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**Original Research Article**

# A Randomized Clinical Comparative Assessment of Dexmedetomidine versus Propofol for Attenuation of Hemodynamic Response to Creation of Pneumoperitoneum in Laparoscopic Cholecystectomies

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**Conflict Of Interest: Nil**

**Abstract**

**Aim:** The aim of the present study was to compare the effectiveness of dexmedetomidine and propofol in attenuating the hemodynamic response to pneumoperitoneum in patients undergoing laparoscopic cholecystectomy.

**Methods:** This retrospective, randomized study was done in the Department of Anesthesia, Vardhman Institute of Medical Science, Pawapuri, Nalanda, Bihar, India from March 2017 to Feb 2018. Written informed consent was taken before enrolling the patient into the study. 100 ASA I and II patients undergoing laparoscopic cholecystectomy under general anesthesia between the ages of 20 and 50 years of both sexes were randomly divided into two groups of 50 patients each using a sealed envelope method, with Group D to receive dexmedetomidine infusion and Group P to receive propofol infusion.

**Results:** The groups were comparable with respect to age, weight, gender ratio and ASA status of patients. There was a significant difference in postoperative mean HR between two groups with HR being lower in dexmedetomidine group. At most of the study stages lower values of mean SBP were observed in the dexmedetomidine group, thus suggesting better control of SBP with dexmedetomidine compared to propofol. Postoperative mean SBP also showed better control in dexmedetomidine group as compared to propofol group. Postoperative DBP was comparable between two groups. Total duration of pneumoperitoneum in dexmedetomidine group was 52.76±12.67 minutes and in propofol group was 57.36±15.34 minutes with p value of 0.155. The time to extubating was 16.80±4.26 minutes in dexmedetomidine group and 14.98±5.42 minutes in propofol group and was statistically insignificant with p-value of >0.05.

**Conclusion:** Dexmedetomidine infusion without loading dose is effective in attenuating hemodynamic response to pneumoperitoneum in patients undergoing laparoscopic cholecystectomy and is better alternative to propofol in such patients.

**Keywords:** Dexmedetomidine, pneumoperitoneum, hemodynamic response



## Introduction

Laparoscopic cholecystectomy is one of the most frequently performed laparoscopic surgeries nowadays. Since the introduction of diagnostic laparoscopic procedures in the early 1970s and the first laparoscopic cholecystectomy procedures in the late 1980s [1] laparoscopy has expanded impressively both in scope and volume. Increasing success of laparoscopic surgery can be attributed to the fact that it results in multiple benefits compared with open procedures, such as reduced trauma to patient, disturbance of homeostasis, morbidity, mortality, recovery time and hospital stay, with consequent reductions in healthcare costs [2-3] Efforts have been made to use the laparoscopic approach for gastrointestinal (e.g., colonic, gastric, splenic, hepatic surgery), gynecologic (e.g., hysterectomy), urologic (e.g., nephrectomy, prostatectomy), and vascular (e.g., aortic) procedures. Despite multiple benefits, any laparoscopic surgery always poses a challenge to its successful anesthetic management, mainly due to significant alteration of hemodynamics, resulting from the combined effects of pneumoperitoneum, patient position, anesthesia, and hypercapnia from the absorbed $CO_2$ that is used to produce pneumoperitoneum. Pneumoperitoneum creation (increased intra-abdominal pressure) is immediately followed by an increased plasma renin activity and increase in plasma levels of norepinephrine and epinephrine. [4] The renin–angiotensin–aldosterone system is also activated. All these changes collectively lead to an elevated arterial pressure, increased systemic and pulmonary vascular resistance, and decreased cardiac output. [5] Various agents such as isoflurane, propofol, β-blockers [6] and antihypertensives [7-8] have been used to reduce hemodynamic changes associated with laparoscopic surgery with variable response. Effects of α2-adrenergic agonist clonidine have also been studied widely. [9-10] Dexmedetomidine is alpha-2 adrenergic receptor agonist that modulates the hemodynamic changes by inhibiting the release of catecholamines and vasopressin. [11] Esmolol, an ultrashort-acting cardio selective beta-1 antagonist, has also been used to control tachycardia and hypertension. [12] Hence, we performed this study so as to compare the efficacy of these two agents and also to compare the safety of these drugs [13] It has been reported in studies that there is a 10–30% reduction in cardiac output during pneumoperitoneum. [4] Increases in arterial pressure can pose a risk for adverse cardiovascular events in patients with pre-existing essential hypertension, ischemic heart disease, or increased intracranial pressure. [14] Hypercapnia and pneumoperitoneum stimulate sympathetic nervous system, causing catecholamine and vasopressin release [15]

The aim of the present study was to compare the effectiveness of dexmedetomidine and propofol in attenuating the hemodynamic response to pneumoperitoneum in patients undergoing laparoscopic cholecystectomy.

## Materials and Methods

This retrospective, randomized study was done in the Department of Anesthesia, Vardhman Institute of Medical Science, Pawapuri, Nalanda, Bihar, India from March 2017 to Feb 2018.. Written informed consent was taken before enrolling the patient into the study.

100 ASA I and II patients undergoing laparoscopic cholecystectomy under general anesthesia between the ages of 20 and 50 years of both sexes were randomly divided into two groups of 50 patients each using a sealed envelope method, with Group D to receive dexmedetomidine infusion and Group P to receive propofol infusion. A preanesthetic checkup was done one day prior to surgery. Patients with history of allergy to the study drugs, uncontrolled diabetes and hypertension, pregnant females and those with deranged liver function test were not included in the study. Patients where conversion to open cholecystectomy was done were also excluded from the study. On arrival to the operating room, a 20 G intravenous line was secured and after applying standard monitoring device (noninvasive blood pressure, electro cardiogram, percent saturation of arterial oxygen, end tidal carbon dioxide monitor) and premedication with injection glycopyrrolate 0.01 mg.kg-1 to reduce airway secretions, all patients were induced with 3 mg.kg-1 bodyweight of sodium thiopentone and airway secured with appropriate sized endotracheal tube after giving injection fentanyl 2 µg.kg-1 and injection Atracurium 0.5 mg.kg-1. Anesthesia was maintained with a mixture of oxygen and nitrous oxide in 50:50 ratio and isoflurane to maintain a minimum alveolar concentration of 1.0. Muscle relaxation throughout surgery was maintained by bolus doses of atracurium. Group D received injection dexmedetomidine infusion (diluted with 24 mL of preservative free normal saline to achieve a dilution of 4µg.mL-1) in a dose range of 0.2 to 0.7 µg.kg-1.h-1 while Group P received injection propofol infusion in a dose range of 25-75 µg.kg-1.h-1. Both the drugs were started immediately after securing the airway and titrated to ensure heart rate and systolic blood pressure did not rise more than 30% of the pre pneumoperitoneum value. Titration was done by starting the drug at the midpoint of the dose range and titrated upwards or downwards depending on the increase or decrease in hemodynamic parameters respectively. The infusions of both the drugs were stopped at the end of pneumoperitoneum. Loading dose of dexmedetomidine was not given as per the study design. The intra-abdominal pressure of pneumoperitoneum was kept constant at 12 mmHg. The study drugs could not be blinded from the anesthesiologist performing the study in view of the physical nature of the drug (propofol being white in color) and need to adjust the dosing as per clinical response. Hemodynamic parameters including heart rate (HR), systolic blood pressure (SBP), diastolic blood pressure(DBP) were noted just before establishing the pneumoperitoneum and every two minutes after establishing the pneumoperitoneum for the first 10 minutes and subsequently every 10 minutes till the end of pneumoperitoneum using an automated multi-channel monitor. Increase in Systolic Blood Pressure (SBP) or Heart Rate (HR) to more than 30% of the pre pneumoperitoneum value even after the highest dose of infusion drugs was described as failure to control the hemodynamic response and was rescued with bolus dose of injection fentanyl 0.5µg.kg-1 and injection esmolol 10 mg bolus dose respectively. Hypotension was

described as fall in SBP below 90 mmHg and treated with bolus dose of injection ephedrine 6 mg while bradycardia was described as fall in heart rate below 50 beats.min-1 and treated with injection atropine 0.6 mg in divided dose. After the establishment of spontaneous respiration and reversal of residual effect of muscle relaxant by injection neostigmine 0.04 mg.kg-1 and glycopyrrolate 10 mcg/kg patients were extubated once they started responding. The data thus obtained was entered into computer using Microsoft Excel. Statistical analysis was done using students t test and chi-square test and p value<0.05 was considered significant.

**Results**

**Table 1: Comparison of demographic parameters between two groups**

| Criterion | Group D n=50 | Group P n = 50 | p-value |
|---|---|---|---|
| Age (years) | 36.33±11.08 | 40.43±12.71 | 0.135 |
| Gender (M/F) | 14/36 | 18/32 | 0.411 |
| Weight (Kgs) | 65.34±9.40 | 63.54±8.52 | 0.381 |
| ASA (I/II) | 38:12 | 36.14 | 0.949 |

The groups were comparable with respect to age, weight, gender ratio and ASA status of patients.

**Table 2: Intergroup comparison of mean heart rate (HR) between two groups**

| Mean HR (beats/min) | | | P – value |
|---|---|---|---|
| | Group D n=50 | Group P n = 50 | |
| Pre –op | 89.74±9.57 | 85.43±11.02 | 0.070 |
| 2 MIN | 92.21±8.46 | 94.60±7.60 | 0.196 |
| 4 MIN | 88.60±7.12 | 86.21±5.64 | 0.106 |
| 6 MIN | 85.63±9.89 | 86.30±7.58 | 0.740 |
| 8 MIN | 88.80±5.89 | 87.11±6.23 | 0.225 |
| 10 MIN | 82.32±11.27 | 89.76±7.3 | 0.264 |
| 20 MIN | 84.70±10.9 | 82.33±10.11 | 0.326 |
| 30 MIN | 80.1±9.23 | 85.30±7.67 | 0.680 |
| 40 MIN | 76.23±9.0 | 83.90±12.03 | 0.174 |
| 50 MIN | 78.34±5.42 | 82.84±7.4 | 0.094 |
| 60 MIN | 78.76±10.34 | 77.5±8.0 | 0.004 |
| POST OP | 82.63±8.67 | 85.79±7.89 | 0.655 |

There was a significant difference in postoperative mean HR between two groups with HR being lower in dexmedetomidine group.

**Table 3: Intergroup comparison of systolic blood pressure (SBP)**

| | Mean SBP (mm Hg) | | P – value |
|---|---|---|---|
| | Group D n=50 | Group P n = 50 | |
| Pre –op | 126.47±11.40 | 123.8±10.7 | 0.293 |
| 2 MIN | 134.21±10.76 | 138.86±9.90 | 0.0523 |
| 4 MIN | 128.50±13.45 | 128.48±11.98 | 0.9945 |
| 6 MIN | 121.66±14.34 | 124.45±17.98 | 0.453 |
| 8 MIN | 117.98±7.4 | 124.23±11.90 | 0.007 |
| 10 MIN | 115.83±6.9 | 120.87±9.78 | 0.012 |
| 20 MIN | 112.14±13.9 | 118.64±16.3 | 0.063 |
| 30 MIN | 112.2±8.6 | 113.73±14.23 | 0.621 |
| 40 MIN | 110.76±9.4 | 114.9±12.67 | 0.819 |
| 50 MIN | 102.09±15.76 | 112.84±16.32 | 0.0009 |
| 60 MIN | 104.6±10.33 | 119.27±17.62 | <0.0001 |
| POST OP | 117.43±12.23 | 130.09±14.54 | <0.0001 |

At most of the study stages lower values of mean SBP were observed in the dexmedetomidine group, thus suggesting better control of SBP with dexmedetomidine compared to propofol. Postoperative mean SBP also showed better control in dexmedetomidine group as compared to propofol group.

**Table 4: Intergroup comparison of diastolic blood pressure (DBP)**

| | Mean DBP (mm Hg) | | P-value |
|---|---|---|---|
| | **Group D n=50** | **Group P n=50** | |
| Pre –op | 73.12±10.26 | 74.31±8.64 | 0.584 |
| 2 MIN | 76.43±8.76 | 77.01±10.23 | 0.789 |
| 4 MIN | 74.72±6.99 | 76.5±7.15 | 0.272 |
| 6 MIN | 71.6±7.28 | 73.24±6.78 | 0.309 |
| 8 MIN | 74.02±7.28 | 72.62±5.27 | 0.337 |
| 10 MIN | 70.23±6.31 | 71.25±6.58 | 0.489 |
| 20 MIN | 68.60±5.86 | 68.90±7.66 | 0.847 |
| 30 MIN | 66.52±4.12 | 67.91±5.82 | 0.229 |
| 40 MIN | 64.23±6.12 | 65.42±5.91 | 0.388 |
| 50 MIN | 63.33±4.21 | 63.81±5.76 | 0.676 |
| 60 MIN | 62.19±6.33 | 66.42±5.99 | 0.003 |
| POST OP | 72.7±6.16 | 74.63±6.88 | 0.198 |

A similar trend of DBP was observed win both groups with values being comparable at corresponding study stages except at 60 minutes where lower DBP was observed in the dexmedetomidine group and the difference was significant (p value<0.05). Postoperative DBP was comparable between two groups.

**Table 5: Comparison of other variables between two groups**

| Criteria | Group D n=50 | Group P n=50 | P value |
|---|---|---|---|
| Duration of pneumoperitoneum(min) | 52.76±12.67 | 57.36±15.34 | 0.155 |
| Time to extubation(min) | 16.80±4.26 | 14.98±5.42 | 0.105 |
| Hypotension | 2 | 1 | 0.220 |
| Rescue fentanyl | 1 | 4 | 0.001 |

Total duration of pneumoperitoneum in dexmedetomidine group was 52.76±12.67 minutes and in propofol group was 57.36±15.34 minutes with p value of 0.155. The time to extubating was 16.80±4.26 minutes in dexmedetomidine group and 14.98±5.42 minutes in propofol group and was statistically insignificant with p-value of >0.05.

## Discussion

Laparoscopic cholecystectomy has become gold standard surgery for cholelithiasis. [16] Advantages of laparoscopic cholecystectomy are shorter hospital stay, early ambulation, smaller scar, and less compromised postoperative respiratory and gastro-intestinal functions. However, the procedure is not risk free as it is associated with significant hemodynamic changes due to creation of pneumoperitoneum, potential for systemic absorption of carbon dioxide, and reverse Trendelenberg position [17] Increase in heart rate and blood pressure in response to pneumoperitoneum produced during laparoscopic cholecystectomy is a challenging situation for a practicing anaesthesiologist. [4,18]

The groups were comparable with respect to age, weight, gender ratio and ASA status of patients. There was a significant difference in postoperative mean HR between two groups with HR being lower in dexmedetomidine group. At most of the study stages lower values of mean SBP were observed in the dexmedetomidine group, thus suggesting better control of SBP with dexmedetomidine compared to propofol. Postoperative mean SBP also showed better control in dexmedetomidine group as compared to propofol group. A similar trend of DBP was observed win both groups with values being comparable at corresponding study stages except at 60 minutes where lower DBP was observed in the dexmedetomidine group and the difference was significant (p value<0.05). Postoperative DBP was comparable between two groups. The results of this study suggest that dexmedetomidine infusion is effective in attenuating the hemodynamic response to pneumoperitoneum in patients undergoing laparoscopic cholecystectomy and may be a better alternative to propofol in attenuating such response. Dexmedetomidine is a highly selective α-2 agonist with central sympatholytic activity. It exerts its sympatholytic effect by activating α-2 receptors in medullary vasomotor center. Activation of these receptors results in decreased central sympathetic outflow. As hemodynamic response to pneumoperitoneum creation is because of sympathetic stimulation, dexmedetomidine seems to be appropriate drug for suppression of this response. Dexmedetomidine has been shown to cause a decrease in serum norepinephrine concentration. It also stimulates parasympathetic outflow as a result of activation of receptors in locus ceruleus of brainstem. [19-21]

Total duration of pneumoperitoneum in dexmedetomidine group was 52.76±12.67 minutes and in propofol group was 57.36±15.34 minutes with p value of 0.155. The time to extubating was

16.80±4.26 minutes in dexmedetomidine group and 14.98±5.42 minutes in propofol group and was statistically insignificant with p-value of >0.05. Our study findings are in concordance with a study conducted by Shah V et al. They compared dexmedetomidine and propofol for hemodynamic changes and depth of anesthesia (using BIS monitor) during laparoscopic surgery. [22] They found dexmedetomidine to be superior to propofol for hemodynamic control of pressor response to pneumoperitoneum. However, in their study dexmedetomidine was used in both loading and maintenance dose. Also BIS monitoring was not done in our study. The results of our study are also in correlation with a study conducted by Manne GR et al [23] who used dexmedetomidine in doses of 0.2 μg/kg/hr and 0.4 μg/kg/hr to assess its effect on hemodynamic stress response, sedation and postoperative analgesic requirement in patients undergoing laparoscopic surgeries and concluded that low dose dexmedetomidine infusion in the dose of 0.4 mcg/kg/h effectively attenuates hemodynamic stress response during laparoscopic surgery with reduction in post-operative analgesic requirements.

## Conclusion

Dexmedetomidine infusion without loading dose is effective in attenuating hemodynamic response to pneumoperitoneum in patients undergoing laparoscopic cholecystectomy and is better alternative to propofol in such patients.

## References


1. Dubois F, Icard PB, Berthelot GA, Levard H. Coelioscopic cholecystectomy: preliminary report of 36 cases. Annals of surgery. 1990 Jan 1;211(1):60-2.
2. Grace PA, Quereshi A, Coleman J, Keane R, McEntee G, Broe P, Osborne H, Bouchier-Hayes D. Reduced postoperative hospitaliz ation after laparoscopic cholecyste ctomy. British journal of surgery. 19 91 Feb;78(2):16 0-2.
3. Joris J, Cigarini I, Legrand M, Jacquet N, De Groote D, Franchimont P, Lamy M. Metabolic and respiratory changes after cholecystectomy performed via laparotomy or laparoscopy. BJA: British Journal of Anaesthesia. 1992 Oct 1;69(4):341-5.
4. Joris JL, Noirot DP, Legrand MJ, Jacquet NJ, Lamy ML. Hemodynamic changes during laparoscopic cholecystectomy. Anesthesia & Analgesia. 1993 May 1;76(5):1067-71.
5. Lenz RJ, THOMAS T, Wilkins DG. Cardiovascular changes during laparoscopy: studies of stroke volume and cardiac output using impedance cardiography. Survey of Anesthesiology. 1976 Dec 1;20(6):549-50.
6. Koivusalo AM, Scheinin M, Tikkanen I, Yli-Suomu T, Ristkari S, Laakso J, Lindgren L. Effects of esmolol on haemodynamic response to CO2 pneumoperitoneum for laparoscopic surgery. Acta anaesthesiologica scandinavica. 1998 May;42(5):510-7.
7. Feig BW, Berger DH, Dougherty TB, Dupuis JF, Hsi B, Hickey RC, Ota DM. Pharmacologic intervention can reestablish baseline hemodynamic parameters during lap-aroscopy. Surgery. 1994 Oct 1;116(4):733-9 .
8. Joris JL, Hamoir EE, Hartstein GM, Meurisse MR, Hubert BM, Charlier CJ, Lamy ML. Hemodynamic changes and catecholamine release during laparoscopic adrenalectomy for pheochromocytoma. Anesthesia & Analgesia. 1999 Jan 1;88(1):16-21.
9. Joris JL, Chiche JD, Canivet JL, Jacquet NJ, Legros JJ, Lamy ML. Hemodynamic changes induced by laparoscopy and their endocrine correlates: effects of clonidine. Journal of the American College of Cardiology. 1998 Nov 1; 32(5):1389-96.
10. Laisalmi M, Koivusalo AM, Valta P, Tikkanen I, Lindgren L. Clonidine provides opioid-sparing effect, stable hemodynamics, and renal integrity during laparoscopic cholecystectomy. Surgical endoscopy. 2001 Nov;15:1331-5.
11. Sharma A, Kumar NJ, Azharuddin M, Mohan LC, Ramachandran G. Evaluation of low-dose dexmedetomidine and neostigmine with bupivacaine for postoperative analgesia in orthopedic surgeries: a prospective randomized double-blind study. Journal of Anaesthesiology Clinical Pharmacology. 2016 Apr 1;32(2):187-91.
12. Harless M, Depp C, Collins S, Hewer I. Role of Esmolol in Perioperative Analgesia and Anesthesia: A Literature Review. AANA journal. 2015 Jun 1;83(3).
13. Srivastava VK, Nagle V, Agrawal S, Kumar D, Verma A, Kedia S. Comparative evaluation of dexmedetomidine and esmolol on hemodynamic responses during laparoscopic cholecystectomy. Journal of clinical and diagnostic research: JCDR. 2015 Mar; 9(3): UC01.
14. Joris JL. Anesthetic management of laparoscopy. Anesthesia.. 1994:2011-29.
15. O'leary E, Hubbard K, Tormey W, Cunningham AJ. Laparoscopic cholecystectomy: haemodynamic and neuroendocrine responses after pneumoperitoneum and changes in position. British journal of anaesthesia. 1996 May 1;76 (5):640-4.
16. Cunningham AJ, Brull SJ. Laparoscopic Cholecystectomy: Anesthetic implications. Anaesth Analg. 1993; 76: 1120–33.
17. Jean LJ. Anaesthesia for Laparoscopic surgery. In: Miller RD, editor. Anesthesia. 7th ed. New York: Churchill Livingstone; 2010. pp. 2185–202.

18. Mann C, Boccara G, Pouzeratte Y, Eliet J, Serradel-Le Gal C, Vergnes C, et al. The relationship among carbon dioxide pneumoperitoneum, vasopressin release, and haemodynamic changes. Anesth Analg. 1999; 89(2):278–83.
19. Talke P, Richardson CA, Scheinin M, Fisher DM. Postoperative pharmacokinetics and sympatholytic effects of dexmedetomidine. Anesth Analg. 1997; 85: 1136–42.
20. Talke P, Chen R, Thomas B, Aggarwall A, Gottlieb A, Thorborg P. The haemodynamic and adrenergic effects of perioperative dexmedetomidine infusion after vascular surgery. Anesth Analg. 2000; 90(4):834–39. Talke P, Lobo E, Brown R. Systemically administeredalpha2-agonist-induced peripheral vasoconstriction in humans. Anesthesiology. 2003;99:65–70.
21. Bhutia MP, Arti A. Attenuation of Haemodynamic Parameters in Response to Pneumoperitoneum during Laparoscopic Cholecystectomy: A Randomized Controlled Trial Comparing Infusions of Propofol and Dexmedetomidine J Clin Diagn Res. 2017; 11(5): UC01– UC04.
22. Manne GR, Upadhyay MR, Swadia VN. Effects of low dose dexmedetomidine infusion on haemodynamic stress response, sedation and post-operative analgesia requirement in patients undergoing laparoscopic cholecys tectomy. Indian J Anaesth. 2014;58:726–31
23. Bhattacharjee DP, Nayek SK, Dawn S, Bandopadhyay G, Gupta K. Effects of dexmeditomidine on haemodynamics in patients undergoing laparoscopic cholecystectomy - A comparative study. J Anaesth Clin Pharmacol 2010;2: 45- 8.