Double Blind Placebo Controlled Study to Compare the Efficacy of Esmolol and Diltiazem in Attenuation of Pressor Response Due to Laryngoscopy and Endotracheal Intubation in Controlled Hypertensive Surgical Patients

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ABSTRACT

Introduction: Pressor response in the form of tachycardia and hypertension are well documented sequels of laryngoscopy and endotracheal intubation which is transient, highly variable and is generally well tolerated in healthy patients. In hypertensive patients this response is exaggerated. The aim of this study is to find a better alternative by comparing esmolol and diltiazem to attenuate the pressor response to laryngoscopy and intubation.

Material and Methods: One hundred fifty hypertensive patients of either sex (ASA II), controlled on antihypertensive medications in 40-60 Year age range scheduled for routine surgical procedures were divided into 3 groups: Group A (10 ml of 5 % Dextrose), Group B (Esmolol 1.5 mg/Kg) and Group C (Diltiazem 0.2 mg/Kg). Heart rate, systolic blood pressure, diastolic blood pressure, mean arterial blood pressure and rate pressure product were noted at baseline level, at 1 min., 3min. and 5min after tracheal intubation.

Results: When compared to control both esmolol and diltiazem showed a statistically significant attenuation of rise in systolic blood pressure, diastolic blood pressure, mean arterial blood pressure and rate pressure product. However Diltiazem failed to reduce rise in heart rate.

Conclusion: Esmolol was found to be a better agent in attenuating the pressor response to laryngoscopy and intubation in these patients.

Keywords: pressor response, diltiazem, esmolol, intubation, laryngoscopy

INTRODUCTION

There are many techniques and drugs which have been used for blunting the hemodynamic response to laryngoscopy and intubation. An important factor influencing cardiovascular response to tracheal intubation is age and the cardiovascular response to laryngoscopy and intubation is exaggerated in hypertensive patients.[1] The proposed mechanisms responsible for exaggerated hemodynamic changes. Arterial lumen narrowing, blunted baro reflex response and increased sympathetic activity.[2]

Various medications like Calcium channel blockers have been used because myocardial depression produced is minimized by reduction in afterload so that cardiac output remains unchanged, but they have no effect on observed tachycardia.[3,4] Beta adrenoreceptor blockade minimizes increase in heart rate and myocardial contractility by attenuating the positive chronotropic and ionotropic effects of increased adrenergic activity.[1,5-6] The study was carried out in a Teritiary Care Medical Facility and the aim was to find a better alternative by comparision between Esmolol and Diltiazem to attenuate the pressor response to laryngoscopy and intubation: the response being more so in hypertensive patients.

MATERIALS AND METHODS

One hundred fifty hypertensive patients of either sex with (American Society of Anesthesiologists Physical Status Classification System) ASA II, controlled on antihypertensive drugs, between age range of 40-60 years scheduled for routine surgical procedures under general anesthesia (Open and Laparoscopic Cholecystectomy, Hydated Cystectomy,

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Common Bile Duct Exploration, AbdominoPerineal Resection, Thyroidectomy, Mastectomy, Exploratory Laparotomy for Carcinomas of Gut and Pancreas, interval Appendicectomy, Hernioplasty) were enrolled in our study. After proper approval from Institutional Review Board & Ethics Committee an informed consent to participate in the study was taken from all the patients. Patients on treatment with calcium channel blocker or β-blockers, history of bronchial asthma; history of cardiac disease; uncontrolled hypertension; History of allergy to any of the study drugs and patients with predicted difficult intubation were excluded. After taking informed consent, the patients were prepared by overnight fasting and sedation with Alprazolam 0.5 mg given orally at bedtime on the night before surgery.

Patients were continued on antihypertensive therapy till the morning of surgery and three hours before the expected time of surgery every patient was given Alprazolam 0.5 mg with water. The patients were divided into three groups of 50 patients each randomly by simple randomization.

Group A: Comprised of 50 patients who received 10 ml of 5 % dextrose water following intravenous induction. This served as a control group for the present study.

Group B: Comprised of 50 patients who received Injection Esmolol 1.5 mg/kg diluted in 10 ml of 5% dextrose water following intravenous induction.

Group C: Comprised of 50 patients who received Injection Diltiazem 0.2 mg/kg diluted in 10 ml of 5 % dextrose water following intravenous induction.

Just before administration of any drugs, parameters, i.e., heart rate, systolic blood pressure, diastolic blood pressure, mean arterial blood pressure and rate pressure product were noted.In all the patients standardized anaesthesia technique was used. Pre-oxygenation was done in all patients for three minutes, followed by Sodium Thiopentone (5 mg/kg of 2.5 % solution) intravenously until loss of eyelash reflex followed by administration of study drug. Succinylcholine 1.5mg/kg was used to facilitate endotracheal intubation and 90 seconds after administration of Succinylcholine, intubation was performed. Patients in whom more than one attempt of laryngoscopy was required and total duration of laryngoscopy exceeded 30 seconds were excluded from the study. The position of endotracheal tube was confirmed and, anaesthesia was maintained using nitrous oxide and oxygen with volatile anaesthetic agent (Isoflurane 0.2 %) delivered through closed circuit. Bolus dose of Atracurium besylate 0.5 mg / kg intravenous initially for muscle relaxation followed by top up doses to maintain muscle relaxation was used. The residual effect of muscle relaxant was reversed with Neostigmine (2.5 mg) and glycopyrrolate (0.5 mg) at the end of the surgery. After full clinical recovery was achieved and after thorough Oropharyngeal suctioning extubation of trachea was done. Thereafter, patients were shifted to recovery room. The study period extended from the induction of anaesthesia to five minutes after intubation. Surgical stimulas was not allowed during study period. Heart rate, Systolic blood pressure, Diastolic blood pressure, Mean blood pressure and Rate pressure product (systolic blood pressure x heart rate) were noted at baseline level, after giving study drug, immediately after laryngoscopy and intubation, at 1 minute, 3 minutes and 5 minutes after the tracheal intubation.

STATISTICAL ANALYSIS

All parameters of the study were statistically evaluated by using student's t-test and chi-square test. Power of study and sample size was estimated assuming any p-value less than 0.05 i.e. ($p < 0.05$) was going to be statistically significant.

RESULTS

There was no statistically significant difference between the groups with respect to age and sex (table 1). Baseline heart rates in the three groups and changes in their levels soon after laryngoscopy and intubation was observed and tabulated in (table 2) in all the three groups. In groups A,B and C respectively showing a highly statistical difference on comparison. The rise was significantly attenuated in the Esmolol group. Thereafter when Group C and A were compared, the heart rate in both the groups showed increase after intubation, that was statistically significant ($p < 0.05$) and it persisted upto 5 five minute after intubation. However the rise in heart rate was statistically more significant in Group A when compared with Group C. When heart rate in Group B and Group C were compared, the rise in heart rate was attenuated in Group B while in Group C there was significant ($p < 0.05$) rise in the heart rate.

The systolic blood pressure at baseline was 126.50 + 6.95 in Group A. A statistically significant rise in systolic blood pressure soon after laryngoscopy and intubation 161.64 + 16.64 and the increase in systolic blood pressure remained statistically significant till 5 minutes after intubation. The systolic blood pressure (table 3) at baseline were 128.77 + 9.59 and 132.04 + 10.80 in Group B and C. The drug B and C successfully attenuated any rise in systolic blood pressure soon after laryngoscopy and intubation 124.76 + 10.24 and128.84 + 14.19 and continued to do so upto 5 min after the intubation 124.94 + 8.36 and 130.98 + 10.63 respectively.

Soon after laryngoscopy and intubation diastolic blood pressure (table 4) in Group A showed statistically significant rise from baseline 77.78 + 5.03 to 105.60 + 18.08 and remained statistically significantly high upto five minutes after intubation 88.52 + 8.26. In Group C the diastolic blood pressure showed a fall from baseline 80.55 + 8.27 to 71.00 + 7.82 at 3 minutes after intubation. Soon after laryngoscopy and

Groups	Gender female (%)	Age (yo) Mean +SD
Group A n = 50	33 (66%)	52.12+13.75
Group B n = 50	39 (78%)	51.72+14.74
Group C n = 50	36 (72%)	49.74+13.97

Table-1: Distribution of gender and age among groups.

Groups	Basal	After study drug	Laryngoscopy & intubation	1 min after intubation	3 min after intubation	5 min after intubation
Group A Mean + SD	88.62+10.03	88.08+12.72	118.24+14.45	112.52+14.45	104.68+17.83	99.04+3.73
Group B Mean + SD	92.77+13.36	88.96+12.51	92.0+13.071	89.48+13.00	88.84+15.38	84.90+11.89
Group C Mean + SD	92.08+13.808	97.24+15.32	100.94+13.69	102.94+13.691	102.94+14.21	103.57 +13.04

Table-2: Comparison of heart rates between the groups A, B and C

Groups	Basal	After study drug	Laryngoscopy & intubation	1 min after intubation	3 min after intubation	5 min after intubation
Group A Mean + SD	126.50+6.95	123.34+8.49	161.64 +16.64	145.12+23.08	139.10+12.45	133.52+10.03
Group B Mean + SD	128.77+9.59	125.28+12.86	124.76+10.24	125.86+12.17	125.45+10.05	124.96+8.39
Group C Mean + SD	132.04+10.80	129.94+11.79	128.84+14.19	129.95+10.15	130.74+10.21	130.98+10.63

Table-3: Comparison of Systolic Blood Pressure between the groups A, B and C

Groups	Basal	After study drug	Laryngoscopy & intubation	1 min after intubation	3 min after intubation	5 min after intubation
Group A Mean + SD	77.78+5.03	78.84+6.50	105.60 +18.08	100.90+10.71	93.18+9.58	88.52+8.26
Group B Mean + SD	81.28+7.61	79.82 +8.20	80.44+9.79	79.90+7.67	78.35+9.56	80.75+8.27
Group C Mean + SD	80.55+8.27	76.51+8.77	74.28 +9.68	74.28+9.68	71.00+7.82	74.82+9.11

Table-4: Comparison of Diastolic Blood Pressure between the groups A, B and C.

intubation the diastolic blood pressure in Group C was 76.67 + 9.82. In Group B diastolic blood pressure insignificantly changed from baseline 81.28 + 7.61. The diastolic blood pressure was 80.44 + 9.79 soon after laryngoscopy and intubation and 80.75 +8.27 at 5 minute after intubation.

In Group A Rate pressure product rose from baseline, peaking at laryngoscopy and intubation 18966.66 + 3032.22 and at 5 minutes after laryngoscopy and intubation 13202.04 + 2043.80. In Group C when rate pressure product was compared at different intervals with baseline 12235.22 + 2258.24, there was insignificant ($p > 0.05$) difference at laryngoscopy and intubation 12508.28 + 2982.23 and at 5 minutes after intubation 12318.86 + 1678.84. In Group B rate pressure product when compared at different interval with baseline 12027.06 + 2271.43, there was insignificant ($P>0.05$) difference at different intervals at laryngoscopy and intubation 12521.35 + 2003.04 and at 5 minutes after laryngoscopy and intubation 11824.51 + 1786.00

DISCUSSION

Laryngoscopy and endotracheal intubation are documented cause of tachycardia and hypertension.[1,7] Cardiovascular response to laryngoscopy and intubation is exaggerated in hypertensive patients.[1] Major determinant of myocardial oxygen consumption is heart rate and there is an increasing evidence that tachycardia is poorly tolerated in patients with coronary artery disease. There is an increased incidence of myocardial ischemia when intra operative heart rates exceed 110/min.[8,9]

After intubation in Group B (Esmolol group) there was significant attenuation in rise of heart rate, systolic blood pressure, diastolic blood pressure, mean arterial pressure and rate pressure product as compared to base line values. These findings are consistent with the result of Miller et al.[10] Esmolol is a cardio selective beta blocker with ultra short duration of action and has been indicated for the treatment of tachycardia and hypertension during tracheal intubation.[11] In the Esmolol group we observed that the increase in heart rate after laryngoscopy and intubation were significantly attenuated and remained throughout the study period. Multiple studies have shown similar results.[8,12,13]

In Group C (Diltiazem group) after laryngoscopy and intubation there was a significant rise in heart rate in and remained so throughout study period when compared with the control group.[14,15] A significant attenuation by group was seen on comparison of Esmolol and Diltiazem and a similar study by Kumar Santoshet al also concluded with the same results.[13]

Systolic blood pressure rose significantly in the control group following laryngoscopy and intubation and remained high thereafter for five minutes following intubation. Esmolol and Diltiazem successfully attenuated the rise in SBP and on comparison showed a statistically significant difference with the control group. These findings were similar to those of the Mikawaand Fuji.[15-16]

Similarly diastolic blood pressure showed a significant rise during laryngoscopy and intubation in group A and persisted upto 5 min. as compared to group B and C when diastolic blood pressure and mean arterial pressure were observed during study period. The rise in diastolic blood pressure was attenuated in Group B while in Group C the diastolic blood pressure showed falling pattern from administration of drug till 3 minutes and then again, at 5 minutes the diastolic blood pressure showed a rise on comparing Group B and C.In the control group mean arterial pressure rose and persisted for 5 min but both Group B and C attenuated the rise in MAP, more efficiently by Esmolol Group.

Rate pressure product is calculated by multiplying systolic blood pressure with heart rate and is good estimate of myocardial oxygen requirement.[17] Significant ($p < 0.05$) rise from baseline, peaking at laryngoscopy and intubation 18966.66 (+ 3032.22) and at 5 minutes after laryngoscopy and intubation 13202.04 (+ 2043.80) was seen in Group A. When comparing rate pressure product between Group B and Group C, there seemed to have significant differences at respective time intervals, but in both groups the rise in rate pressure product is insignificant.

Menkhaus and Miller also concluded that esmolol is effective in controlling systolic, diastolic and mean arterial pressure following laryngoscopy and intubation.[10,18,19] Findings in Group C (Diltiazem group) showed significant attenuation in rise in systolic, diastolic and mean arterial pressure when compared with base line. These are consistent with the findings of the Mikawaand Fuji.[15,16]

On comparing the changes in heart rate, systolic blood pressure, mean arterial pressure and rate pressure product after intubation between Group B (Esmolol) and Group C (Diltiazem) it was found that esmolol attenuated the rise in above mentioned parameters better. These findings are consistent with the findings of Kumar Santoshet al.[13]

CONCLUSION

The esmolol had better attenuating effect of pressor response when compared with diltiazemin the form of alterations in heart rate, systolic blood pressure and rate pressure product when compared between the two study groups. Diltiazem does not prevent rise in the heart rate observed during laryngoscopy and intubation. Hence, esmolol proved to be very effective agent in attenuating the pressor response of laryngoscopy and intubation in controlled hypertensive patients.

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