Original Research Paper

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"COMPARISON OF THE EFFECT OF DILTIAZEM AND ESMOLOL IN ATTENUATING THE CARDIOVASCULAR RESPONSES TO ENDO-TRACHEAL EXTUBATION AND EMERGENCE FROM ANAESTHESIA"

Sharma Mukul V 3rd Year Resident, Dept. of Anaesthesiology, S.B.K.S. M.I. & R.C., Piparia

Sharma Tejash H* Assistant professor, Dept. of Anaesthesiology, S.B.K.S. M.I. & R.C., Piparia
*Corresponding Author

Chauhan Dinesh K. Professor & Head, Dept. of Anaesthesiology, S.B.K.S. M.I. & R.C., Piparia.

ABSTRACT

INTRODUCTION: Endotracheal extubation is almost always associated with haemodynamic changes. This increase in sympatho-adrenal activity may result in hypertension, tachycardia and arrhythmias and is more hazardous to the patients with hypertension, myocardial insufficiency or cerebro-vascular disease.

AIMS: To compare the effects of diltiazem and esmolol in attenuating the cardiovascular responses to tracheal extubation.

MATERIAL AND METHOD: After ethical committee's approval, this observational study was carried out on ASA class I-II patients. After pre-anaesthetic checkup, 60 patients were randomly allocated to 3 equal groups by using chit method. Patients were given 10 ml saline in Group – S, 0.1mg/kg of diltiazem diluted in 10 ml saline in Group – D and 1mg/kg of esmolol diluted in 10 ml saline in Group – E. These drugs were given 3 minutes after reversal and 2 minutes before extubation.

STATISTICAL ANALYSIS: The results were analyzed using ANOVA, student's paired t-test and chi-square test. 'p' value of <0.05 was statistically significant and <0.001 was highly significant.

RESULTS: Both drugs had greater attenuating effects on haemodynamic changes than control group. Attenuation on changes of heart rate was greater with esmolol whereas of blood pressure was greater with diltiazem.

CONCLUSION: Diltiazem 0.1mg/kg or esmolol 1mg/kg i.v. given at 2 min before extubation was of value in attenuating the cardiovascular changes during tracheal extubation & emergence from anaesthesia. Esmolol is more effective in attenuating the heart rate changes while Diltiazem is more effective in attenuating the systolic blood pressure changes.

KEYWORDS : Diltiazem, Esmolol, Haemodynamics, Endotracheal extubation.

INTRODUCTION

Haemodynamic changes due to reflex sympathetic discharge caused by epipharyngeal and laryngopharyngeal stimulation are almost always associated with endotracheal extubation. This increase in sympatho adrenal activity may result in hypertension, tachycardia and arrhythmias.[1,2] This increase in blood pressure and heart rate are usually transitory, variable,unpredictable and more hazardous to the patient with hypertension, myocardial insufficiency or cerebrovascular diseases.[3] Many pharmacological agents have been used to reduce the extent of haemodynamic events accompanying extubation e.g esmolol, alfentanil, fentanyl, diltiazem.[1,2,7] Esmolol is an ultrashort-acting, highly cardioselective beta-adrenerenergic receptor antagonist[8] and Diltiazem, a calcium channel blocker[1] has been used extensively to blunt the haemodynamic responses associated with laryngoscopy and tracheal extubation.

METHOD

Study type: Observational study
Duration of study: one year and 6 months

Sample size: Selected 60 patients were allocated into equal three groups by chit method.

After obtaining approval of the ethical committee & informed consent 60 patients of ASA status I & II were randomly divided into 3 groups using chit method (20 patients per group). Patients were given 10 ml saline in Group – S, 0.1mg/kg of diltiazem diluted in 10 ml saline in Group – D and 1mg/kg of esmolol diluted in 10 ml saline in Group – E. These drugs were given 3 minutes after reversal and 2 minutes before extubation.

Patients belonging to ASA I&II status, age between 18-60 years of either sex, posted for surgery under general anaesthesia were included whereas patients with cardiovascular or respiratory disease, history of allergy to study drugs, comorbidities like hypertension, diabetes mellitus and anticipated difficult intubation were excluded from the study.

In the operation theatre i.v line was secured with 18G veinflow & standard monitors ECG, NIBP, SPO2 were attatched, baseline values noted. All patients were pre-medicated with inj. glycopyrolate 0.004mg/kg i.v., inj. ondansetron 0.1mg/kg, inj. midazolam 0.02 mg/kg i.v., inj. tramadol 1mg/kg i.v. Standard maintenance i.v. fluids continued prior to induction of anaesthesia as per NPO guidelines. Pre-oxygenation with 100% O_2 for 3 minutes done. Induction was done with inj. thiopentone sodium 5-7mg/kg i/v. Tracheal intubation was facilitated with inj. succinylcholine 1.5 to 2 mg/kg i.v. Maintenance of anaesthesia was with O_2, N_2O, Isoflurane (0.2 -1%), inj. vecuronium loading dose 0.1 mg/kg i.v and intermittently 0.02 mg/kg i.v. Pulse, NIBP, ECG, SPO_2, were monitored throughout anaesthesia. After completion of surgery isoflurane and N_2O were discontinued and residual muscle relaxation was reversed by inj. neostigmine (0.05 mg/kg) + inj. gycopyrrolate (0.008 mg/kg) i/v. Three minutes after reversal, 1 mg/kg esmolol diluted to 10 ml or diltiazem 0.1 mg/kg diluted to 10 ml or saline 10 ml were given. Extubation was done 2minutes after administering these drugs. Immediately before tracheal extubation we confirmed that patients could breathe spontaneously and open the eyes on command. Oropharyngeal secretions were aspirated just prior to extubation. Laryngoscopy was not performed during extubation. After tracheal extubation 100% O_2 was given for 5 minutes.

The systolic blood pressure (SBP), diastolic blood pressure (DBP), and heart rate (HR) measured at the end of surgery served baseline values. Hemodynamic data obtained from 3 minutes after the injection of neostigmine-glycopyrrolate (reversal agents) was analyzed for cardiovascular changes associated with emergence from anesthesia and tracheal extubation. Values of SBP, DBP, HR and Mean arterial pressure (MAP) recorded after completion of reversal, at the time of administration of esmolol or diltiazem or saline (3 minutes after reversal-taken as 0 minute) and at 1, 2, 3, 4, 5, 7, 10 and 15 minutes after administration of drugs and these values were also compared with baseline values within individual study groups. Any haemodynamic effects of i.v injection of drugs were monitored for first 2 hours post-operatively.

STUDY PARAMETERS

HR, SBP, DBP and MAP.

OBSERVATIONS & RESULTS:

There were no significant differences in demographic data in all three groups.

Table 1: Changes in mean Heart Rate between Esmolol, Diltiazem and Saline groups

Conditions	Esmolol (n=20)	Diltiazem (n=20)	Saline (n=20)
	Mean ± SD		
Preoperative	92.5 ± 12.18	86.05±7.79	80.45±10.95
Reversal	96.45 ±15.60	89±10.37	86.65±10.93
During drug administration	97.2 ±14.45	91.35±10.79	91.65±9.32
After 1 minute	82.3 ±13.04	85.75±11.9	96.2±10.30
Extubation	74.4 ±11.63	85±12	100.05±11.40
E1	70.3 ±11.35	83±10	109.9±9.08
E2	68.4 ±10.79	84±10	102.1±9.26
E3	69±9.83	84±11	98.7±8.65
E5	71±9.48	86±11	96.4±8.66
E10	74±9.31	87±11	94.45±8.81
E 15	78.4±9.61	89±11	82.1±7.72

The heart rate in the group E was found to be significantly lower than those in group S and group D during extubation and 1,3 and 5 minutes after extubation.

Chart 1: Changes in mean heart rates between diltiazem, esmolol and saline groups

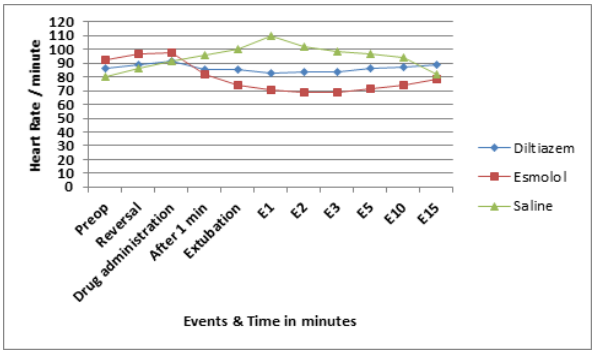


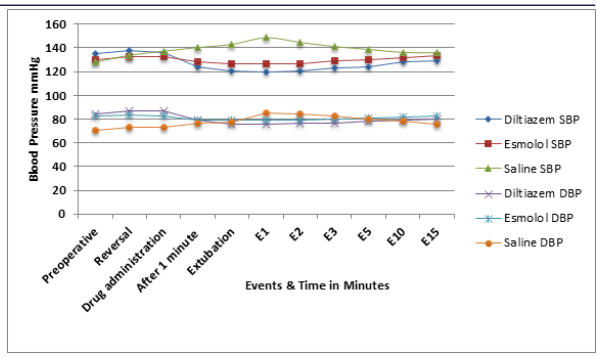
Table 2: Changes in mean SBP & DBP between Diltiazem, Esmolol and Saline group

Conditions	Systolic BP (Each group n=20)			Diastolic BP (Each group n=20)		
	Mean ± SD			Mean ± SD		
	Diltiazem	Esmolol	Saline	Diltiazem	Esmolol	Saline
Preoperative	134.9±7.47	130±5.27	128.1±7.07	84.35±6.62	82.3±4.95	70.7±4.20
Reversal	137.75±5.67	133.05±6.25	133.95±6.21	87.25±8.35	83.6±6.66	73.55±4.91
During drug administration	136.0±8.53	132.6±6.49	137.3±5.64	87.0±8.52	82.9±7.85	73.3±3.38
After 1 minute	124.0±6.41	128±5.73	140.45±6.38	79.6±6.31	79.55±7.22	76.75±3.76
Extubation	121.0±6.3	126.65±5.33	143.05±4.90	76.0±6	79.3±6.19	77.8±4.34
E1	120.0±4.88	127±4.92	148.65±6.40	76.0±5	78.9±6.88	85.3±6.02
E2	121.0±4.5	126.65±5.11	144.7±5.13	77.0±5	78.9±6.37	84.65±6.83
E3	123±5.5	128.9±7.21	141.2±4.16	77.0±6	80.45±6.88	82.5±6.54
E5	124±6.4	129.9±7.57	138.85±3.73	78.0±5	81.25±7.60	80.05±6.09
E10	128±4.6	132±7.45	136.3±4.49	79±4.9	81.75±6.60	78±5.30
E15	129±4.4	133.78±7.16	136±4.69	80±5.5	82.6±5.92	76.1±4.71

The SBP in the group D was found to be significantly lower than those in group E and group S during extubation and 1,3 and 5 minutes after extubation.

The DBP in the group D was not found to be significantly lower than those in group E and group S during extubation and at 1, 3 and 5 minutes after extubation.

Chart 2: Changes in mean SBP & DBP between Diltiazem, Esmolol and Saline group



DISCUSSION

Tracheal extubation often provokes hypertension and tachycardia as does tracheal intubation due to reflex sympathetic discharge caused by pharyngeal and laryngeal stimulation. This stimulation is associated with increase in plasma epinephrine concentration.[8] These cardiovascular responses to tracheal extubation are probably of little consequence in healthy individuals, but may be more severe and more hazardous in patients with hypertension, coronary artery disease and cerebrovascular disease.[9]

Several methods and drugs have been used to provide haemodyanamic stability during extubation and in early post-operative period.[4,5,6]

A number of pharmacological agents including lidocaine, esmolol, alfentanyl, fentanyl and diltiazem have been recommended for the attenuation of haemodynamic changes associated with extubation.[9]

We studied patients in ASA physical status I & II without any cardiovascular disease. This population was chosen to ensure the safety.

In this study we compared the effects of intravenous Diltiazem 0.1mg/kg (Group D), Esmolol 1mg/kg (Group E) & Saline 10ml (Group S) given 3minutes after inj.neostigmine and glycopyrrolate and 2 minutes before extubation.

All the study groups were assessed for any significant differences between the demographic data such as Age variation, male: female ratio. It was then concluded that there was no significant differences in the demographic data between the 3 groups (P>0.05)

The onset of antihypertensive action of diltiazem 0.1mg/kg occurs within approximately 30 sec after a single i.v. injection with a peak effect occurring at 1.5- 2 minutes.[9] The decision to give the drug 2 minutes prior to tracheal extubation was based on this data. The same also holds true regarding esmolol. Intravenous administration of the mixture of neostigmine and atropine increases heart rate within 1 minute, the effect peaking 1-2 minutes after injection. The heart returns to basal values 3 minutes after injection.[10] This was the rationale for administering esmolol, diltiazem or saline, 3 minutes after reversal for attenuation of hemodynamic response to extubation.

Esmolol was used by **Andrew Dyson et al**[8] in 1990 to attenuate the cardiovascular responses associated with extubation in a dose of 1mg/kg, 1.5mg/kg, 2mg/kg. They have concluded that the increase in heart rate that occurs during extubation can be successfully attenuated by bolus injection of 1 mg/kg esmolol, although this dose is insufficient to effectively block increases in SBP. A dose of 1.5 mg/kg blocks the maximal increase in HR and controls SBP. Doses of 2 mg/kg produce significant (>20%) decreases in SBP without further attenuation of the pressor or HR responses. The use of esmolol before extubation maybe beneficial in patients with ischemic heart disease and good left ventricular function, especially in the presence of borderline hypertension.

Similarly In our study, by using esmolol 1mg/kg during extubation, increase in heart rate was attenuated successfully and this dose did not have much effect on SBP, DBP & MAP.

Dae Hue Nam[11] **et al** in 1996 used esmolol in the dose of 1.5 mg/kg and diltiazem in the dosage of 0.2mg/kg to attenuate cardiovascular responses to tracheal extubation, They have concluded that at a bolus dose of i.v. esmolol 1.5mg/kg or diltiazem 0.2mg/kg given 2 min

before extubation was of value in attenuating the cardiovascular changes occurring in association with tracheal extubation and emergence from anaesthesia. Esmolol is more effective than diltiazem in attenuating the heart rate changes. Diltiazem is more effective than Esmolol in attenuating the systolic blood pressure changes. Thus their findings were comparable to our study also.

Habib Boston, Ahmed Eroglu[13] in 2012 had used esmolol in the dose of 1 mg/kg in preventing the haemodynamic responses to endotracheal intubation and extubation. They concluded that when administered before induction and emergence from anaesthesia, 1mg/kg of esmolol is effective in controlling the haemodynamic response to laryngoscopy, intubation and extubation. Thus their findings were comparable to ours.

Esmolol, with its rapid onset and extremely short duration of action ($t^{1/2}$ -9 minutes), would appear to be ideal drug for preventing acute increase in heart rate and systolic blood pressure. However, we would advice caution when using bolus dose of esmolol during extubation unless the patient has received atropine or glycopyrrolate (as part of the reversal of neuromuscular blockade) because tracheal stimulation in the presence of beta blockade may potentially produce profound bradycardia.

Nishina MD et al[2] have reported that calcium channel antagonists like diltiazem, verapamil and nicardipine are also effective in controlling the hemodynamic responses associated with extubation in normotensive as well as in hypertensive patients. In their study found that diltiazem is effective in blunting the haemodynamic responses associated with extubation. The probable mechanism of action of diltiazem are direct vasodilator properties and negative chronotropic and dromotropic properties.

So the use of diltiazem 0.3 mg /kg did not seem to be justified. In view of this in the present study we employed 0.1 mg/kg of diltiazem.

Kahoru Nishina et al[1], **Yujii Morimotoet al**[12] **and Katsuya Mikawaet al**[2] administered diltiazem 0.2 mg/kg 2 minutes before tracheal extubation based on the fact that the onset of antihypertensive action of diltiazem (0.2mg/kg) occurs obviously within approximately 30 sec after a single iv injection, with a peak effect occurring at 1.5-2 minutes.

We noticed that diltiazem 0.1mg/kg i.v. given 2 minutes before extubation was simple, effective and practical method for blunting cardiovascular responses to tracheal extubation. This suppressive effect of diltiazem was compared with esmolol 1mg/kg.

However further studies are required to evaluate the advantage, beneficial effects and safety of diltiazem and esmolol in comparison with other drugs when used for the purpose of attenuating the haemodynamic changes associated with extubation in patients with coronary artery disease and cerebrovascular disease.

CONCLUSION

We concluded that SBP, DBP and heart rate in the control group increased significantly in association with tracheal extubation.

Diltiazem hydrochloride given in dose of 0.1mg/kg i.v. given 3 minutes after reversal and 2 minutes before extubation is more effective in decreasing the blood pressure than the heart rate during tracheal extubation as compared to esmolol. Diltiazem has more effect on the systolic blood pressure than diastolic blood pressure.

Esmolol given in a dose of 1mg/kg, 3 minute after reversal and 2 minutes before extubation is more effective in decreasing the heart rate than the blood pressure as compared to diltiazem during tracheal extubation.

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