

Research Article

COMPARISON OF DILTIAZEM AND ESMOLOL IN ATTENUATING THE CARDIOVASCULAR RESPONSES TO TRACHEAL EXTUBATION.

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ABSTRACT

Background: Endotracheal extubation is almost always associated with haemodynamic changes. This increase in sympathoadrenal activity may result in hypertension, tachycardia and arrhythmias and is more hazardous to the patients with hypertension, myocardial insufficiency or cerebrovascular disease. The aim of this randomized double blind study was to compare the effect of diltiazem and esmolol in attenuating the cardiovascular responses to tracheal extubation. **Methods:** Changes in heart rate(HR), systolic blood pressure(SBP), diastolic blood pressure(DBP) and mean arteial blood pressure(MAP) were measured during extubation and emergence from anaesthesia in 150 ASA physical status I patients to assess the effect of esmolol and diltiazem. The patients were randomly assigned to one of three groups (n=50 for each group): saline 10ml(as control), 0.1mg/kg diltiazem and 1mg/kg esmolol. The medications were given 3 minutes after reversal and 2 min before tracheal extubation. **Results:** Both esmolol and diltiazem had greater attenuating effects on changes of HR, SBP and DBP than control group. The inhibitory effects on changes of heart rate was greater with esmolol than diltiazem, but the attenuating effect on changes of SBP and DBP was greater with diltiazem than esmolol. **Conclusion:** We concluded that a bolus dose of intravenous diltiazem 0.1mg/kg or esmolol 1mg/kg given at 2 min before extubation was of value in attenuating the cardiovascular changes occurring in association with tracheal extubation. 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.

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INTRODUCTION

Extubation of trachea should be devoid of changes in hemodynamic parameters and adverse events such as coughing, breath holding and laryngospasm is almost always associated with hemodynamic changes. The hemodynamic changes at extubation are due to reflex sympathetic discharge caused by epipharyngeal and laryngopharyngeal stimulation. This increase in sympathoadrenal activity may result in hypertension, tachycardia and arrhythmias which are transient, variable and unpredictable^{1,2}. It is more hazardous to the patient with hypertension, myocardial insufficiency or cerebrovascular disease.³

Many pharmacological methods have been devised to reduce the extent of hemodynamic events accompanying extubation, including esmolol, alfentanil, fentanyl, diltiazem, high dose of opioids, local anesthetics like lignocaine.⁴⁻⁷

Esmolol is an ultrashort-acting, highly cardioselective beta-adrenergic receptor antagonist. Its

rapid elimination is due to conversion to an inactive free acid metabolite by plasma esterases.⁵ Diltiazem, a calcium channel blocker has been used extensively to maintain perioperative haemodynamic stability. This drug is effective in blunting the haemodynamic responses associated with laryngoscopy and tracheal extubation as well as intubation.¹

The mechanism responsible for tachycardia and hypertension during tracheal extubation is unknown but these changes may be related to the release of catecholamines⁸.

The various pharmacological and non-pharmacological approaches mentioned for attenuation of hemodynamic responses to extubation are not entirely satisfactory. Hence the present study was undertaken to evaluate the ability of diltiazem and esmolol in attenuating the cardiovascular responses to tracheal extubation.

MATERIALS AND METHODS

This study was randomised double blind study which was carried out after obtaining approval of the ethical committee of institution and informed consent from the patients.150 patients with ASA physical status I undergoing elective surgery under general anaesthesia with endotracheal intubation were randomly divided into 3 groups using random number tables.

The groups were organized as follows:

Saline group (Group S,n=50): 10 ml of normal saline

Diltiazem group(Group D,n=50): 0.1mg/kg of Diltiazem

Esmolol group (Group E,n=50): esmolol 1mg/kg. These drugs were given 3 min after injection of neostigmine and glycopyrrolate and 2 minutes before tracheal extubation.

Inclusion criteria were: ASA 1 patient, age range 18 - 60 years ,of either sex and any operation performed under general anaesthesia with tracheal intubation. Exclusion criteria were: cardiac and respiratory diseases, a history of allergy to the study drugs, antihypertensive medication, and any patient with difficult intubation.

All patients were premedicated with intramuscular glycopyrrolate 0.2mg, 30 min before induction of anaesthesia. In the operation theatre i.v. line secured with 20G intracath and standard monitors including ECG, NIBP, SPO₂ were attached and baseline values noted. All the patients received inj. Midazolam 0.02mg/kg i.v. and inj fentanyl 1-2 mcg/kg i.v. preinduction. Anaesthesia was induced with 5-7mg/kg of thiopental sodium and patients were intubated under the effect of succinylcholine 1.5 to 2 mg/kg. Maintenance of anaesthesia was done with 50% O₂ and N₂O each and Isoflurane(0.2 -1%) and intermittent top up of vecuronium 0.02mg/kg. For all patients heart rate(HR), Systolic blood pressure(SBP), Diastolic blood pressure(DBP), Mean arterial pressure(MAP) and peripheral oxygen saturation(SPO₂) were monitored throughout anaesthesia. At the end of surgery, all anaesthetics were discontinued and patients were ventilated with 100% oxygen. Neuromuscular block was antagonized with inj neostigmine (0.04mg/kg) + inj. glycopyrrolate(0.01mg/kg) i.v. Three minutes after reversal, 1mg/kg esmolol or diltiazem 0.1 mg/kg or saline 10 ml were given i.v.. These medications had been prepared

beforehand by an assistant and their identities were unknown to the anaesthetist. The trachea was extubated 2 min after administration of these drugs. Immediately before tracheal extubation we confirmed that patients could breathe spontaneously and open their eyes on command. Furthermore, oropharyngeal secretions were aspirated just prior to extubation. Laryngoscopy was not performed during extubation. Immediately after tracheal extubation, 100% Oxygen was given via face mask for 5 minutes.

Values of HR, SBP, DBP, MAP were recorded after completion of reversal, at the time of administration of study drugs (3min after reversal taken as 0 min), 1 and 2 minutes after administration of drugs and 1 min, 2 min, 3 min, 5 min, 10 min and 15 minutes after extubation.

Statistical analysis: The results were analysed using student's paired t-test, student's unpaired t-test and chi-square test. A 'p' value of <0.05 was considered as statistically significant whereas 'p' value of <0.001 was taken as highly significant.

RESULTS

Table 1 indicates that no statistically significant differences were found between saline, diltiazem and esmolol groups in the demographic data

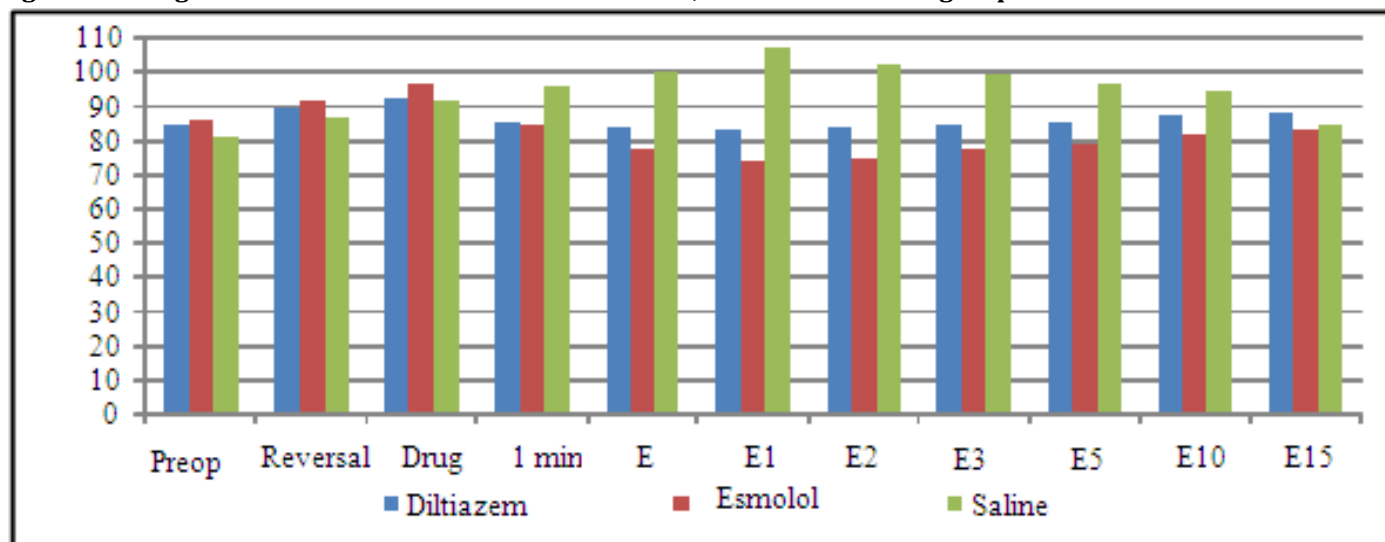
Table 1: Demographic data of the study population

| Parameter | Diltiazem (n=50) | Esmolol (n=50) | Saline (n=50) | p value |
|--------------------------|------------------|----------------|---------------|---------------------|
| Age (years) ^a | 31.1±9.3 | 33.5±13.6 | 32.0±10.5 | 0.570 ^{ns} |
| Gender ^b | | | | |
| Male | 17 (34.0) | 21 (42.0) | 18 (36.0) | 0.690 ^{ns} |
| Female | 33 (66.0) | 29 (58.0) | 32 (64.0) | 0.632 ^{ns} |

Values are mean ± standard deviation of mean. One way ANOVA test is used to compare difference in mean values of study groups. Values are frequency (percent). Chi-square test is used to test difference in proportions. NS: Statistically Not Significant p>0.05.

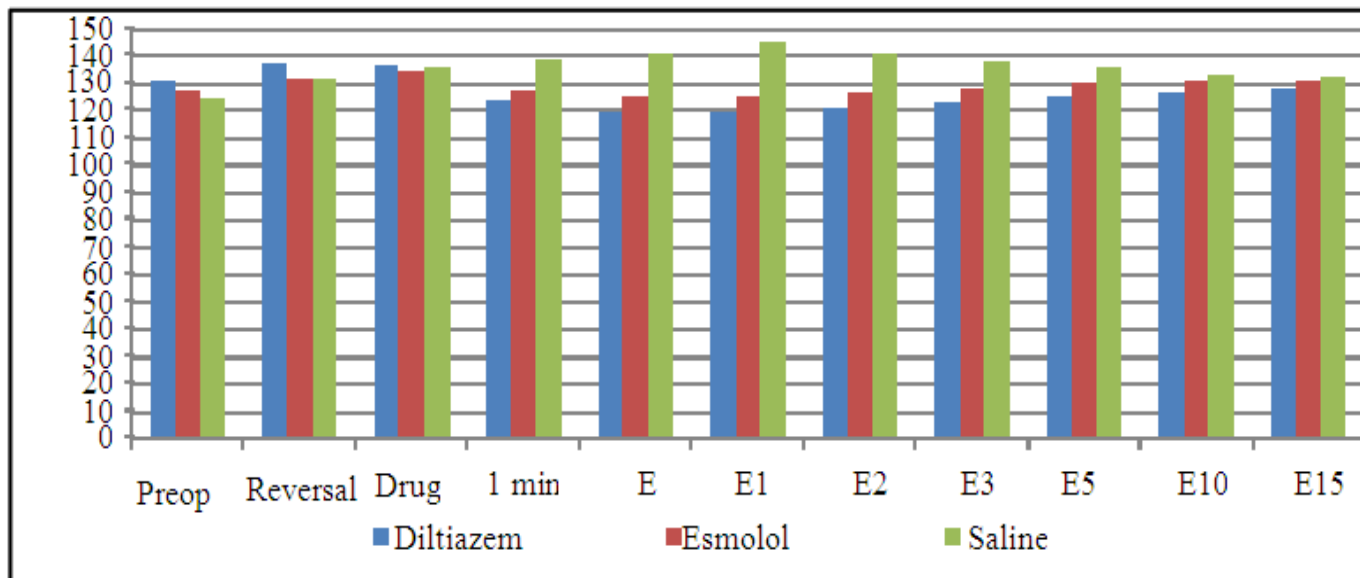
Heart rate: The heart rate in the esmolol group was significantly lower than saline group and diltiazem group at extubation and 1,3,5, 10 minutes after extubation.

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



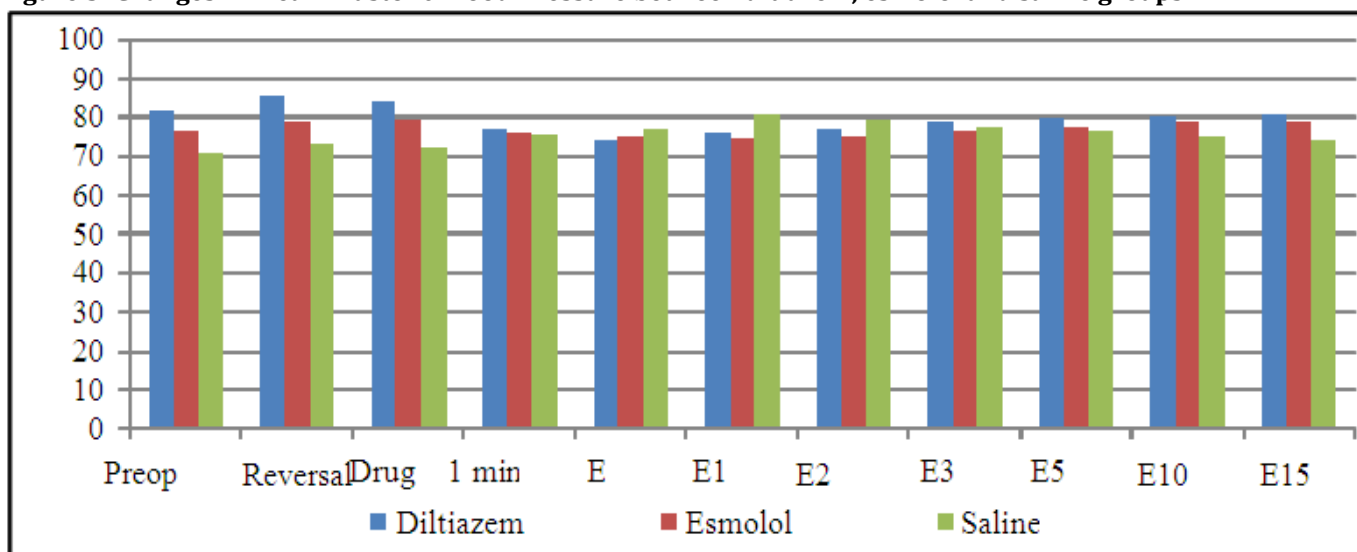
Systolic blood pressure (SBP): The SBP in diltiazem group was found to be significantly lower than in esmolol group and saline group at extubation and 1, 3, 5, 10 minutes after extubation. Statistical evaluation between the groups showed that decrease in SBP observed in diltiazem group was statistically highly significant when compared to SBP in esmolol group.

Figure 2: Changes in mean Systolic Blood Pressure between Diltiazem, esmolol and saline groups



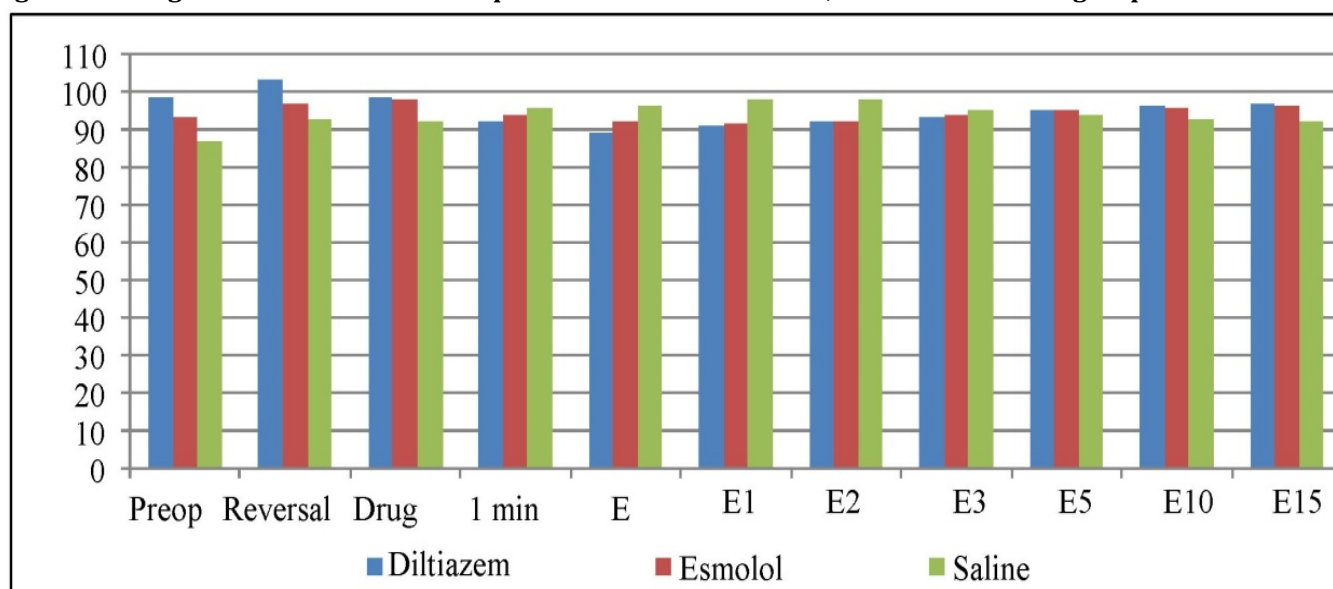
Diastolic BP: The DBP in the diltiazem group was not found to be significantly lower than DBP in esmolol group at extubation and 1, 3, 5, 10 minutes after extubation.

Figure 3: Changes in mean Diastolic Blood Pressure between diltiazem, esmolol and saline groups



Mean arterial blood pressure(MAP): There was no statistically significant difference in MAP between diltiazem and esmolol group at extubation and 1,3,5,10 minutes after extubation

Figure 4: Changes in Mean arterial blood pressure between diltiazem, esmolol and saline groups



DISCUSSION

Tracheal intubation often provokes significant increase in arterial blood pressure and heart rate. Tracheal extubation also causes hypertension and tachycardia.⁹ These cardiovascular changes during intubation and extubation may lead to an imbalance between myocardial oxygen demand and supply in patients with coronary artery disease and in those with risk factors for heart disease.^{9,10}

A number of pharmacological agents including lignocaine, esmolol, alfentanil, fentanyl, diltiazem have been recommended for the attenuation of hemodynamic changes with extubation.⁴⁻⁷ The goal of our study was to investigate the effect of 1 mg/kg of esmolol and 0.1mg/kg of diltiazem on the control of hemodynamic response to extubation.

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.¹¹ 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 min after injection. The heart returns to basal values 3 minutes after injection.¹² 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 al⁵ in 1990 to attenuate the cardiovascular responses associated with extubation in a dose of 1mg/kg, 1.5mg/kg and 2 mg/kg. They have concluded that increase in heart rate that occurs during extubation can be successfully attenuated by bolus injection of 1mg/kg esmolol, although this dose is insufficient to effectively block increase SBP. Thus our findings were similar to them.

Dae Hue Namet al¹³ in 1996 used esmolol in the dose of 1.5 mg/kg and diltiazem in the dose of 0.2mg/kg to attenuate cardiovascular responses to tracheal extubation. They have concluded that esmolol is more effective than diltiazem in attenuating the heart rate changes and diltiazem is more effective than esmolol in attenuating the systolic blood pressure changes, thus our findings were comparable to theirs.

Kovac et al¹⁴ in 1998 in their study compared nicardipine and esmolol for attenuation of haemodynamic responses to anaesthesia emergence and extubation and Habib Boston, Ahmed Eroglu¹⁵ had used esmolol in the dose of 1mg/kg for attenuation of hemodynamic responses to intubation and extubation and our findings were comparable to theirs. **Nishina MD et al¹** 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 as follows.

1. Direct vasodilator properties.
2. Negative chronotropic and dromotropic properties.

Diltiazem has been employed in various doses for blunting the cardiovascular responses to extubation. Intravenous diltiazem 0.2mg/kg was employed by kahanu Nishina et al¹, Katsuya Mikawa et al², Yoshitaka Fuji et al³. Kahoru Nishina et al¹ employed i.v. diltiazem

0.1mg/kg, 0.2 mg/kg and 0.3mg/kg but with 0.3 mg/kg i.v. diltiazem patient had hypotension. So the use of diltiazem 0.3mg/kg did not seem to be justified. In view of this in the present study we employed 0.1mg/kg of diltiazem.

We studied patients in ASA physical status I without any cardiovascular disease. 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 hemodynamic changes associated with extubation in patients with coronary artery disease and cerebrovascular disease.

CONCLUSION

Diltiazem is more effective than esmolol in attenuating systolic blood pressure changes and esmolol is more effective than diltiazem in attenuating heart rate changes during tracheal extubation.

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