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

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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 Dexmedetomidine group there was a statistically significant decrease in heart rate before pneumoperitoneum (84.24±9.17) and 10 minutes after pneumoperitoneum (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

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Introduction
Laparoscopy cholecystectomy has revolutionised 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 has its own drawbacks like adverse hemodynamic cardiovascular, respiratory, stress response and acid base physiology. 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. Dexmedetomidine 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 workers. 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 $n = \frac{2(Z_a+Z_b)^2\bar{S}^2}{d^2}$ where $n$= sample size in each group, $Z_a=1.96$ at 95% confidence level and $Z_b=0.84$ 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. Dexmedetomidine group - patient received bolus dose of 1 mcg/kg iv Dexmedetomidine over 10 minutes before pneumoperitoneum followed by an infusion of 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 Ondanetron 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**

| Time interval | Baseline | After 10 minutes | After 20 minutes | After 30 minutes | After 40 minutes | After 50 minutes | After extubation |
|---------------|----------|----------------|----------------|----------------|----------------|----------------|------------------|
| Heart rate (HR) | 71.96±12.88 | 79.34±11.17 | 87.56±11.23 | 87.56±11.23 | 87.56±11.23 | 87.56±11.23 | 87.56±11.23 |
| Systolic blood pressure (SBP) | 70.40±13.15 | 79.12±12.48 | 86.60±10.78 | 86.60±10.78 | 86.60±10.78 | 86.60±10.78 | 86.60±10.78 |
| Diastolic blood pressure (DBP) | 79.40±8.54 | 79.34±11.17 | 86.60±10.78 | 86.60±10.78 | 86.60±10.78 | 86.60±10.78 | 86.60±10.78 |

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 Dexmedetomidine group (84.24±9.17), compared to Esmolol Group (91.40±5.98) before pneumoperitoneum and 10 minutes after pneumoperitoneum Dexmedetomidine Group (79.40±7.41) and Esmolol group (95.18±14.17).

There was statistically significant decrease in MAP in Dexmedetomidine group (86.53±6.13) at 30 minutes as compared to Esmolol group (91.25±8.97), at 50 minutes in Dexmedetomidine group (77.95±4.85) as compared to Esmolol group (94.34±12.64) and after release of pneumoperitoneum Dexmedetomidine group (92.42±3.91) as compared to Esmolol group (102.5±10.44), as well as after extubation in Dexmedetomidine group (99.50±11.81) in comparison to Esmolol group (112.39±11.15).

**Table 1: Demographic data of the patient**

| Gender (M/F) | 3:47 | 6:44 |
|-------------|------|------|
| Weight (kg) | 57.32±8.65 | 58.04±7.79 |
| P value     | 0.218 | 0.485 |

There was no significant decrease in heart rate in Dexmedetomidine group (84.24±9.17), compared to Esmolol Group (91.40±5.98) before pneumoperitoneum and 10 minutes after pneumoperitoneum Dexmedetomidine Group (79.40±7.41) and Esmolol group (95.18±14.17).
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 in 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 regimen 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.

**References**

[1] Bruhat MA, Chapron C,Mage G, Poully JL, Canis M, Wattez A, The benefits and risks of laparoscopic surgery, Revue française de gynecologie et d’obstétrique. 86(1993) 84-88. PMID:8469869
[2] Myre K, Rostrup M, Buanes T, Stokland O, Plasma catecholamines and haemodynamic changes during pneumoperitoneum, Acta Anaesthesiologica Scandinavica. 42(1998) 343-347. PMID:9542563
[3] Mann C, Boccare G, Pouzeratte Y, Eliet J, Serradeil-Le Gal C, Vergnes C, The relationship among carbon dioxide pneumoperitoneum, vasopressin release, and hemodynamic changes, Anesthesia & Analgesia. 89(1999) 278-283. PMID:10439730
[4] Walder AD, Aitkenhead AR, Role of vasopressin in the haemodynamic response to laparoscopic cholecystectomy, British journal of anaesthesia. 78(1997) 264-266.https://doi.org/10.1093/bja/78.3.264
[5] Toyoyama H, Kariya N, Hase I, Toyoda Y, The Use of Intravenous Nitroglycerin in a Case of Spasm of the Sphincter of Oddi during Laparoscopic Cholecystectomy, Anesthesiology. 94(2001) 708-709.PMID:11379694
[6] Koivusalo A, Scheinin M, Tikkanen I, Yli-Suomu T, Ristikari S, Laaks 8 et al., Effects of esmolol on haemodynamic response to CO2 pneumoperitoneum for laparoscopic surgery, Acta Anaesthesiologica Scandinavica. 42(1998) 510-517. PMID:9605365
[7] Damen S, Clevers G, Vergnes C, The relationship among carbon dioxide pneumoperitoneum, vasopressin release, and haemodynamic response to laparoscopic cholecystectomy, Acta Anaesthesiologica Scandinavica. 42(1998) 510-517. PMID:9605365
[8] Pitino P, Name S, Jhouwenhuijs V, Joosten W, Hemodynamics during laparoscopic cholecystectomy, A Randomized Blinded Trial, Journal of Laparoendoscopic& Advanced Surgical Techniques. 14(2004) 87-92. PMID:15107217
[9] Pandey CK, Priye S, Ambesh SP, Singh S, Singh U, Singh PK, Prophylactic gabapentin for prevention of postoperative nausea and vomiting in patients undergoing laparoscopic cholecystectomy: a randomized, double-blind, placebo-controlled study, Journal of postgraduate medicine. 52 (2006) 97. PMID:16879671
[9] Peng PW, Li C, Farcas E, Haley A, Wong W, Bender J, Use of low-dose pregabalin in patients undergoing laparoscopic cholecystectomy, Br J Anaesth. 105 (2010) 155-161. PMID:20581215

[10] Jee D, Lee D, Yun S, Lee C, Magnesium sulphate attenuates arterial pressure increase during laparoscopic cholecystectomy, Br J Anaesth. 103(2009) 484-489. PMID:19617379

[11] Kaur M, Liddle D, Verghese M, Balakrishnan I, Singh M, Choudhury A, The comparative evaluation of intravenous with intramuscular clonidine for suppression of hemodynamic changes in laparoscopic cholecystectomy, Saudi J Anaesth. 7(2013) 181-186. PMID:23956720

[12] Yennawar SD, Memon NY, Nandanwankar NK, Evaluation of Effect of Infusion of Dexmedetomidine on Attenuation of Hemodynamic Response During Laparoscopic Surgeries, JMed Sci clin Res. 05(2017) 22846-22854. DOI: https://dx.doi.org/10.18535/jmscr/v5i6.08

[13] Cekic B, Geze S, Ozkan G, Besir A, Sonmez M, Karahan S et al, The Effect of Dexmedetomidine on Oxidative Stress during Pneumoperitoneum, BioMed ResInt. (2014)1-5.DOI: http://dx.doi.org/10.1155/2014/760323

[14] Hedeker D, Gibbons R, Waternaux C, Sample size estimation for longitudinal designs with attrition, Journal of Educational and Behavioral Statistic. 24 (1999) 70-93. DOI:https://doi.org/10.3102/10769986024001070

[15] 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. 9(2015) UC01-UCOS. PMID:25954683

[16] 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 JAnaesth. 7 (2013) 175. PMID: 23956719

[17] Zuberi A, Tiwary V, Rastogi B, Gupta K, Kumar A, Farooqui R, Comparison of hemodynamic responses of intravenous dexmedetomidine and esmolol infusion during laparoscopic cholecystectomy, Int J Res Med Sci. 6(2018) 1429-1434. DOI:http://dx.doi.org/10.18203/2320-6012.ijrms20181309

[18] Iwase K, Takenaka H, Ishizaka T, Ohata T, Oshima S, Sakaguchi K, Serial Changes in Renal Function during Laparoscopic Cholecystectomy, European Surgical Research, 25(1993) 203-212. PMID:8330637

[19] 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. 100(2008) 211-214. PMID:18037672

[20] 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. PMID:17959952

[21] Ibrahim A, Kamal M, Lofty A, Comparative study of clonidine versus esmolol on hemodynamic responses during laparoscopic cholecystectomy, Egypt J Anaesth. 32(2016) 37-44. DOI:http://dx.doi.org/10.1016/j.ejga.2015.10.001