International Journal of Science and Research (IJSR)
ISSN (Online): 2319-7064
Index Copernicus Value (2015): 78.96 | Impact Factor (2015): 6.391

A Comparative Study of Dexmedetomidine and Esmolol for Attenuation of Haemodynamic Response to Laryngoscopy and Endotracheal Intubation

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Abstract: ***Background and Aims: The present study compared the efficacy of Esmolol and Dexmedetomidine for attenuation of the haemodynamic stress response to laryngoscopy and intubation in elective general surgical patients. Study Design: Prospective randomized double blinded study. Material And Methods: Total of 60 patients aged 20-60 years with ASA physical status I or II of either sex, scheduled for elective surgical procedures under general anaesthesia were included in this study. Patients were randomly allocated to two equal groups of 30 each. Group D received an IV infusion of 1 µg/kg of dexmedetomidine diluted up to 50 ml with 0.9% saline and Group E received 2 mg/kg of Esmolol diluted up to 50 ml with 0.9% saline. All the drugs were infused over a period of 10 min. General anaesthesia was induced and patients were intubated after 3 minutes as per the study protocol. The parameters monitored were Heart rate (HR), Systolic Blood Pressure(SBP), Diastolic Blood Pressure (DBP) and Mean Arterial Pressure (MAP)at baseline, post intubation and at intervals of 3, 5, 7 and 10 minutespost orotracheal intubation. Results: Data was compared using paired t-test and the reduction in Heart Rate was found to be statistically significant (p< 0.05) at all intervals. There was also significant decrease in Systolic, Diastolic and Mean Arterial Pressuresduring the immediate post intubation period and at 10 minute interval (p< 0.05). Conclusion: Dexmedetomidine 1 µg/kg IV infusion is more effective than Esmolol IV infusion for attenuating the sympathomimetic response to laryngoscopy and intubation in elective general surgical patients.***

Keywords: Dexmedetomidine, Esmolol, Haemodynamic response

1. Introduction

Increase in heart rate and blood pressure are well documented sequelae of Direct Laryngoscopy and Endotracheal intubation in normotensive individuals. [1, 2, 3, 4]

This transient, self-limitingrise in heart rate and blood pressure are innocuous in healthy individuals but may be hazardous to patients with hypertension, coronary insufficiency or with cerebrovascular disease.[5]

Various anaesthetic agents and agents acting on the sympathetic system have been used to attenuate this sympathetic response to direct laryngoscopy and tracheal intubation, such as opioids, calcium channel blockers, local anaesthetics, beta-blockers, magnesium sulphate, dexmedetomidine, esmolol etc.[6]

Dexmedetomidine is a highly selective alpha-2 agonist, which has been used to attenuate the sympathetic response to Direct Laryngoscopy and Endotracheal intubation and also for its anaesthetic sparing effects, anxiolysis and analgesia without respiratory depression. [7]

Esmolol is an ultra-short acting β1-cardioselective adrenergic receptor blocker with a distribution half-life of 2 min and an elimination half-life of 9 min that reduces heart rate and blood pressure. Esmolol lowers arterial blood pressure through a decrease in cardiac output secondary to negative chronotropic and ionotropic effects of β adrenergic antagonism [8]

No single anaesthetic technique has been accepted to be completely effective in preventing or attenuating this sympathetic response. The methods which are being used either produce undesirable side effects or are partially effective.

Hence we undertook this study to compare the efficacy of Dexmedetomidine and Esmolol in attenuating the stress response to laryngoscopy and intubation.

2. Study Design, Materials and Methods

A prospective, interventional, randomized double blinded clinical study, using a sample size of 60withpatients agedbetween 20 to 60 years of ASA physical status I or II were included in the study. Sample size was derived using 95% confidence interval and power of the study as 80% using the statistical formula.

After approval from ethical committee and obtaining written informed consent from each patient, a detailed history and complete clinical examination was done. All patients were worked up and prepared for surgery according to the institutional protocol. Routine blood investigations and ECG was done for all patients. Detailed airway examination was done to rule out anticipated difficult airway. Patients on beta-blockers, alpha-2 agonists or any other cardiac medications or with known history of allergy to the study drugs, pregnant and lactating patients, patients with preoperative ECG abnormalities and those patients who required more than 1 attempt to intubate were also excluded

from the study.

Patients and the Observer recording the parameters were blinded to the study. Patients were asked to choose a sealed envelope containing the name of the study drug to be used and were asked to stay nil per oral (NPO) from 12 midnight. They were premedicated with tab ranitidine 150 mg and tab diazepam 5 mg orally on the previous night.

After the patients were shifted to the operation theater standard monitors like NIBP, SPO2and ECG were connected and baseline parameters were recorded. Loading dose of the study drug was infused as per group allotted and administered by a qualified anesthesiologist who was not part of the study.Group D was infused with intravenous (IV) Dexmedetomidine(1 mcg/kg body wt.) diluted in 50 ml normal saline over 10 minutes before inducing general anesthesia.Group E was given IV infusion ofEsmolol at dose of 2 mg/kg diluted in 50ml NS over 10 min pre induction. Patients were preoxygenated during infusion of the study drug after which general anesthesia was induced with IV thiopentone sodium (5mg /kg body wt.)and paralyzed for intubation using IV succinylcholine (1.5 mg / kg body wt.).Laryngoscopy was attempted 90 seconds after the administration of succinylcholine using appropriate sized Macintosh curved bladeand intubated with appropriate size (8.5 for male and 7.5 for female) cuffed disposable oral Endotracheal tube. Laryngoscopy and intubation time was limited to 15-20 sec in all patients and patient with failure to in tubate within this period with single attempt was excluded from the study.After confirming the ETT position, anesthesia was maintained with 66% N_2O in 33% oxygen and 1% sevoflurane in 6 litres of fresh gas flow. Paralysis was maintained with Vecuronium bolus IV dose of 0.08 mg/kg wt followed by intermittent doses of 0.02 mg/kg wt. Vital parameters such as HR, SBP, DBPand MAP were recorded at baseline, after study drug infusion, immediately after induction, and at 3, 5, 7 and 10 min after intubation using standard monitors by the observer who is blinded to the study drug used. No surgical intervention was allowed throughout the study period of 10 min.

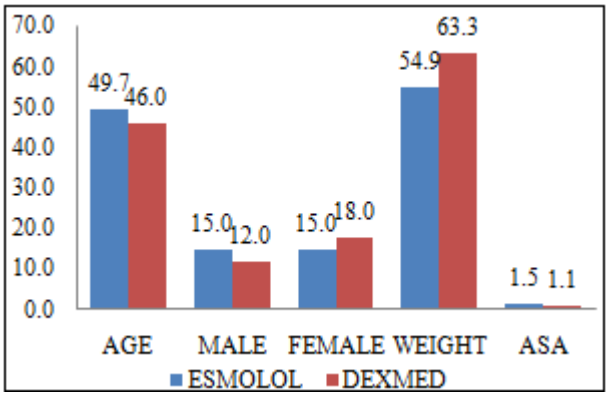
Haemodynamic alterations like a decrease in MAP greater than 20% below the baseline value or SBP less than 90 mm of Hg was defined as hypotension and treated primarily by increasing the IV fluid infusion rate and then reducing sevoflurane concentration or incremental doses of mephentermine 6 mg bolus IV and excluded from the study . Decrease in HR (<50 beats/min) was defined as bradycardia and treated with atropine 0.6 mg IV and excluded from the study and noted.

3. Statistical Analysis

All statistical methods were carried using SPSS 23 for Windows. Demographic data was presented in frequency and percentage .Statistical analysis of data was determined with t-test, Mann-Whitney U test and Analysis of variance for repeated measures (ANOVA). Chi-square test and Fisher's exact test was used to find out possible associations.P<0.05 was considered significant and p<0.01 was considered highly significant.

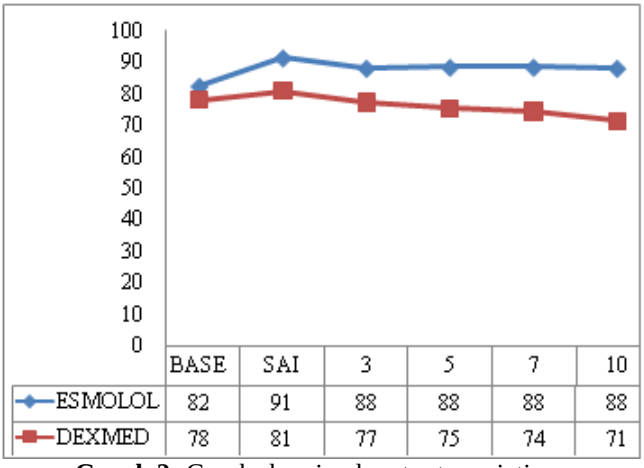
4. Results

All cases were selected from general surgery and from orthopaedic surgeries for upper limb. All the 60 patients completed the study. Demographic profile of the patients in terms of age, body weight, male: female ratio, ASA status were comparable and there was no significant inter-group difference (Graph1)



Graph 1: Demographic data

Though there was decrease in heart rate in both the study groups after infusion of study drugs, we found a relative increase in heart rate in the Esmolol group (9bpm) when compared to the Dexmedetomidine group (3bpm) soon after intubation. Heart rate reached baseline values by 3 min in Group D and also dropped below baseline (maximum drop by 8% at 10 min) while it took more than 10 min to reach baseline in Group E. There was also statistically significant difference in heart rate at all time intervals in our study. (Graph2, Table 1)



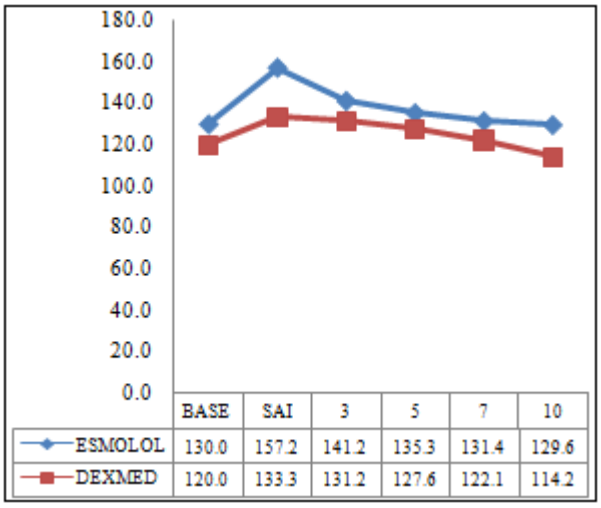
Graph 2: Graph showing heart rate variations

Table 1: Table Showing Heart Rate Variations

changes in heart rate (HR)			
	GROUP	Mean±SD (mmHg)	P Value
Baseline	group D	78 ± 9.6	0.073
	group E	82 ± 15.0	
soon after intubation	group D	81 ±10.2	0.000
	group E	91 ±10.8	
3 min after intubation	group D	77 ± 10.4	0.000
	group E	88 ±10.5	
5 min after intubation	group D	75 ± 9.8	0.000
	group E	88 ± 13.4	

7 min after intubation	group D	74 ± 10.1	0.000
	group E	88 ± 13.4	
10 min after intubation	group D	71 ± 10.9	0.000
	group E	88 ± 12.6	

There was statistically significant difference in SBP (Systolic Blood Pressure)soon after intubation($p<0.01$)) and at 10 min after intubation ($p<0.01$). We also found that both drugs could not completely abolish rise in SBP soon after intubation. There was 10.8% rise in SBP in Group D compared to 20.1% rise in Group E immediately after laryngoscopy and intubation. (Graph 3, Table 2)

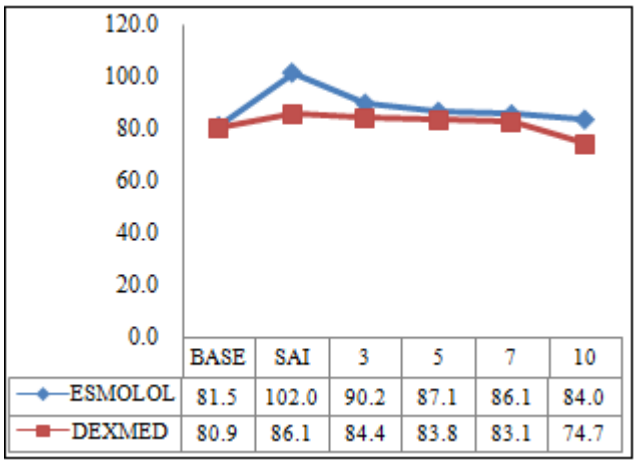


Graph 3: Graph showing changes in systolic blood pressure

Table 2: Table showing SBP variations

changes in systolic blood pressure (SBP)			
	GROUP	Mean±SD (mmHg)	P VALUE
Baseline	group D	120 ± 10.1	0.240
	group E	130 ± 13.9	
soon after intubation	group D	133.3 ± 9.1	0.000
	group E	157.2 ± 27.1	
3 min after intubation	group D	131.2 ± 9.9	0.065
	group E	141.2 ± 25.2	
5 min after intubation	group D	127.6 ± 8.9	0.128
	group E	135.3 ± 23.9	
7 min after intubation	group D	122.1 ± 10.4	0.065
	group E	131.4 ± 23.2	
10 min after intubation	group D	114.2 ± 7.6	0.003
	group E	129.6 ± 23.1	

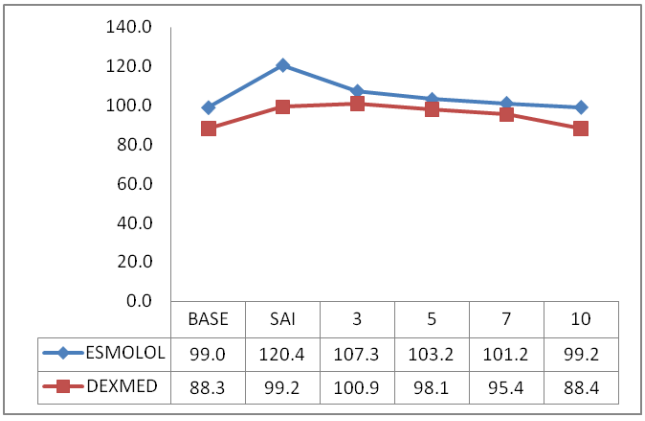
Similar trend was also found in DBP (diastolic blood pressure) as per Graph 4, Table 3 and MAP (mean arterial pressure) as evidenced by Graph 5 and Table 4 where statistically significant difference was found immediately after intubation and also at 10 min interval. But values were lower in Group D as compared to Group E at all time intervals in our study.



Graph 4: Changes in diastolic blood pressure

Table 3: Changes in diastolic blood pressure

changes in diastolic blood pressure (DBP)			
	GROUP	Mean±SD (mmHg)	P value
Baseline	group D	80.9 ± 5.6	0.807
	group E	81.5 ± 9.5	
soon after intubation	group D	86.1 ± 7.2	0.002
	group E	102 ± 20.5	
3 min after intubation	group D	84.4 ± 8.4	0.211
	group E	90.2 ± 19.5	
5 min after intubation	group D	83.8 ± 9.4	0.481
	group E	87.1 ± 18.7	
7 min after intubation	group D	83.1 ± 9.4	0.472
	group E	86.1 ± 18.4	
10 min after intubation	group D	74.7 ± 7.7	0.024
	group E	84 ± 18.7	



Graph 5: Changes in mean arterial pressure

Table 4: Variations in Mean Arterial Pressure

changes in mean arterial pressure (MAP)			
	GROUP	Mean±SD (mmHg)	P VALUE
Baseline	group D	88.3 ± 8.6	0.059
	group E	99 ± 9.6	
soon after intubation	group D	99.2 ± 8.3	0.000
	group E	120.4 ± 21.8	
3 min after intubation	group D	100.9 ± 9.2	0.175
	group E	107.3 ± 20.8	
5 min after intubation	group D	98.1 ± 8.9	0.262
	group E	103.2 ± 20.1	
7 min after intubation	group D	95.4 ± 10.4	0.178
	group E	101.2 ± 19.5	
10 min after intubation	group D	88.4 ± 8.4	0.014
	group E	99.2 ± 19.8	

As per above mentioned results Dexmedetomidine is more effective than Esmolol in controlling heart rate rise during intubation response at all time intervals .Both the drugs in the doses used in our study could not completely abolish the pressor response but Dexmedetomidine was better than Esmolol for the purpose. We also did not have episodes of bradycardia or hypotension as defined in our methodology.

5. Discussion

Our study demonstrated that the use of both Esmolol and Dexmedetomidine were effective in decreasing the hypertensive response to laryngoscopy and intubation though the use of Dexmedetomidine was more effective for the same. Laryngoscopy and Endotracheal intubation provoke a transient, but marked sympathetic and response leading to hypertension and tachycardia. In situations when laryngoscopy and intubation is difficult or when a high risk patient is involved (coronary artery disease, intracranial hypertension, and intracranial aneurysm) it would seem prudent to pharmacologically attenuate blood pressure surges associated with laryngoscopy and intubation. Various drugs have been used to attenuate this post intubation hemodynamic response such as opioids, beta blockers, calcium channel blockers, local anaesthetics, magnesium sulphate etc [6]

No single drug or anaesthetic technique has been accepted to be completely effective in attenuating this sympathetic response. The methods which are being used are either partially effective or produce undesirable side effects.

The α-adrenoceptors are involved in regulating the autonomic nervous system and cardiovascular systems. α2- -adrenoceptors are located on blood vessels, where they mediate vasoconstriction and on sympathetic presynaptic terminals where they inhibit epinephrine and nor-epinephrine release. α2-adrenoceptors are also located within the central nervous system and their activation leads to sedation, a reduction of tonic levels of sympathetic outflow and an augmentation of vagal activity. This can result in a decrease in HR and cardiac output. The use of α_2 -agonists in the peri-operative period has been associated with reduced anaesthetics requirements and attenuated HR and blood pressure responses to stressful events. [9, 10]

Different authors postulate that brief periods of hypertension during induction of anaesthesia in neurosurgical patients may result in bleeding or increase in cerebral oedema. [2]

Dexmedetomidine is α2-adrenergic agonist which produces its action by decreasing the catecholamine release from locus cereleus in the brain. It decreases the cerebral blood flow (CBF) while preserving the CBF-cerebral metabolic rate coupling, decrease ICP, attenuation of hypoxic injury to brain as well as decrease the vasodilation produced by use of inhalational agents.[11,12] Hence it is a potentially attractive adjunct for neuro-anaesthesia to attenuate hemodynamic response. It has also been found to influence the catecholamine surge associated with endotracheal intubation. [9]

Various studies have used Dexmedetomidine in doses ranging from 0.5 to 10 μg/kg/hr with not so much conclusive data but definitely associated with a significant incidence of bradycardia and hypotension in higher doses. [13, 14, 15]

Rapid administration of Dexmedetomidine might produce tachycardia and hypertension followed by bradycardia and hypotension. We administered Dexmedetomidine at 1.0 μg/kg as IV infusion over 10 min in our study and no bradycardia or hypotension was noticed.

Among the β-adrenergic blocking drugs, Esmolol seems to be an appropriate selection for attenuating the haemodynamic response to laryngoscopy and endotracheal intubation, because of its cardio selectivity, rapid onset of action and short elimination half-life. [16]

Liu *et al*used Esmolol infusion to control haemodynamic responses associated with intubation and found significant decreases in HR and SBP prior to induction and post-intubation.The increase was 50% less in the Esmololtreated patients compared to the placebo group. [17]

Esmolol decreases the force of contraction and HR by blocking beta-adrenergic receptors of the sympathetic nervous system which are found in the heart, blood vessels and other organs of the body. Esmolol prevents the action of two naturally occurring neurotransmitters epinephrine and nor-epinephrine, thereby attenuates tachycardia and hypertensive responses to laryngoscopy and tracheal intubation.

In our study we found increase in heart rate was more in Esmolol group (9bpm) compared to Dexmedetomidine group (3bpm) immediately after intubation. Heart rate reached baseline values by 3 min in Group D and also dropped below baseline, but maximum drop in HR was by 8% by the end of 10 min interval. It took more than 10 min to reach baseline in Esmolol group (Group E). There was also statistically significant difference in HR at all time intervals in our study with values lower in Group D. This confirms that Dexmedetomidine is better in controlling heart rate associated with Laryngoscopy and Endotracheal Intubation.

There was 10.8% rise in SBP in Group D compared to 20.1% rise in Group E immediately after laryngoscopy and intubation. SBP reached baseline values by 7 min in Group D as compared to 10 min in Group E which states that SBP is stabilised early in Dexmedetomidine group.

DBP was also drastically increased in Group E soon after intubation (21mmHg) as compared to Group D (6mmHg). So we see that Esmolol is not so effective in reducing DBP which results in a significant rise in MAP. DBP reached baseline values by 7 min in Group D but not before 10 min in Group E (Esmolol)

We also found statistically significant changes in MAP immediately after intubation and at 10 min interval after intubation where values were lower in Dexmedetomidine group (Group D) as compared to Esmolol group. (Group E).

6. Conclusion

Dexmedetomidine as an intravenous infusion (1 µg/kg wt.) infused over 10 minutes is more effective than Esmolol infusion(2mg/kg) infused over 10 min for attenuation of haemodynamic response to laryngoscopy and endotracheal intubation.

7. Limitations

7.1 Plasma catecholamine levels were not assessed by us to know the degree of suppression of neurohumoral pathway.

7.2 We did not have a control group to compare effectiveness of Esmolol to abolish haemodynamic response as compared to placebo group.

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