e-ISSN: 0975-1556, p-ISSN:2820-2643
Available online on www.ijpcr.com
International Journal of Pharmaceutical and Clinical Research 2024; 16(8); 698-704

Original Research Article

Comparison of Intravenous Esmolol versus Dexmedetomidine for Attenuation of Hemodynamic Responses during Laryngoscopy and Endotracheal Intubation in Adult Patients Undergoing Laproscopic Surgeries: A Prospective Randomized, Interventional Study in Department of Anesthesia, S.M.S Medical College, Jaipur.

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Received: 25-05-2024 / Revised: 23-06-2024 / Accepted: 25-07-2024
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Conflict of interest: Nil

Abstract:

Context: Direct laryngoscopy and endotracheal intubation directly affect severe sympathoadrenal responses, which increase arterial blood pressure, catecholamine levels, heart rate, and dysrhythmias in some cases.

Aims: This study was aimed to compare the effect of dexmedetomidine and esmolol on hemodynamic response to laryngoscopy and endotracheal intubation in patients undergoing Laparoscopic surgeries under general anaesthesia.

Settings & Designs: Interventional tertiary care hospital based prospective randomised study.

Materials & Methods: A total of 70patients were selected and randomised into two groups. Group A received inj. Dexmedetomidine 0.5mcg/kg IV diluted with 10ml normal saline and injected IV slowly over 10minutes and Group B patients will receive inj. Esmolol bolus 0.5mg/kg diluted to 10 ml. 3minutes after the completion of infusion patients were induced with general anaesthesia Baseline parameters such as heart rate(HR), systolic blood pressure (SBP), diastolic blood pressure (DBP), mean arterial blood pressure(MAP), were recorded before administration of study drugs and at 1,3,5,7, and 10minutes after intubation.

Results: Mean HR, SBP, DBP, MAP values remained significantly lower in Group A than that of Group B at all time intervals up to 10minutes after intubation.

Conclusions: Both drugs suppressed hemodynamic response to intubation, but dexmedetomidine is more effective than esmolol in maintaining hemodynamic stability following laryngoscopy and intubation.

Introduction

Haemodynamic stability is an integral and essential goal of any anaesthetic management plan. Laryngoscopy and intubation are the gold standard for airway management. The induction of anaesthesia, laryngoscopy and endotracheal intubation are associated with mechanical stimulation of the respiratory tract [1] leading to sympatho-adrenal stimulation, which in turn leads to increased plasma norepinephrine concentration which manifest season increase in heart rate, blood pressure and cardiac complications [2] and may evoke life threatening complications. The pressor response during laryngoscopy and intubation was first explained by Reid and Brace in 1940. Yu et al. [3] reported that the tachycardia and hypertension are the main cause of morbidity and mortality in perioperative myocardial infarction (MI). In healthy patients, these sympatho-adrenergic reactions are likely to have minimal clinical-impact. Complications Lichess cerebral haemorrhage, LVF and have been due to an abrupt increase in systemic arterial BP and an increase in pulse rate [4]. These issues are more likely to develop in people who already have Hypertension, CHD, overactive airways, intracranial pathology and cerebral vascular disease. In order to lessen the sun desirable hemodynamic reactions during laryngoscopy and endotracheal intubation, numerous systemic as well as topical medicines are tested. Narcotics, vasodilators, beta blockers, calcium channel blockers, lignocaine and other sympatholytic are among the frequently used techniques. The ideal

agent used for controlled hypotension must have certain characteristics such as a short onset time, rapid elimination without toxic metabolites, easy to administer, an effect that disappears quickly when administration is discontinued, and dose dependent predictable effects.

Esmolol, a rapid-onset, ultrashort-acting, water-soluble, cardio-selective blocker has been added to the anesthesiologist's toolbox to help manage procedures that involve high sympathetic activation like laryngoscopy and endotracheal intubation. Use Of Esmolol is effective blunting pressure response and provides hemodynamic stability in risk patients [5,6]. Esmolol Blocks Theβ-adrenergic receptors and also reduces the force of contraction and heart rate. It has rapid onset of action of bolus IV injection and infusion with Varying doses of esmolol0.5–2mg/kg have been used in the past [7]. Upon termination of infusion gradual recovery of arterial blood pressure to the pre infusion level occurred without development of rebound hypertension. [8]

Dexmedetomidine is a highly specific and selectiveα2 adrenoreceptor agonist. It is currently used for sedation, anxiolysis, and analgesia without respiratory depression.[9] It causes a dose dependent reduction in serum norepinephrine concentration, resulting in decreased heart rate and arterial blood pressure. It has been studied for attenuation of hemodynamic effects after laryngoscopy in different doses (0.5, 0.75 or 1 μg/kg) with promising results. It is currently used in ICU for sedation and analgesia in mechanically ventilated patients and produces rapid recovery after discontinuation. It has been found that minimum alveolar concentration (MAC) of volatile anesthetics also decreases significantly up to90%. Hence decreases the requirement of Inhalation al anesthetics [10] In this study we compare effectiveness of Esmolol and Dexmedetomidine for attenuating the pressure response to laryngoscopy and endotracheal intubation under general anaesthesia with respect to heart rate (HR), SBP, diastolic blood pressure, MAP and RPP. In this study we compared the relative effectiveness of intravenous Esmolol versus Dexmedetomidine for attenuation of stress response following direct laryngoscopy and endotracheal intubation in normal adult patients undergoing laparoscopic surgeries.

Materials and Methods

Following clearance given by Ethics committee, SMS Medical College, and after getting registered in Clinical Trials Registry India (CTRI/2023/06/054104) on June 15, 2023 a prospective and omized interventional study was carried out in operation theater of general surgery in SMS Hospital with the signed informed consent of patient and their relatives for undergoing elective laparoscopic surgeries under general anaesthesia. where in 72 patients were included between the age group of 18 and 60 years, belonging to ASA grade I and II. Patients having history of convulsion and history of allergy to anesthetic agents used in study, anticipated difficult intubation i.e Mallampati class 3 or more were excluded. The sample size calculated at 80% study power and α error of 0.5 assuming standard deviation of 13.2 as main detectable mean difference of 9.5/min. change in heart rate from baseline. The sample size required was 32 cases in each group which was further enhanced and rounded off to 35 cases in each both groups as final sample size expecting 10% loss to follow up/ dropped out/ attrition. Therefore, the study was conducted in two groups having 35 patients each. Group A patients received inj**.** Dexmedetomidine 0.5mcg/kg IV infusion diluted with normal saline to make a total volume of 10 ml and injected IV slowly over 10 minutes and Group B patients received inj. Esmolol bolus 0.5mg/kg diluted to 10 ml and given IV. On arrival of patient in the operation theatre, fasting status, written informed consent and PAC was checked. Routine noninvasive monitors and baseline parameters i.e. ECG (Electrocardiogram), NIBP (non-invasive blood pressure), SPO_2 (pulse oximeter) were attached, and baseline values were recorded. Peripheral Intravenous line was procured in all patients and Infusion of Ringer's lactate started as per the standard calculation of perioperative fluid replacement therapy. Patients were premedicated with Inj. Metoclopramide (0.1mg/kg), inj. Glycopyrrolate (0.004mg/kg) IV and inj. Midazolam (0.01mg/kg) IV 20 minutes prior to study drug. Baseline hemodynamic variables (HR, MAP, SBP, DBP) were recorded before starting infusion of study drug in both groups. Infusion of Study drugs, Dexmedetomidiene and Esmolol, as per study group started. Group A received intravenous infusion of inj. Dexmedetomidine 0.5mcg/kg IV diluted with normal saline to make a total volume of 10 ml and injected IV slowly over 10 minutes and in Group B, inj. Esmolol bolus 0.5mg/kg in 10 ml NS IV was given. Induction was done 10 min. after completion of infusion of study drug. Patient preoxygenated with 100% O_2 for three minutes, Induction was done with inj. Propofol 2mg/kg iv followed by inj. Atracurium 0.5 mg/kg IV for neuromuscular blockade and ventilated with 100% oxygen for 3 minutes. Following induction and adequate paralysis, Direct laryngoscopy performed using a Macintosh laryngoscope blade and patient intubated with appropriate size high volume, low pressure, cuffed Endotracheal Tube (E.T.T) in each patient. Bilateral air entry was checked & tube was fixed. Patients, intubated after more than 1 attempt or took more than 45 seconds were excluded from the study. Heart rate (HR), systolic blood pressure

(SBP), diastolic blood pressure (DBP), Mean Arterial Pressure (MAP), and peripheral oxygen saturation (SpO_2) were recorded at the following time intervals: Baseline (before the start of infusion of study drugs), after the completion of study drug infusion, just after

laryngoscopy and intubation, and then at 1, 3, 5, 10 minutes after laryngoscopy and intubation. Any episode of arrhythmia, apnoea or desaturation was noted during the administration of study drugs. Complications like arrythmia, myocardial infarction, cardiac failure, cardiac arrest, intracranial haemorrhage, increased intracranial pressure, pulmonary oedema were also recorded. The study ended at this point. After intubation Inj. Atracuronium 0.5 mg/kg IV was given. Intra operative Anaesthesia maintained with 60% N_2O + 40% O_2 and inj. atracurium0.1 mg/kg I.V and Gas Isoflurane 0.4 % MAC. At the end of the surgery patient was reversed with Inj. Neostigmine (0.05mg/kg i.v.) and Inj. Glycopyrrolate (0.008mg/kg i.v.) & was smoothly extubated. After meeting standard extubation criteria, patient was shifted to recovery room to see immediate post op complications and observe side effects.

Results and Discussion

In this study, we aimed to compare two different drugs intravenous dexmedetomidine and Esmolol in attenuating hemodynamic response to endotracheal intubation under general anaesthesia. 70 patients were randomly assigned to two groups of 35 patients each. The study was focused on events from the time of injection of study drugs to 10 min after intubation. On arrival to operation theatre, during laryngoscopy and intubation and after 1, 3, 5 and 10 mins. of intubation, HR, SBP and DBP, SpO2 readings were noted and MAP and RPP were calculated.

The groups were collectively matched for their demographic data [Table 1]. No significant differences were found among the general demographic data of patients such as age, weight, gender, ASA and Mallampatti grade.

Table 1: Distribution of study population

Variables		Mean ± SD	
		Dexmedetomidine	Esmolol
Age		44.80 ± 11.21	42.14 ± 12.82
Weight		54.09 ± 10.64	54.03 ± 8.96
Gender	Male	22(62.9%)	19(54.3%)
	Female	13(37.1%)	16(45.7%)
ASA Grade	I	24(68.6%)	23(65.7%)
	II	11(31.4%)	12(34.3%)
Mallampatti grade	I	20(57.1%)	20(57.1%)
	II	15(42.9%)	15(42.9%)

Table 2 : Changes in Mean Heart Rate

Variables			Mean ± SD			
	Baseline	1 min after induction		After intubation		
			1 min	3 min	5 min	10 min
Dexmedetomidine	89.8 ± 11.48	76.6 ± 13.83	79.14 ± 12.05	80.11 ± 13.52	75.09 ± 13.34	71.86 ± 12.44
Esmolol	90.14 ± 11.94	83.34 ± 14.63	95.26 ± 15.02	93.83 ± 15.89	90.37 ± 14.62	86.66 ± 15.45
P	0.903	0.052	<0.001 (S)	<0.001 (S)	<0.001 (S)	<0.001 (S)

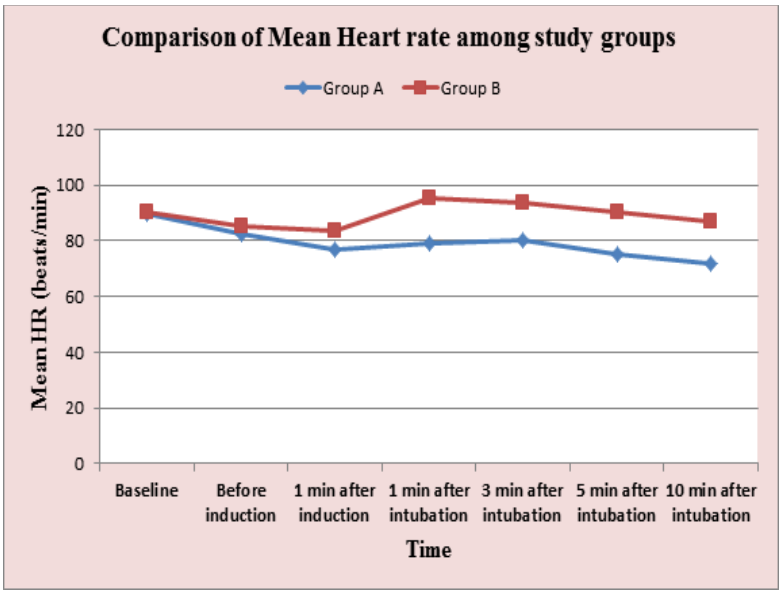

Figure 1: Comparison of Mean Heart rate (beats/min) among study groups.

In our study, both the groups were compared with respect to baseline heart rate value without any significant statistical difference (p>0.05). Among patients of Esmolol group B mean heart rate at 1, 3,

5 and 10 mins post intubation were 95.26 ± 15.02, 93.83 ± 15.89, 90.37 ± 14.62,86.66 ± 15.45 beats/min. respectively, while in dexmedetomidine group A mean heart rate at 1, 2, 3, 5 and 10 mins. post intubation were 79.14 ± 12.05, 80.11 ± 13.52, 75.09 ± 13.34, 71.86 ± 12.44 beats/min. respectively was found to be statistically significant (p value <0.05). Lesser heart rate in group A (dexmedetomidine) was observed which was statistically significant at 1, 3, 5, 10 mins. after intubation and showed better haemodynamics. HR variability decreases with increasing age.[11] Keeping it in view, patients between 18 and 60 years were considered in this study. Laryngoscopy has a linear relation with presser response during the first 48 sec. and with further prolongation has little effect [12]. Keeping it as a guide, laryngoscopy and intubation were limited. Beta blockers have been used for blunting hemodynamic response to laryngoscopy and intubation. However, they blunt the HR response better than blood pressure response.

Esmolol is an ultrashort acting cardio selective beta blocker with rapid onset of action and short elimination half-life; these properties make it a valuable agent to obtund the cardiovascular response.(16) It decreases the force of contraction and HR by blocking the beta adrenergic receptors, thereby attenuating tachycardia and hypertensive response to intubation. It has been used in doses ranging from 0.5 to 2 mg/kg IV to provide hemodynamic stability during laryngoscopy and intubation in previous studies [13,14,15]. Kindler et al.[13] observed that esmolol administration in the doses of 1 and 2 mg/kg before laryngoscopy was sufficient to control HR after intubation but did not affect SBP. Sharma et al.[16] concluded that esmolol in the dose of 1–1.5 mg/kg is most effective in controlling the response to laryngoscopy and intubation. Hence, we decided to preoperatively administer 0.5mg/kg esmolol in one group of patients and 0.5 µg/kg dexmedetomidine in another group and we found that these doses effectively suppressed the hemodynamic responses caused by endotracheal intubation without serious side effects. In our study, all hemodynamic parameters were significantly lower at 10 mins after intubation than at baseline and showed a decreasing trend from 1 min to 10 mins after intubation. However, at 10 mins after intubation, the hemodynamic values were still in the normal range (changes within 20%) and the commencement of surgical procedures halted this decreasing trend. Heart rate values were statistically significantly lower in the Dexmedetomidine group at all-time intervals and an increase in heart rate after intubation was observed in all patients in our study but the increase was more in patients who received intravenous esmolol as compare with dexmedetomidine. This difference was statistically highly significant between the groups till 10 min. after intubation. We found that decrease in heart rate was in a dose dependant manner.

The mean of the MAP increased significantly from baseline values in the Esmolol group, particularly during and 1 and 3 mins following laryngoscopy and endotracheal intubation. There was a substantial decrease in the hypertensive response to laryngoscopy and endotracheal intubation in the Dexmedetomidine group's mean of MAP. [Table 3 and Figure 2).

Table3:Changes in Mean Arterial Blood Pressure (MAP)

Variables	**Mean ± SD**					
	Baseline	**1min.After intubation**	**After Intubation**			
			1min	**3min**	**5min**	**10min**
Dexmedetomidine	126.46± 8.66	120.17 ± 6.21	135.11± 7.4	133.06± 7.5	131.14± 7.1	122.23± 6.08
Esmolol	125.71± 8.27	118.6±6.17	141.57±8.81	140±8.59	139.69±8.42	130.6±6.1
P	0.715	0.292	0.001 (S)	<0.001(S)	<0.001(S)	<0.001(S)

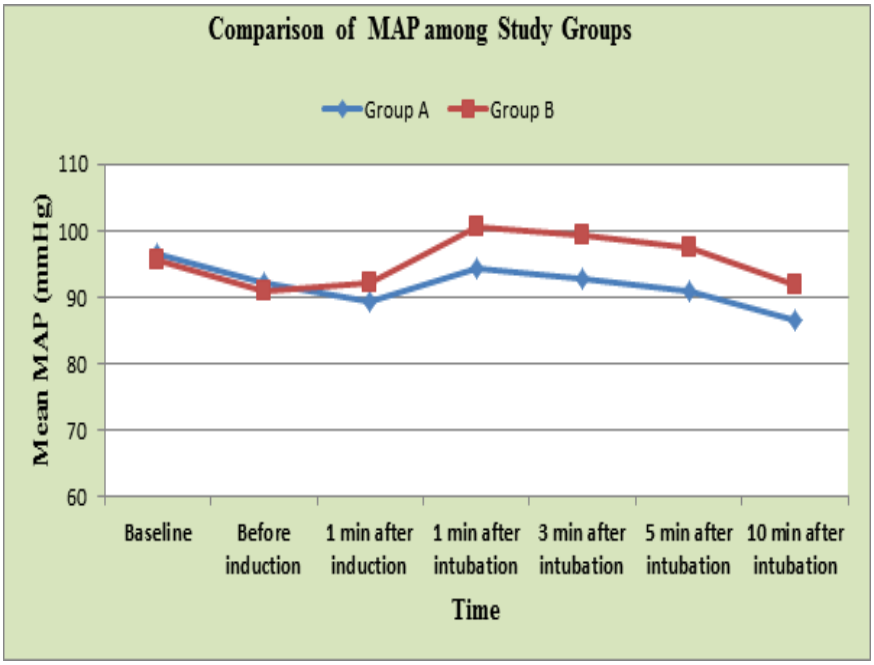

Figure 2: Comparison of MAP (mmHg) among study groups

The systolic blood pressure, diastolic blood pressure and mean arterial pressure at baseline were not significantly different between the two groups. Patients who were treated with inj. dexmedetomidine, 10 minutes before induction of anesthesia had significant decrease in SBP, DBP and MAP after administration of loading dose. This dexmedetomidine induced hemodynamic profile can be attributed to the known sympatholytic effect of α2 agonists. This observation was similar to Basar et al. [17] who investigated the effect of single dose of dexmedetomidine 0.5 µg/kg administration 10 min. before induction of anesthesia and reported significant reduction in MAP and HR. There was a significant decrease in SBP, DBP and MAP after loading of esmolol. Esmolol lowers arterial blood pressure through a decrease in cardiac output secondary to negative chronotropic and ionotropic effects of β adrenergic antagonism. This observation was similar to Shen et al. [18] who studied the effects of intravenous infusion of esmolol on patients undergoing Laparoscopic surgeries and found that blood pressure significantly decreased with Esmolol injection.

There was statistically significant difference in SBP, DBP and MAP between the two groups after loading of study drug, after induction, after intubation and intraoperative period. It was statistically significantly higher (p value <0.05) in Esmolol group as compared to Dexmedetomidine group during surgeries and at the end of surgery. This trend in blood pressure is because of shorter context sensitive half-life of esmolol as compared to dexmedetomidine. Recently, α-2 agonists such as clonidine and dexmedetomidine have been tried for attenuating response to intubation without any of the side effects. Dexmedetomidine is a direct α-2 adrenergic agonist with sedative, anxiolytic, analgesic, and sympatholytic effects. It is better than clonidine for suppressing the hemodynamic response to laryngoscopy and intubation because of higher selectivity to α-2 receptors (α-1:α-2 = 1:1620) than clonidine (α-1:α-2 = 1:220). Shailaja and Srikantu [19] study in hypertensive patients received normal saline, esmolol 1.5 mg/kg, and esmolol 1.5 mg/kg with fentanyl 2 µg/kg during laryngoscopy and endotracheal intubation and concluded that esmolol 1.5 mg/kg is effective in attenuating hemodynamic response to laryngoscopy and intubation, but the combination of the drug causes hypotension following intubation. Talwar et al. [20] study reported that esmolol (1.5 mg/kg) and esmolol with diltiazem were both effective in attenuating heart rate, SBP, DBP, and MAP after laryngoscopy and endotracheal intubation. At the same time, we infused the drug as slow IV infusion over 10 min. as rapid administration of dexmedetomidine has been reported to reduce tachycardia and hypertension. In our study, we observed that both dexmedetomidine and esmolol significantly attenuated the rise in HR after intubation however, dexmedetomidine suppressed the response to intubation more than esmolol. While comparing SBP, DBP and MAP, we found that dexmedetomidine attenuated the rise in these parameters significantly up to 10 mins. after intubation, but there were no significant differences in values between both groups and showing that dexmedetomidine showed greater hemodynamic stability than esmolol.

There were some limitations in our study. Present study depends on the hemodynamic parameters for assessment of the attenuation of the cardiovascular responses to airway manipulation without

measuring the blood catecholamine and cortisol levels. Secondly, adequate depth of anesthesia and neuromuscular blockade were monitored only by clinical observations. Use of bispectrality index and neuromuscular monitoring could have been a better guide. No invasive blood pressure monitoring was done which could give more accurate value at the appropriate timing but it was not indicated usually in the surgeries which have less chances of hemodynamic instability. We included only normotensive patients Thus, further studies are awaited in the future for blunting hemodynamic response in patient with hypertension, cardiac diseases and other comorbidities.

Conclusion

Dexmedetomidine when used as an infusion in the loading dose of 0.5 µg/kg 10 min. before intubation is more effective than loading dose of 0.5 mg/kg of Esmolol in attenuating of hemodynamic responses to laryngoscopy and intubation but without any significant side effects like hypotension and bradycardia. Hence comparatively better drug dexmedetomidine in dose of 0.5 µg/kg may offer clinical advantage.

Acknowledgement: The authors thank the surgeons and nursing staff of general surgery OT, SMS medical college, Jaipur.

Funding: The authors did not receive support from any organization for the submitted work.

Authors' contributions: SKJ, SM, SS, VKK; study concept and design, data collection and processing, analysis and interpretation of the data, drafting of the manuscript, revision of the manuscript for important intellectual content, administrative, technical, material support, literature research and study supervision.

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