Research Article

Effect of dexmedetomidine on hemodynamic stability during laparoscopic surgeries: A randomized double-blind controlled trial

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Abstract

Background: Certain drugs have been tried to increase hemodynamic stability during different phases of laparoscopic cholycystectomy. The pathophysiologic hemodynamic changes can be prevented by optimizing preload before pneumoperitoneum and by vasodilating agents.

Objective: A randomized double-blind controlled trial was planned with an objective to evaluate the effect of intraoperative dexmedetomidine with or without propofol in hemodynamic stability during laparoscopic surgery.

Material and Methods: A randomized double-blind controlled trial was conducted between November 2009 and August 2011. Patients were divided into two groups of 50 each according to table of computer generated random numbers. Group I patients received dexmedetomidine with propofol. Group II patients received propofol with normal saline (placebo) in the same volume and rate.

Results: The number of the patients with Ramsay sedation score of 2 was more in group II compared to group I. The sedation score subsequently was comparable in both the groups till next one hour. The pain as measured with numerical rating scale (median value) was lower in group I compared to group II at 1 h postoperatively and therefore the requirement of rescue fentanyl was less in group I compared to group II ($p < 0.05$).

Conclusion: It was concluded that the addition of dexmedetomidine with propofol provides better hemodynamic stability in normal patients undergoing laparoscopic surgeries and decreases the analgesic requirements preoperatively. Patients receiving dexmedetomidine in addition to the propofol are more sedated in early phase of postoperative period though became alert later.

KEY WORDS: Dexmedetomidine, hemodynamic stability, laparoscopic surgery

Introduction

Laparoscopic cholecystectomy results in multiple postoperative benefits including less trauma, less pain, less pulmonary dysfunction, quicker recovery, and shorter hospital stay.[1]

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However, intraoperative pneumoperitoneum decreases thoracopulmonary compliance,[2–4] which results into ventilatory and respiratory changes ($Paco_2$ increases due to CO_2 absorption from the peritoneal cavity).[5] The effects of pneuoperitoneum on hemodynamics like vagal stimulation, phasic change in cardiac output, decreased organ perfusion,[6] are further accentuated in high-risk cardiac patients.[7]

Certain drugs have been tried to increase hemodynamic stability during different phases of laparoscopic cholycystectomy. The pathophysiologic hemodynamic changes can be prevented by optimizing preload before pneumoperitoneum and by vasodilating agents.[8] Clonidine, a centrally acting partial α_2-adrenergic agonist (220:1 α_2 to α_1), has been used for hemodynamic stability during various surgeries.

Dexmedetomidine is more selective to α_2-receptor with a 1600 greater selectivity for the α_2-receptor compared with the

α_1 receptor. Dexmedetomidine is considered as a full agonist of the α_2-adrenoceptor thus adverse effect caused by α_1-agonist action can be avoided. It provides sympatholysis sedation, anxiolysis, hypnosis, and analgesia. It was hypothesized that perioperative use of dexmedetomidine will produce better hemodynamic stability, perioperative analgesia, and postoperative recovery.

Therefore, a randomized double-blind controlled trial was planned with an objective to evaluate the effect of intraoperative dexmedetomidine with or without propofol in hemodynamic stability during laparoscopic in surgery.

Material and Methods

The study was conducted after the approval from institutional ethical board between November 2009 and August 2011. After written informed consent, 100 ASA grade I and II patients of either sex, aged between 18 and 60 years, undergoing elective laparoscopic cholecystectomy under general anesthesia with endotracheal intubation, were included in the study.

The patients who were operated on emergency basis, pregnant female, anticipated difficult airway, e.g., Mallampati III, IV, allergic to the study drug, patient with clinically significant cardiovascular, respiratory, renal, hepatic, neuropsychiatry, or endocrinal disease, anticoagulant used within preceding 4 weeks, laparoscopic procedure converted to laparotomy and patients with incomprehensive ability like deaf and mute, etc. were excluded from study. Patients were divided into two groups of 50 each through computer generated random number table.

Group I (n = 50): Patients received dexmedetomidine with propofol.

Group II (n = 50): Patients received propofol with normal saline (placebo) in the same volume and rate.

Briefly, 100 solutions of normal saline in 50 ml syringes were prepared by an anesthesiologist not participating in the study by adding the dexmedetomidine in 50 syringes. These 100 syringes with two types of solutions labeled as solution A and solution B were randomly used in laparoscopic surgeries and obtained data were recorded after each surgery as result of group A or result of group B. After 100 surgeries, groups were renamed as group I and group II according to drug.

All patients premedicated with 10 mg of metoclopramide and 50 mg of ranitidine intravenously after insertion of intravenous line 1 h before time of surgery.

Midazolam 3 and 0.2 mg glycopyrrolate were given intravenously 15 min before induction of anesthesia. The monitoring included electrocardiogram, noninvasive blood pressure, pulse oxymetry, and temperature. All patients were preoxygenated for 5 min then anesthesia was induced by fentanyl (2 μg/kg lean body weight (LBW)), lidocaine (1.5 mg/kg LBW), and propofol (1–2 mg/kg LBW). The assigned drugs were given intravenously over 10 min as a loading dose followed by maintenance infusion. Succinylcholine in the dose of 1.5 mg/kg LBW was administered to facilitate endotracheal intubation, followed by a loading dose of atracurium 0.25 mg/kg LBW followed by top-up doses of 0.1 mg/kg LBW every 20–30 min based on neuromuscular stimulation which was applied over the ulnar nerve in order to maintain the train of four (TOF) count of 1 or 2.

Radial artery cannulation was performed with 22G cannula in the non-dominant hand for continuous recording of arterial blood pressure. All patients were maintained on propofol infusion at the rate of 10 mg/kg LBW/h for the initial 10 min, then reduced to 6 mg/kg LBW/h. Propofol infusion was adjusted during surgery between 6 and 10mg/kg LBW/h, in order to keep the systolic blood pressure (SBP) and heart rate within 20% of baseline value.

All patients in both groups received volume infusion of 10 ml/kg/h of Ringer's lactate solution during anesthesia. Patients were mechanically ventilated with a mixture of 50% air in oxygen, tidal volume of 10 ml/kg LBW, and respiratory rate was adjusted to maintain normocarbia (end tidal CO_2 35–40 mmHg).

Measurements

All parameters were noted down at an interval of 15 min. All patients were examined in the post-operative period for recovery profile, degree of pain relief, and need for extra dose of rescue analgesia (Fentanyl). Sedation was evaluated by Ramsay sedation scoring. Pain was evaluated on Numerical Rating Scale (0–10) with 0 meaning no pain and 10 relating to the worst pain ever perceived. Rescue fentanyl was given when the perceived pain was more than 3 on NRS. Nausea and vomiting was treated with ondansetron (4 mg IV). Ramsay sedation scoring (1–6) was done.

Statistical Analysis

Statistical Package for Social Sciences (SPSS) version 15.0 (Chicago, Inc., USA) was used for statistical analysis and $p < 0.05$ was considered as significant. Demographic data were analyzed for matching between groups. Hemodynamic data was compared with Student's *t*-test. Hemodynamic data, i.e., HR, SBP, DBP, MBP were presented as mean and standard deviation. Within the groups, comparison of hemodynamic data was done using repeated measure test. Difference among the groups was analyzed using paired *t*-test.

Results

There was no significant difference in demographic variables between the groups ($p > 0.05$). Most of patients were between 31 and 40 years of age group both groups. The mean ages of the patients belonging to group I and group II were 40.70 ± 9.52 and 40.04 ± 6.99 years, respectively. Overall male to female sex ratio was 45:55. The male and female ratio in group I and group II were 23:27 and 22:28, respectively (Table 1).

Table 1: Demographic characteristics of patients

Variable (Mean ± SD)	Group 1 (*n* = 50)	Group 2 (*n* = 50)	*P*-value
Age (year)	40.70 ± 9.52	40.04 ± 6.99	0.07
Weight (kg)	67.60 ± 6.39	68.42 ± 6.185	0.933
Height (cm)	159.58 ± 4.74	160.50 ± 3.89	0.096
Sex (M/F)	23/27	22/28	0.754

In group I, there was no change in the HR form baseline at 15 min. However, HR decreased from 15 to 30 min, 30 to 45 min, and 45 to 60 min ($p < 0.002$). In group II, initially HR decreased from baseline to 15 min ($p = 0.013$). Thereafter, the HR was remained stable and did not changed significantly till 60 min ($p > 0.05$). In group I, there was significant decrease in systolic blood pressure (SBP) from baseline value at 15 min however it remained stable at 30 min. In group II, there was significant increase in SBP from baseline value at 15 min however it remains stable at 30 min. In group I, mean blood pressure (MBP) at 15 min was lower than the baseline value ($p = 0.01$). In group II, MBP were higher than the baseline value at 15 min and between 30 and 45 min of time interval ($p < 0.001$) (Table 2).

Intergroup comparison of HR showed that baseline HR was comparable in both groups ($p > 0.05$). There was significant change in the heart rate at 15, 30, 45, and 60 min interval ($p < 0.002$). The HR was lower in group 1 than group II at 15, 30, 45, and 60 min ($p < 0.05$). In intergroup comparison, baseline SBP was comparable in both groups ($p > 0.05$). After that, at different time interval, SBP variability was not significant between both groups ($p > 0.076$). In group I, diastolic blood pressure (DBP) variability was not significant from baseline to 15 min time interval ($p = 0.078$). Subsequently, DBP was decreased between 15 to 30, 30 to 45 min, and 45 to 60 min ($p < 0.008$). At 60 min, DBP was comparable to baseline value ($p = 0.828$). In group II, DBP was significantly higher at 15 min comparing baseline ($p = 0.000$). In intergroup comparison, baseline mean blood pressure was comparable in both groups ($p > 0.05$). Subsequently, there was no significant variability in MBP at any time interval (Table 3).

Sedation as measured by Ramsay sedation score was more in the group I compared to group II immediately after extubation ($p < 0.05$). The number of the patients with Ramsay sedation score of 2 was more in group II compared to group I. The sedation score subsequently was comparable in both the groups till next one hour (Table 4).

Table 2: Intragroup hemodynamics change

Time interval	Group 1 (*n* = 50)	Group 2 (*n* = 50)
Systolic blood pressure changes		
0–15 min	131.20 ± 8.31–124.38 ± 8.12	122.92 ± 9.46–138.44 ± 8.83
15–30 min	124.38 ± 8.12–116.38 ± 7.91	138.44 ± 8.83–140.32 ± 8.31
30–45 min	116.38 ± 7.91–113.42 ± 7.39	140.32 ± 8.31–129.32 ± 8.50
45–60 min	113.42 ± 7.39–109.62 ± 7.76	129.32 ± 8.50–123.00 ± 11.63
0–60 min	131.20 ± 8.31–109.62 ± 7.76	122.92 ± 9.46–123.00 ± 8.83
Diastolic blood pressure changes		
0–15 min	79.18 ± 5.15–76.24 ± 6.18	77.40 ± 5.56–87.08 ± 7.39
15–30 min	76.24 ± 6.18–72.02 ± 4.64	87.08 ± 7.39–84.16 ±16.30
30–45 min	72.02 ± 4.64–70.24 ± 3.74	84.16 ± 16.30–81.90 ± 5.18
45–60 min	70.24 ± 3.74–66.54 ± 5.14	81.90 ± 5.18–77.38 ± 7.03
0–60 min	79.18 ± 5.15–66.54 ± 5.14	77.40 ± 5.56–77.38 ± 7.03
Mean blood pressure changes		
0–15 min	96.74 ± 5.90–92.42 ± 6.98	92.78 ± 6.74–104.28 ± 7.54
15–30 min	92.42 ± 6.98–86.86 ± 5.43	104.28 ± 7.54–105.52 ± 6.45
30–45 min	86.86 ±5.43–84.74 ± 4.84	105.52 ± 6.45–98.78 ± 5.24
45–60 min	84.74 ± 4.84–81.20 ± 5.81	98.78 ± 5.24–92.78 ± 8.19
0–60 min	96.74 ± 5.90–81.20 ± 5.81	92.78 ± 6.74–92.78 ± 7.54
Heart rate changes		
0–15 min	75.32 ± 7.30–70.38 ± 7.02	74.30 ± 8.51–70.96 ± 28.36
15–30 min	70.38 ± 7.02–66.24 ± 4.96	70.96 ± 28.36–76.24 ± 21.69
30–45 min	66.24 ± 4.96–63.52 ± 5.64	76.24 ± 21.69–78.96 ± 11.73
45–60 min	63.52 ± 5.64–61.36 ± 6.34	78.96 ± 11.73–73.16 ± 8.12
0–60 min	75.32 ± 7.30–61.36 ±6.34	74.30 ± 8.51–73.16 ± 8.12

Table 3: Comparison of hemodynamics between two groups at different time intervals intraoperatively

Time interval	Group 1 (*n* = 50), Mean ± SD	Group 2 (*n* = 50), Mean ± SD	*p*-Value
Systolic blood pressure			
Baseline	131.20 ± 8.31	122.92 ± 9.47	0.058
15 min	124.38 ± 8.11	138.44 ± 8.83	0.125
30 min	116.38 ± 7.90	140.32 ± 8.31	0.930
45 min	113.42 ± 7.38	129.32 ± 8.50	0.927
60 min	109.62 ± 7.76	123.00 ± 11.63	0.076
Diastolic blood pressure			
Baseline	79.18 ± 5.15	77.40 ± 5.56	0.191
15 min	76.24 ± 6.17	87.08 ± 7.39	0.011
30 min	72.02 ± 4.64	84.16 ± 16.30	0.006
45 min	70.24 ± 3.73	81.90 ± 5.18	0.088
60 min	66.54 ± 5.14	77.38 ± 7.03	0.222
Mean blood pressure			
Baseline	96.74 ± 5.90	92.78 ± 6.74	0.112
15 min	92.42 ± 6.98	104.28 ± 7.54	0.071
30 min	86.86 ± 5.43	105.52 ± 6.45	0.050
45 min	84.74 ± 4.84	98.78 ± 5.24	0.272
60 min	81.20 ± 5.81	92.78 ± 8.19	0.178
Heart rate change (in beat/minute)			
Baseline	75.32 ± 7.30	74.30 ± 8.51	0.892
15 min	70.38 ± 7.02	70.96 ± 28.58	0.000
30 min	66.24 ± 4.96	76.24 ± 21.69	0.000
45 min	63.52 ± 5.64	78.96 ± 11.73	0.000
60 min	61.36 ± 6.34	73.16 ± 8.12	0.002

Table 4: Comparison of Ramsay sedation scoring between two groups at different time interval in postoperative period

Ramsay sedation score	0 min		15 min		30 min	
	Group 1 (*n* = 50)	Group 2 (50)	Group 1 (*n* = 50)	Group 2 (50)	Group 1 (*n* = 50)	Group 2 (50)
1						
2		4	41	42	50	50
3	40	38	9	8		
4	10	8				
5						
6						

The pain as measured with numerical rating scale (median value) was lower in group I compared to group II at 1 h post-operatively and therefore the requirement of rescue fentanyl was less in group I compared to group II ($p < 0.05$) (Table 5).

Table 5: Comparison of numerical rating scale between two groups in postoperative period at 1 h: median (interquartile range)

Group 1 (*n* = 50)	Group 2 (*n* = 50)
2(1)	4(1)

Discussion

The current study was aimed to know perioperative applications of the novel α_2-adrenoceptor agonist, dexmedetomidine during laparoscopic surgery. In the present study, addition of dexmedetomidine with propofol and fentanyl during maintenance phase of anesthesia resulted in decrease hemodynamic variability that was occurring during creation of pneumoperitonium.

The results of the present study showed that the dexmedetomidine provided a good condition for maintenance of anesthesia during laparoscopic surgery. Dexmedetomidine

decreased the analgesic requirement periopearively. The patients received dexmedetomidine though sedated initially however they were alert for rest of the postoperative period.

The present study examined only laparoscopic cholecystectomy. This population was selected because the surgery is standardized and common. Characteristics of this surgical population include a short length of surgery (45–90 min), hemodynamic variability is more than many other surgeries. Despite our negative results regarding blood pressure changes and postoperative recovery profile, it remains possible that dexmedetomidine would be more advantageous in more extensive and longer duration laparoscopic surgeries. In addition, the dexmedetomidine dose ranged we studied was 0.2 μg/kg LBW/h. This was purposeful, as doses of dexmedetomidine > 0.7 μg/kg LBW/h are causative of bradycardia, sedation, and hypotension. In a study, when used during bariatric surgery, a Dex infusion rate of 0.2 *μ*g/kg/h was recommended to minimize the risk of adverse cardiovascular side effects.[9] The findings of this study were comparable to many other studies.[10–12]

Our measurements had only relied on hemodynamic parameters, however, elaboration of monitoring in the form of cardiac output, systemic vascular resistance, pulmonary vascular resistance, and cardiac index would be further high lightened the effect of dexmedetomidine on cardiovascular physiology, when used with propofol during laparoscopic surgery.

Conclusion

It was concluded from the present study that the addition of dexmedetomidine with propofol provides better hemodynamic stability in normal patients undergoing laparoscopic surgeries and decreases the analgesic requirements perioperatively. Patients receiving dexmedetomidine in addition to the propofol were more sedated in early phase of postoperative period though became alert later.

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