



Evaluation of Effect of Infusion of Dexmedetomidine on Attenuation of Hemodynamic Response During Laparoscopic Surgeries

Authors

Dr S.D.Yennawar¹, Dr Nazima Y Memon², Dr N.K Nandanwankar³

^{1,3}Associate Professor, ²Assistant Professor, Department of Anaesthesiology
Dr Shankarrao Chavan Government Medical College, Vishnupuri, Nanded (MS) India

Corresponding Author

Dr Nazima Y Memon

Assistant Professor, Department of Anaesthesiology

Dr Shankarrao Chavan Government Medical College, Vishnupuri, Nanded (MS) India

Abstract

Background: *Laparoscopic Surgeries have recently gained much popularity because of its minimal invasiveness and fast recovery. These surgeries require creation of Pneumoperitoneum with carbon dioxide which results in undesirable hemodynamic effects. To overcome these effects various drugs have been tried. Recently dexmedetomidine, a selective α -2 agonist, is used for same purpose. Various studies have found that use of dexmedetomidine is associated with blunting of haemodynamic instability associated with creation of Pneumoperitoneum for the purpose of laparoscopic surgeries.*

Aims and Objectives: *The purpose of the study was (1) To study the effect of dexmedetomidine on attenuation of hemodynamic responses associated with Pneumoperitoneum during laparoscopic surgeries (2) To study the incidence of adverse effects like bradycardia, hypotension, and Postoperative nausea and vomiting (3) To study the effect on postoperative pain relief.*

Material and Methods: *The study included 60 patients of ASA grade I/II divided into two groups, Group A (n=30) Patients received Dexmedetomidine infusion 1mcg/kg/min over 10 minutes prior to induction followed by dexmedetomidine infusion at 0.3 mcg/kg/min till end of surgery. Group B (n=30) received normal saline infusion at same rate.*

Conclusion: *Patients receiving dexmedetomidine infusion had better hemodynamic profile without any significant side effects than patient receiving saline infusion. Also the requirement of analgesic in postoperative period was reduced significantly in dexmedetomidine group. Moreover incidence of adverse effects like bradycardia, hypotension and Postoperative vomiting was considerably less in patients who received dexmedetomidine.*

Keywords: *Laparoscopic surgery, Pneumoperitoneum, Dexmedetomidine, hemodynamic response.*

Introduction

Laparoscopic Surgery was first introduced by Philip Mouret in 1987^[1]. Since then it has gained immense popularity. The laparoscopic interventions may include diagnostic laparoscopy and

therapeutic laparoscopic surgeries. The diagnostic laparoscopic procedures may include suspected acute appendicitis, localization of undescended testis, metastatic carcinoma, gynecological conditions, pancreatic malignancies, abdominal

kochs and perforated peptic ulcer disease. Common therapeutic surgeries done laparoscopically include cholecystectomy, adrenalectomy for pheochromocytoma, pyeloplasty, appendicectomy and peritoneal lymph nodes dissection in various malignancies^[2].

The benefits of laparoscopic surgery include minimal invasiveness which causes less pain, early mobilization, shorter hospital stay and better cosmetic results^[3]. On the other hand these surgeries are complicated and hence require a prolonged learning curve. There is increase in average time for surgery and hence may cause surgeons' fatigue. The most important problem associated with these surgeries from an anesthetists' perspective is hemodynamic instability of the patient during laparoscopic surgeries^[4]. The mean arterial pressure generally decreases after induction of anaesthesia but there is increase in MAP after peritoneal insufflation. There is an increased risk of cardiac dysfunction in patients in whom cardiac function is already compromised to some extent^[5]. In obese patients Pneumoperitoneum creation during laparoscopic surgeries is fraught with the danger of diastolic dysfunction. Gas insufflation causes raised intra-abdominal pressure followed by pooling of blood from splanchnic circulation to systemic circulation which causes increased venous return followed by increased cardiac output. The systemic vascular resistance is increased not only due to increased abdominal pain but also because of an increase in the release of circulating catecholamines. The increasing systemic vascular resistance, raised blood pressures and tachycardia results in a increase in myocardial workload^[6]. This increased workload may eventually cause hypotension which is more pronounced in patients who have pre-existing cardiovascular disease. The other systemic involvement in laparoscopic surgeries due to gas insufflation includes respiratory affection in the form of airway collapse, atelectasis, ventilation-perfusion mismatch, hypoxemia and hypercarbia^[7]. Renal impairment in the form of reduced GFR may be

seen. Raised intracranial pressure and decreased cerebral perfusion pressure may also be seen following gas insufflations to create Pneumoperitoneum for the purpose of laparoscopic surgeries^[8].

Many drugs like nitroglycerine, esmolol, fentanyl, propofol, and alpha-2-adrenergics have been tried to overcome hemodynamic perturbations during laparoscopy. Dexmedetomidine is a recently introduced alpha-2-adrenergic agonist, which has affected the perioperative pain management considerably^[9]. It is a sedative drug, having significant analgesic, opioid sparing and sympatholytic property, without causing significant respiratory depression. Since the distribution half life of dexmedetomidine is short (6 minutes) it can be effectively used in short procedures like laryngoscopy. It can be used as a useful adjuvant to general anaesthesia in laparoscopic procedures, diagnostic and therapeutic surgeries as well^[10]. We conducted this study to evaluate the effect of dexmedetomidine infusion on attenuation of hemodynamic response during laparoscopic surgeries.

Aims and Objectives

1. **Primary outcome:** Attenuation of hemodynamic response for laparoscopic surgeries.
2. **Secondary outcome:** (i) Attenuation of hemodynamic response of laryngoscopy and intubation. (ii) Postoperative pain relief.

Materials and Methods

This was a double blind randomized case control study. After approval from institutional Ethical Committee and written informed consent from the patients, the present study was carried out in 60 patients, belonging to ASA I/II, undergoing laparoscopic appendicectomy and cholecystectomy. All surgeries were performed under general anesthesia. The patients were divided in 2 groups:

The patients were divided in 2 groups:

Group A: 30 patients receiving Dexmedetomidine 1 mcg/kg bolus in 50 ml NS over 10 min prior to induction followed by Dexmedetomidine 0.3mcg/kg/min till end of surgery.

Group B: 30 patients receiving 50 ml normal saline over 10 min.

Following details were noted in the given proforma.

1. Demographic Profile

Age of the patient (b) Sex (c) ASA (d) Height of the patient (e) Weight of the patient (f) Type of surgery (g) Duration of surgery (h) Types of surgeries.

2. Relevant Observations related to the study

Perioperative heart rate Monitoring. (b)

Perioperative blood pressure monitoring. (c)

Postoperative VAS Score Monitoring. (d)

Sedation Score Monitoring (e) Adverse Effects

Inclusion Criteria:

1. ASA I/II patients.
2. Age of patient- 18 to 50 years
3. Patients undergoing elective Laparoscopic surgery.
4. Surgery lasting for 2 hours.

Exclusion criteria

1. ASA III or more
2. Emergency Surgery
3. Pregnant patient
4. Patient with difficult airway
5. Patient with known allergy of the drug
6. Obese patient (BMI > 35)

Routine Monitoring was done with NIBP, SpO₂, Respiratory rate, ECG and EtCO₂ monitoring. All patients received general anesthesia. All patients were premedicated with IV Glycopyrrolate 0.2 mg, IV Midazolam 1 mg, IV Pentazocine 30 mg and IV Ondansetron 4 mg. The study drug (Dexmedetomidine or normal saline) was started @ 1mcg/kg over 10 min followed by 0.3mcg/kg/min.. Induction was done with IV Propofol and IV Scoline 100mg. Maintenance of general anesthesia was done with oxygen, nitrous oxide and sevoflurane as inhalational agents. IV Vecuronium was used as muscle relaxant. Vital

parameters (mainly MAP, Heart rate and SpO₂) and Postoperative VAS Score were noted at following timings: Baseline, after infusion, after intubation, 10 minutes after creation of Pneumoperitoneum, every 10 minutes till the end of surgery, after extubation, every hourly for 4 hours, and then 4 hourly till end of surgery. Postoperative pain relief was assessed with VAS score. Rescue analgesia was given in the form of IV Dynapar 75 mg when VAS Score > 4. Sedation was assessed in postoperative period by 6 point Ramsay Sedation Scale:

1 = Anxious or agitated and restless or both.

2 = Cooperative, oriented and tranquil.

3 = Drowsy but responds to commands.

4 = Asleep, brisk response to light glabellar tap or loud auditory stimulus.

5 = Asleep, sluggish response to light glabellar tap or loud auditory stimulus.

6 = Asleep and unarousable.

Sedation score >3 was considered an undue sedation. The results of the study were subjected to statistical analysis. Statistical tests were performed using Statistical Package for the Social Sciences software, version 12.0 (SPSS Inc., Chicago, Illinois, USA). *t-test* was used to compare the study group and the control group. Paired *t-test* was used to compare the variables before and after the intervention. Chi-square test was used to analyze the categorical data and for testing the association between the variables. For comparison of continuous data such as hemodynamic parameters, ANOVA test was used. The results were expressed as mean \pm 0 standard deviation (SD). $p < 0.05$ was considered as significant.

Observation and Results

The present study was conducted on 60 ASA grade I & II patients who were scheduled for elective laparoscopic surgeries under general anesthesia.

Demographic Data

The analysis of demographic data of both the groups revealed that the mean age of patients was

33.96 years and 36.06 years in Group A and Group B respectively. The difference was not statistically significant. In group A 14 males and 16 females were present while group B consisted of 17 males and 13 females. The mean weight was 52.4 and 54.2 in group A and B respectively. While the mean height was 152 cms and 151 cms in group A and Group B respectively [Table 1]

Table 1: demographic data in group A and Group B.

	Group A (n = 30)	Group B (n=30)	p value	Significan t
Mean age	33.96 ± 8.41	36.06	> 0.05	No
Sex	14/16	17/13	> 0.05	No
Mean weight	52.4 +/- 4.52 Kg	54.2 +/- 5.48 kg	> 0.05	No
Mean Height	152 +/- 10 cms	151 +/- 9 cms	> 0.05	No

Amongst the studied cases out of 30 patients belonging to group A (Dexmedetomidine Group) 10 (33.33%) patients underwent laparoscopic cholecystectomy while 20 (66.66%) patients underwent laparoscopic appendectomy. While in group B 8 (26.66%) patients underwent laparoscopic cholecystectomy and 22 (73.33%) patients underwent laparoscopic appendectomy. The common indications for laparoscopic cholecystectomy were cholelithiasis and chronic cholecystitis [Figure 1].

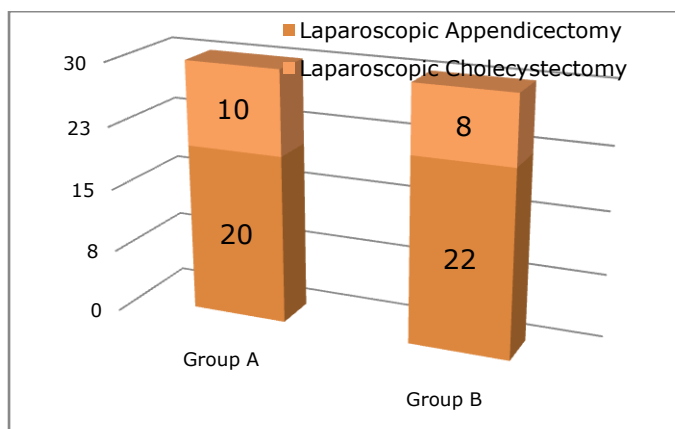


Figure 1: Type of surgeries done in both the groups

The average duration of the surgery was 102 +/- 21 minutes in group A while the duration of surgery in group B was 98 +/- 18 minutes. The average duration of Pneumoperitoneum in Group A and B was 60 +/- 22 minutes and 56 +/- 20 minutes respectively. The P value in both these cases was found to be more than 0.05 (Not significant) [Figure 2].

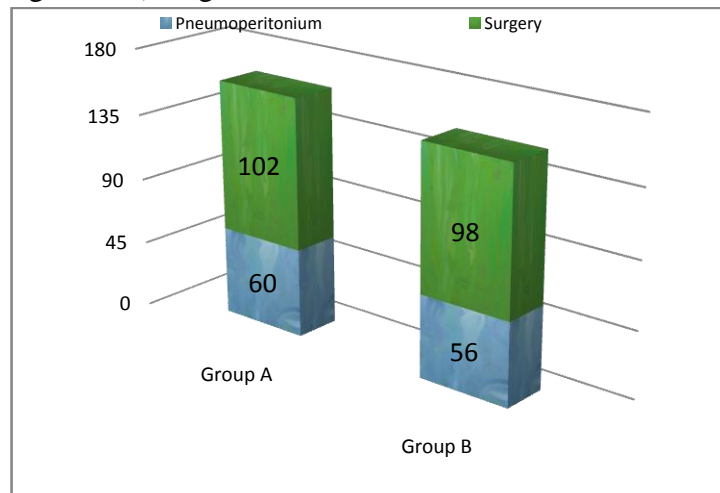


Figure 2: Graph showing duration of Pneumoperitoneum and surgery in group A and Group B respectively.

Vital parameters during surgery:

The study of vital parameters like heart rate, systolic blood pressure, diastolic blood pressure and mean arterial pressure was done. All these vital parameters were noted during study and scatter diagrams were made [Figure 3].

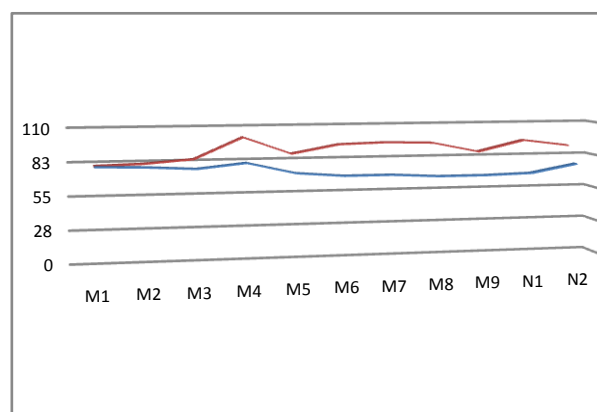


Figure 3: Graph Showing Heart rate during various phases of surgery in Group A and Group B

The analysis of the heart rate during surgery revealed that heart rate increased in group B increased significantly when compared to group A

after intubation, before Pneumoperitoneum, 5, 10 and 20 minutes after Pneumoperitoneum, at the end of Pneumoperitoneum and eventually after reversal of neuromuscular blockade and 1 hour post-operatively. During other phases of surgery heart rate was considerably less in group A than in group B. One patient in Group A had bradycardia which was easily treated with IV Atropine 0.6mg. Dexmedetomidine does not appear to have any direct effects on the heart. A biphasic cardiovascular response has been described after the application of Dexmedetomidine. The administration of a bolus of Dexmedetomidine initially results in a transient increase of the blood pressure and a reflex decrease in heart rate, especially in younger, healthy patients.

The analysis of systolic blood pressure was done. The values of systolic blood pressure during different phases of surgery were determined. The values were analyzed by plotting them on scatter diagram [Figure 4].

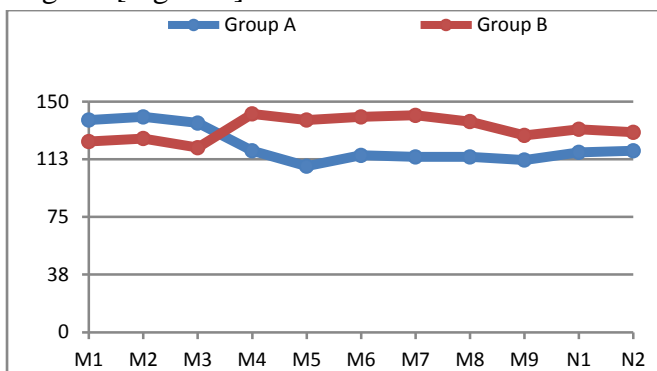


Figure 4: Graph showing systolic blood pressure during various phases of surgery in Group A and Group B.

The analysis of systolic blood pressure showed significantly higher levels of systolic blood pressures in group B. Initially there was an increase in systolic blood pressure after administration of Dexmedetomidine but during later stages of surgery the systolic blood pressure was decreased. This increase in systolic blood pressure in group B was more evident at induction, after intubation, before and after pneumoperitoium (5, 10 and 20 minutes), before reversal of neuromuscular blockade and 1 hour postoperatively. The analysis of the difference of

systolic blood pressure in group A and group B showed that the difference of systolic blood pressure was statistically significant ($P < 0.05$). The initial response lasts for 10-15 minutes and was followed by a decrease in blood pressure of approximately 15% to 20% below baseline and a stabilization of the heart rate, also below baseline values; both of these effects were seen due to inhibition of the central sympathetic outflow overriding the direct stimulating effects.

The analysis of diastolic blood pressure during various stage of was done which showed significant increase in diastolic blood pressure at various levels especially at induction, after intubation, before and after Pneumoperitoneum, at the end of Pneumoperitoneum, after reversal of neuromuscular blockade and 1 hour postoperatively. The analysis of these values showed that the difference was statistically significant ($P < 0.05$). The values of diastolic blood pressure were lower in Dexmedetomidine group probably due to inhibition of the central sympathetic outflow [Figure 5].

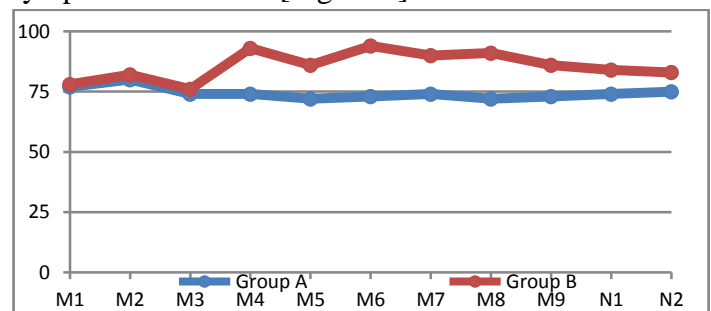


Figure 5: Graph showing diastolic blood pressure during various phases of surgery in Group A and Group B.

Finally an analysis of mean arterial pressure between group A and group B during various stages of surgery was done. It showed a significant increase in mean arterial pressure in group B when compared to group A at induction, after intubation, before and after Pneumoperitoneum, after reversal of neuromuscular blockade and 1 hour postoperatively. The analysis of the difference in mean arterial pressures of these 2 groups showed that the difference of MAP was statistically significant ($P < 0.05$) [Figure 6].

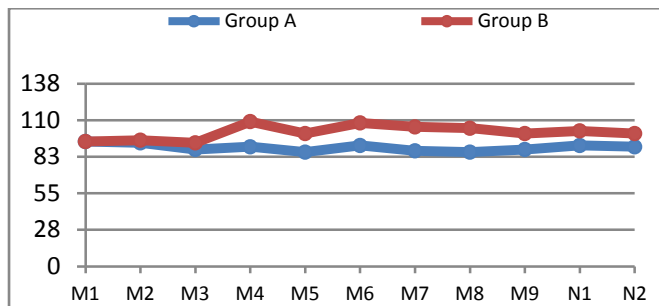


Figure 6: Graph showing mean arterial pressure during various phases of surgery in Group A and Group B.

The analysis of need to give analgesics in Group A and Group B revealed that there was a statistically significant difference between average requirements of analgesics in post-operative period in these 2 groups. The average requirement of analgesic was 110 +/- 42 mg and 180 +/- 70 mg in Group A and Group B respectively. The statistical analysis showed this difference to be significant ($P < 0.05$) [Figure 7].

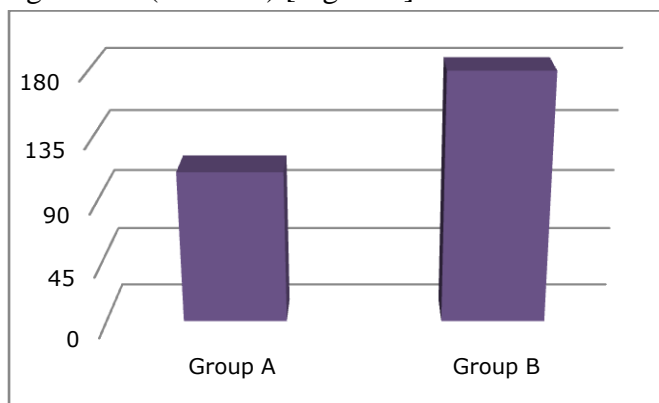


Figure 7: Requirement of analgesic in group A and Group B.

Postoperative pain relief

Postoperative pain relief was assessed by VAS Score at 0,2,4,6,8,12,16,20,24 and also by requirement of rescue analgesic in postoperative period. VAS Score was much reduced in Dexmedetomidine group with early mobility and early discharge. Requirement of rescue analgesic was reduced in Dexmedetomidine group by 50-60% as compared to saline group.

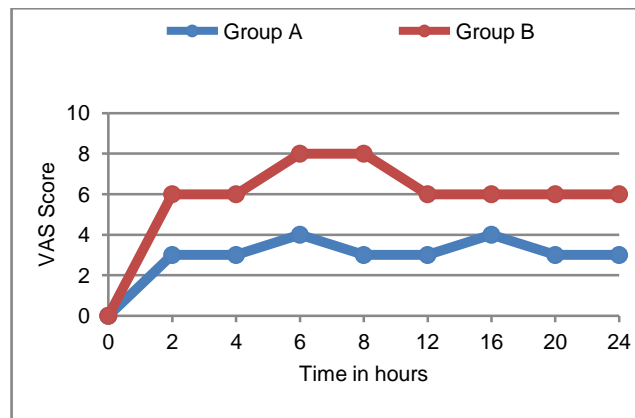


Figure 8 : Graph showing postoperative VAS score in Group A and Group B.

Incidence of complications

The use of IV Dexmedetomidine was associated with decrease in heart rate and decrease in blood pressure which was easily managed by iv atropine and iv fluids. Tachycardia, hypertension and arrhythmias were common in saline group. Sedation observed in patients receiving Dexmedetomidine but patient was comfortable and easily arousable.

Table 2: Incidence of complications in Group A & Group B

	Group A (n=30)	Group B (n=30)
Bradycardia	1	0
Hypotension	1	0
Tachycardia	0	10
Arrhythmias(Ventricular premature beats)	0	1
Hypertension	0	8
Postoperative nausea and vomiting	1	2
Sedation	3	0

Discussion

Pneumoperitoneum created during laparoscopic surgeries cause increase in systemic vascular resistance and blood pressure simultaneously [11]. Pneumoperitoneum causes increase in intra-abdominal pressure which decreases venous return. Consequent to a decrease in venous return there is reduction in preload which causes reduction in cardiac output. All these changes are responsible for increase in heart rate, mean arterial

pressure and systemic vascular resistance^[12]. These hemodynamic changes can produce significant stress in patients undergoing laparoscopic surgery. Patients with pre-existing co-morbid conditions and cardiovascular disorders are more prone for developing exaggerated hemodynamic instability in patients undergoing laparoscopic surgeries^[13]. Cephalad displacement of diaphragm causes decrease vital capacity decreased functional reserve capacity and increased intrathoracic pressure. These changes again are responsible for pulmonary complications^[14]. An awareness of such an eventuality in these patients is essential for successful anesthetic management of patients.

Dexmedetomidine is an imidazole compound having selective α_2 adrenergic receptor agonistic action. It is eight times more specific for α_2 receptors than clonidine (α_2 : α_1 ratio for Dexmedetomidine is 1620:1 and that of clonidine is 220:1). It induces sedation by decreasing activity of noradrenergic neurons in the locus ceruleus in the brain stem, thereby increasing the activity of inhibitory gamma-aminobutyric acid (GABA) neurons in the ventrolateral preoptic nucleus. It has an analgesic effect at the level of spinal cord and higher centres. It is notable for its ability to provide sedation without risk of significant respiratory depression. Many studies have proved that the use of Dexmedetomidine was associated with reduced ICU stay and time of extubation^[15].

Dexmedetomidine causes potentiating of anesthetic effects of all intraoperative anesthetic agents regardless of the method of administration. α_2 adrenergic receptors mediated action is found to be responsible for this significant reduction in anesthetic requirement. In their study Buhner M et al found that Dexmedetomidine decreases thiopental dose requirement by 15-30% . They found this effect due to Dexmedetomidine-induced decrease in thiopental distribution volume and distribution clearances. They finally concluded that Dexmedetomidine reduces thiopental

distribution most probably by decreasing cardiac output and regional blood flow^[16].

The hemodynamic effects of Dexmedetomidine are due to central sympatholytic and peripheral vasoconstrictive effects. It causes a dose dependent decrease in heart rate, systolic blood pressure and a decrease in serum norepinephrine concentrations. The mechanism of action of Dexmedetomidine at central nervous system level is by activation of receptors in the medullary vasomotor center, reducing norepinephrine turnover and decreasing central sympathetic outflow. All these changes are responsible for alterations in sympathetic function, thereby suppressing the hemodynamic response to intubation, extubation without any side effects like respiratory depression and post-operative nausea and vomiting^[17].

In patients undergoing general or gynecological surgery, numerous studies have shown that Dexmedetomidine blunts the cardiovascular responses to intubation. Dexmedetomidine is found to be useful for maintenance of anesthesia in patients anesthetized with thiopental, fentanyl, nitrous oxide, and oxygen. It was also found to reduce the requirement of isoflurane by > 90%. The heart rate response to endotracheal intubation was also found to be significantly blunted^[18].

In their study Lawrence and De Lange found that a single dose of 2 $\mu\text{g}/\text{kg}$ of Dexmedetomidine before induction of anesthesia was responsible for attenuation of hemodynamic response to intubation and extubation. This drug related cardiovascular side effects were related to dosage and the speed of administration of the drug. Similar to our study, other studies demonstrated that Dexmedetomidine attenuates sympathoadrenal response to tracheal intubation, reduces perioperative anesthetic requirement and maintains hemodynamic stability^[19].

As in our study the need for administration of post-operative analgesics is also found to be reduced in various studies. A recent double-blind randomized clinical trial conducted by Dong-Jian Ge et al concluded that intraoperative

Dexmedetomidine promotes postoperative analgesia and recovery in patients after abdominal hysterectomy. They further concluded that no differences were observed in postoperative adverse effects between the two groups during the first 24 hours. The patients who received Dexmedetomidine suffered less adverse effects, such as nausea, vomiting, than those in the saline group^[20].

Conclusion

Use of Dexmedetomidine during laparoscopic surgeries was associated with better hemodynamic profile without any significant side effects. The requirement of analgesic in postoperative period was reduced significantly in Dexmedetomidine group. Use of Dexmedetomidine was associated with reduced recovery time. Moreover incidence of adverse effects like bradycardia, hypotension and Postoperative nausea and vomiting was considerably less in patients who received Dexmedetomidine.

Conflict of Interest: None

References

1. Blum CA, Adams DB. Who did the first laparoscopic cholecystectomy? *Journal of Minimal Access Surgery*. 2011;7(3):165-168.
2. Litynski GS. Profiles in laparoscopy: Mouret, Dubois, and Perissat: The laparoscopic breakthrough in Europe (1987-1988) *JLS*. 1999;3:163-7
3. Bruhat MA, Chapron C, Mage G, Pouly JL, Canis M, Wattiez A, Glowaczower E. The benefits and risks of laparoscopic surgery]. *Rev Fr Gynecol Obstet*. 1993 Feb;88(2):84-8
4. Pisarska M, Pędziwiatr M, Budzyński A. Perioperative hemodynamic instability in patients undergoing laparoscopic adrenalectomy for pheochromocytoma. *Gland Surgery*. 2016;5(5):506-511.
5. Sadhu S, Sarkar S, Jahangir TA, et al. Laparoscopic Cholecystectomy in Patients with Cardiac Dysfunction. *The Indian Journal of Surgery*. 2011;73(2):90-95.
6. Srivastava A, Niranjana A. Secrets of safe laparoscopic surgery: Anaesthetic and surgical considerations. *Journal of Minimal Access Surgery*. 2010;6(4):91-94.
7. Sha M, Kohno M, Yamagami J, Fujiwara Y, Hiroshima N, Kitahara M, Yamauchi K, Ohmura A. [Pulmonary complications following laparoscopic cholecystectomy in patients with abnormal spirometry]. *Masui*. 2001 Dec;50(12):1332-6.
8. Josephs LG, Este-McDonald JR, Birkett DH, Hirsch EF. Diagnostic laparoscopy increases intracranial pressure. *J Trauma*. 1994 Jun;36(6):815-8;
9. Gertler R, Brown HC, Mitchell DH, Silvius EN. Dexmedetomidine: a novel sedative-analgesic agent. *Proceedings (Baylor University Medical Center)*. 2001;14(1):13-21.
10. Kaur M, Singh PM. Current role of dexmedetomidine in clinical anesthesia and intensive care. *Anesthesia, Essays and Researches*. 2011;5(2):128-133.
11. Nguyen NT, Wolfe BM. The Physiologic Effects of Pneumoperitoneum in the Morbidly Obese. *Annals of Surgery*. 2005;241(2):219-226.
12. Perugini RA, Callery MP. Complications of laparoscopic surgery. In: Holzheimer RG, Mannick JA, editors. *Surgical Treatment: Evidence-Based and Problem-Oriented*. Munich: Zuckschwerdt; 2001.
13. Speicher PJ, Ganapathi AM, Englum BR, Vaslef SN. Laparoscopy is safe among patients with congestive heart failure undergoing general surgery procedures. *Surgery*. 2014;156(2):371-378.
14. Ntutumu R, Liu H, Zhen L, et al. Risk factors for pulmonary complications following laparoscopic gastrectomy: A

- single-center study. Zhang. L, ed. *Medicine*. 2016;95(32):e4567.
15. Constantin JM, Momon A, Mantz J, Payen JF, De Jonghe B, Perbet S, Cayot S, Chanques G, Perreira B. Efficacy and safety of sedation with dexmedetomidine in critical care patients: a meta-analysis of randomized controlled trials. *Anaesth Crit Care Pain Med*. 2016 Feb;35(1):7-15.
 16. Bühner M, Mappes A, Lauber R, Stanski DR, Maitre PO. Dexmedetomidine decreases thiopental dose requirement and alters distribution pharmacokinetics. *Anesthesiology*. 1994 Jun;80 (6):1216-27.
 17. Hunter JC, Fontana DJ, Hedley LR, Jasper JR, Lewis R, Link RE, Secchi R, Sutton J, Eglen RM. Assessment of the role of alpha 2-adrenoceptor subtypes in the antinociceptive, sedative and hypothermic action of dexmedetomidine in transgenic mice. *Br J Pharmacol*. 1997;122:1339–1344.
 18. Aantaa R, Jaakola ML, Kallio A, Kanto J. Reduction of the minimum alveolar concentration of isoflurane by dexmedetomidine. *Anesthesiology*. 1997 May;86(5):1055-60.
 19. Lawrence CJ, De Lange S. Effects of a single pre-operative dexmedetomidine dose on isoflurane requirements and peri-operative haemodynamic stability. *Anaesthesia*. 1997 Aug;52(8):736-44.
 20. Ge D-J, Qi B, Tang G, Li J-Y. Intraoperative Dexmedetomidine Promotes Postoperative Analgesia and Recovery in Patients after Abdominal Hysterectomy: a Double-Blind, Randomized Clinical Trial. *Scientific Reports*. 2016;6:21514.