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RESEARCH ARTICLE

Dexmedetomidine Infusion an Effective Intra-Operative Medication for Patients Undergoing Laparoscopic Cholecystectomy

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Abstract

Background: Laparoscopic surgeries involves creation of pneumo-peritoneum with insufflation of gas usually CO_2 thereby increasing intra-abdominal pressure. The Intra-abdominal pressure above 10 mmHg causes adverse hemodynamic changes. Various agents have been used to attenuate these adverse effects. Dexmedetomidine alpha-2 agonist has sedative, sympatholytic, analgesic and anxiolytic properties and used in laparoscopic cholecystectomies for attenuation of adverse hemodynamic changes and to maintain hemodynamic stability.

Material and methods: 60 patients of ASA 1-2 undergoing elective laparoscopic cholecystectomy were randomly allotted to two groups. Each group consists of 30 patients. Group 1 patients received dexmedetomidine infusion @0.2 microgram/kg/hour and group 2 patients received normal saline @0.2 microgram/kg/hour after intubation. The medication was stopped at the end of peritoneal deflation. Intra-operative hemodynamic stability was assessed by monitoring heart rate and Mean arterial pressure.

Results: In Dexmedetomidine group, the haemodynamic response was significantly attenuated.

Conclusion: Dexmedetomidine infusion in the dose of 0.2 µg/kg/hour effectively attenuates haemodynamic stress response to pneumo-peritoneum during laparoscopic surgery.

Keywords

Dexmedetomidine, Laparoscopic Cholecystectomy

Introduction

Laparoscopic surgery is a modern surgical technique involving insufflation of gas (usually CO_2) into the peritoneal cavity, under pressure, to separate the organs within the abdominal cavity [1]. Because of its minimal scar, less postoperative pain, decreased length of hospital stay and obviously less mortality, it has become the gold standard for treatment of gall bladder diseases [2]. Laparoscopic cholecystectomy is one of the most commonly undertaken procedures in general surgery, with overall complication rate being less than 1.5% and the overall mortality rate of less than 0.1% [3]. However pneumoperitoneum (PNP) required for this procedure affects several systems leading to alterations in cardiovascular, respiratory, stress response and acid-base physiology. The nature of changes in cardiovascular system associated with pneumoperitoneum includes an increase in mean arterial pressure, decrease in cardiac output and increase in systemic vascular resistance which can lead to altered tissue perfusion. These changes though better tolerated in ASA I and II patients can be detrimental in elderly and ASA III patients particularly with compromised cardiovascular system physiology. Various surgical methods like change in nature of insufflating gas, [4] use of low intra-abdominal pressure [5,6], use of abdominal wall lift methods [7] have been tried to decrease the hemodynamic alterations seen with pneumoperitoneum, but all with practical limitations. Various anesthetic interventions like use of epidural, segmental spinal [8], combined epidural and general anaesthesia [9], use of various pharmacologic interventions like nitroglycerine [10], esmolol [11], magnesium sulphate [12] have been used with varying

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success and practical limitations. Aho, et al. [13] used alpha 2 adrenergic receptor agonist for prevention of hemodynamic responses associated with laparoscopic surgery. They found that dexmedetomidine effectively reduces the maximum heart rate response after intubation and pneumoperitoneum. As laparoscopic cholecystectomy is a routinely performed surgery, it is desirable to have a stable intraoperative haemodynamic status. Hence in this study, it has been attempted to study the beneficial effect of α-2 adrenergic agonist dexmedetomidine in maintaining the perioperative parameters during laparoscopic cholecystectomy.

Materials and Methods

The present study was carried out in 60 patients of ASA Grade I and II between the age group of 20-60yrs of both genders scheduled to undergo elective laparoscopic cholecystectomy. They were randomly divided into two groups of 30 patients each. Group I (n = 30): Dexmedetomidine group-200 mcg (2 ml) in 38 ml of 0.9% NS @ 0.2 µg/kg/hr infusion was given. Group II (n = 50): Control group-0.9% saline was given at same rate.

Exclusion criteria: Patients with chronic hypertension, ASA physical status III, AV block, morbid obesity (> 50% above ideal body weight), acute cholecystitis, chronic use of opioid analgesics or β-blockers, asthma or reactive airway disease and those with severe renal, hepatic, endocrine and cardiac dysfunction was excluded from the study. A thorough pre-anesthetic evaluation was done a day prior to surgery and all the necessary investigations were carried out including specific investigations if required. A written informed consent was taken from every patient. All the patients were kept fasting overnight and were given tablet ranitidine 150 mg a night before surgery. On arrival to operation theatre, intravenous (IV) line was secured and crystalloid intravenous infusion of 6-8 ml/kg/hr was started. Routine monitoring like ECG, NIBP and pulse oximetry was started and baseline parameters were recorded. All patients were premedicated with IV Injection midazolam 1-2 mg and Glycopyrrolate 0.02 mg/kg. After preoxygenation for 3 minutes with 100% oxygen, general anaesthesia was induced with inj. propofol 2 mg/kg, O_2 and N_2O. Analgesia was given using Fentanyl 2 microgram/kg. After preoxygenation, endotracheal intubation was facilitated by muscle relaxant Atracurium 0.5 mg/kg. Group I patients were given dexmedetomidine by IV infusion @0.2 µg/kg/hr intraoperatively after tracheal intubation. This drug was prepared in identical 50 ml syringe by adding Dexmedetomidine 200 µg (2 ml) in 0.9% saline (38 ml) making a total volume of 40 ml (resulting concentration will be 5 µg/ml). Group II patients were given 0.9% saline at the same rate. Anesthesia was maintained with O_2:N_2O (50:50), isoflurane, IPPV. Supplemental neuromuscular blockade was achieved with Atracurium 0.1 mg/kg. End-tidal carbon dioxide ($EtCO_2$) was maintained between 35-40 mmHg. Pneumoperitoneum was created and Intra-abdominal pressure was maintained between 12-14 mmHg throughout the laparoscopic procedure. Intraoperatively patients were monitored for NIBP and heart rate at every 5 min interval. Hypotension defined as NIBP < 20% of the baseline or systolic BP < 90 mmHg was treated by increasing the intravenous crystalloid infusion rate and additionally with vasoactive drugs. Bradycardia, defined as heart rate < 20% of the baseline or less than 50 beats/min, was treated with 0.02 mg/kg atropine. After the release of pneumoperitoneum, infusion of the drug was stopped. Injection ondansetron 4 mg was given before reversal of neuromuscular blockade by neostigmine 0.05 mg/kg and Glycopyrrolate 0.02 mg/kg and patient was extubated. After extubation, time to response to verbal commands was recorded. Post-operatively 100% oxygen was given by face mask for 15 minutes. The results obtained in the study are presented in tabulated manner. Statistical analysis was done using student's t-test and Chi square test was performed for nonparametric values. P value < 0.05 was considered statistically significant.

Observations and Results

Two groups were comparable with respect to age, gender, weight and duration of surgery (Table 1). There was no significant difference in preoperative values between the two groups (Table 2). After 5 minutes of dexmedetomidine infusion, mean arterial pressure (MAP) and heart rate decreased significantly in group

Table 1: Patient characteristics and duration of surgery.

	Group 1	Group 2	P value	Statistical significance
Age (years)	35.4 ± 11.1	36.6 ± 10.5	> 0.05	NON-Significant
Gender (M/F)	22/24	23/27	> 0.05	NON-Significant
Weight	57.8 ± 8	58.8 ± 8.7	> 0.05	NON-Significant
Duration of surgery	52.25 ± 3.81	50.20 ± 10.87	> 0.05	NON-Significant

Table 2: Pre-operative vitals in Group I and Group II.

	Group 1		Group 2			
Parameters	Mean	SD	Mean	SD	P value	Statistical Significance
HR/min	83.86	9.15	84.60	7.12	0.58	NS
SBP	122.82	10.74	120.74	8.67	0.27	NS
DBP	78.54	5.92	76.44	4.98	0.12	NS
MBP	93.73	6.11	91.63	5.22	0.09	NS

Table 3: Changes in HR at different time interval in Group I and Group II.

Group	Group 1		Group 2			
Time interval	N	Mean ± SD	N	Mean ± SD	p-value	Statistical Significance
Preoperative	50	83 ± 9.3	50	84.5 ± 6.6	0.67	NS
Postintubation	50	110 ± 8.76	50	107.8 ± 8.45	0.08	NS
Post pneumoperitoneum M 5	50	83.2 ± 12.0	50	102 ± 10.5	0.00	S
M10	50	83.2 ± 12.1	50	101.5 ± 11.8	0.00	S
M15	50	84.8 ± 11.2	50	103.3 ± 10.6	0.00	S
M20	50	83.2 ± 10.5	50	98.8 ± 11.7	0.00	S
M25	50	80.6 ± 11.5	50	94.7 ± 10.4	0.00	S
M35	50	81.9 ± 11.0	50	96.5 ± 11.7	0.00	S
M40	50	82.2 ± 11.5	50	92.2 ± 11.5	0.00	S
M45	50	81.6 ± 10.8	50	94.8 ± 11.1	0.00	S
M50	50	82.2 ± 10.9	50	95.4 ± 11.3	0.00	S
M55	50	81.5 ± 10.8	50	91.4 ± 9.3	0.00	S
M60	50	82.4 ± 9.5	50	92.7 ± 10.7	0.00	S
M65	50	81.8 ± 10.6	50	101.5 ± 11.6	0.00	S
Post deflation	50	84 ± 10.7	50	103.3 ± 10.6	0.00	S
Post extubation	50	82.0 ± 11.7	50	101.6 ± 10.7	0.00	S

Table 4: Changes in MBP at different time interval in Group I and Group II.

Group	Group 1		Group 2			
Time interval	N	Mean ± SD	N	Mean ± SD	p-value	Statistical Significance
Preoperative	50	93.7 ± 6.5	50	91.7 ± 7.4	0.12	NS
Postintubation	50	102.02 ± 7.5	50	99.55 ± 8.0	0.07	NS
Post pneumoperitoneum M5	50	87.5 ± 8.5	50	100.6 ± 10.4	0.00	S
M10	50	89.5 ± 8.0	50	101.1 ± 11.2	0.00	S
M15	50	86.8 ± 8.7	50	100.4 ± 10.5	0.00	S
M20	50	84.0 ± 7.3	50	100.5 ± 9.6	0.00	S
M25	50	88.5 ± 7.4	50	97.5 ± 8.1	0.00	S
M35	50	85.7 ± 6.7	50	98.7 ± 12.0	0.00	S
M40	50	87.5 ± 5.5	50	94.5 ± 9.5	0.00	S
M45	50	88.0 ± 9.1	50	97.6 ± 11.7	0.00	S
M50	50	86.0 ± 9.3	50	94.7 ± 7.1	0.00	S
M55	50	87.7 ± 7.3	50	95.2 ± 9.5	0.00	S
M60	50	85.8 ± 7.2	50	96.4 ± 12.6	0.00	S
M65	50	84.2 ± 8.56	50	95.7 ± 9.5	0.00	S
Post deflation	50	90.67 ± 7.67	50	102.56 ± 11.6	0.00	S
Post extubation	50	88.6 ± 8.54	50	101.54 ± 10.55	0.00	S

I than in group II ($P < 0.05$). MAP and heart rate was significantly lower ($P < 0.05$) during pneumoperitoneum, remained lower throughout the surgery and in postoperative period in group I as compared to group II (Table 3 and Table 4).

Discussion

Laparoscopic cholecystectomy is one of the routine procedures done in general surgery. However pneumoperitoneum and positioning required for this procedure alters the cardiovascular, respiratory, neuroendocrine and acid base physiology. α-2 adrenoceptor agonists are now being frequently used in anesthesia as they decrease sympathetic tone and attenuate the stress responses to intubation and surgery. Infusion doses of dexmedetomidine varying from 0.1 to 10 µg/kg/h [14,15] have been studied. Even the low dose infusion of 0.25-0.5 µg/kg/h are effective in blunting stress response and decrease in systemic catecholamines [16]. In our study dose of 0.2 µg/kg/hr infusion had significant hemodynamic stability during intra and post-operative period. It is an effective alternative to benzodiazepine and opioids in patients undergoing monitored anaesthesia care because of its analgesic, arousal sedation and lack of respiratory depression properties [17]. α-2 adrenoceptors are found in many sites in the central nervous system, highest densities in the locus ceruleus, the predominant noradrenergic nuclei of the brainstem which contributes to the maintenance of arousal or wakefulness. Presynaptic activation of the α-2 adrenoceptor in the locus ceruleus inhibits the release of norepinephrine and results in the sedative and hypnotic effects. Dexmedetomidine infusion also enables smooth extubation without causing hemodynamic instability, undue sedation and maintains plasma noradrenaline concentration [18]. Dexmedetomidine in a dose of 0.2 µg/kg/hr is effective in blunting stress response to pneumoperitoneum [19]. Bhattacharjee DP, et al. [20] showed the effects of Dexmedetomidine

infusion (0.2 µg/kg/hour) for hemodynamic stability in patients undergoing laparoscopic cholecystectomy and found that heart rate in Dexmedetomidine group was significantly less after intubation and throughout the period of pneumoperitoneum [20]. In our study the mean heart rate was also significantly lower in dexmedetomidine group.

Conclusion

Low dose infusion of dexmedetomidine at the rate of 0.2 µg/kg/hr serves as a very useful anaesthesia adjuvant to control hemodynamic stress response to pneumoperitoneum and extubation in patients undergoing laparoscopic cholecystectomy.

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