ISSN: 0975-8585

Research Journal of Pharmaceutical, Biological and Chemical Sciences

A Comparative Evaluation Of Dexmedetomidine And Esmolol On Haemodynamic Responses To Pnuemoperitoneum During Laparoscopic Surgeries.

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ABSTRACT

Laparascopic surgery is a routinely performed surgery and it is desirable to have a stable intraoperative haemodynamic state by avoiding hypertension and tachycardia. Various drugs have been employed to attenuate these hemodynamic responses. No single drug is satisfactory. Thus there is a need to find a simple efficient and reliably consistent method. The aim is to compare the effects of dexmedetomidine and esmolol on haemodynamic responses due to pneumoperitoneum during laparoscopic surgeries. The study prospective, randomized, controlled, single blinded trial conducted in 60 patients of both sex, belong to ASA I and ASA II of age group 20-60 years admitted at Government Medical College, Kallakurichi, Tamil Nadu , India in the year 2023 comparing dexmedetomidine (alpha 2-agonist) and esmolol (beta 1- antagonist) done by allocating into two groups. They were randomly divided into two groups of 30 patients each- Group- D (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 0.5microgram/kg/hr throughout pnuemoperitonium. Group-E (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 0.5mg/kg/hr throughout pnuemoperitonium. Heart rate and systolic blood pressure were significantly lower in Group D after induction, after intubation, and maintained throughout the intraoperative and postoperative period compared to Group E. Diastolic blood pressure were significantly lower in Group D after intubation, and maintained throughout intraoperative period and at extubation compared to Group E. Diastolic blood pressure were not significant after induction, at postoperative period. Mean blood pressure was significantly lower in Group D after induction, after intubation, and maintained throughout intraoperative period and at extubation compared to Group E. Mean blood pressure were not significant at postoperative period. This study concluded that Dexmedetomidine(1mcg/kg followed by 0.5mcg/kg/hr) is more effective agent than esmolol(1mg/kg followed by 0.5mg/kg) in attenuation of hemodynamic response to intubation and reduces the elevation of heart rate, systolic blood pressure, diastolic blood pressure and mean arterial pressure during and after pneumoperitoneum in laparoscopic surgeries.

Keywords: pneumoperitoneum, laparoscopic surgeries, Dexmedetomidine, esmolol

https://doi.org/10.33887/rjpbcs/2024.15.2.31

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ISSN: 0975-8585

INTRODUCTION

Laparoscopic surgeries involve insufflation of a CO2 gas into the peritoneal cavity producing apneumoperitoneum. This causes an increase in intra- abdominal pressure. Carbon dioxide is insufflated into the peritoneal cavity at the rate of 4-6 lit/min to a presnsure of 10-15mm Hg. The pneumoperitoneumis maintained by a constant gas flow of 200-400 mL/min. Peritoneal insufflation induces alterations of haemodynamics, characterized by decrease in stroke volume and cardiac output, elevation of mean arterial pressure, and increase of systemic and pulmonary vascular resistance. Haemodynamic changes are accentuated in high-risk cardiac patients [1]. General anaesthesia has been supplemented on ocassions 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 anaesthesia is yet another strategy employed by anaesthesiologists to control perioperative haemodynamic instability, with limited success. But the search for the ideal agent to control this instability in haemodynamics is still on. The pathophysiologic haemodynamic changes can be attenuated or prevented by optimizing preload before pneumoperitoneum and by vasodilating agents, α2-adrenergic receptor agonists, high doses of opioids, and β blockers.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-3hours.Dexmedetomidineis considered full agonist at α2 receptors as compared to clonidine, which is considered as a partial agonist. 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 has analgesic, anxiolytic, sedative and sympatholytic properties. It might be useful adjunct for premedication, especially for patients susceptible to preoperative and perioperative stress. Dexmedetomidine also attenuates the haemodynamic response to tracheal intubation, decreases plasma catecholamine concentration during anaesthesia and decreases perioperative requirement of inhaled anesthetics. 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 β1 receptors of myocardium, it also inhibits β2 receptors of smooth muscles of bronchial and vascular walls at higher doses.2 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]. Hence, the present study was designed to compare the effects of dexmedetomidine and esmolol on haemodynamic response Pneumoperitoneum during laproscopic surgeries i.e. laproscopic appendectomy, splenectomy, cholecystectomy.

MATERIALS AND METHODS

The study entitled a comparative and prospective evaluation of Dexmedetomidine and Esmolol on haemodynamic responses to Pnuemoperitoneum during Laparoscopic surgeries is undertaken in at Gandhi hospital Secunderabad, after obtaining approval of ethics committee of hospital and with written informed consent to evaluate the efficacy of dexmedetomidine and esmolol on haemodynamic response during laparoscopic surgeries. at Government Medical College, Kallakurichi, Tamil Nadu , India in the year 2023 Sixty patients who fulfill the following criteria were included in the study. The duration of study is one year. Patients were randomly allocated to 2 groups namely D and E.Inclusion criteria were age group of 20-60 years, patients of ASA physical grade I and II undergoing laparoscopic surgeries. Exclusion criteria were patients who underwent emergency surgeries, who had hypertension, who had renal and hepatic insufficiency, patients with cardiac or pulmonary diseases, patients with morbid obesity, hypersensitivity to dexmedetomidine and esmolol. Patients selected were explained regarding the surgical procedure, anaesthesia and drugs to be used in their own language. A written informed consent was obtained in each case. Sixty patients (N=60) were divided into two groups group D (dexmedetomidine n=30), group E (esmolol n=30) were taken. Pre-anaesthetic 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 following investigations such as complete haemogram, blood grouping and typing, bleeding time and clotting time, electrocardiogram, blood urea, serum creatinine, prothrombin time, liver function tests and 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-D (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), followedby maintainence with 0.5microgram/kg/hr throughout pnuemoperitonium. Group-E (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 0.5mg/kg/hr throughout pnuemoperitonium.

All patients included in the study were premedicated with tablet Alprazolam 0.5mg and tablet ranitidine 150mg orally at bed time the previous night before surgery. They were kept nil orally 10pm onwards on the previous night.

Intraoperative Period

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, non-invasive measurement of SBP, DBP, MAP, EtCO2 and continuous ECG monitoring and oxygen saturation. The baselin systolis, 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 0.05mg/kg, inj. ondansetron 0.1mg/kg, inj. fentanyl 1.5microgm/kg and inj. glycopyrrolate 0.2mg. In the group D dexmedetomidine 1microgm/kg was given 15 min prior to induction followed by maintained with 0.5microgm/kg/hr throughout pnuemoperitonium. In the group E esmolol 1mg/kg was given 5mim prior to induction followed by maintained with 0.5mg/kg/hr throughout pnuemoperitonium. 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. Anaesthesia was maintained by N2O (60%) and O2(40%). Intermittent boluses of vecuronium bromide intravenously. Intra-abdominal pressure was restricted to 10-14 mmHg. EtCO2 was maintained below 35 mmHg at any course of the procedure. Atropine was kept ready to counter the bradycardia, and Inotropes 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 parameters recorded were heart rate, systolic blood pressure, diastolic blood pressure & mean arterial pressure. The recordings were noted at various intervals such as pre-operative, after study drug administration, after induction, after intubation, after 15 mins, 30 mins, 45 mins, 60 mins after creation of pneumoperitoneum, post pneumoperitoneum (PP), post-operative period (PO) after 15 mins.

Statistical Analysis

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 P value means $P<0.05$ and highly significant P value means $P<0.01$. The Statistical software namely graph pad was used for the analysis of the data and Microsoft word and Excel have been used to generate graphs, tables etc.

RESULTS

[Table 1] shows that age of the patients in both the groups was comparable. Majority of the patients in both Group D and Group E belonged to 41-50 years age group (40% and 36.7% respectively). In group D, 56.7% of the patients were females, while in Group E 53.3% of the patents were males.[Table 2] shows that the preoperative values of heart rate(HR) were comparable between the two groups with no

significant difference. The heart rate were significantly less in dexmedetomidine group throughout study time compared with the esmolol group.[Table 3] shows that the preoperative values of systolic blood pressure(SBP) were comparable between the two groups with no significant difference. The systolic blood pressure were significantly less in dexmedetomidine group throughout study time compared with the esmolol group. [Table 4] shows that 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 at postoperatively after 15 min(p=0.0517).[Table 5] shows that 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>0.05).[Table 6] shows that In Group D, only three patients out of thirty had hypotension in the intraoperative period. No such adverse effect was seen in Group E. 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 is clinically not significant. [Table 7] shows that Only two patients in Group E 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 is clinically not significant.

Table 1: Distribution based on demographic data such as age, sex.

Age in years	Group D (n=30)	Group E (n=30)
20-30	3 (10%)	4 (13.3%)
31-40	7 (23.3%)	6 (20%)
41-50	12 (40%)	11 (36.7%)
51-60	8 (26.7%)	9 (30%)
Gender	Group D (n=30)	Group E (n=30)
Male	13 (43.3%)	16 (53.3%)
Female	17 (56.7%)	14 (46.7%)
Total	30 (100%)	30 (100%)

Table 2: Haemodynamic Parameters: Comparison of heart rate between two groups

Time interval	Group D (n=30)	Group E (n=30)	p-value
Preoperative	86.65±8.72	85.10±7.65	0.338
After Study Drug	78.09±8.97*	82.21±7.91	<0.05
After Induction	81.34±7.87*	86.03±7.44	<0.05
After Intubation	86.24±8.27	95.38±10.17*	<0.01
P 15	82.38±7.62	91.07±8.20*	<0.001
P 30	81.45±6.04*	90.28±7.97*	<0.001
P 45	80.14±6.77*	92.21±6.40*	<0.001
P 60	78.71±7.23*	91.34±7.06*	<0.001
PP	78.00±10.51*	88.59±6.70	<0.001
PO	77.38±10.74*	87.76±7.18	<0.001

Table 3: Comparison of systolic blood pressure between two groups.

Time interval	Group D (n=30)	Group E (n=30)	p-value
Preoperative	121.54±7.54	122.68±9.71	0.679
After Study Drug	110.28±8.62*	112.10±9.53*	0.022
After Induction	105.42±7.37*	114.21±7.55*	<0.01
After Intubation	123.63± 7.32	137.76±9.17*	<0.001
P 15	116.50±8.51	134.07±7.06*	<0.001
P 30	119.84±7.29	132.93±6.57*	<0.001
P 45	116.72±9.01	134.03±5.92*	<0.001
P 60	118.23±768	136.86±7.35*	<0.001
PP	110.54±8.21*	126.97±6.77	<0.001
PO	116.68±7.53*	120.24±8.11	<0.01

Table 4: Comparison of diastolic blood pressure between two groups.

Time interval	Group D (n=30)	Group E (n=30)	p-value
Preoperative	79.62±8.08	78.55±8.69	0.355
After Study Drug	73.07±7.38*	74.67±8.72	<0.05
After Induction	68.31±6.07*	70.86±7.80*	<0.001
After Intubation	79.07±8.17	89.67±8.02*	<0.001
P 15	75.17±7.34	88.35±7.07*	<0.001
P 30	73.76±8.10	82.97±7.83	<0.001
P 45	73.28±7.31	85.48±8.45*	<0.001
P 60	75.34±7.82	80.52±8.13	<0.01
PP	72.34±5.59*	76.63±7.15	<0.001
PO	68.83±6.12*	73.65±7.85*	<0.001

Table 5: Comparison of mean arterial pressure between two groups.

Time interval	Group D (n=30)	Group E (n=30)	p-value
Preoperative	87.63±9.46	88.72±8.64	0.515
After Study Drug	82.97±7.57*	86.28±6.74	0.024
After Induction	76.41±7.74*	80.24±9.53*	<0.05
After Intubation	90.54±8.62	102.55±8.02*	<0.001
P 15	84.31±6.95	99.07±661*	<0.001
P 30	86.90±7.62	96.14±8.91	<0.001
P 45	83.87±9.54	98.10±7.60*	<0.001
P 60	85.64±8.67	94.45±7.30*	<0.001
PP	82.74±6.65*	89.03±10.19	<0.001
PO	80.65±7.46*	86.59±8.62	<0.01

Table 6: Comparison of adverse effects between two groups.

Adverse effects	Hypotension	No adverse effect	p value
GROUP D	3	27	0.2373
GROUP E	0	30	

Table 7: Use of other drugs in both the groups.

	Use of other drugs	No use of other drugs	p value
GROUP D	0	30	0.4915
GROUP E	2	28	

DISCUSSION

In laparoscopic surgery, CO2 is routinely used to create pneumoperitoneum. Elevated intra-abdominal pressure induced by pneumoperitoneum and CO2 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 some characteristic haemodynamic alterations, which include decreased cardiac output (25-35%), elevated mean arterial pressure, increased systemic or pulmonary vascular resistance. Laparoscopic surgeries are 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 haemodynamics. Pneumoperitoneum used for laparoscopic procedures is a complex patho- physiologic phase with significant hemodynamic variation. CO2 is most commonly used as it is colorless, non-combustible, highly soluble andpermeable in tissues thus reducing the risk of gas embolism. The hemodynamic changes associated with pneumoperitoneum are the result of both increased intra-abdominal pressure and hypercarbia. There is marked increase of vasopressin and plasma catecholamines, 5 mins after the

beginning of pneumoperitoneum, Plasma concentration of vasopressin then decreased. Plasma concentrations of epinephrine, norepinephrine and renin also increased during laparoscopy.

The preoperative values of heart rate (HR) were comparable between the two groups of group D86.65±8.72 and group E 85.10±7.65 with no significant difference. The heart rate were significantly less in dexmedetomidine group throughout study time compared with the esmolol group (p= <0.05) in the present study. Kalpana S. Vora et al [4] conducted a randomized blind study which consisted of a total of 70 patients ASA I or II scheduled for elective laparoscopic surgeries and received bolus infusion of dexmedetomidine (group D) or saline(group S) 1mcg/kg/hr, followed by continuous infusion of same, at the rate of 0.5mcg/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 surgeries. Patients were randomly divided into two groups (group D and group N). Prior to induction group D received 1mcg/kg of dexmedetomidine and group N received normal saline infusion over 20 minutes. Dexmedetomidine 0.5mcg/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 surgeries. Patients were divided into two groups. Group E received esmolol loading dose 0.5mg/kg in 30ml isotonic saline before induction followed by infusion of 0.05mcg/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 8th 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 with86.67% in group C.The preoperative values of systolic blood pressure (SBP) in group D 121.54±7.54 and group E122.68±9.7 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 [7] 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 was125 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 [8] 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. Vinit K. Srivastava et al [9] 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 0.5mcg/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. 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 pnuemoperitonem period. In group D there was no statistically significant increase after intubation and at any time intervals of pneumoperitoneum.

The preoperative values of diastolic blood pressure(DBP) in group D 79.62±8.08 and in group E 78.55±8.69 no significant difference. The diastolic blood pressure was significantly less in dexmedetomidine group throughout study time compared with the esmolol group and not significant at postoperatively after 15 min(p=0.0517).

The preoperative values of mean arterial pressure (MAP) in group D 87.63±9.46 and group E 88.72±8.64 with no significant difference. The mean arterial pressure was 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 0.5mcg/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 [10] 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 dexmedetomidine over 15 mins before induction and maintained with 0.3mcg/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 anaesthesia care unit. There was attack of hypertension included 5 patients in group D and 14 patients in group C(p=0.035).

CONCLUSION

This study concluded that Dexmedetomidine (1mcg/kg followed by 0.5mcg/kg/hr) is more effective agent than esmolol (1mg/kg followed by 0.5mg/kg) in attenuation of hemodynamic response to intubation and reduces the elevation of heart rate, systolic blood pressure, diastolic blood pressure and mean arterial pressure during and after pneumoperitoneum in laparoscopic surgeries.

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