_2) level between 35-40mmHg and intra-abdominal pressure below 14 mmHg, significant rise was observed in heart rate, diastolic, systolic and mean arterial blood pressure in control group when compared to dexmedetomidine group.

Emergence from anaesthetic effects and extubation are equally essential as is laryngoscopy, surgical period and intubation. Dexmedetomidine allows a smooth transition from the time of administration of reversal to the post-extubation phase by suppressing the CNS sympathetic activity which leads to high quality of extubation with minimum haemodynamic changes, as we observed in majority of our patients in same group. We also observed the haemodynamics during emergence from anaesthesia i.e. time for extubation and time to respond to oral commands was similar in either group. These findings are correlated with the earlier studies. [17, 23]

In present study, it was observed that in intraoperative period, the patients who received dexmedetomidine infusion had HR, DBP, SBP and MAP on the lesser side as compared to that of control group which received normal saline infusion in immediate postoperative period. The difference observed was statistically significant ($p< 0.05$). There were more requirements of fentanyl top-ups in control group because of postoperative nausea and vomiting incidences (13.3%). Whereas in Dexem group, there was no single patient with postoperative nausea and vomiting. This results are in agreement with the findings of other studies.[16,24,25]

5. Conclusion

Dexmedetomidine IV infusion in the dose range of 0.2µg/kg/hr reduces the rise in heart rate, diastolic, systolic and mean arterial pressure associated with the creation and maintenance of pneumoperitoneum during the laparoscopic surgical procedures. Thus, it offers perioperative haemodynamic stability in ASA I/II class patients during laparoscopic cholecystectomy because of their sedative, hypnotic, sympatholytic and anxiolytic properties.

Hence, Dexmedetomidine infusion of 0.2µg/kg/hr as an anaesthetic adjuvant is recommended in laparoscopic cholecystectomy to provide perioperative haemodynamic stability and to facilitate smooth emergence from anaesthesia. It also affords added advantage of reduction in post-operative complications such as nausea-vomiting. However further study is required to evaluate its effect on haemodynamic parameters in high risk group patients with compromised cardio-respiratory function undergoing laparoscopic surgical procedures.

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