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ATTENUATION OF THE HAEMODYNAMIC RESPONSES ARISING OUT OF LARYNGOSCOPY AND ENDOTRACHEAL INTUBATION: A COMPARATIVE STUDY OF ESMOLOL, METOPROLOL AND DILTIAZEM.

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ABSTRACT

Background: Maintenance of hemodynamic responses during laryngoscopy and tracheal intubation is a perpetual challenge for anaesthetists. The drugs commonly used to maintain the hemodynamic responses are ß-blockers, calcium channel and sodium channel blockers.
Objective: To assess and compare the efficacy of Esmolol, Metoprolol and Diltiazem in controlling the hemodynamic responses. Materials and Methods: The study was conducted in the Dept. of Gynaecology, Gandhi Hospital, after the permission from Institutional Ethics Committee. Eligible Patients(N=75) were randomly enrolled into one of the three study groups(n=25). Each group received Esmolol, Metoprolol and Diltiazem respectively 3minutes before laryngoscopy and endotracheal intubation. Haemodynamic parameters i.e., Heart rate, Systolic, Diastolic, Mean arterial pressures and ECG were recorded before, during and after the intubation at 1, 3 and 5 minutes. Results: Esmolol found to be more effective in suppressing the haemodynamic responses followed by Diltiazem and then by Metoprolol.

KEYWORDS: Esmolol, Diltiazem, Metoprolol, Laryngoscopy, Endotracheal intubation, Haemodynamic responses.

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INTRODUCTION

The reflex cardiovascular responses to Laryngoscopy and tracheal intubation were known to anaesthesiologists since a long time[1]. Anaesthesiologists aim at suppressing the sympathetic responses at the time of laryngoscopy and tracheal intubation, and quickly get back the protective sympathetic reflexes thereafter. Failure to blunt the responses to intubation may have disastrous consequences like Cardiac failure, Myocardial infarction, Cerebrovascular accidents and precipitates the condition in patients with coronary artery disease, systemic arterial hypertension and aneurysmal vascular disease. Effect of drugs on the haemodynamic responses can be known by monitoring the heart rate(HR), respiratory rate(RR), Blood pressure, Mean arterial pressure(MAP), electrocardiography(ECG) and by calculating the Rate pressure product (RPP= HR * Systolic Blood Pressure)[2,3]. ß adrenergic blocking drugs[4] and calcium channel blocking drugs[5,6] have been in use for blunting the hemodynamic responses during intubation procedures. Hence this study was carried to find the better and safe drug among the Esmolol, Metoprolol and Diltiazem in suppressing the hemodynamic responses.

Aim

To assess and compare the effect of Esmolol, Metoprolol and Diltiazem in blunting the hemodynamic responses aroused out of laryngoscopy and endotracheal intubation. Hemodynamic responses measured were HR, Systolic blood pressure (SBP), Diastolic blood pressure (DBP), MAP as well as an electrocardiogram(ECG).

MATERIALS & METHODS

The present study was a randomised three arm parallel group study conducted in the Dept. of Gynaecology after the permission of institutional ethics committee for the study period of one year. The female patients of age group 20-50 years of bodyweight 40-70kgs of Grade 1 ASA (American Society of Anaesthesiology) posted for elective laparoscopic gynaecological surgery under general anaesthesia without any chronic disease were included in the study. Written informed consent was taken from the patients before enrolling into the study. The number of patients included in the study was 75 and each group (I, II & III) consists of 25 patients. Preoperatively all the patients were assessed clinically i.e., general build of the patient, heart rate, blood pressure and respiratory rate. Laboratory investigations were done to rule out the exclusion criteria. The patients with the following criteria were excluded from the study, i.e., the patients with history of respiratory problems, heart block (Atrioventricular conduction block) greater than first degree, congestive heart failure, cardiac arrhythmias, valvular heart diseases, history of angina, coronary artery diseases, Diabetes mellitus, Hypertension, Hepatic /Renal problems and other major medical problems. And also patients with Baseline heart rate<60/min, Baseline systolic BP <90mm Hg and who are on treatment with beta blockers or calcium channel blockers and patients with predicted difficult intubation were excluded from the study.

Division of groups

For Group – I patients, Esmolol 0.5 mg/kg (25mg) intravenous (IV) bolus dose was given 3 minutes before laryngoscopy and intubation. For Group – II Metoprolol 0.075mg/kg (4mg) IV bolus was given 3minutes before laryngoscopy and intubation. And for Group-III Diltiazem 0.2mg/kg (10 mg) was given as IV bolus 2 minutes before laryngoscopy and intubation.

Study procedure

Preoperatively no sedation was given on the night before surgery. Inj.Glycopyrrolate 0.2mg and Inj.Midazolam 2mg were given intramuscularly 45minutes prior to surgery. Non invasive blood pressure monitor, pulse oximeter and electrocardiographic leads [limb lead II] were connected to the patient prior to induction of anaesthesia. All the patients were oxygenated for 3 minutes, with 100% oxygen before induction of anaesthesia and all the hemodynamic parameters were assessed. Induction was achieved with Inj.Thiopentone

sodium 2.5% solution (5mg/Kg) and intubation was done using Inj.Vecuronium (0.1 mg/kg). The test drugs were given 3minutes prior to laryngoscope and intubation for group I and II patients, whereas 2 minutes before for group III patients. Intubation was carried out by the aid of mackintosh laryngoscope and oral cuffed red rubber tube/portex tracheal tube of appropriate size was used. Time taken for intubation did not exceed 15-20 seconds. Anaesthesia was maintained with vecuronium bromide and intermittent positive pressure ventilation using closed circuit system. Heart rate, Systolic, Diastolic, Mean arterial pressures and ECG were recorded before, during and after the intubation at 1, 3 and 5 minutes. Surgery was allowed to commence after the study was completed. At the end of surgery patients were reversed with Neostigmine [0.05mg/kg] and atropine [0.02-0.04mg/kg].

Statistical Analysis

Data was spread in Microsoft excel sheet; Mean and standard deviations was calculated. Intergroup comparison was done by one way ANOVA method using Prism software and $p<0.05$ was considered significant.

RESULTS

Prior to the study period the mean age and weight in group-1 patients was 30.88±7.50, 55.36±8.23, in group II patients were 32±7.33, 58.48±6.97 and in group III patients were 33.16±9.04, 57.16±6.26 respectively. No significant difference noted in age (p=0.604), weight (p=0.31) and hemodynamic parameters (HR, SBP, DBP and MAP) in between the groups. The Mean±SD of the HR (Table1, Fig 1), SBP(Table2, Fig 2), DBP(Table3, Fig 3), MAP(Table4, Fig 4) was calculated at basal time, during laryngoscopy and intubation and after intubation at 1, 3 and 5 minutes. We noted that there was no significant difference in HR in between the groups prior to induction (basal). We observed a higher increase in HR in Metoprolol group followed by Diltiazem group and least rise in Esmolol group. We also observed that HR returned to basal rate in Esmolol group, 1 minute after intubation but in the other two groups it did not come to the basal rate even after 5 minutes of intubation. Significant difference was noted in between the groups during the time of laryngoscopy and intubation (p=0.018) as well as 1(p=0.006) and 3(0.013) minutes after intubation.

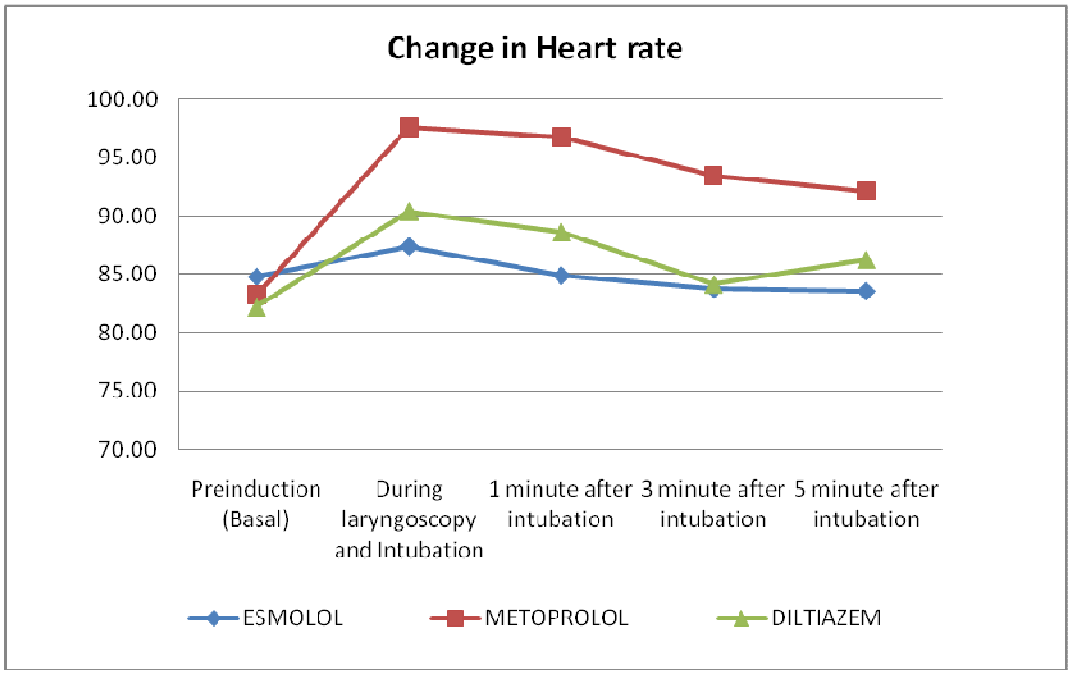
Table1

Change in Heart rate (Mean ±SD) in Esmolol, Metoprolol & Diltiazem Groups

Change in Heart rate	ESMOLOL (Group-I)	METOPROLOL (Group-II)	DILTI AZEM (Group-III)	p-value
	Mean ±SD	Mean ±SD	Mean ±SD	
Preinduction (Basal)	84.76±8.64	83.20±10.62	82.20± 10.12	0.652
During laryngoscopy and Intubation	87.36±11.81	97.60±14.11	90.42±12.35	0.018*
1 minute after intubation	84.88±11.18	96.74±15.12	88.62±12.14	0.006*
3 minute after intubation	83.72±12.40	93.46±14.28	84.15±11.42	0.013*
5 minute after intubation	83.54±11.98	92.12±15.20	86.26±12.10	0.069

p-value is significant

Figure 1
Change in Heart rate (Mean ±SD) in Esmolol, Metoprolol & Diltiazem Groups



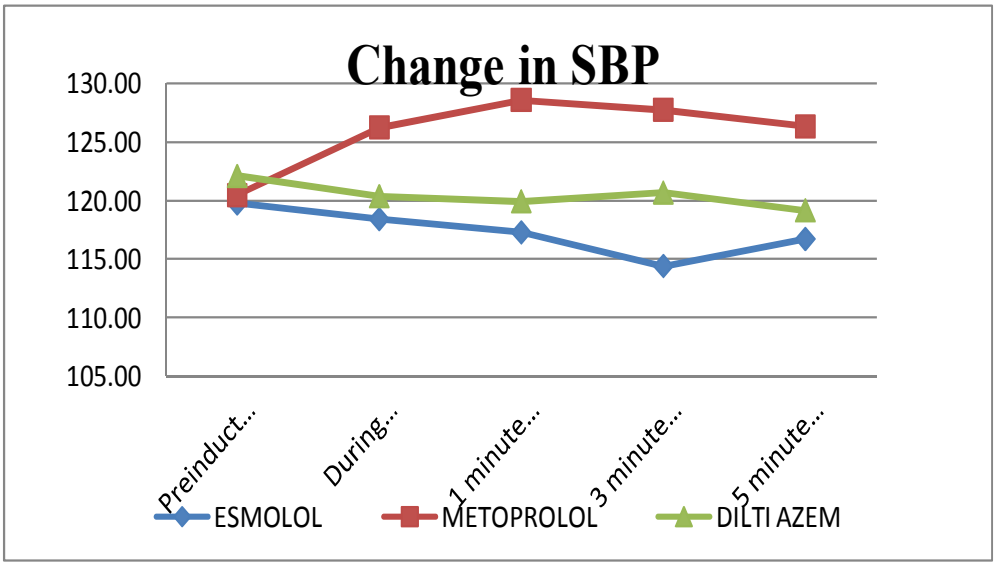
When the SBP was compared there was a significant difference in SBP in between the groups at 1(P=0.022), 3(P=0.007) and 5(P=0.04) minutes after intubation (Table 2, Fig 2). When compared to the basal SBP we observed greater rise in SBP in Metoprolol group till 1 minute after intubation followed by little fall in SBP but did not reach the basal SBP. But in the other two groups instead of rise there is a fall in BP when compared to the basal SBP.

Table 2
Change in SBP (Mean±SD) in Esmolol, Metoprolol and Diltiazem Groups

Change in SBP	ESMOLOL	METOPROLOL	DILTI AZEM	p-value
	Mean±SD	Mean±SD	Mean±SD	
Preinduction (Basal)	119.76±11.13	120.48±10.55	122.10± 11.65	0.749
During laryngoscopy and Intubation	118.42±14.12	126.24±13.24	120.36±15.90	0.145
1 minute after intubation	117.28±16.10	128.56±13.80	119.92±14.26	0.022*
3 minute after intubation	114.40±15.15	127.72±13.59	120.68±14.24	0.007*
5 minute after intubation	116.72±14.70	126.32±12.42	119.14±13.66	0.04*

p-value is significant

Figure 2
Change in SBP (Mean±SD) in Esmolol, Metoprolol and Diltiazem Groups



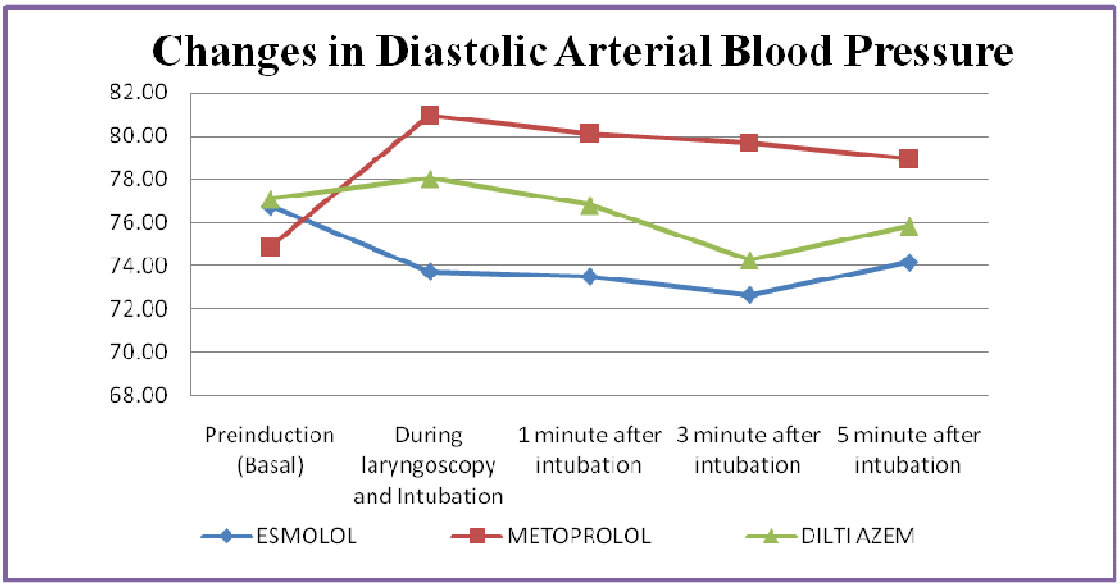
When DBP is measured, we observed there was decrease in DBP in group 1 patients in contrast to the rise in DBP in group II and III patients during laryngoscopy and intubation and significant difference noted in between the groups(p=0.05). In group II patients DBP did not come to basal level even 5 minutes after intubation and in group III, though initially DBP was raised, it came down to basal level by 1minute after intubation (Table 3, Fig.3).we also observed significant difference(p=0.04) in between the groups at 3 minutes after intubation.

Table 3
DBP (Mean± SD) in Esmolol, Metoprolol and Diltiazem Groups

DBP	ESMOLOL	METOPROLOL	DILTI AZEM	p-value
	Mean±SD	Mean±SD	Mean±SD	
Preinduction (Basal)	76.76±8.15	74.88±6.64	77.10±.8.92	0.571
During laryngoscopy and Intubation	73.72±9.64	80.96±11.15	78.04±10.40	0.05
1 minute after intubation	73.50±10.14	80.12±11.26	76.81±10.92	0.102
3 minute after intubation	72.64±10.26	79.70±9.84	74.26±10.14	0.04*
5 minute after *intubation*	74.16±9.66	78.96±9.28	75.84±10.12	0.213

p-value is significant

Figure 3
Changes in DBP with Esmolol, Metoprolol and Diltiazem



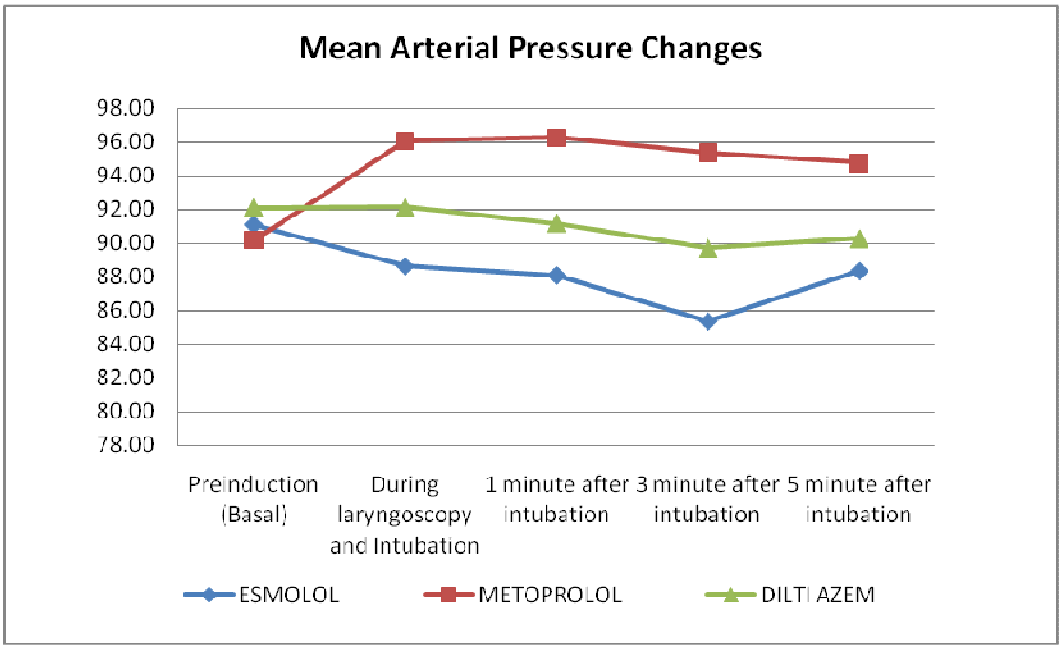
When MAP was measured in Group I patients, we observed a slight decrease in MAP during laryngoscopy and intubation and further decrease was noted 3minutes after intubation and came to basal level after 5 minutes in contrast to other groups. In Group II there was a higher rise in MAP during laryngoscopy and intubation compared to other two groups and it did not reach the basal level even 5 minutes after intubation. In group III initially there was a slight rise in MAP during laryngoscopy and intubation but decreased one minute after intubation. We observed significant difference in MAP in between the groups during laryngoscopy and intubation (P=0.041) and after intubation at 1(P=0.05) and 3(P=0.006) minutes. We also observed higher rise in MAP in group II at 5 minutes after intubation.

Table 4
Changes in Mean Arterial Pressure (Mean±SD) between Esmolol, Metoprolol and Diltiazem Groups

Mean Arterial Pressure Changes	ESMOLOL	METOPROLOL	DILTIAZEM	P VALUE
	Mean±SD	Mean±SD	Mean±SD	
Preinduction (Basal)	91.09±8.39	90.18±7.95	92.10± 9.35	0.732
During laryngoscopy and Intubation	88.62±9.94	96.05±10.48	92.14±10.12	0.041*
1 minute after intubation	88.09±10.90	96.26±12.82	91.18±11.43	0.05*
3 minute after intubation	85.35±10.96	95.37±10.14	89.73±11.14	0.006*
5 minute after intubation	88.34±10.45	94.74±9.68	90.27±10.82	0.087

p-value is significant

Table 4
Changes in Mean Arterial Pressure between Esmolol, Metoprolol and Diltiazem Groups



ECG Changes were found to be within normal limits in all the groups before induction, during laryngoscopy and intubation and after intubation at 1, 3 and 5minutes. In summary in the patients treated with Esmolol, all the hemodynamic parameters were decreased during laryngoscopy and intubation and maintained near to the basal level till five minutes after the intubation. In Group II patients who were treated with Metoprolol there was significant increase in all the hemodynamic parameters and did not come to basal level even 5 minutes after intubation. In group III patients who were treated with Diltiazem, there was increase in the hemodynamic parameters during laryngoscopy and intubation but returned to the basal level by one to three minutes after intubation.

DISCUSSION

Endotracheal intubation and anaesthesia have become an integral part of the anaesthesiologist's contribution to the patient care. Endotracheal intubation is the translaryngeal placement of endotracheal tube into the trachea. Attempts were made to differentiate between effects of laryngoscopy and those of Tracheal intubation and their individual contribution to haemodynamic changes. Prys Roberts et al (1971) observed that a majority of patients produced reflex tachycardia and hypertension well before the act of intubation and was often enhanced by intubation[7, 8]. So it is laryngoscopy rather than endotracheal intubation which generates the stimulus. These changes are probably of little consequence in healthy individuals but of great Consideration and potentially dangerous in patients with hypertension, ischemic heart disease, and other states of cardiovascular compromise. Anaesthetists want to suppress sympathetic responses at one time (e.g., before tracheal intubation) but observed enhanced responses very soon after intubation. Strategies to blunt these responses include minimizing duration of laryngoscopy to less than fifteen seconds, the administration of IV lidocaine/ vasodilators/ narcotics/beta blockers. In this aspect selective beta adrenergic blocking agents are paid more attention to prevent the reflex sympathetic discharge mediated tachycardia and hypertension during procedures of laryngoscopy and endotracheal intubation. Esmolol and Metoprolol[9, 10] are cardioselective ß1-blockers commonly used by the anaesthesiologists. Esmolol is an ultra short acting (half life -10 minutes), with low lipid

solubility and 55% bound to plasma proteins. Given intravenously, it has rapid onset of action with peak effects occurring within 6–10 minutes of administration of a loading dose, and there is a substantial attenuation of ß blockade within 20 minutes of stopping an infusion. Esmolol is not having significant intrinsic sympathomimetic or membrane stabilizing activity at therapeutic dosage. The duration of action of Esmolol is brief because of esterases in erythrocytes which rapidly degrade the drug.

Metoprolol on the other hand is long acting (with plasma half-life: 3-7 hrs) non irritating intravenous agent without intrinsic sympathomimetic activity but have membrane stabilizing activity at high doses. It is having moderate lipid solubility and metabolised in liver CYP2D6 and a little excreted unchanged in urine. It is an age old beta blocker which is in use for blunting the haemodynamic response. ß1-blockers have negative chronotropic effect by which it decreases the heart rate, thereby decreasing the Myocardial oxygen consumption. Diltiazem is a calcium channel blocker belonging to Benzothiazepine group. It is used in the treatment of hypertension, angina pectoris, and some types of arrhythmia and for prevention of migraine. It is a class 3 anti-anginal drug, and a class IV antiarrhythmic agent. On heart it has negative Ionotropic, chronotropic and dromotropic effects thereby decreasing the contractility, HR and conduction. It is a potent coronary and peripheral vasodilator[11].

In this study when bolus dose of Esmolol(25mg), Metoprolol 4 mg and Diltiazem 10mg (0.2mg/kg) were given, we observed that Esmolol was superior to the other two drugs in controlling the hemodynamic responses. In Esmolol treated patients there was decrease in all the hemodynamic parameters during and after laryngoscopy and intubation. In patients who received Metoprolol showed a significant increase in various parameters during laryngoscopy and intubation, while the haemodynamic parameters in Diltiazem group were intermediate between Esmolol and Metoprolol groups. Our study findings that Esmolol attenuates the hemodynamic responses were comparable to the findings of other studies done by Menkhaus G.et al[12]. The other finding of our study was superiority of Esmolol over Metoprolol in decreasing the hemodynamic parameters were similar to the study findings of Dr Javaid A. Zargar et al[13]. The hemodynamic responses with Diltiazem and Esmolol are comparable with the findings of the study done by Santhosh Kumar et al[14].

CONCLUSION

Esmolol in a bolus dose (25 mg) was effective in attenuating the haemodynamic responses to laryngoscopy and endotracheal intubation like heart rate, systolic, diastolic and mean arterial blood pressure. And Esmolol was comparatively better than Metoprolol and Diltiazem in this regard.

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