COMPARISON OF DEXMEDETOMIDINE VERSUS ESMOLOL IN ATTENUATING HAEMODYNAMIC RESPONSES DURING AND IMMEDIATELY AFTER TRACHEAL INTUBATION

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ABSTRACT

BACKGROUND

Laryngoscopy and tracheal intubation produce sympathetic overdrive by catecholamine release resulting in complications like hypertension, tachycardia, cardiac arrhythmias, cerebrovascular accidents, which can be detrimental to the patient's life. Various agents are being tried to combat the intubation responses over years and dexmedetomidine and esmolol are the newer ones.

The aim of the study is to compare dexmedetomidine versus esmolol in attenuating haemodynamic responses during and immediately after tracheal intubation.

MATERIALS AND METHODS

Ninety patients scheduled for general anaesthesia were divided into three groups, D, E and C with 30 patients in each group. Group-D patients received dexmedetomidine 0.5 mcg/kg; Group-E patients received esmolol 0.5 mg/kg and Group-C patients received 0.9% 20 mL saline as intravenous premedication over 5 minutes before anaesthesia induction. Systolic, diastolic and mean arterial pressures along with heart rate were measured at various time points. The percentage change in haemodynamic parameters at different time points from the baseline were compared between the groups.

Statistical Analysis Used- Descriptive and inferential statistical methods were used to analyse the data.

Settings and Design- This was a prospective randomised double-blind controlled study.

RESULTS

The percentage change of all haemodynamic parameters from baseline were less in the dexmedetomidine group than in esmolol group at all time points of measurement. However, a statistically significant differences were observed often at the time points between endotracheal intubation and at 3 mins. after tracheal intubation. The increase in heart rate, systolic, diastolic and mean arterial pressures were significantly lesser in dexmedetomidine group ($P<0.05$) than compared to other two groups immediately after intubation to 3rd minute.

CONCLUSION

Dexmedetomidine is superior to esmolol in attenuating the haemodynamic responses to laryngoscopy and immediately (<3 minutes) after tracheal intubation.

KEYWORDS

Dexmedetomidine, Esmolol, Haemodynamics, Intubation, Laryngoscopy.

HOW TO CITE THIS ARTICLE: Mishra JC. Comparison of dexmedetomidine versus esmolol in attenuating haemodynamic responses during and immediately after tracheal intubation. J. Evid. Based Med. Healthc. 2017; 4(81), 4765-4769. DOI: 10.18410/jebmh/2017/951

BACKGROUND

During general anaesthesia, airway control is generally provided by laryngoscopy and intubation. Laryngoscopy and intubation leads to mechanical and chemical stimuli. Mechanical stimuli causes reflex responses in cardiovascular and respiratory systems, which reaches its peak within 1 minute and ends by 5 to 10 minutes after intubation.[1] Chemical stimuli is mediated through release of catecholamines, which causes tachycardia, hypertension and arrhythmias. The degree of the reflex response of laryngoscopy and intubation is related with the deepness of anaesthesia, patient's age and the presence of diabetes or heart disease.[2] Some treatment modalities to prevent or reduce haemodynamic responses include topical lignocaine sprays, deeper planes of anaesthesia by inhalational/intravenous (IV) agents or narcotics, calcium channel blockers, vasodilators such as sodium-nitroprusside; nitroglycerine, etc.

Dexmedetomidine is a selective α_2 adrenergic agonist. Its effects on cardiovascular system are particularly prominent.[1,3] It produces dose-dependent sedation, anxiolysis and analgesia due to its effect on central adrenergic outflow. Esmolol is a cardioselective β adrenergic blocker that has an effect with rapid onset and shorter duration.[2] While it inhibits β_1 receptors of myocardium, it

Financial or Other, Competing Interest: None.
Submission 02-09-2017, Peer Review 20-09-2017,
Acceptance 03-10-2017, Published 06-10-2017.
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DOI: 10.18410/jebmh/2017/951

also inhibits β_2 receptors of smooth muscles of bronchial and vascular walls at higher doses.[4]

In this study, we aimed to compare the effects of dexmedetomidine and esmolol in attenuating haemodynamic responses during and after endotracheal intubation.

MATERIALS AND METHODS

Ninety elective surgery patients who were in American Society of Anesthesiology (ASA) I and II groups and whose ages were between 21 and 65 years were included in the study. Informed written consent were taken. The study was planned as a prospective, double blind and randomised controlled study. Those in whom difficulty in intubation was expected, who had coronary artery disease, hypertension, chronic obstructive pulmonary disease or diabetes and who were using any cardiovascular medication were excluded.

All patients were examined one day before and their laboratory results were reviewed. Included patients received necessary information about the study and gave their written consents. Before admittance to operation room, vascular access was obtained from the back of the hand with 20G cannula and 10 mL/kg/hour Ringer's lactate infusion was started. Following transferring to operation room, premedication with 0.01 mg/kg Intravenous (IV) midazolam, 0.08 mg/kg glycopyrrolate was performed. ECG (electrocardiogram) and Heart Rate (HR) were monitored, Systolic (SAP), Diastolic (DAP) and Mean (MAP) Arterial Pressures were monitored via automatic noninvasive blood pressure measurements and peripheral oxygen saturation (SpO_2) was monitored via pulse oximetry.

The patients were randomised into three groups. The subjects were blinded to the treatment they received. The anaesthesiologists who prepared and administered the medications were provided to be different. Group D (n=30) received 0.5 µg/kg, dexmedetomidine with infusion in 5 mins., Group C (n=30) received 20 mL 0.9% normal saline and Group E received 0.5 mg/kg, esmolol 2 mins. before induction. Then, 5 mg/kg thiopental and 0.1 mg/kg vecuronium were administered intravenously. Three minutes later, laryngoscopy and intubation were performed by the same anaesthesiologist. The patients in whom endotracheal intubation could not be achieved within 45 seconds were excluded from the study. All patients received 50% O_2 (2 L/mins.), 50% N_2O (2 L/min.) and 1.5 MAC sevoflurane (Sevorane®, Abbott) during maintenance of anaesthesia. These parameters (heart rate, blood pressure) were measured and recorded before induction, after induction, before intubation and 1, 3, 5 and 10 mins. after intubation in all patients. The measurements before induction were considered as basal levels and all of other measurements were compared with these basal levels. Surgical incisions were started following completion of the data collection process. The patients were ventilated in order to maintain end-tidal CO_2 levels between 30 and 35 mmHg. During the operations, HR, SAP, MAP, DAP and SpO_2 levels were recorded with 5 mins. intervals. After the operations, the subjects were monitored in recovery room for 60 mins. following awakening and then were transferred to inpatient clinics.

Statistical Analysis

SPSS (Statistical Package for Social Sciences) for Windows version 10.0 was used for statistical analysis. One-way ANOVA and Student's t-test were used for comparison of quantitative data besides descriptive statistical methods (mean, standard deviation) in evaluation of study data. Chi-square test was employed for comparison of qualitative data.

After the pilot study, it was decided that a 20% of difference should be the minimum detectable difference of means in all groups. The Standard Deviation (SD) of residual was also kept at (20% of average difference between the groups). The α value was 0.05 and the power of the study was 0.80. Thus, the calculated sample size for each group was 24 patients. So, we decided to include 30 patients in each group. The comparisons were considered as not significant ($p > 0.05$), significant ($p < 0.05$) or extremely significant ($p < 0.001$) in a confidence interval of 95%.

RESULTS

All cases were selected from General Surgery only. All the 90 patients completed the study. The demographic profile of the patients in terms of age, bodyweight, male:female ratio, ASA status, Mallampati class were comparable and there were no significant differences among the 3 groups ($P > 0.05$) Table 1.

Variables	Group C	Group E	Group D	P value
Age (years)	44.11 ± 8	45 ± 7.6	45.7 ± 8.8	0.800
Weight (kg)	53 ± 5.6	53.4 ± 4.3	53 ± 4.9	0.9348
Height (cm)	153.25 ± 7.9	153.9 ± 4.4	153.8 ± 7.4	0.946
BMI (kg/sq. m.)	22.65 ± 1.5	22 ± 1.6	22.7 ± 2	>0.05
Sex (male:female)	10:20	10:20	12:18	0.823
ASA status I/II	8/22	8/22	9/21	0.946
MP grade I/II	7/23	7/23	8/22	0.941
Baseline SpO2	98.2 ± 0.5	99.3 ± 0.6	98.23 =/- 0.58	0.815

Table 1. Patient's Characteristics

Values are mean ± SD, BMI- Body mass index; ASA- American Society of Anaesthesiologists; MP- Mallampati; SpO2- Oxygen Saturation; SD- Standard Deviation.

The increase in mean HR after intubation was seen in all the three groups. But, the mean increase was statistically minimal in Group D compared to other two groups immediately after intubation (P = 0.0004) and 3 minutes after intubation (P = 0.0027) Table 2.

HR (/Min.)	Group C	Group E	Group D	P Value
Baseline	80 ± 4	82 ± 4	84 ± 4	0.762
After study drug	80 ± 6	76 ± 2	80 ± 4	0.727
After induction	80 ± 6	76 ± 2	80 ± 4	0.727
After intubation	104.8	90	84.5	0.0004*
3rd min.	102.5	90	84	0.0027*
5th min.	96	88	82.6	0.079
7th min.	88.5	84	78	0.219
10th min.	82	80	78	0.832

Table 2. Mean Heart Rate of Patients in all the Groups

HR- Heart Rate.

The mean SAP levels in Group D were significantly lower than Groups C and E immediately after intubation (P <0.001) and at 3rd minute (P=0.001) and 5th minute (P=0.003) after intubation. Esmolol does not prevent the raise in SAP following intubation, but the raise was less when compared with the patients in Group C, Table 3.

Mean SAP (mmHg)	Group C	Group E	Group D	P Value
Baseline	122 ± 9.5	121.5 ± 11.0	121.4 ± 4.5	0.985
After study drug	126 ± 12.8	131 ± 17.5	127.5 ± 15	0.710
After induction	114 ± 6	114 ± 12	122 ± 13.8	0.439
After intubation (1 min.)	166 ± 13.5	156 ± 13	125 ± 18.6	0.0001***
3rd min.	142 ± 18.47	148 ± 21.9	117 ± 12.7	0.0001***
5th min.	133.80 ± 16.4	132 ± 22.2	111.15 ± 11.6	0.003*
7th min.	124 ± 12.8	125 ± 18	111 ± 12.3	0.078
10th min.	122 ± 12.5	120.5 ± 18.5	114.2 ± 14.3	0.461

Table 3. Comparison of SAP in all the Groups

Values are mean ± SD, *significant, **highly significant, ***extremely significant.
SD- Standard deviation, SAP- Systolic arterial pressure.

The DAP levels in Group D were significantly lower than Groups C and E immediately after intubation (P=0.0001) at 3rdminute (P=0.003) Table 4.

Mean DAP (mmHg)	Group C	Group E	Group D	P Value
Baseline	78 ± 8.7	77.8 ± 8.7	79.2 ± 8.75	0.980
After study drug	76 ± 8.7	77.5 ± 8.4	81.4 ± 14	0.688
After induction	78 ± 5.3	72.3 ± 10.5	78.1 ± 13.4	0.517
After intubation (1 min.)	100.5 ± 18.5	94.5 ± 10.8	79.37 ± 16.22	0.0001***
3rd min.	97.8 ± 11.7	84.5 ± 13.5	76.3 ± 12.9	0.0003**
5th min.	81 ± 10	78 ± 8.7	71.7 ± 12.2	0.305
7th min.	80.2 ± 21.3	72 ± 10.4	71.6 ± 10.3	0.323
10th min.	75 ± 9.4	70.5 ± 11.8	70.7 ± 11.9	0.766

Table 4. Comparison of DAP in all the Three Groups

Values are mean ± SD, *significant, **highly significant, ***extremely significant.
SD- Standard deviation, DAP- Diastolic arterial pressure.

The MAP was comparable in all the three groups at baseline level and after induction. There was raise in MAP in all three groups after intubation. The raise in MAP was significantly minimal in Group D immediately after intubation (P=0.0001) and at 3rd minute (P = 0.034) after intubation Table 5.

Mean MAP (mmHg)	Group C	Group E	Group D	P Value
Baseline	92.3 ± 9.4	92.5 ± 8	93.5 ± 6.5	0.962
After study drug	91.5 ± 10	95 ± 11.8	96.5 ± 13.6	0.781
After induction	88.4 ± 6.2	87.6 ± 14	96.6 ± 14	0.371
After intubation (1 min.)	122 ± 16	116.5 ± 10	95.4+/17.6	<0.0001***
3rd min.	107 ± 11.8	104.5 ± 15	91 ± 11.8	0.034*
5th min.	99 ± 10.5	95.3 ± 12	85 ± 12.3	0.140
7th min.	93 ± 8.4	89.4 ± 11.4	84 ± 11	0.486
10th min.	93 ± 8.4	88 ± 11.5	85.3 ± 11.7	0.560

Table 5. Comparison of MAP in Three Groups

Values are ± SD,
*Significant, **Highly significant,
***Extremely significant.
***Extremely significant, SD- Standard deviation.

DISCUSSION

Endotracheal intubation may lead to many systemic effects in the body, few of them are cardiovascular haemodynamic responses characterised with hypertension, tachycardia, arrhythmia and increase in sympathoadrenergic activity. Although, cardiovascular haemodynamic responses carry risk for all patients who receive anaesthesia that risk is more prominent in those who have cerebrovascular or coronary artery disease, thus preventing the increase in sympathoadrenergic activity due to endotracheal intubation is an important aspect.[5] Dexmedetomidine is a selective α_2 adrenergic agonist and esmolol is a short-acting β adrenergic receptor blocker, which are generally used for attenuating the haemodynamic responses.

Among the β-adrenergic blocking drugs, esmolol has some features like cardioselectivity, rapid onset of action and short elimination half-life.[5] There have been several reports discussing the effects of esmolol on both HR and arterial blood pressure during laryngoscopy and ET intubation compared with placebo.[6] Miller et al[6] in their study have reported that 100 mg of single bolus dose of esmolol was effective for controlling the haemodynamic response to tracheal intubation in a Canadian multicenter trial. Liu et al who used esmolol infusion to control haemodynamic responses associated with intubation found significant decreases in HR and SAP prior to induction and post-intubation, the increase was 50% less in the esmolol-treated patients compared to the placebo group.[7]

In our study, we found that the haemodynamic parameters increased after intubation in all the groups, but the response was statistically minimal in Group D when compared to other groups immediately after intubation and at 3rd minute after intubation.

Ugur et al[8] used 1.5 mg/kg esmolol, 1 µg/kg fentanyl and 1.5 mg/kg lidocaine 2 mins. before intubation and found that esmolol prevented the increase in heart rate. On the other hand, Hussain et al[4] compared the effects of 2 µg/kg fentanyl and 2 mg/kg esmolol that were administered 2 mins. before laryngoscopy and intubation and reported that fentanyl was inadequate to prevent the increases in heart rate and blood pressure. They also showed that esmolol prevented the increase in heart rate, but did not have any effect on blood pressure.

Scheinin et al[9] reported that 0.6 µg/kg dexmedetomidine decreased, but not totally suppressed the haemodynamic response to tracheal intubation in healthy individuals. Keniya et al stated that the pretreatment with dexmedetomidine 1.0 µg/kg attenuated, but not totally obtunded the cardiovascular response to tracheal intubation after induction of anaesthesia.[10]

The alpha-2 adrenoreceptors plays important role in autonomic nervous system. The α_2-adrenoceptors are located on blood vessels where they mediate vasoconstriction and on sympathetic presynaptic terminals where they inhibit epinephrine and norepinephrine release.[11] α_2-adrenoceptors in the central nervous system produces sedation on activation, 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, hence the use of alpha-2 agonists in premedication before intubation to attenuate haemodynamic response is substantiated.[12,13]

Patient's characteristics like age, sex and others were statistically matched such that they will not influence the result of the study.

No complications in the form of hypotension, bradycardia and arrhythmias were found in any of the groups studied.

CONCLUSION

Dexmedetomidine is superior to esmolol in attenuating the haemodynamic responses to laryngoscopy and immediately (<3 minutes) after tracheal intubation.

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