Original Research Article

A study to compare the efficacy of dexmedetomidine with esmolol on hemodynamic response during laparoscopic cholecystectomy

Maskuri Soujanya[1], Nama Nagarjuna Chakravarthy[2*], G. Venkateshwarlu[3]

[1]Post Graduate, [2]Assistant Professor, [3]HOD and Professor
Department of Anesthesiology, Gandhi Medical College, Secunderabad, Telangana, India
[*]Corresponding author email: **drnag.cn@gmail.com**

International Archives of Integrated Medicine, Vol. 5, Issue 8, August, 2018.
Copy right © 2018, IAIM, All Rights Reserved.
Available online at http://iaimjournal.com/
ISSN: 2394-0026 (P) **ISSN: 2394-0034 (O)**
Received on: 12-07-2017 **Accepted on:** 17-07-2017
Source of support: Nil **Conflict of interest:** None declared.
How to cite this article: Maskuri Soujanya, Nama Nagarjuna Chakravarthy, G. Venkateshwarlu. A study to compare the efficacy of dexmedetomidine with esmolol on hemodynamic response during laparoscopic cholecystectomy. IAIM, 2018; 5(8): 17-29.

Abstract

Introduction: Laparoscopic surgery is a routinely performed surgery and it is desirable to have stable intra-operative hemodynamic states by avoiding hypertension and tachycardia. Various drugs have been employed to attenuate this hemodynamic response. No single drug is satisfactory. Thus there is a need to find a simple efficient and reliably consistent method.

Aim: The present study was undertaken to evaluate the comparison of Dexmedetomidine and Esmolol on perioperative hemodynamic response during laparoscopic cholecystectomy.

Materials and methods: Prospective, randomized, controlled, single blinded trial comparing dexmedetomidine (alpha 2- agonist) and esmolol (beta 1-antagonist) done by allocating into two groups. It was conducted in 60 patients of both sex, belong to ASA I and ASA II of age group 20-60 years admitted for laparoscopic surgery from 2016-2017. They were randomly divided into two groups of 30 patients each. The Heart rate (HR), Systolic blood pressure (SBP), Diastolic blood pressure (DBP), Mean arterial pressure (MAP) were recorded prior to induction, after the induction, after the intubation, 15 min, 30 min, 45 min, 60 min after creation of pneumoperitoneum, post pneumoperitoneum, after extubation.

Results: Heart rate and systolic blood pressure were significantly lower in Group A after induction, after intubation, and maintained throughout intraoperative and postoperative period compared to

Group B. Diastolic blood pressure were significantly lower in Group A after intubation, and maintained throughout intraoperative period and at extubation compared to Group B. Diastolic blood pressure was not significant after induction, at postoperative period. Mean blood pressure were significantly lower in Group A after induction, after intubation, and maintained throughout intraoperative period and at extubation compared to Group B. Mean blood pressure were not significant at postoperative period.

Conclusion: Dexmedetomidine is more effective agent than esmolol in maintaining stable hemodynamics during and after pneumoperitoneum in laparoscopic cholecystectomy.

Key words

Laparoscopic surgeries, Dexmedetomidine, Esmolol, Cholecystectomy.

Introduction

Laparoscopic surgeries involve insufflation of a CO2 gas into the peritoneal cavity producing a pneumoperitoneum. This causes an increase in intra-abdominal pressure. Carbondioxide is insufflated into the peritoneal cavity at the rate of 4-6 lit/min to a pressure of 10-15 mm of Hg. The pneumoperitoneum is maintained by a constant gas flow of 200-400 mL/min. Peritoneal insufflation induces alterations of hemodynamics, characterized by decrease in stroke volume and cardiac output, elevation of mean arterial pressure, and increase of systemic and pulmonary vascular resistance. Hemodynamic changes are accentuated in high-risk cardiac patients [1].

General anesthesia has been supplemented on occasions with intraoperative infusions of propofol due to its intrinsic ability to inhibit catecholamine secretion, infusions of nitroglycerine or beta blockers to control perioperative stress. Again combined GA with epidural anesthesia is yet another strategy employed by anesthesiologists to control perioperative hemodynamic instability, with limited success. But the search for the ideal agent to control this instability in hemodynamics is still on. The pathophysiological hemodynamic changes can be attenuated or prevented by optimizing preload before pneumoperitoneum and by vasodilating agents, α_2-adrenergic receptor agonists, high doses of opioids, and β blockers [2].

Alpha 2 agonists produce diverse responses including analgesia, anxiolysis, sedation and sympatholysis, each of which has been reported in the treatment of surgical and chronic pain patients and in panic disorders as well. The food and drug administration (FDA) registered novel alpha-2 adrenergic agonists Dexmedetomidine.

The α2 agonists dexmedetomidine decrease central sympathetic outflow and modify intraoperative cardiovascular responses to surgical stimuli and laryngoscopy. The reduction in tachycardia, hypertension and sympathetic activity may be of benefit in patients at risk of myocardial ischemia.

Dexmedetomidine is an α2 adrenergic receptor agonist with high selectivity for the alpha2 receptor (α2 to α1 1620:1) and it is seven to ten times more selective for α2 receptors compared to clonidine, and has a shorter duration of action with a elimination half-life of 2-3 hours. Dexmedetomidine is considered full agonist at α2 receptors as compared to clonidine, which is considered as a partial agonist. Dexmedetomidine also attenuates the hemodynamic response to tracheal intubation, decreases plasma catecholamine concentration during anesthesia and decreases perioperative requirement of inhaled anesthetics.

Dexmedetomidine has analgesic, anxiolytic, sedative and sympatholytic properties. It might be useful adjunct for premedication, especially for patients susceptible to preoperative and

perioperative stress. The hypnotic response is probably mediated by activation of the α2 adrenoreceptors. The α2 adrenergic mechanism causes dose-dependent reduction in blood pressure (BP) and heart rate (HR). Dexmedetomidine is proved to have antinociceptive effects and reduce the neurohumoral properties. These properties render dexmedetomidine an ideal preanesthetic medication for surgical procedures. Esmolol is a rapid onset, short acting selective beta-1 adrenergic antagonist. While it inhibits β_1 receptors of myocardium, it also inhibits β_2 receptors of smooth muscles of bronchial and vascular walls at higher doses. Dose is 0.5-2 mg/kg. It is effective in blunting the increase in systolic blood pressure and heart rate, which occurs during tracheal intubation [2]. Elimination half-life is around 9 minutes [3].

Materials and methods

Prospective, randomized, controlled, single blinded study was conducted in Department of Anesthesiology and Critical Care, Gandhi Hospital, Secunderabad from 2016 to 2017 on 60 patients aged between 20-60 years posted for elective laparoscopic cholecystectomy. The purpose of study was to compare the efficacy of dexmedetomidine with esmolol on hemodynamic response to pneumoperitoneum during laparoscopic cholecystectomy. Sixty patients who fulfill the following criteria were included in the study.

Inclusion criteria: Age group 20-60 years undergoing laparoscopic cholecystectomy of both 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.

Patients selected were explained regarding the surgical procedure, anesthesia and drugs to be used in their own language. A written informed consent was obtained in each case.

Total Sixty patients (N=60) were divided into two groups group A (dexmedetomidine n=30), group B (esmolol n=30) were taken.

Preoperative period

Pre-anesthetic evaluation was done on the evening before surgery with complete history, clinical, airway and systemic examination of cardiovascular and respiratory system was done.

All patients underwent the baseline investigations as complete hemogram, Blood urea and serum creatinine, Liver function tests, TFT, Chest X-ray PA view, Serum electrolytes, HIV and HbSAg viral screening.

All the selected patients were allocated into two groups consisting of 30 patients each. Blinding was done by using SNOSE (sequentially numbered opaque sealed envelope) technique.

Group - A (Dexmedetomidine + Standard Procedure) – in this group, patients received a loading dose of 1microgram/kg of dexmedetomidine over a period of 15 minutes (15 minutes before induction), followed by maintenance with 0.5 microgram/kg/hr throughout pneumoperitoneum.

Group-B (Esmolol+Standard Procedure) - in this group, patients received a loading dose of 1mg/kg of esmolol over a period of 5 minutes (5 minutes before induction), followed by maintenance with 0.5 mg/kg/hr throughout pneumoperitoneum. All patients included in the study were kept nil orally 10 pm onwards on the previous night.

On arrival of patient in the operating room, an 18 gauge intravenous cannula was secured and an infusion of ringer lactate was started. The patients were connected to multiparameter monitor that records heart rate, noninvasive measurement of SBP, DBP, MAP, EtCO2 and continuous ECG monitoring and oxygen saturation. The baseline systolic, diastolic blood pressure, mean arterial pressure and heart rate

were recorded. The cardiac rate and rhythm were also monitored from a continuous visual display of electrocardiogram from lead II. All patients were premedicated intravenously 15 min prior to induction with inj. midazolam 0.05 mg/kg, inj. ondansetron 0.1 mg/kg, inj. fentanyl 1.5 microgm/kg and inj. glycopyrrolate 0.2 mg.

In the group A, dexmedetomidine 1 microgm/kg was given 15 min prior to induction followed by maintained with 0.5 microgm/kg/hr throughout pneumoperitoneum. In the group B esmolol 1mg/kg was given 5mim prior to induction followed by maintained with 0.5mg/kg/hr throughout pneumoperitoneum.

The patients were preoxygenated with 100% O2 by face mask for 3min. Induction was done with inj. propofol 2mg/kg and after 30sec relaxation achieved with inj. succinyl choline 2mg/kg 90sec later the patient was intubated using a macintosh laryngoscope. Tracheal tubes of 7.0 mm and 8.5 mm were used for female and male patients respectively. Anesthesia was maintained by N_2O (60%) and O_2 (40%). Intermittent boluses of vecuronium bromide intravenously. Closed circuit with sodalime was used. Most of the laparoscopic cholecystectomy surgeries are last from one and half hour to two hours.

- Intra abdominal pressure was restricted to 10-14 mmHg.
- Atropine was kept ready to counter the bradycardia, and Ionotropes were kept ready to counter any untoward hypotension.

At the end of surgery, neuromuscular blockade was reversed with inj. neostigmine (40microgm/kg) and inj. glycopyrrolate (10microgm/kg).

The recordings were noted at various intervals as Preoperative, after induction, after intubation15 min, 30 min, 45 min, 60 min after creation of pneumoperitoneum, post pneumoperitoneum, post-operative period after 15 min.

EtCO2 recordings were noted after intubation, 15 min, 30 min, 45 min, 60 min after pneumoperitoneum and at post pneumoperitoneum.

Descriptive statistical analysis had been carried out in the present study. Results on continuous measurements were presented on Mean ± SD and results on categorical measurements were presented in Number. Student t test (two tailed, independent) had been used to find the significance of study parameters on continuous scale between two groups (Inter group analysis) on metric parameters. Fisher Exact test has been used to find the significance of study parameters on categorical scale between two or more groups.

Significant figures

- Significant (P value: P< 0.05)
- Highly significant (P value: P<0.01)

Statistical software

The Statistical software namely Graphpad was used for the analysis of the data and Microsoft word and Excel have been used to generate graphs, tables etc.

Results

The average age was 35.86 years in group A and 36.2 years in group B. Youngest patient in the study group was 28 years and oldest was 48 years. The average weights of the patients were 55.53 in group A and 56.63 in group B respectively. There was no significant difference in age and weight between the two groups. There was no significant difference in gender between the two groups (**Table – 1**).

Hemodynamic parameters

Statistical analysis of changes in heart rate at preoperatively, after induction, after intubation and different time intervals after creation of pneumoperitoneum are presented. The preoperative values of heart rate (HR) were comparable between the two groups with no significant difference. The heart rate was significantly less in dexmedetomidine group throughout study time compared with the esmolol group (**Figure – 1**).

Table - 1: Comparison of Demographic distribution between the groups (N=30).

	Group A	**Group B**	**P Value A And B**
Mean Age (Years)	35.86±4.73	36.2±4.49	0.77
Weight (Kg)	55.53±10.36	56.63±10.63	0.6863
Male/Female	15/15	16/14	1

Figure - 1: Comparison of heart rate.

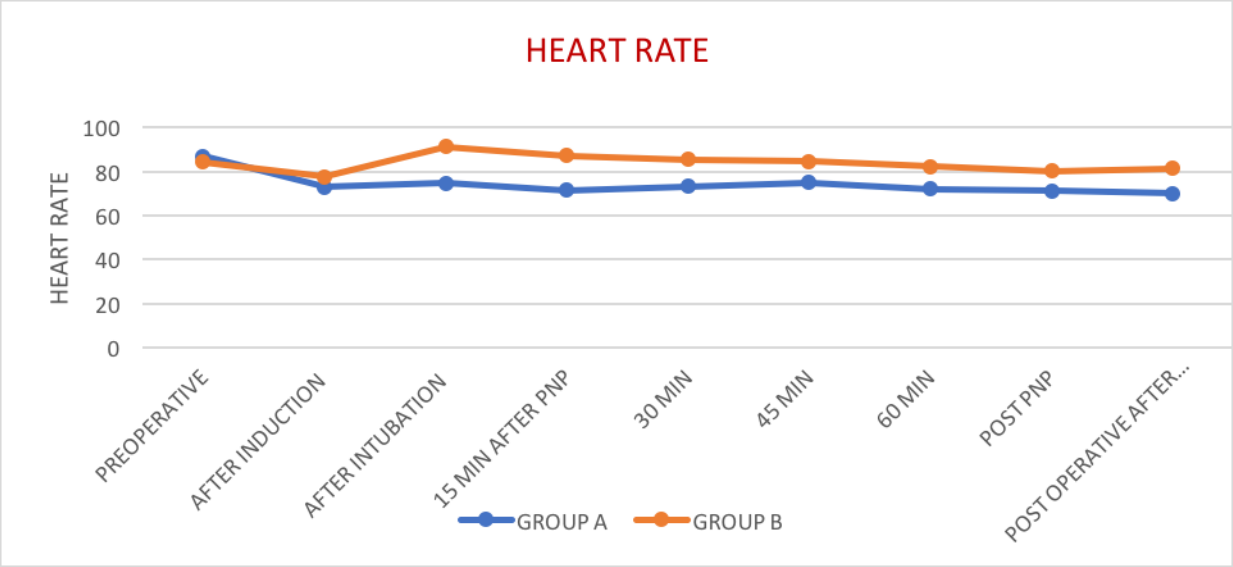
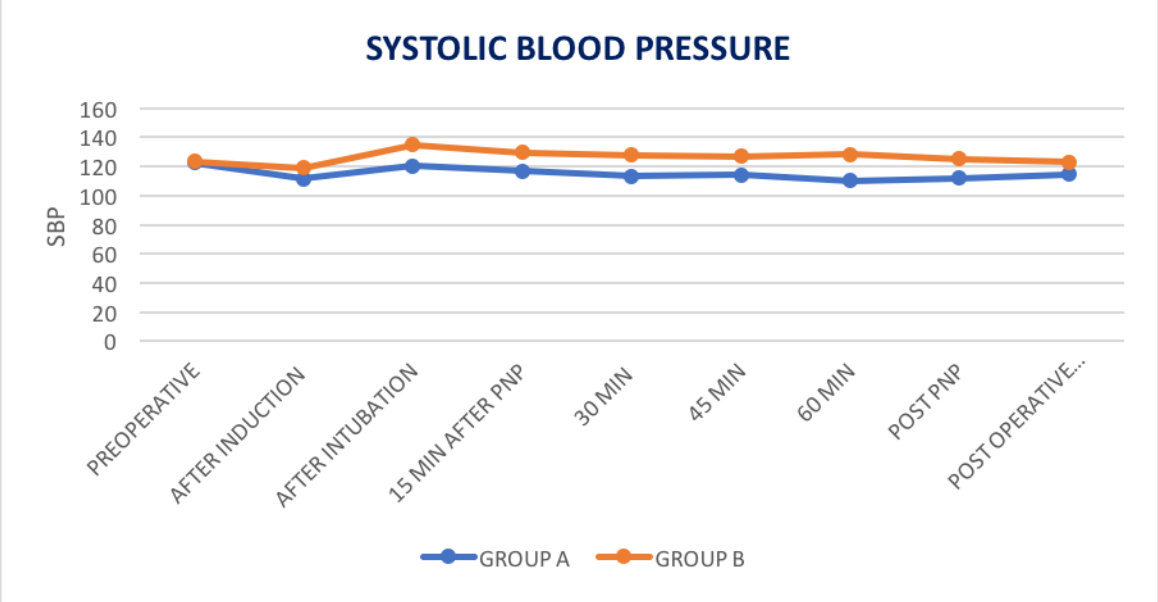


Figure - 2: Comparison of systolic blood pressure.



Statistical analysis of changes in systolic blood pressure at preoperatively, after induction, after intubation and different time intervals after creation of pneumoperitoneum were presented. The preoperative values of systolic blood pressure (SBP) were comparable between the two groups with no significant difference. The systolic blood pressure was significantly less in dexmedetomidine group throughout study time compared with the esmolol group (**Figure – 2**).

Figure - 3: Comparison of diastolic blood pressure.

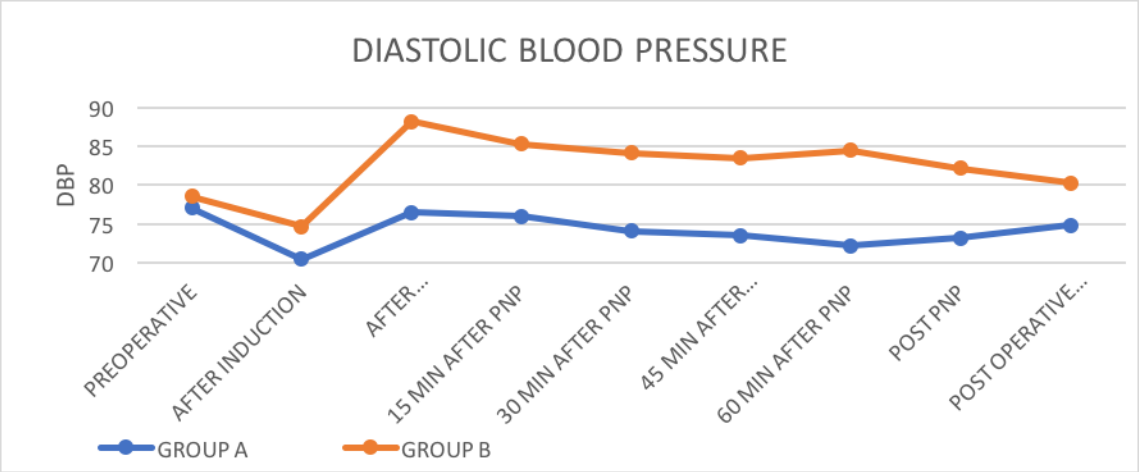


Figure - 4: Comparison of mean arterial pressure.

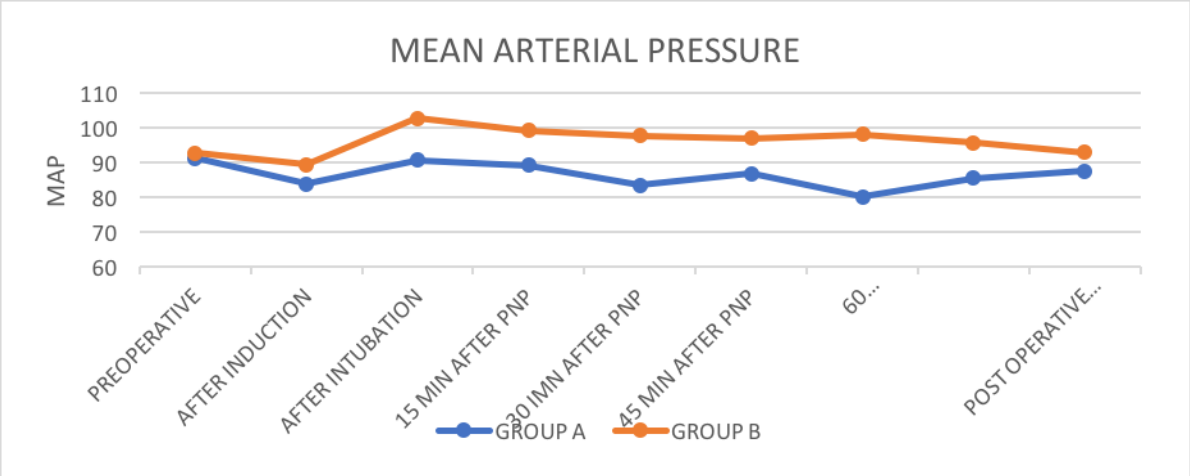


Table - 2: Comparison of endotracheal CO2 between two groups.

ETCO2	Group A (Mean±SD)	Group B (Mean±SD)	P value
After intubation	33.3±3.13	34.3±2.99	0.21
15 min after PNP	36.53±3.29	37.53±1.75	0.147
30 min after PNP	38.06±1.89	38.33±1.15	0.506
45 min after PNP	37.13±2.3	36.9±2.27	0.698
60 min after PNP	35.96±2.63	36.26±2.75	0.667
Post PNP	32.2±2.08	31.7±1.6	0.301

Table - 3: Comparison of adverse effects between two groups.

	Hypotension	No Adverse Effect	P Value
Group A	3	27	0.2373
Group B	0	30	

Table - 4: Use of other drugs in both the groups.

	Use of other drugs	No use of other drugs	P value
Group A	0	30	**0.4915**
Group B	2	28	

The preoperative values of diastolic blood pressure (DBP) were comparable between the two groups with no significant difference. The diastolic blood pressure were significantly less in dexmedetomidine group throughout study time compared with the esmolol group and not significant after induction (0.08) and at postoperatively after 15 min (p=0.0517) as per **Figure - 3**.

The preoperative values of mean arterial pressure (MAP) were comparable between the two groups with no significant difference. The mean arterial pressure were significantly less in dexmedetomidine group throughout study time compared with the esmolol group and MAP was not significant postoperatively after 15 min (p=0.075) as per **Figure - 4**.

ETCO2: Endotracheal CO2 was recorded as it was influencing the hemodynamic parameters like heart rate, systolic blood pressure, diastolic blood pressure and mean arterial pressure. ETCO2 was maintained between 30-40 mm of Hg (**Table – 2**).

In Group A, only three patients out of thirty had hypotension in the intraoperative period. No such adverse effect was seen in Group B. there were no other adverse effects observed. This analysis was done by using Fisher's exact test which provided a P value of 0.2373 which was clinically not significant (**Table – 3**).

Only two patients in Group B developed hypertension during pneumoperitoneum which was managed with nitroglycerine infusion. Statistical analysis was done by using Fisher's exact test which provided a P value of 0.4915 which was clinically not significant (**Table – 4**).

Discussion

In laparoscopic surgery, CO_2 is routinely used to create pneumoperitoneum. Elevated intra-abdominal pressure induced by pneumoperitoneum and CO_2 itself produce some adverse effects on the cardiovascular system.

Immediately after pneumoperitoneum, plasma level of norepinephrine, epinephrine and plasma renin activity is increased. Increased catecholamine level activates the renin-angiotensin-aldosterone-system (RAAS) leading to hemodynamic alterations, which include:

- Decreased cardiac output (25-35%)
- Elevated mean arterial pressure.
- Increased systemic / pulmonary vascular resistance.

Laparoscopic cholecystectomy is performed in reverse Trendelenburg position. This particular position causes diminished venous return which ultimately leads to further decrease in cardiac output. Normal heart can cope with the increase in afterload under physiologic conditions. But patients with compromised cardiac function may not be able to tolerate the changes in afterload produced by pneumoperitoneum and it may have deleterious effects on their hemodynamics. Pneumoperitoneum used for laparoscopic procedures is a complex pathophysiologic phase with significant hemodynamic variation.

CO_2 is most commonly used as it is colorless, non-combustible, highly soluble and permeable in tissues thus reducing the risk of gas embolism. There is marked increase of vasopressin and plasma catecholamines, 5 mins after the beginning of pneumoperitoneum, Plasma concentration of vasopressin then decreased. The vasopressin levels were in line with the changes in SVR.

Dexmedetomidine, a highly selective α2 receptor agonist, provides excellent sedation and analgesia with minimal respiratory depression. Esmolol, an ultra short-acting cardio-selective β1- receptor antagonist having little sedative effect, but no analgesic activity. The pharmacologic profiles and anesthetic sparing effects of dexmedetomidine and esmolol suggested that these drugs could be a suitable anesthetic adjuvant for attenuating acute intraoperative hemodynamic stress responses in laparoscopic cholecystectomy without interfering with the recovery process.

Informed consent was obtained from all the patients. Patients with hypertension, cardiopulmonary problems, morbid obesity, with renal insufficiency and hepatic insufficiency are excluded from study. A total of 60 patients within the age group of 20 – 60 years were included in study with 30 in each group. Heart rate (HR), Systolic blood pressure (SBP), diastolic blood pressure (DBP), mean arterial pressure(MAP) were recorded preoperative, after induction, after intubation, 15 min, 30 min, 45min, 60min after pneumoperitoneum, post pneumoperitoneum and post-operative period after 15 min were noted.

Laparoscopic cholecystectomy is a minimally invasive surgery. Pneumoperitoneum using CO2 for laparoscopic surgery causes a rapid and immediate increase in plasma catecholamines and vasopressin, due to increase in intraperitoneal pressure and stimulation of peritoneum by CO2. The increase in these stress hormones induces a cardiovascular response characterized by abrupt elevations of arterial pressure, SVR and HR. The increase in these hemodynamic values significantly increases the incidence of myocardial ischemia, infarction and causes increased intracranial pressure and increased intraocular pressure.

To attenuate this hemodynamic response, a wide variety of agents are being used both during premedication and induction. Research fellows have tried beta blockers, α2 agonists, magnesium sulfate, opioids, vasodilators, and gasless approach to negate the hemodynamic variations. Previous studies report that dexmedetomidine infusion rates ranging from 0.2 to 10 mcg/kg/hr have been used. The studies with higher dose had more incidences of hypotension and bradycardia.

Most studies used dexmedetomidine loading dose 1 mcg/kg over 10-15 minutes followed by continuous infusion 0.2 to 0.5 mcg/kg/hr for maintenance and concluded that dexmedetomidine attenuates the increase in heart rate and blood pressure by altering the stress-induced sympathoadrenal response. In this study, we also used dexmedetomidine loading dose 1 mcg/kg over 15 minutes, followed by maintenance dose 0.5 mcg/kg/hr, which is similar to the dose used in above mentioned studies.

Beta adrenergic receptor antagonists have also been used by various authors during surgery with intention to attenuate the stress response and decrease the unwanted perioperative hemodynamic response. The effect of esmolol on hemodynamic response to CO_2 pnuemoperitoneum is mediated by blockade of peripheral beta adrenergic receptors.

However studies to compare the dexmedetomidine with esmolol are lacking. The average age was 35.86 years in group A and 36.2 years in group B. The average weights of the patients were 55.53 in group A and 56.63 in group B respectively. There was no significant difference in age and weight between the two groups. There was no significant difference in gender between the two groups.

Hemodynamic parameters

The preoperative values of heart rate (HR) were comparable between the two groups of group A 86.96±8.21 and group B 84.16±9.92 with no significant difference. The heart rate were significantly less in dexmedetomidine group throughout study time compared with the esmolol group (p= <0.05).

Kalpana S. Vora, et al. [4], conducted a randomized blind study consists of a total of 70 patients ASA I or II scheduled for elective laparoscopic surgeries were received bolus infusion of dexmedetomidine (group D) or saline (group S) 1 mcg/kg/hr, followed by continuous infusion of same, at the rate of 0.5 mcg/kg/hr. baseline mean HR was not significant between two groups (p >0.05). There was a significant reduction in HR following the loading dose of dexmedetomidine, after intubation, after 20 min of pneumoperitoneum, after 60 min of pneumoperitoneum, after infusion was stopped,

after extubation, in group D as compared to group S.

Nandlal Bhagat, et al. [5], conducted a randomized single blind study with 120 patients of ASA I and II who underwent laparoscopic cholecystectomy. Patients were randomly divided into two groups (group D and group N). Prior to induction group D received 1 mcg/kg of dexmedetomidine and group N received normal saline infusion over 20 minutes. Dexmedetomidine 0.5 mcg/kg/hr in group D and volume matched NS in group N was continued throughout the surgery. Heart rate decreased intraoperatively by 5.7% from the baseline in group D while it increased in group N by 16% from baseline ($p < 0.0001$).

Ritima Dhir, et al. [6], conducted a randomized study consisting of 60 patients of ASA I and II of either sex scheduled for laparoscopic cholecystectomy. Patients were divided into two groups. Group E received esmolol loading dose 0.5 mg/kg in 30 ml isotonic saline before induction followed by infusion of 0.05 mcg/kg/min till the completion of surgery. Group C patients received 30ml of isotonic saline as loading dose and continuous infusion till completion of surgery. The baseline HR at 0 min was almost similar in both the groups. At 8^{th} minute (time of intubation) HR increased significantly in group C as compared to group E and remained higher than group E till the end of surgery. Only 10% of patients in group E showed statistically significant ($p=0.004$) increase in intraoperative HR as compared with 86.67% in group C.

Dhurjoti Prosad Bhattacharjee, et al. [7], conducted a randomized single blind placebo controlled study consisting of 60 patients of either sex undergoing laparoscopic cholecystectomy, were randomly allocated into three groups containing twenty patients each. group E received bolus dose of 500 mcg/kg IV esmolol before pneumoperitoneum followed by infusion of 100mcg/kg/min. group D received bolus dose of 1mcg/kg IV dexmedetomidine before pneumoperitoneum followed by infusion of 0.2 mcg/kg/hr. group S received saline 0.9%. There is no significant difference was found between the preoperative HR and the HR values following intubation and before pneumoperitoneum among all three groups ($p > 0.05$). However, following pneumoperitoneum, HR values in group E and group D were significantly lower compared to group S at 10, 20, 30, 40, and 50 min after pneumoperitoneum, following the release of CO2 and after extubation ($p < 0.05$). On comparing patients in group E and group D, no significant difference in HR was found at any interval.

Vinit K. Srivastava, et al. [8], conducted a prospective randomized study consisting of 90 patients of ASA I or II of either sex scheduled for laparoscopic cholecystectomy. Group D received loading dose of 1mcg/kg of dexmedetomidine before induction followed by maintenance of 0.5 mcg/kg/hr. group E received esmolol loading dose of 1mg/kg before induction followed by maintenance of 0.5 mg/kg/hr. group C received same volume of normal saline. There was no significant difference in preoperative HR between the groups. After administration of study drugs, there was a significant decrease in heart rate in group D ($p < 0.05$). Intubation and pneumoperitoneum caused an increase in the heart rate in the group E ($p < 0.05$), comparison to preoperative values, however this increase was not seen in group D ($p > 0.05$).

Systolic blood pressure

The preoperative values of systolic blood pressure (SBP) in group A 122.53±4.23 and in group B 123.46±6.05 with no significant difference. The systolic blood pressure were significantly less in dexmedetomidine group throughout study time compared with the esmolol group ($p < 0.05$).

Poonam S Ghodki, et al. [9], in their study of 30 patients of, ASA I and II, aged 18 to 50 years of either gender undergoing laparoscopic surgeries received loading dose infusion of dexmedetomidine 1mcg/kg over 15 min and

maintenance infusion of 0.2mcg/kg/hr. Mean systolic blood pressure (SBP) to start with was 125 and fell to 113 with loading dose of Dex (p=0.009) after that minimal change was observed for entire duration of infusion.

Rajdip Hazra, et al. [10], in their study found that group D received dexmedetomidine 1mcg/kg over 15 min before induction, those were scheduled for elective laparoscopic cholecystyectomy. Group K (Control group) received same volume of normal saline. Systolic arterial pressure was significantly higher in group K specially after intubation, at P30 and after extubation.

Nupur chakravorty, et al. [11], conducted a randomized study with patients undergoing elective laparoscopic cholecystectomy. Group E received esmolol 2 mg/kg before extubation. The systolic blood pressure was significantly low before and after extubation compared to group N.

Vinit K. Srivastava, et al. [8], conducted a prospective randomized study consisting of 90 patients of ASA I or II of either sex scheduled for laparoscopic cholecystectomy. Group D received loading dose of 1mcg/kg of dexmedetomidine before induction followed by maintenance of 0.5 mcg/kg/hr. group E received esmolol loading dose of 1mg/kg before induction followed by maintenance of 0.5 mg/kg/hr. group C received same volume of normal saline. SBP values were statistically significantly lower in the group D after induction, intubation and all time observations of pneumoperitoneum, when compared with the group E ($p < 0.001$). In group E, there was a statistically significant increase after intubation and during pneumoperitoneum period. In group D there was no statistically significant increase after intubation and at any time intervals of pneumoperitoneum.

Diastolic blood pressure

The preoperative values of diastolic blood pressure (DBP) in group A 77.03±8.43 and in group B 78.56±6.56 with no significant difference. The diastolic blood pressure were significantly less in dexmedetomidine group throughout study time compared with the esmolol group and not significant after induction (0.08) and at postoperatively after 15 min (p=0.0517).

Rajdip Hazra, et al. [10], in their study found that group D received dexmedetomidine 1mcg/kg over 15 min before induction, those were scheduled for elective laparoscopic cholecystyectomy. Group K (Control group) received same volume of normal saline. The diastolic blood pressure was significantly higher in group K specially after intubation, at P20, P30 and after extubation. It was significantly lower in group D.

Vinit K. Srivastava, et al. [8], conducted a prospective randomized study consisting of 90 patients of ASA I or II of either sex scheduled for laparoscopic cholecystectomy. Group D received loading dose of 1mcg/kg of dexmedetomidine before induction followed by maintenance of 0.5 mcg/kg/hr. group E received esmolol loading dose of 1mg/kg before induction followed by maintenance of 0.5mg/kg/hr. group C received same volume of normal saline. DBP values were statistically significantly lower in the group D after induction, intubation and all time observations of pneumoperitoneum, when compared with the group E ($p < 0.001$). In group E, there was a statistically significant increase after intubation and during pneumoperitoneum period. In group D there was no statistically significant increase after intubation and at any time intervals of pneumoperitoneum.

Mean arterial pressure

The preoperative values of mean arterial pressure (MAP) in group A 91.17±5.8 and group B 92.6±5.08 with no significant difference. The mean arterial pressure were significantly less in dexmedetomidine group throughout study time compared with the esmolol group and MAP was not significant postoperatively after 15 min ($p > 0.05$).

Kalpana S. Vora, et al. [4] conducted a randomized blind study consists of a total of 70 patients ASA I or II scheduled for elective laparoscopic surgeries were received bolus infusion of dexmedetomidine (group D) or saline (group S) 1mcg/kg/hr, followed by continuous infusion of same, at the rate of 0.5 mcg/kg/hr. Baseline MAP was not significant between two groups ($p>0.05$). Decrease in MAP was found after loading dose, after intubation, after 20 min of pneumoperitoneum, after 60 min of pneumoperitoneum, after infusion stopped, after extubation, in group D compared to group S, which was significant ($p<0.05$).

Rabie Soliman, et al. [12], conducted a study including 80 cardiac patients with ASA III-IV scheduled for elective laparoscopic cholecystectomy. The patients were randomly classified into two groups. Group D patients received a loading dose of 1 mcg/kg dexmedetomodine over 15 min before induction and maintained with 0.3 mcg/kg/hr infusion during the procedure. Group B received equal amount of normal saline. The mean arterial blood pressure was increased greatly after induction in the group C compared with the group D ($P<0.05$) and remained elevated during the procedures and post anesthesia care unit. There was attack of hypertension included 5 patients in group D and 14 patients in group C ($p=0.035$).

Ritima Dhir, et al. [13], conducted a randomized study consisting of 60 patients of ASA I and II of either sex scheduled for laparoscopic cholecystectomy. Patients were divided into two groups. Group E received esmolol loading dose 0.5 mg/kg in 30 ml isotonic saline before induction followed by infusion of 0.05 mcg/kg/min till the completion of surgery. Group C patients received 30 ml of isotonic saline as loading dose and continuous infusion till completion of surgery. The baseline MAP at 0 min was almost similar in both the groups. At 8^{th} minute (time of intubation) MAP increased significantly in group C as compared to group E and remained higher than group E till the end of surgery. Only 6.67% of patients in group E showed statistically significant increase in intraoperative MAP as compared with 80% in group C.

Dhurjoti Prosad Bhattacharjee, et al. [7], conducted a randomized single blind placebo controlled study consisting of 60 patients of either sex undergoing laparoscopic cholecystectomy, were randomly allocated into three groups containing twenty patients each. Group E received bolus dose of 500 mcg/kg IV esmolol before pneumoperitoneum followed by infusion of 100 mcg/kg/min. group D received bolus dose of 1mcg/kg IV dexmedetomidine before pneumoperitoneum followed by infusion of 0.2 mcg/kg/hr. group S received saline 0.9%. There is no significant difference was found between the preoperative MAP and the MAP values following intubation and before pneumoperitoneum among all three groups ($p >0.05$). However, following pneumoperitoneum, MAP values in group E and group D were significantly lower compared to group S at 10, 20, 30, 40, and 50 min after pneumoperitoneum, following the release of CO_2 and after extubation ($p <0.05$). On comparing patients in group E and group D, no significant difference in MAP was found at any interval.

Vinit K. Srivastava, et al. [8], conducted a prospective randomized study consisting of 90 patients of ASA I or II of either sex scheduled for laparoscopic cholecystectomy. Group D received loading dose of 1mcg/kg of dexmedetomidine before induction followed by maintenance of 0.5 mcg/kg/hr. group E received esmolol loading dose of 1mg/kg before induction followed by maintenance of 0.5mg/kg/hr. group C received same volume of normal saline. MAP values were statistically significantly lower in the group D compared to group E after intubation, all time observations of pneumoperitoneum, post pneumoperitoneum and post-operative period ($p<0.001$). There was no significant increase in MAP in group D, compared to preoperative values at any time intervals of pneumoperitoneum, while it was a significant

increase in group E during pneumoperitoneum ($p<0.05$).

Conclusion

To conclude, Dexmedetomidine (1 mcg/kg followed by 0.5 mcg/kg/hr) is more effective agent than esmolol (1 mg/kg followed by 0.5 mg/kg/hr) in maintaining stable hemodynamics during and after pneumoperitoneum in laparoscopic cholecystectomy with significant P values in all variables. Only three patients in group Dexmedetomidine had hypotension as adverse effect. It was managed by fluid boluses and vasopressors. Only two patients in group esmolol developed hypertensive response during pneumoperitoneum. It was managed with nitroglycerine infusion.

References

1. Wittgen CM, Andrus CH, Fitzgerald SD, et al. Analysis of the hemodynamic and ventilatory effects of laparoscopic cholecystectomy. Arch Surg., 1991; 126(8): 997-1001.
2. Ronald D. Miller. Miller's anesthesia laparoscopic cholecystectomy, 7th edition, New York; Churchill Livingstone; chaper 68, 2010.
3. Figueredo E, Garcia-Fuentes EM. Assessment of the efficacy of esmolol on the hemodynamic changes induced by laryngoscopy and tracheal intubation: a meta-analysis. Acta Anaesthesiol Scand., 2001; 45: 1011–22.
4. Vora KS, Baranda U, Shah VR, Modi M, Parikh GP, Butala BP. The effects of dexmedetomidine on attenuation of hemodynamic changes and there effects as adjuvant in anesthesia during laparoscopic surgeries. Saudi J Anaesth., 2015; 9: 386-392.
5. Nandlal B, Yunus M, Habib MR, Ranendra H, Prithwis B, Manorama S. Dexmedetomidine in attenuation of hemodynamic response and dose sparing effect on opioid and anesthetic agents in patients undergoing laparoscopic cholecystectomy - A randomized study. J Clin Diagn Res., Nov 2016; 10(11): UC01-UC05.
6. Ritima D, Mirley RS, Tej KK, et al. Effect of intravenous esmolol on analgesic requirements in laparoscopic cholecystectomy. J Anaesthesiol Clin Pharmacol., Jul-Sept 2015; 31(3): 375-379.
7. Bhattacharjee DP, et al. effects of dexmedetomidine on hemodynamics. J Anaesth Clin Pharmacol., 2010; 26(1): 45-48.
8. Vinit KS, Vaishali N, Sanjay A, Diwakar K, Amit V, Sunil K. Comparative evaluation of dexmedetomidine and esmolol on hemodynamic responses during laparoscopic cholecystectomy. J Clin Diagn Res., March 2015; 9(3): UC01-UC05.
9. Ghodki PS, Thombre SK, Sardesai SP, Harnagle KD. Dexmedetomidine as an anesthetic adjuvant in laparoscopic surgery: An observational study using entropy monitoring. J Anaesthesiol Clin Pharmacol., 2012; 28: 334-338.
10. Hazra R, Manjunatha SM, Manuar MD, Basu R, Chakraborty S. Comparison of the effects of intravenously administered dexmedetomidine with clonidine on hemodynamic responses during laparoscopic cholecystectomy. Anaesth Pain & Intensive Care, 2014; 18(1): 25-30.
11. Nupur C, Devashish C, et al. Comparison of esmolol and nitroglycerine on hemodynamic parameters during extubtion in obese patients following laparoscopic cholecystectomy: a prospective randomized study. Anaessth, Pain and Intensive Care, Oct-Dec 2015; 19(4).
12. Rabie S, Gomaa Z. Assessment of the effect of dexmedetomidine in high risk cardiac patients undergoing laparoscopic cholecystectomy. Egypt J Anesth., Apr 2016; 32(2): 175-180.

13. Ritima D, Mirley RS, Tej KK, et al. Effect of intravenous esmolol on analgesic requirements in laparoscopic cholecystectomy. J Anaesthesiol Clin Pharmacol., Jul-Sept 2015; 31(3): 375-379.