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Original Research Article

Comparative Study of Dexmedetomidine and Esmolol on Hemodynamic Responses during Laparoscopic Cholecystectomy

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Conflict of interest: Nil

Abstract

Background: Laparoscopic surgeries have revolutionized surgeries and it has now become the "gold standard" of many surgical procedures, and has been promoted, as a "gentle surgery". However, this procedure is not risk free. In fact it produces significant haemodynamic changes especially in elderly and haemodynamically compromised patients. Aim of the study to evaluate the type and extent of haemodynamic changes associated with laparoscopic surgery and also to find out the efficacy of dexmedetomidine and Esmolol in prevention of such haemodynamic changes.

Materials and Methods: Total of 100 patients aged 18-60 years, American Society of Anaesthesiologists (ASA) physical status I or II, of either sex, planned for laparoscopic cholecystectomy were included. 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 15 minutes before pneumoperitoneum followed by 0.6 mcg/kg/hr in infusion. Heart rate (HR), systolic blood pressure, diastolic blood pressure and mean arterial pressure (MAP) were recorded preoperative, after study drug, after induction, after intubation, after pneumoperitoneum at 15 min intervals, post pneumoperitoneum and postoperative period after 15 min. Propofol induction dose, intraoperative fentanyl requirement and sedation score were also recorded.

Results: 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: Comparison of Dexmedetomidine and esmolol in hemodynamic responses to pneumoperitoneum in elective laparoscopic cholecystectomy, Dexmedetomidine is more

effective than esmolol. Dexmedetomidine and esmolol also reduced fulfill the requirements of anaesthetic agents.

Keywords: α2 agonist, General anesthesia, Pneumoperitoneum

Background

Laparoscopic cholecystectomy has become the milestone accomplishment in the modern arena of surgical practice as a great advance in the management of patients with symptomatic gallbladder diseases. It has also become an integral component of ambulatory and one-day procedures; hence, it requires a balanced anesthesia technique to obtain a smooth post-operative recovery. It has the advantages of lesser tissue trauma, reduced post-operative pain, shorter hospital stay, more rapid return of normal activities with significant cost savings [1].

However, the pneumo-peritoneum created during laparoscopy can induce stimulation of the neuro -endocrinal pathway which in turn increase the levels of several mediators such as catecholamines, renin, vasopressin, prostaglandins and cortisol with subsequent various hemodynamic and respiratory effects that may be harmful to the patients [2,3].

Methods to reduce these effects include administration of some pharmacological preparations to the patients, which will modify the response of anesthetic drugs [4,5].

Dexmedetomidine modulates the hemodynamic changes induced by pneumoperitoneum by inhibiting the release of catecholamines and vasopressin. Esmolol, an ultra-short-acting cardio-selective β1-receptor antagonist, has been shown to blunt hemodynamic responses to perioperative noxious stimuli. There are few studies demonstrating the effectiveness of esmolol and dexmedetomidine individually in attenuation of hemodynamic response during laparoscopy. However, there is no study to compare the effects of esmolol and dexmedetomidine on hemodynamic response during laparoscopic cholecystectomy. Hence, the present prospective, randomized study is designed to evaluate and compare the efficacy of esmolol and dexmedetomidine on hemodynamic response during laparoscopic cholecystectomy.

Material and Methods

This prospective Comparative Study was conducted in Nalanda Medical College and Hospital, Patna, Bihar from November 2021 to July 2022. A total of 100 patients, aged 18-60 years, ASA physical status I or II, of either sex, scheduled for elective laparoscopic cholecystectomy under general anesthesia were taken as subjects for the study.

Inclusion criteria: Age group 18-60 years undergoing laparoscopic cholecystectomy of genders, ASA physical status I and II.

Exclusion criteria: Patients with history of hypertension, with morbid obesity, Contraindication/ allergy to either dexmedetomidine or esmolol being used, with renal insufficiency, hepatic insufficiency, with cardiopulmonary problems.

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.

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 Isobutane intermittent boluses of Vecuronium (0.01mg/kg).

Ventilation was adjusted to maintain an end-tidal carbon dioxide ($ETCO_2$) 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.

Statistical Analysis

Statistical analysis was performed using the Microsoft Excel 12.0 version. Patient characteristic data were analysed with one-way analysis of variance (ANOVA) for continuous variables and Chi-square test for categorical variables. Intergroup comparison of heart rate, systolic blood pressure, diastolic blood pressure and mean arterial pressure were done with one way analysis of variance (ANOVA), followed by an unpaired t-test. Repeated measure analysis of variance (ANOVA) with the *post-hoc* Tukey test was used to compare means for hemodynamic variables in intragroup comparison to baseline parameters. Sedation score was analysed by the Kruskal-Wallis test. A P-value of <0.05 was considered statistically significant.

Results

A total of 100 patients, aged 18-60 years, ASA physical status I or II, of either sex, scheduled for elective laparoscopic cholecystectomy under general anesthesia were taken as subjects for the study.

Table 1: Demographic Data of Both group of patients

	Esmolol Group (n=50)	Dexmeditomidine Group (n=50)	P value
Age in years	37.44±12.05	40.48±12.48	0.218
Gender (M/F)	3 male 47 female	6 male 44 female	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 of both groups of patients

Time interval	Esmolol Group (n=50)	Dexmeditomidine Group (n=50)	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
After 10 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
After 50 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 of both group of patients

Time interval	Esmolol Group (n=50)	Dexmeditomidine Group (n=50)	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
After 10 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
After 50 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 of Both group of patients

Time interval	Esmolol Group (n=50)	Dexmeditomidine Group (n=50)	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
After 10 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
After 50 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 of Both group of patients

Time interval	Esmolol Group (n=50)	Dexmeditomidine Group (n=50)	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
After 10 minutes	87.56±11.13	86.60±10.78	0.644
After 20 minutes	87.56±11.13	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
After 50 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

Our study confirms that dexmedetomidine and esmolol were successfully used to control hemodynamic changes during pneumoperitoneum in laparoscopic cholecystectomy; however dexmedetomidine is more effective than esmolol to attenuate these changes. Esmolol showed fewer 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*. [6] was used to find out its efficacy to attenuate the hemodynamic response to pneumoperitoneum during laparoscopic cholecystectomy. Similarly Koivusalo *et al*. [7] recommended that Esmolol blocks peripheral β-adrenergic receptors which ultimately decrease the hemodynamic response to CO_2 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 [8] 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* [10] and Zuberi *et al* [9]. 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 [11]. In Srivastava V *et al* [6], 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 [12], Collard *et al* [13], Ibrahim *et al*. [14], Srivastava V *et al* [6].

There are some limitations to our study: (1) the no of patients is too small for broad generalizations (2) plasma catecholamines and antidiuretic hormone levels were not assessed by us to know the degree of suppression of neurohumoral pathway (3) we did not measure the postoperative fentanyl requirement and extubation criteria.

Conclusion

Incidence of hemodynamic changes during laproscopic procedure is proven, and various methods of stress attenuation to pneumoperitonium is advised. We decided to study the use of dexmedetomidine and esmolol for attenuation of hemodynamic response to pneumoperitoneum in laparoscopic cholecystectomy. Dexmedetomidine is more effective than esmolol in preventing such hemodynamic responses in laparoscopic surgery. In addition, dexmedetomidine and esmolol also reduce the induction dose of other anaesthetic agents i.e. propofol and intraoperative fentanyl requirement.

References

1. Jean LJ. Anaesthesia for laparoscopic surgery. In: Miller RD, editor. Anesthesia. 7th ed. Philadelphia: Church ill Livingstone, New York; 2010; 2185–2202.
2. Sharma KC, Brandstetter RD, Brensilver JM, *et al*. Cardiopulmonary physiology and patho -physiology as a consequence of laparoscopic surgery. Chest. 1996; 110(3):810–815.
3. Larsen JF, Svendsen FM, Pedersen V. R andomized clinical trial of the effect of pneumoperitoneum on cardiac function and haemodynamics during laparoscopic cholecystectomy. Br. J. Surg. 2004; 91(7):848–854.
4. Koivusalo AM, Scheinin M, Tikkanen I, *et al*. Effects of esmolol on haemodynamic response to CO_2 pneumoperitoneum for laparoscopic

surgery. Acta Anaesthesiol Scand. 1998; 42(5):510–517.
5. Aho M, Scheinin M, Lehtinen AM, *et al*. Intramuscularly administered dexmedetomidine attenuates hemodynamic and stress hormone responses to gynecologic laparoscopy. Anesth Analg. 1992; 75(6):932–939.
6. Srivastava VK, Nagle V, Agrawal S, Kumar D, Verma A, Kedia S, Comparative evaluation of dexmedetomidine and esmolol on hemodynamic responses during laparoscopic cholecystectomy, J Clin Diagn Res. 2015;9:UC01-UCO5.
7. Koivusalo A, Scheinin M, Tikkanen I, Yli-Suomu T, Ristkari S, Laakso J *et al,* Effects of esmolol on haemodynamic response to CO_2 pneumoperitoneum for laparoscopic surgery, Acta Anaesthesiologica Scandinavica.1998; 42:42:510-517.
8. Shams T, El Bahnasawe N, Abu-Samra M, El-Masry R, Induced hypotension for functional endoscopic sinus surgery: A comparative study of dexmedetomidine versus esmolol, Saudi J Anaesth. 2013; 7:175.
9. Zuberi A, Tiwary V, Rastogi B, Gupta K, Kumar A, Farooqui R, Comparison ofhemodynamic responses of intravenous dexmedetomidine and esmolol infusion during laparoscopic cholecystectomy, Int J Res Med Sci. 2018;6:1429-1434.
10. Yennawar SD, Memon NY, Nandanwankar NK, Evaluation of Effect of Infusion of Dexmedetomidine on Attenuation of Hemodynamic Response During Laparoscopic Surgeries, J Med Sci clin Res. 2017;05:22846-22854.
11. Iwase K, Takenaka H, Ishizaka T, Ohata T, Oshima S, Sakaguchi K, Serial Changes in Renal Function during Laparoscopic Cholecystectomy, European Surgical Research. 1993; 25: 203-212.
12. Ozturk T, Kaya H, Aran G, Aksun M, Savaci S, Postoperative beneficial effects of esmolol in treated hypertensive patients undergoing laparoscopic cholecystectomy, Br J Anaesth. 2008;100:211-214.
13. Collard V, Mistraletti G, Taqi A, Asenjo J, Feldman L, Fried G *et al*, Intraoperative Esmolol Infusion in the Absence of Opioids Spares Postoperative Fentanyl in Patients Undergoing Ambulatory Laparoscopic Cholecystectomy, Anesth Analg. 105; 2007:1255-1262.
14. Ibrahim A, Kamal M, Lotfy A, Comparative study of clonidine versus esmolol on hemodynamic responses during laparoscopic cholecystectomy, Egypt J Anaesth. 2016;32:37-44.