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Original Article

A Comparative Study of Dexmedetomidine and Esmolol on Hemodynamic Responses During Laparoscopic Cholecystectomy

Sangeeta Subba* [1], **Richa Mishra** [1], **Rupak Bhattarai** [1] **and Arjun Chhetri** [2]

[1]Department of Anesthesiology, Critical Care and Pain Management, Nobel Medical College Teaching Hospital, Biratnagar, Nepal, [2]Department of Anesthesiology and Critical Care, Neuro Cardio and Multispeciality Hospital Pvt. Ltd., Biratnagar, Nepal

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Abstract

Background

Laparoscopic surgery has various advantages like minimal invasiveness and quick recovery. However carbon dioxide used for pneumoperitoneum during laparoscopic surgery causes increase in heart rate, blood pressure and systemic vascular resistance. The present study compared the efficacy of Dexmedetomidine and Esmolol on hemodynamic responses during laparoscopic cholecystectomy.

Material and Methods

A total of 100 patients scheduled for laparoscopic cholecystectomy were randomly allocated in two groups, 50 in each group. Esmolol group received bolus dose of 1 mg/kg intravenous Esmolol just before pneumoperitoneum followed by an infusion of 200 mcg/kg/min and Dexmeditomidine group received bolus dose of 1 mcg/kg iv Dexmedetomidine over 10 minutes before pneumoperitoneum followed by 0.6 mcg/kg/hr in infusion. Hemodynamic parameters like Heart rate, Mean arterial pressure, Systolic blood pressure, Diastolic blood pressure were recorded at different time intervals.

Results

It was found that in Dexmeditomidine group there was a statistically significant decrease in heart rate before pneumoperitoneum (84.24±9.17) and10 minutes after pneumoperitoneumc (79.40±7.41) compared to Esmolol Group before pneumoperitoneum (91.40±5.98) and 10 minutes after pneumoperitoneum (95.18±14.17). There was statistically significant decrease in Mean arterial pressure in Dexmeditomidine group at 30 minutes (86.53±6.13), 50 minutes (77.95±4.85) , after release of pneumoperitoneum (92.42±3.91) and after extubation (99.50±11.81) compared to Esmolol group at 30 minutes (91.23±8.97), 50 minutes (94.34±12.64) after release of pneumoperitoneum (102.5 ±10.44) and after extubation (112.39±11.15).

Conclusion

Dexmedetomidine was found to be more effective than Esmolol in attenuating the hemodynamic responses following pneumoperitoneum during laparoscopic cholecystectomy.

Keywords: *Cholecystectomy, Dexmedetomidine, Hemodynamic*

***Corresponding author**
Dr Sangeeta Subba
Lecturer
Email: sangytasubba@hotmail.com
ORCID: https://orcid.org/0000-0003-3107-8911

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Introduction

Laparoscopy cholecystectomy has revolutionalised the management of patients with gall bladder diseases and has rapidly emerged as the gold standard for the surgical treatment and is now available worldwide. It has various advantages over the conventional cholecystectomy to the patient in terms of decreased tissue damage, early ambulation, reduced hospital stay, decreased analgesic needs, and cost effectiveness [1]. However creation of pneumoperitoneum had its own drawbacks like adverse hemodynamic cardiovascular, respi- ratory, stress response and acid base physio- logy. Increased release of vasopressin, catecholamines, or both are responsible for these hemodynamic responses [2,3,4]. Various drugs like nitroglycerine [5], beta blockers [6], opioids [7], gabapentin [8], pregabalin [9], magnesium sulphate [10], clonidine [11] and dexmedetomidine [12] are used to provide hemodynamic stability during pneumoperitoneum with variable success rate. Dexmedet-omidine inhibits the release of catecholamines and vasopressin, thus modulating the hemodynamic changes induced by pneumoperitoneum [12-13]. Esmolol, is an ultrashort-acting cardio-selective β1 receptor antagonist, which blunts hemodynamic responses to perioperative noxious stimuli [6]. Stress response during anaesthetic induction especially intubation and effects of various drugs to reduce this is extensively done by several worker. But there are few research work done on the effects of drugs to attenuate haemodynamic responses after pneumoperitoneum that also for operations on gall bladder. Therefore, the present prospective comparative study was designed to evaluate and compare the efficacy of Esmolol and Dexmedetomidine on hemodynamic response after pneumoperitoneum during laparoscopic surgery.

Materials and Methods

After obtaining ethical approval from Institutional Review Board, this prospective Comparative Study was conducted in Nobel Medical College and Teaching Hospital, Biratnagar, Nepal from September 2018 to April 2019. Sample size was calculated using formula $n=2(Z\alpha+Z\beta)^2S^2/d^2$ where n= sample size in each group, $z\alpha=1.96$ at 95% confidence level and $Z\beta=0.84$ at 80% power Assuming effect size = (d/S) 2 = 0.6 in determining differences in mean in two groups, we took 50 as 45 was minimum calculated sample size. Therefore, Sample size was 100 patients, divided into 2 groups, 50 in each group [14]. A total of 100 patients aged 18 to 60 years, American Society of anesthesiologist (ASA) Physical status I and II of either sex scheduled for elective laparoscopic cholecystectomy under general anaesthesia were taken as subjects for study after taking informed consent. Patient unwilling to participate in the study, Patients with bleeding disorders, cardiopulmonary diseases, severe obstructive lung diseases, pregnancy, Patients with Morbid obesity, Cirrhosis, Portal hypertension, Previous abdominal surgeries, CBD stones, CBD polyps, patients with difficult airway mallampati grade III, IV ASA physical status III and IV Hypersensitivity to any drug used in study and Patient with lack of communication were excluded from the study.

All patients underwent routine pre anaesthetic checkup one day prior to surgery and were kept Nil per Oral 8 hours prior to surgery. They were premedicated with oral Diazepam 5 mg and Ranitidine 150 mg, on the evening prior to surgery and 2 hours before surgery.

In the operating room, intravenous cannulation with an 18 gauze cannula was done and an infusion of intravenous fluid Ringers Lactate at 60ml\hr was started for all the patients. Standard anaesthetic monitoring equipment was attached (Five-lead electrocardiogram (ECG) monitoring, pulse oximetry and noninvasive blood pressure monitoring and baseline vitals [heart rate (HR), systolic blood pressure (SBP), diastolic blood pressure (DBP), mean arterial blood pressure (MAP)] were recorded. Randomization was done by computer generated numbers. Senior anaesthesiologist prepared the drugs in different syringes and infusion pumps. Same group of person were involved in preparation and administration of drugs in all patients.

Esmolol group- Patients received bolus dose of 1 mg/kg intravenous Esmolol just before pneumoperitoneum followed by an infusion of 200 mcg/kg/min. Dexmeditomidine group - patient received bolus dose of 1 mcg/kg iv Dexmedetomidine over 10 minutes before pneumoperitoneum followed by 0.6 mcg/kg/hr in infusion. All patients were pre-oxygenated with 100% oxygen by a face mask for 3 min. Inj Midazolam 0.05 mg/kg, Inj Fentanyl 1.5 mcg/kg was given as a premedication and anesthesia was induced with Propofol 1.5 mg/kg body weight followed by Vecuronium 0.15 mg/kg body weight. Bag and mask ventilation with oxygen followed by orotracheal intubation was done with an appropriate size cuffed endotracheal tube. Dexmedetomidine /Esmolol infusion were started before creation of pneumoperitoneum. Maintenance of anaesthesia was done with oxygen, Air and Isoflurane intermittent boluses of Vecuronium (0.01mg/kg).

Ventilation was adjusted to maintain an end-tidal carbon dioxide (ETCO2) value between 35 and 40 mm Hg. Intraabdominal pressure was maintained to 12 mmHg throughout the laparoscopic procedure. Patients were also given Injection Ondansetron 4mg and Injection Diclofenac 75 mg. At the end of surgery residual neuromuscular blockade was reversed with Neostigmine (50 mcg/kg) and Glycopyrrolate (10 mcg/kg). Both the group of drug infusion was stopped after extubation.

Throughout the surgery HR, SBP, DBP, MAP, were monitored and documentation was done at various time intervals (Baseline recording was documented as soon as patient arrived in OT , followed by 3 minutes of intubation, before pneumoperitoneum , at 10 minutes, 20 minutes, 30 minutes, 40 minutes, 50 minutes of pneumoperitoneum, after release of pneumoperitoneum and after extubation) using Proforma. Data was collected and analyzed by statistical package for the social sciences (SPSS) version 17.0 using independent t test for numerical data. Statistical significance was taken if p value <0.05.

Results

A total of 100 patients of both sexes belonging to ASA class I and Class II between the age group of 18-60 years who were willing to participate were included in the study. Table 1 shows the demographic data of the patients.

Table 1: Demographic data of the patient

	Esmolol Group (n=50)	DexmeditomidineGroup (n=50)	P value
Age (years)	37.44±12.05	40.48±12.48	0.218
Gender (M\F)	3\47	6\44	0.485
Weight (kg)	57.32±8.65	58.04±7.79	0.663

There was no significant difference amongst the groups with regard to demographic variables. The higher number of female patients in both groups indicates normal demographic distribution of the disease and its increased prevalence in the female sex.

There was statistically significant decrease in heart rate in Dexmeditomidine group (84.24±9.17) ,compared to Esmolol Group (91.40±5.98) before pneumoperitoneum and 10 minutes after pneumoperitoneum Dexmeditomidine Group (79.40± 7.41) and Esmolol group (95.18±14.17).

Table 2: Heart rate (HR)

Time interval	Esmolol Group	Dexmedetomidine Group	P value
Baseline	88.36±10.76	84.38±10.41	0.063
3 minutes after intubation	88.70±6.67	90.60±7.27	0.179
Before pneumoperitoneum	91.40±5.98	84.24±9.17	< 0.001
After10 minutes	95.18±14.17	79.40±7.41	<0.001
After 20 minutes	87.86±12.72	87.60±11.99	0.916
After 30 minutes	86.52±17.49	85.42±16.45	0.71
After 40 minutes	87.91±12.77	87.59±6.26	0.894
After50 minutes	89±12.24	81.91±7.37	0.22
After release of pneumoperitoneum	87.56±12.70	88.86±12.12	0.602
After extubation	100.92±13.12	99.32±13.09	0.543

Table 3: Mean arterial pressure (MAP)

Time interval	Esmolol Group	Dexmeditomidine Group	P value
Baseline	92.36±8.60	91.96±7.88	0.809
3 minutes after intubation	97.20±21.67	98.10±21.80	0.836
Before pneumoperitoneum	94.26±13.17	95.66±13.65	0.61
After10 minutes	97.31±13.79	95.50±12.77	0.458
After 20 minutes	93.47±11.76	98.36±11.30	0.65
After 30 minutes	91.23±8.97	86.53±6.13	<0.001
After 40 minutes	94.34±8.20	84.88±7.59	0.001
After50 minutes	94.34±12.64	77.95±4.85	<0.001
After release of pneumoperitoneum	102.5±10.44	92.42±3.91	<0.001
After extubation	112.39±11.15	99.50±11.81	<0.0001

There was statistically significant decrease in MAP in Dexmeditomidine group (86.53±6.13) at 30 minutes as compared to Esmolol group (91.23±8.97), at 50 minutes in Dexmeditomidine group (77.95±4.85) as compared to Esmolol group (94.34±12.64) and after release of pneumoperitoneumin Dexmeditomidine group (92.42±3.91) as compared to Esmolol group (102.5±10.44), as well as after extubation in Dexmeditomidine group (99.50±11.81) in comparison to Esmolol group(112.39±11.15).

Table 4: Systolic blood pressure (SBP)

	EsmololGroup	Dexmeditomidine Group	P value
Baseline	122.90±14.47	122.06±14.63	0.773
3 minutes after intubation	125.90±13.64	126.80±14.14	0.747
Before pneumoperitoneum	124.90±13.63	126.28±13.50	0.612
After10 minutes	124.90±13.63	126.28±13.50	0.612
After 20 minutes	119.50±10.09	117.50±9.45	0.309
After 30 minutes	118.64±9.28	116.96±9.49	0.375
After 40 minutes	109.90±9.10	108.42±8.80	0.483
After50 minutes	119.21±10.87	116.75±10.55	0.453
After release of pneumoperitoneum	124.04±8.62	122.78±7.90	0.448
After extubation	137.70±14.17	136.26±14.40	0.615

Table 5: Diastolic blood pressure (DBP)

Table 5: Diastolic blood pressure (DBP) Time interval	EsmololGroup	Dexmeditomidine Group	P value
Baseline	71.96±12.88	70.40±13.15	0.555
3 minutes after intubation	79.34±11.11	79.12±11.41	0.922
Before pneumoperitoneum	77.60±11.13	78.28±11.21	0.761
After10 minutes	87.56±11.23	86.60±10.78	0.644
After 20 minutes	87.56±11.23	86.60±10.78	0.664
After 30 minutes	82.50±11.67	79.92±11.06	0.259
After 40 minutes	79.90±8.54	78.78±8.18	0.505
After50 minutes	76.54±10.43	73.27±10.52	0.817
After release of pneumoperitoneum	79.33±11.32	75.30±8.90	0.203
After extubation	83.52±8.24	81.96±7.36	0.321

Comparison of systolic and diastolic blood pressure showed no statistically significant difference between two groups.

Discussion

It was seen that use of both Dexmedetomidine and Esmolol perioperatively was effective in maintaining better hemodynamic stability during laparoscopic cholecystectomy. Esmolol showed less fluctuations in BP and HR due to attenuation of sympathetic stimuli but, the response was better at all time intervals in dexmedetomidine group. In the current study similar regimen (loading dose 1 mcg/kg over 10 minutes followed by continuous infusion 0.6 mcg/kg/hr used by Srivastava V et al. [15] was used to find out its efficacy to attenuate the hemodynamic response to pneumoperitoneum during laparoscopic cholecystectomy. Similarly Koivusalo et al. [6]recommended that Esmolol blocks peripheral β-adrenergic receptors which ultimately decreases the hemodynamic response to CO2 pneumoperitoneum.In the present study Esmolol at a dose of 1 mg/kg intravenous followed by an infusion of 200 mcg/kg/min was used. Similar dose regime was used by Shams et al. in [16] but they used it for controlled hypotension.

In this study, after initiation of infusion of the study drugs i.e before pneumoperitoneum, there was a significant decrease in heart rate in Dexmedetomidine group in comparison to Esmolol group. The decrease in HR was also seen 10 minutes after pneumoperitoneum in Dexmedetomidine group. These effects were similar with Yennawar et al [12] and Zuberi et al [17]. The reason of this decrease in HR immediately after start of infusion may be due to biphasic cardiovascular response which has been described after the start of Dexmedetomidine. Dexmedetomidine injected as a bolus dose results in a transient rise in the blood pressure initially followed by a reflex decrease in heart rate, especially in healthy young patients [18]. In Srivastava V et al [15], Dexmedetomidine group had a decrease in MAP when compared to Esmolol Group, after creating pneumoperitoneum at 15 minutes, 45 minutes, and 60 minutes interval, Similar result was seen in present study where there was significant decrease in MAP in Dexmedetomidine group at 30 minutes , 50, minutes of pneumoperitoneum, which was found to be statistically significant.

The MAP of Esmolol group was higher than Dexmedetomidine group at some of the time intervals of pneumoperitoneum i.e at 30 minutes, 40 minutes, and 50 minutes of pneumoperitoneum and after release of pneumoperitoneum. However the MAP was not below 20 % of baseline value in Esmolol group in any of the observed data, so Esmolol could also provide better hemodynamic stability as Dexmedetomidine. This kind of effects of Esmolol has been shown by various researchers like Ozturk T [19], Collard et al [20], Ibrahim et al. [21], Srivastava V et al [15]. Limitations of this study was that dose of Propofol, Fentanyl requirement during surgery and sedation score were not analysed in the present study. The sample size of the study was small and was carried out at only one institution; hence it couldn't be representative of general population.

Conclusion

This study concludes that both the drugs were effective in attenuating the hemodynamic responses following pneumoperitoneum during laparoscopic cholecystectomy but Dexmedetomidine was found to be better, when compared with Esmolol.

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