Original Article

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Comparison of Dexmedetomidine Versus Esmolol to Decrease the Stressor Responses during Tracheal Intubation and Immediately Thereafter

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Abstract

Context: Endo-tracheal intubation following laryngoscopy may cause sympathetic stimulation by releasing catecholamines and may result in complications like hypertension, tachycardia, cardiac arrhythmias, cerebro-vascular accidents, which can be detrimental to the patient's life. Many drugs and techniques are being tried to reduce the stressor responses to intubation over years, and Dexmedetomidine and esmolol are the newer drugs.

Aims: This study was aimed at comparing dexmedetomidine versus esmolol in attenuating hemodynamic responses during and immediately after tracheal intubation.

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

Subjects and Methods: Ninety patients posted for surgery under general anesthesia were divided into three groups, D and E and C with thirty patients in each group. Group-D patients received the first study drug dexmedetomidine 0.5 µg/kg, Group-E patients received the second study drug esmolol 1 mg/kg and Group-C patients received 0.9% 20ml saline as intravenous over 5 minutes before anaesthesia induction. The subject's Systolic blood pressure, diastolic and mean arterial blood pressures with heart rate were measured at 1st, 3rd 5th, 7th, 10th minute post- intubation.

Statistical Analysis: The statistical methods employed were descriptive and inferential methods for the analysis of the obtained data.

Results: A statistically significant differences were seen in the period between endo-tracheal intubation and at 3 minute post intubation in Group D. The heart rate, systolic, diastolic pressure and mean arterial pressures showed statistically significantly lesser increase in dexmedetomidine group ($P<0.05$) than compared to other two groups at immediate post intubation and till 3minutes thereafter.

Conclusions:

Dexmedetomidine is more efficient than esmolol in reducing the stressor responses to tracheal intubation and immediately (< 3minutes) thereafter.

Keywords: Dexmedetomidine; Esmolol; Hemodynamics; Intubation; Laryngoscopy.

Introduction

During general anaesthesia airway control is provided by endo-tracheal intubation. Laryngoscopy and intubation leads to mechanical and chemical stimuli. Mechanical and chemical stimuli may cause undesired responses in cardiovascular (tachycardia, arrhythmias) and respiratory systems (bronchospasm, laryngospasm), which reaches its peak within 1 minute and ends by 5 to 10 minutes after intubation [4]. Chemical stimuli are mediated through release of sympathetic neurotransmitters (catecholamines) which causes tachycardia, hypertension, arrhythymias. The degree of these responses is related to how deep the anaesthesia plain is? The deeper the plain, lesser is the stressor response. Patient's age and association with diabetes mellitus or heart disease can also influence the pressor responses [6]. Some measures which can be taken to reduce the reflex responses are; using lignocaine 4% spray, opioid drugs, using inhalation anesthetics to deepen the plain of anaesthesia, before laryngoscopy and intubation.

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Dexmedetomidine is a selective α_2 adrenergic agonist. It produces sedation, anxiolysis, and analgesia due to its effect on central nervous system to reduce sympathetic outflow. Esmolol is a β receptor blocker (cardio-selective) that has quick onset of action and is of shorter duration[6]. It is cardio-selective because it inhibits β_1 receptors of the heart and not β_2, but at large doses it can inhibit β_2 receptors also which are present in the bronchial smooth muscles and vascular walls [7].

In our study, we have compared the effects of dexmedetomidine versus esmolol in attenuating hemodynamic responses during and after endo-tracheal intubation.

Methods

Ninety patients posted for elective surgery (general surgery) under general anaesthesia and who were in ASA I and II groups and aged between 20 and 60 years were taken as the subjects for the study. The study was conducted at P.E.S. Medical college and hospital, Kuppam, Andhra Pradesh. Informed consent was taken from the each subject. The present study was a prospective, double blind and randomized controlled study.

Exclusion Criteria

Patients in whom difficult airway and possible difficult intubation was expected, who had Ischemic heart disease, obstructive pulmonary diseases (COPD), diabetes mellitus, hypertension etc and who were using any medications for cardiac diseases were excluded.

All included patients were explained about the procedure and informed written consent was taken. In the pre-operative room intravenous line was secured with 20Gauge cannula and 8 mL/kg/hour Ringer's lactate infusion was initiated. After shifting to operation room, the patients were premedicated with with 0.01 mg/kg intravenous (i.v) midazolam, 0.08 mg/kg glycopyrrolate. The following monitors were connected, Electro Cardio Gram to monitor heart rate (HR) and rhythm, non-invasive blood pressure to monitor systolic blood pressure, diastolic and mean arterial pressure (SAP, DAP and MAP respectively), and pulse oximeter to monitor peripheral oxygen saturation (SpO_2) .

The patients were grouped into three groups randomly by closed envelope technique. The blindness of the study was maintained as the anaesthesiologists preparing the medications and administering them were different. Group D (n = 30) received 0.5 ìg/kg dexmedetomidine with infusion over 5 minutes, Group C (n = 30) received 20 ML 0.9% normal saline and Group E received 1 mg/kg esmolol over 5minutes before anaesthesia induction. Then, 5 mg/kg thiopental sodium and 0.1 mg/kg vecuronium intravenous was given. Laryngoscopy and intubation were performed. Those patients in whom failure of intubation was seen within 30 seconds were excluded. All patients received 50%O_2 (2.5 L/min), 50% N_2O (2.5 L/min) and 1 MAC Isoflurane during maintenance of anaesthesia. Arterial blood pressure, Heart Rate were noted before induction, after the patient is induced, noted before intubation and at 1st, 3rd, 5th, 7th and 10th minute post intubation for all subjects. The measurements taken before induction were designated as base level measurements and all others were compared with those levels.

The Surgery was allowed to commence once the data collection is over. The patients were artificially ventilated using pressure controlled ventilation and end tidal CO_2 levels were maintained between 30 and 35 mm Hg. During the procedure the above said parameters were recorded with 5 min intervals. After the surgery, the subjects were transferred to recovery room and monitored for an hour and then shifted to post-operative room.

Statistical Analysis

The statistical software SPSS 10.0 was used for statistical analysis. Quantitative data was compared using ANOVA and student's t test and the results were presented in mean, standard deviation. Qualitative data was compared using Chi-square test. After the pilot study, we came to know that a 20% of difference should be the detectable difference (minimum) of means in the groups studied. The standard deviation (SD) was also kept at (average difference of 20% among the groups). The α value was 0.05 and the power of the study was 0.80(80%). The sample size calculated for each group was 24 patients, so we included 30 patients in each group. The data when compared was not significant if ($p > 0.05$), significant ($p < 0.05$) in a confidence interval of 95%. To reject null hypothesis the significant level was taken as $P<0.05$.

Results

All the patients completed the study. The demographic parameters of the patients with respect

to age (years), body weight (kilograms), male and female ratio, American Society of Anaesthesiology status, Mallampatti Class were statistically comparable (P> 0.05) among the groups (Table 1).

As soon as the intubation was over, immediately the heart rate increased in all the three groups. But the mean increase was statistically minimal in Group D compared to other two groups at immediate post-intubation (P= 0.0004) and 3 minutes after intubation (P=0.0027) (Table 2).

The mean systolic blood pressure in Group D increased by significantly lesser extent than Groups C and E at immediate post intubation (P< 0.001) and at 3rd minute(P=0.001), and at 5th minute(P=0.003)

Table 1: Patient's characteristics

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/sqm)	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

Values are mean+/-SD, BMI: Body mass index; ASA: American society of anaesthesiologists; MP: Mallampati; SpO2: Oxygen saturation; SD: Standard deviation

Table 2:

HR (/Minutes)	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	85	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

HR- Heart Rate

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

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

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

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

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

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

post intubation. Esmolol didn't prevent the increase in SAP at immediate post- intubation, but the increase was lesser than that in patients in Group C (Table 3).

The DAP increased to significantly lesser extent in Group D than that in Groups C and E at immediate post intubation (P=0.0001), and at 3rdminute (P=0.003)(Table 4).

The baseline MAP was comparable in all the studied groups, both before and post induction. The MAP increased in all the studied groups post intubation, but it was to significantly lesser extent in Group D at immediate post intubation (P=0.0001) and at 3rd minute (P= 0.034) post intubation (Table 5).

Discussion

Endo-tracheal intubation may lead to many systemic effects in the body like, cardiovascular responses in the form of hypertension, tachycardia, arrhythmias. These responses may be detrimental to the patients, especially on those patients who have cardiac and cerebro-vascular diseases [8]. Thus, preventing the excessive increase in sympathetic activity post intubation is very important. Dexmedetomidine, is a selective α_2 adrenergic agonist, and esmolol, is a short acting β receptor blocker which are used to reduce the stress responses.

Among the β– receptor blocking drugs, esmolol has some special features like, quick onset of action, and faster elimination and it is cardio-selective [8]. There are many reports showing its effects on HR and arterial blood pressure after endo-tracheal intubation when it was compared with placebo [9]. Miller *et al* [9] showed that esmolol 100mg bolus effectively controlled the stress response to tracheal intubation. Liu *et al*. used esmolol infusion to control intubation responses, showed that it prevented increase in heart rate and systolic blood pressure prior to and post intubation, when compared to the placebo group [10].

In this study we found that the hemodynamic parameters increased after intubation in all the groups but the response was minimal and significantly lower in dexmedetomidine group when compared to other groups after intubation. The increase in heart rate after intubation was 1.19% in dexmedetomidine group (P=0.0004) when compared to 9.75% in Group E and 31.25% in Group C. And it was also lower for Group D at 3rd minute (P=0.0027).

With respect to increase in SBP and DBP in Group D at 1 minute and 3rd minute it was significantly less(P=<0.0001) when compared to Group E and Group C.

In a study done by Ugur et al [12], he observed that esmolol 1.5mg/kg along with fentanyl 1µg/kg and 1.5 mg/kg lidocaine given 2 minute before intubation prevented the raise in the heart rate.

Scheinin *et al*. [13][3] showed that dexmedetomidine 0.6µg/kg decreased stress response to intubation in individuals. Keniya *et al*. showed that pre-medication with dexmedetomidine 1.0 µg/kg decreased the cardiovascular responses to endo-tracheal intubation post induction of anaesthesia [14].

The α_2 adreno-receptors plays important role in autonomic nervous system. The α_2 –adrenergic-receptors are found on the blood vessels, where their stimulation leads to vasoconstriction and there are also seen in the presynaptic sympathetic terminals, where they inhibit adrenaline and nor-adrenaline release [15]. α_2 -adrenoceptors in the central nervous system produces sedation on activation, cause reduction in sympathetic outflow such that the Vagal activity takes predominance. This can result in a decrease in HR and cardiac output, hence the use of α_2 agonists used before intubation can decrease the stress responses, and hence its use in our study is substantiated [15].

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, arrhythmias were found in any of the groups studied.

Conclusion

Dexmedetomidine is more efficient than esmolol in attenuating the hemodynamic responses to tracheal intubation and immediately (< 3minutes) thereafter.

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