



## Original Research Article

# An observational study to compare the efficacy of intravenous dexmedetomidine versus intravenous esmolol for attenuation of pressor response during laryngoscopy and endotracheal intubation

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## ABSTRACT

**Background:** Laryngoscopy and endotracheal intubation during general anaesthesia is an invasive stimulus associated with release of circulating catecholamine leading to hemodynamic and cardiovascular responses resulting in tachycardia, hypertension and arrhythmias. Many prophylactic drugs have been used to decrease cardiovascular response to laryngoscopy & intubation. Aim of this study is to compare effectiveness of Dexmedetomidine 1µg/kg and Esmolol 1 mg/kg intravenously in attenuating cardiovascular response during laryngoscopy and intubation during general anaesthesia.

**Materials and Methods:** This randomised double blinded prospective study was conducted on 50 patients, of either gender between age group 18-60 years and American Society of Anaesthesiology (ASA) classification I & II, undergoing various surgeries under General anaesthesia requiring intubation. Patients were randomly divided into 2 groups of 25 patients each.

Group D patients received intravenously Inj. Dexmedetomidine 1 mcg/kg as an infusion in 100ml Normal Saline over 20 minutes before induction of general anaesthesia.

Group E patients received intravenously Inj. Esmolol 1 mg/kg diluted with normal saline to volume of 10ml given just before induction of general anaesthesia.

Hemodynamic parameters such as Heart rate (HR), systolic blood pressure (SBP), diastolic blood pressure (DBP) and mean arterial pressure (MAP) were recorded at baseline, after study drug administration, after induction, at laryngoscopy and intubation and 1, 3, 5 and 7 min after Endotracheal intubation.

**Results:** Comparison of two groups reveals that dexmedetomidine shows less rise in heart rate (P-0.0003) and mean arterial pressure (P-0.0106) at the laryngoscopy and intubation. It also shows less rise in systolic and diastolic blood pressure after induction and after intubation (P< 0.05) than Esmolol.

**Conclusion:** This study suggests that Dexmedetomidine 1µg/kg was more effective in attenuating the stress response to laryngoscopy and intubation as compared to Esmolol 1mg/kg.

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## 1. Introduction

Laryngotracheal intubation is a noxious stimulus associated with a marked autonomic response which manifests as

increased heart rate and blood pressure.<sup>1</sup> Laryngoscopy and intubation leads to an average 40 to 50% rise in blood pressure and 20% rise in heart rate.<sup>2</sup> This sympathetic over activity is due to increased firing of cardio acceleratory fibres resulting in release of catecholamines in the circulation from adrenergic nerve

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endings and adrenal medulla. Parasympathetic response is more common in children but can occur in some adults.<sup>1,3</sup> These haemodynamic changes are of little concern in normal healthy patients but can have deleterious effect in patients with hypertension, coronary heart disease, valvular heart disease, preeclampsia and patients with intracranial pathology.<sup>4</sup>

Cardiovascular response to laryngoscopy and endotracheal intubation is enhanced in hypertensive patients<sup>5</sup> leading to marked pressure response, which may lead to life threatening complications such as arrhythmias, myocardial ischemia and intracranial haemorrhage.<sup>6</sup> We should be very much vigilant and cautious in hypertensive patients at the time of laryngoscopy and intubation. Various pharmacological agents have been used to prevent the stress response like opioids,<sup>7</sup>  $\beta$  blockers,<sup>8</sup>  $\alpha$ -adrenergic agonists,<sup>9</sup> calcium channel blockers,<sup>10</sup> vasodilators<sup>11</sup> and lignocaine<sup>12</sup> with varying results.

Esmolol is fast acting, cardio-selective  $\beta$ -adrenergic antagonist with favourable properties such as controlling tachyarrhythmias, decreasing myocardial oxygen demand, increasing coronary perfusion and restriction of infarct size.<sup>13</sup> Esmolol suppresses the action of catecholamine on beta-receptors leading to prevention of cardiovascular response of laryngoscopy and intubation. Esmolol 1 mg/kg is very effective in suppressing the pressure response without any deleterious effects on heart and provided hemodynamic stability in risk patients in various studies.<sup>14</sup>

Dexmedetomidine is an imidazole derivative and selective alpha 2 adrenergic receptor agonist<sup>15</sup> having advantageous property such as sedation with very easy arousal, neuroprotection and analgesia. Alpha 2 adrenergic agonists produce hyperpolarisation of noradrenergic neurons and suppression of neuronal firing in the locus coeruleus which leads to decreased systemic noradrenaline release resulting in attenuation of sympathetic responses during laryngoscopy and tracheal intubation.<sup>16</sup> Dexmedetomidine blunts hemodynamic response and provides stable hemodynamic during the placement of endotracheal tube.<sup>17,18</sup>

Hence, this study was done to compare the efficacy of intravenous (iv) Dexmedetomidine versus iv Esmolol in attenuating the haemodynamic response during laryngoscopy and endotracheal intubation which is our primary outcome in patients undergoing general anaesthesia. The secondary outcome was to study any side effects of these two drugs.

## 2. Materials and Methods

This randomised double blinded prospective study was conducted at Tertiary care centre, Institutional Ethical Committee approval was obtained under: SVIEC/MEDI/SRP/JUNE/24/127. Total 50 Patients of either gender aged between 18-60 years belonging to

grade I & II of American Society of Anaesthesiologists (ASA) classification who underwent elective surgeries under general anaesthesia with endotracheal intubation were randomly divided by computer generated random number sequence into 2 groups of 25 patients each. Patients unwilling to participate in the study, patients having arrhythmias or heart block, patient with psychiatric disease, Pregnancy & lactating women, Patients on beta blockers, History of allergy to the study drugs, BMI >30, Patients with ASA physical status III and above, Patient with suspected difficult airway and Mallampatti Grade III and IV were excluded from our study.

Sample size was calculated using open epi software based on reference study done by Reddy SV et al<sup>16</sup> and study done by us. It was decided that a 20% of difference should be the minimum detectable difference of calculated means for hemodynamic variables in both groups between his study and our study. The standard deviation (SD) among both the studies was also considered as 20% average difference between the groups. The  $\alpha$  value was 0.05 and the power (1- $\alpha$ ) of the study was 0.80. Thus, the calculated sample size for each group was 25 patients.

Patients were divided into two groups for comparison: Group D and Group E.

1. Group D: Patients received intravenous dexmedetomidine at a dose of 1  $\mu$ g/kg as an infusion in 100 ml of normal saline over 20 minutes before the induction of general anesthesia. Additionally, these patients were administered 10 ml of normal saline just before induction, provided by a separate anaesthesiologist who was not involved in the study.
2. Group E: Patients received intravenous esmolol at a dose of 1 mg/kg, diluted with normal saline to a total volume of 10 ml, given just before the induction of general anesthesia. Furthermore, these patients were also given 100 ml of normal saline 30 minutes before the induction, administered by a separate anaesthesiologist who was not part of the study.

This methodology was designed to ensure that the volume of intravenous fluids administered was consistent across both groups, with additional normal saline infusions given at specific times to maintain blinding and control for any potential volume-related effects on hemodynamic responses.

Pre-anaesthetic check-up was done a day before surgery. Patients were informed about the procedure and written informed consent was obtained. On the day of surgery intravenous access was taken and baseline parameters like Heart rate (HR), non-invasive systolic blood pressure (SBP), diastolic blood pressure (DBP) and mean arterial pressure (MAP), continuous ECG monitoring and oxygen saturation by pulse oximetry (SpO<sub>2</sub>) were taken.

Patients received infusion of study drug according to divided group by the anaesthesiologist who was not part of the study. After arrival in the operation theatre hemodynamic parameters (HR, SBP, DBP and MAP) were taken and considered as after study drug parameters.

Premedication of Inj. Glycopyrrolate 0.004mg/kg iv., Inj. Ondansetron 0.1mg/kg iv., Inj. Tramadol 2mg/kg iv. & Inj. Ranitidine 50 mg iv were given to all the patients. Patients were pre-oxygenated with 100% oxygen for 3 minutes via face mask.

Patients were given Inj. Propofol 2mg/kg iv. for induction and Inj. Succinylcholine 2mg/kg iv. to facilitate intubation after confirmation of ventilation. Intubation of trachea was done with appropriate size cuffed endotracheal tube, bilateral equal air entry was checked and tube was secured with adhesive tap. Anaesthesia was maintained with O<sub>2</sub>, N<sub>2</sub>O at 1:1 ratio and Isoflurane using close system. Neuromuscular monitoring was done and loading dose of inj. Atracurium 0.5mg/kg iv. was administered followed by maintenance with 0.1 mg/kg iv. Patients were mechanically ventilated on Volume Control mode to maintain eucapnia.

Monitoring of hemodynamic parameters i.e. HR, SBP, DBP, MAP and SPO<sub>2</sub> were noted by consultant anaesthesiologist after induction, during laryngoscopy and intubation and at 1,3,5 ,7 minutes after intubation.

After completion of surgery, neuromuscular blockade reversal was done with Inj. Neostigmine (0.05mg/kg) iv. and Inj. Glycopyrrolate (0.008mg/kg) iv after ensuring that the patient’s breathing was normal with sufficient tidal volume and rate. After adequate reversal, the endotracheal tube was removed and patients were taken to the recovery room.

During the study fall in HR less than 50/min was taken as Bradycardia and treated with Inj. Atropine 0.6mg iv. Fall in SBP less than 80 mmHg was considered as hypotension and first treated with bolus Ringer Lactate fluid upto 200 ml and then Inj. Mephentermine 6 mg iv. if there is no improvement with fluid trial.

Post-operative complications like Nausea, vomiting, Bradycardia, hypotension, Respiratory depression, Dryness of mouth or any other complications were noted.

2.1. Statistical analysis

Data were collected in tabulated form. Numerical variables were calculated as mean & standard deviation (SD) while categorical variables were calculated as frequency and percentage. For numerical variables; tests like unpaired student-t test and/or ANNOVA were used whenever appropriate for between-groups comparisons, while for categorical variables; chi-square test was used. P value <0.05 was considered statistically significant.

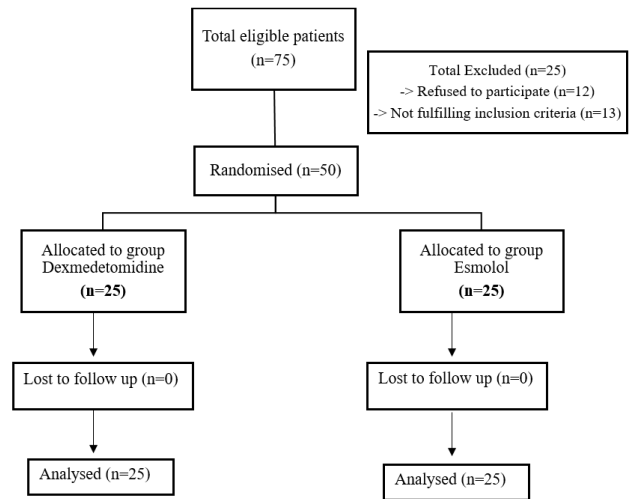


Diagram 1: Consort flow diagram

3. Results

Total 50 patients were enrolled in the study with 25 patients in each group. Both the groups were similar in terms of age, weight, gender and ASA status.(Table 1)

Table 1: Results of demographic parameters

Parameter	Group D	Group E	P-value
	Mean ±SD	Mean ±SD	
Age (years)	33.08 ±6.89	35.12 ±10.85	0.4313(NS)
Weight (kg)	68 ±7.85	64.44 ±11.57	0.2091(NS)
<b>Gender</b>	N (%)	N (%)	
Male	13 (52%)	15 (60%)	0.7757(NS)
Female	12 (48%)	10 (40%)	
<b>ASA</b>			
I	20 (80%)	19 (76%)	1.0000(NS)
II	5 (20%)	6 (24%)	

(\*NS- Non significant)

Baseline haemodynamic variables were comparable in both the groups. Both the groups exhibited rise in HR but the rate of rise was statistically significantly low in Group D as compared to Group E during laryngoscopy and intubation and at 1min, 3min, 5min, 7min after intubation as compared to Group E. (p < 0.005). Dexmedetomidine shows better hemodynamic stability as compare to esmolol.(Table 2)

There was significant fall in SBP noted in both the groups (p<0.05) after induction. There was less rise in SBP in Group D following laryngoscopy and intubation, at 1min, 3min, 5min, 7 min of intubation as compared to Group E (p<0.005).(Table 3) There is fall in blood pressure after induction which may be because of effect of induction agent also, but during laryngoscopy and intubation significant rise is seen in esmolol group as compared to dexmedetomidine group.

**Table 2:** Comparison of heart-rate

Parameter Heart rate	Group D	Group E	P-value
	Mean $\pm$ SD	Mean $\pm$ SD	
Baseline	80.68 $\pm$ 6.87	78.28 $\pm$ 6.79	0.2201 (NS)
After test drug	77.76 $\pm$ 6.89	76.36 $\pm$ 6.53	0.4645 (NS)
After induction	73.72 $\pm$ 6.62	75.2 $\pm$ 6.38	0.4249(NS)
At laryngoscopy & intubation	87.72 $\pm$ 4.91	93.76 $\pm$ 5.98	0.0003 (HS)
1 min	83.48 $\pm$ 5.75	91.36 $\pm$ 5.82	P<0.0001 (HS)
3 min	80.88 $\pm$ 5.95	88.68 $\pm$ 5.81	P<0.0001 (HS)
5 min	76.68 $\pm$ 5.09	87.12 $\pm$ 5.38	P<0.0001 (HS)
7 min	72.72 $\pm$ 5.53	84.6 $\pm$ 5.63	P<0.0001 (HS)

**Table 3:** Comparison of systolic blood pressure

Parameter Systolic blood pressure	Group D	Group E	P-value
	Mean $\pm$ SD	Mean $\pm$ SD	
Baseline	121.68 $\pm$ 7.9	119.36 $\pm$ 6.53	0.2634 (NS)
After test drug	117.28 $\pm$ 7.78	117.52 $\pm$ 5.94	0.9029 (NS)
After induction	112.36 $\pm$ 6.61	116.04 $\pm$ 5.75	0.0410 (S)
At laryngoscopy & intubation	132.4 $\pm$ 7.9	141.56 $\pm$ 8.6	0.0003 (HS)
1 min	127.2 $\pm$ 7.52	137.84 $\pm$ 6.67	P < 0.0001 (HS)
3 min	123.2 $\pm$ 7.47	135.4 $\pm$ 6.25	P < 0.0001 (HS)
5 min	118.44 $\pm$ 7.14	132.44 $\pm$ 5.2	P < 0.0001 (HS)
7 min	113.84 $\pm$ 7.21	129.88 $\pm$ 5.24	P < 0.0001 (HS)

(\*HS- Highly Significant, NS- Non significant, S- Significant)

There was no significant difference noted in DBP after laryngoscopy and intubation but at 1min, 3min, 5min and 7 min of intubation statistically significant fall in DBP was noted in groups D ( $p < 0.005$ ). (Table 4)

There was no statistically significant change in MAP was noted in both the groups after test drug and after induction, but statistically significant rise in MAP was noted in Group E as compared to Group D at laryngoscopy and intubation and after that. ( $p < 0.005$ ). (Table 5)

In this study, Group D and Group E both the drugs were effective for decreasing hypertensive stress response of laryngoscopy and intubation. In fact, there is less increase in SBP, DBP and MAP compared to the baseline values was observed in Group D among both the groups. None of the patients were observed bradycardia or hypotension in this study.

#### 4. Discussion

Laryngoscopy and endotracheal intubation plays very critical role during general anaesthesia as they produce transient but very remarkable sympathetic response. These procedures lead to increase in blood pressure and heart rate. Sympathetic nervous system activation leads to adverse hemodynamic effects on myocardium and therefore it is better to be suppressed by supplementing drugs which blocks adrenergic receptors like  $\beta$ -blockers, others like opioids, calcium channel blockers,  $\alpha_2$  agonist drugs etc. can be used to achieve this effects.

In present study, we compared Dexmedetomidine which is a selective alpha 2 adrenergic receptor agonist and Esmolol which is  $\beta$ -blocker. All the patients received study drug as well as normal saline to make it double blind.

In a study conducted by Shivanand Y. Hulakund , Archana R. Endigeri (2017), they compared intravenous Dexmedetomidine (Group D)  $1\mu\text{g}/\text{kg}$  diluted in 10 ml NS given over 10 minutes and Esmolol (Group E)  $1\text{mg}/\text{kg}$  diluted to 10 ml and given over 1 min. The decrease in mean HR, SBP, DBP, MAP at 1, 3, 5 and 10 minutes after intubation was better in dexmedetomidine group as compare to esmolol group which is similar to our study.<sup>19</sup> They observed hypotension in 5 patients and bradycardia in 3 patients of dexmedetomidine group which did not need any medication. However, no patients in group E had such side effects. But in our study, there was no hypotension or bradycardia noted in any of the groups.

Beta blockers are being frequently used for suppressing hemodynamic response to laryngoscopy and intubation. However, they blunt the HR response better than blood pressure response. Esmolol is an ultrashort-acting cardioselective beta blocker with rapid onset of action and short elimination half-life; these properties make it a very useful agent to decrease the cardiovascular response.<sup>20</sup> 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

**Table 4:** Comparison of diastolic blood pressure

Parameter Diastolic blood pressure	Group D	Group E	P-value
	Mean $\pm$ SD	Mean $\pm$ SD	
Baseline	80.48 $\pm$ 7.75	78.08 $\pm$ 5.42	0.2106 (NS)
After test drug	78.44 $\pm$ 7.64	76.08 $\pm$ 4.7	0.1946 (NS)
After induction	75.32 $\pm$ 7.13	74.88 $\pm$ 5.4	0.8068 (NS)
At laryngoscopy & intubation	89 $\pm$ 8.39	92.2 $\pm$ 5.6	0.1193 (NS)
1 min	85.8 $\pm$ 9.25	90.28 $\pm$ 5.26	0.0405 (S)
3 min	82.36 $\pm$ 9.85	87.24 $\pm$ 5.1	0.0327 (S)
5 min	78.76 $\pm$ 9.26	85.2 $\pm$ 4.63	0.0031 (HS)
7 min	74.84 $\pm$ 9.32	83.16 $\pm$ 5.14	0.0003 (HS)

(\*HS- Highly significant, NS- Non significant, S- Significant)

**Table 5:** Comparison of mean arterial pressure

Parameter Mean arterial pressure	Group D	Group E	P-value
	Mean $\pm$ SD	Mean $\pm$ SD	
Baseline	94.24 $\pm$ 7.39	91.92 $\pm$ 5.23	0.2063 (NS)
After test drug	91.44 $\pm$ 7.12	90 $\pm$ 4.61	0.4002 (NS)
After induction	88.08 $\pm$ 6.27	88.36 $\pm$ 5.22	0.8645 (NS)
At laryngoscopy & intubation	103.48 $\pm$ 7.56	108.68 $\pm$ 6.19	0.0106 (S)
1 min	99.6 $\pm$ 8.04	105.4 $\pm$ 5.28	0.0041 (HS)
3 min	96 $\pm$ 8.42	103.32 $\pm$ 5	0.0005 (HS)
5 min	92.28 $\pm$ 7.89	101.04 $\pm$ 4.4	P < 0.0001 (HS)
7 min	88.04 $\pm$ 8.05	98.68 $\pm$ 4.42	P < 0.0001 (HS)

(\*NS- Non significant, S-Significant, HS- Highly significant)

in previous studies.<sup>21–23</sup> We have taken esmolol at 1 mg/kg dose and have shown similar results.

Similar to our study Venkatesh Selvaraj, Karthik Raj conducted a prospective randomized study by double-dummy blinding method which is similar to our study. Group A patients were given dexmedetomidine 1 mcg/kg diluted in 50 ml with normal saline and infused over 10 min before induction, patients also received 20 ml of normal saline intravenous (IV) 2 min before endotracheal intubation. Group B patients were given 50 ml of normal saline infusion over 10 min before induction and IV bolus of esmolol 0.5 mg/kg diluted in 20 ml of normal saline given 2 min before intubation. They also concluded that Dexmedetomidine group showed statistically significant reduction in heart rate, blood pressure and mean arterial pressure at all the time intervals following intubation.<sup>24</sup> While esmolol group showed significant reduction of HR, SBP, and MAP following intubation but there was no reduction in DBP.

Dexmedetomidine acts on the  $\alpha$ -2 adrenergic receptors located on sympathetic presynaptic terminals where they inhibit epinephrine and norepinephrine release. It decreases central sympathetic outflow by acting on locus coeruleus. Thus, it attenuates the hemodynamic response to intubation and also reduces intraoperative anesthetic agents and opioid requirements.

Srivastava VK et al., compared the efficacy of esmolol and dexmedetomidine in elective neurosurgical patients.

Patients were randomly divided to three equal groups of 30 each. Control group (group C) received 20 ml of 0.9% saline intravenous (IV), group dexmedetomidine (group D) received 1  $\mu$ g/kg diluted with 0.9% saline to 20 ml IV and group esmolol (group E) received 1.5 mg/kg diluted with 0.9% saline to 20 ml IV.<sup>25</sup> All the drugs were infused over 10 min of period and after 2 min induction of anaesthesia done. Even though increasing the dose of esmolol compare to our study in group E, there was a statistically significant increase in blood pressure after intubation and after 1, 2, and 3 min and HR up to 5 min in study conducted by Sanjay Agrawal and team. In group D, there was no significant increase in HR and blood pressure was noted after intubation at any time intervals.

Reddy SV et al., conducted a randomized double-blind clinical study similar to our study to compare the clinical effects of dexmedetomidine with esmolol and for controlling presser response during laryngoscopy. The patients were randomly divided into three groups (n = 30). Group C received placebo, Group E received 2.0 mg/kg of esmolol and Group D received 1.0  $\mu$ g/kg of dexmedetomidine, intravenously over 10 min and 3 min before induction of general anaesthesia. The mean arterial pressure was significantly increased in patients receiving placebo and esmolol after laryngoscopy and intubation compared with baseline value and Group D (P = 0.6294).<sup>16</sup> The rise in HR (P = 0.08481) and rate pressure product (P = 0.0666) at the time of intubation were minimal and

was statistically significant up to 15 min in Group D. It was observed that pediatric and hypertensive patients show more stress response to laryngoscopy and intubation, but we have taken only adults and normotensive patients.

Many studies have used different drugs and different doses of dexmedetomidine and esmolol during induction and extubation of patients during general anaesthesia. We also observed dexmedetomidine is better for controlling stress response of laryngoscopy and intubation.

## 5. Limitations

The limitations of our study are: First, there is no placebo group in our study so there are no comparison with patients with saline group. Second, we have considered hemodynamic changes up to 7 minutes after intubation so effect of Dexmedetomidine and Esmolol on hemodynamic parameters are not considered intraoperatively. Since this is a hospital-based study, it has limited generalisability.

## 6. Conclusion

This study suggests that both Dexmedetomidine and Esmolol are effective for attenuation of haemodynamic response to laryngoscopy & intubation. However, Dexmedetomidine 1µg/kg provides better and effective haemodynamic stability as compare to Esmolol 1mg/kg during airway manipulation.

## 7. Source of Funding

Nil.

## 8. Conflict of Interest

There are no conflicts of interest.


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