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ORIGINAL RESEARCH

Evaluating drugs Esmolol, Diltiazem and combination of Esmolol and Diltiazem to see haemodynamic response to laryngoscopy and intubation

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ABSTRACT

Background: In major surgeries, endotracheal intubation has been proved to be the most effective way to maintain and secure airway. The present study evaluated drugs Esmolol, Diltiazem and combination of Esmolol and Diltiazem to see haemodynamic response to laryngoscopy and intubation. **Materials & Methods:** 90 patients were randomly divided into three Groups - D, E and combination group (D+E) of 30 each by using a closed envelope method. GROUP D (30 patients): r e c e i v e d Diltiazem I/V (0.2 mg/kg), group E (30 patients): Esmolol I/V (1.5 mg/kg), group D+E (30 patients): Combination of Diltiazem (0.1 mg/kg) and Esmolol (0.75 mg/kg). **Results:** There was significant difference ($p < 0.05$) in heart rate at all intervals of time except for the base line values. There was significant difference ($p < 0.05$) in systolic BP at all intervals of time except for the base line values. A reduced diastolic BP in combination group compared to the diltiazem and esmolol group after laryngoscopy which is denoted by a significant p value ($p < 0.05$). **Conclusion:** A combination fo**r** drug esmolol and diltiazem in minimal effective doses can be used safely for attenuating hemodynamic responses during laryngotracheal intubation.

Keywords: diltiazem, endotracheal intubation, esmolol

INTRODUCTION

In major surgeries, endotracheal intubation has been proved to be the most effective way to maintain and secure airway.[1] Instrumentation of the upper airways during laryngoscopy and intubation causes sympathoadrenal responses. These responses result in increased circulatory catecholamines, increase in heart rate, blood pressure, arrhythmias and thus it is a reason of concern for the anaesthesiologists. The response following laryngoscopy and intubation peaks at 1-2 minutes and returns to normal within 5-10 minutes. Many non- pharmacological techniques like use of Mc Coy laryngoscope blade, I-gel or LMA, fiber optic bronchoscopic intubation with blocking of glossopharyngeal nerve, Recurrent laryngeal nerve and superior laryngeal nerve are employed for attenuation of cardiovascular responses.

Various pharmacologic interventions have been hypothesized to blunt the hemodynamic responses of laryngoscopy and intubation for e.g. deep anaesthesia, topical anaesthesia, use of ganglionic blocker, inhalational agents, opioidnarcotics, alpha 2 agonists, beta blockers, antihypertensives such as phentolamine, combined alpha-beta blockers, nitroglycerine, calcium channel blockers, etc.[4,5]

Esmolol is short-acting cardio selective (beta 1 selective) beta-blocker that is employed in perioperative management of arrythmias, tachycardia and hypertension. It can be therefore used for management of tachycardia response towards laryngoscopy and intubation. In the literature, different doses of esmolol have been reviewed, but the selection of an effective dose of esmolol is essential to balance the desired effects and adverse effects.[6]

Diltiazem, a calcium channel blocker, is used as antihypertensive drug. It is a benzothiazepine class of compound and is an intermediate class between phenylalkylamine and dihydropyridines in their

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selectivity for vascular calcium channels. It effectively decreases the rise in blood pressure, but not the increase in heart rate associated with stress response. On the other hand, Esmolol is effective in controlling heart rate and arrhythmias but is not as effective in controlling the rise in blood pressure.[8,9,10] Therefore there is always a need to explore the newer possibility of obtunding this pressor response and prevent perioperative morbidity and mortality. We therefore, hypothesized that a combination of esmolol and diltiazem would be more efficacious in blunting the hemodynamic changes associated with s laryngoscopy and intubation, than when either drug is used alone.

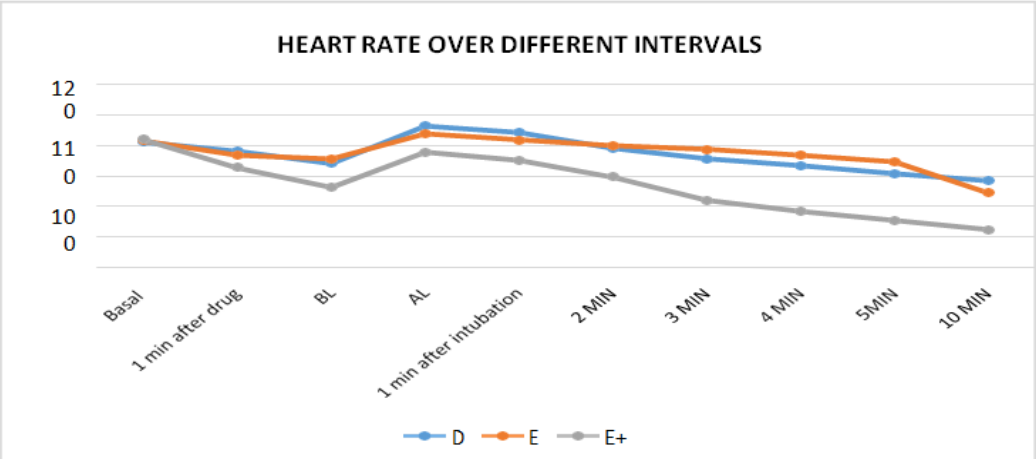
MATERIALS AND METHODS

After approval from Institutional Ethics Committee, this study was conducted in the Department of Anaesthesiology, Gandhi Medical College, Hamidia Hospital Bhopal, from January 2021 – July 2022. This prospective, randomized, double-blind, comparative study included 90 patients of either genders of ASA physical status I and II aged 20–60 years, scheduled for an elective surgery under general anaesthesia with endotracheal intubation. Patients receiving beta blockers or calcium channel blockers; with significant hepatorenal disease, uncontrolled hypertension, diabetes, significant respiratory or cardiovascular diseases or presenting as difficult tracheal intubation were excluded from the study. After obtaining written and informed consent, the patients were randomly divided into three Groups - D, E and combination group (D+E) of 30 each by using a closed envelope method. GROUP D (30 patients): received Diltiazem I/V (0.2 mg/kg), group E (30 patients): Esmolol I/V (1.5 mg/kg), group D+E (30 patients): Combination of Diltiazem (0.1 mg/kg) and Esmolol (0.75 mg/kg).

All the groups received the aforementioned drug as a bolus 2 min before laryngoscopy and intubation. Upon arrival in the operation theatre, all standard noninvasive monitors were attached to the patients, and their baseline vitals were recorded and monitored. The appropriate IV fluid was started. Patients were premedicated with Glycopyrrolate (0.2 mg, IV) and Midazolam (0.5 – 1 mg, IV) and simultaneously preoxygenation was done with 100% oxygen for 3 min. Anaesthesia was induced with IV Propofol (1%, 2.5 mg/Kg), I/V Fentanyl 2 mcg/kg and Succinylcholine (1.5 mg/Kg) followed by administration of study drugs. Laryngoscopy was performed using a Macintosh laryngoscope, and intubation was performed using an appropriately sized, cuffed endotracheal tube. Laryngoscopy and intubation were performed within 15–20s, with careful monitoring of haemodynamic parameters—Heart rate, blood pressure, oxygen saturation and electrocardiographic changes which were observed at baseline, 1 minute after drug administration, immediately after intubation, and at 1, 3, and 5 min, 10 minutes after intubation. These parameters were noted by anaesthesiologist who was blinded about the study drugs. Any surgical stimulus was avoided during the study period. Anaesthesia was maintained on IPPV with 66% nitrous oxide, 33% oxygen, 1% isoflurane and a nondepolarizing muscle relaxant, Vecuronium. Ventilation adequacy was monitored clinically with ETCO2, and SpO2 was maintained at 99%–100%. At the end of the surgery, neuromuscular blockade was reversed with injection neostigmine (0.05 mg/Kg) and injection glycopyrrolate (0.008 – 0.01 mg/Kg). Extubation was performed after the return of the protective airway reflex and the patients were shifted to the recovery room for further observation. The incidence of Hypotension/Hypertension, Tachycardia/Bradycardia and Dysrhythmia or any other side effects were recorded throughout the study period and compared among the groups. Continuous variables were compared among groups using ANOVA, while categorical variables were compared using Chi-square or Fisher's exact test depending on the distribution. For all the statistical interpretation *p* value less than 0.05 was consideredsignificant.

RESULTS

Line diagram 1: Heart rate of all three groups over different time intervals



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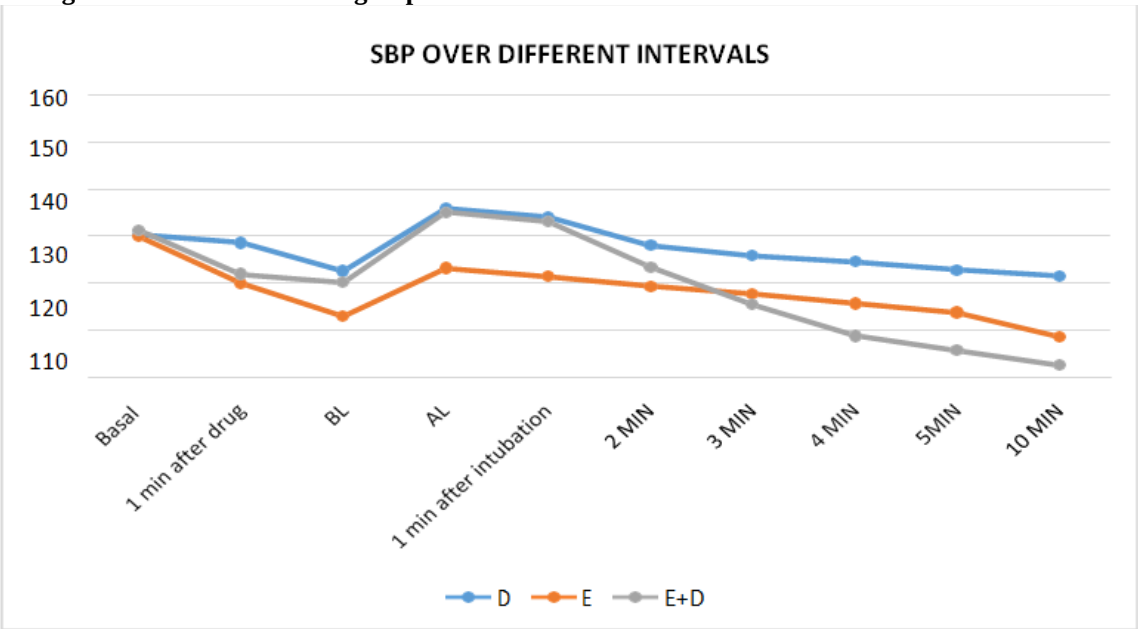
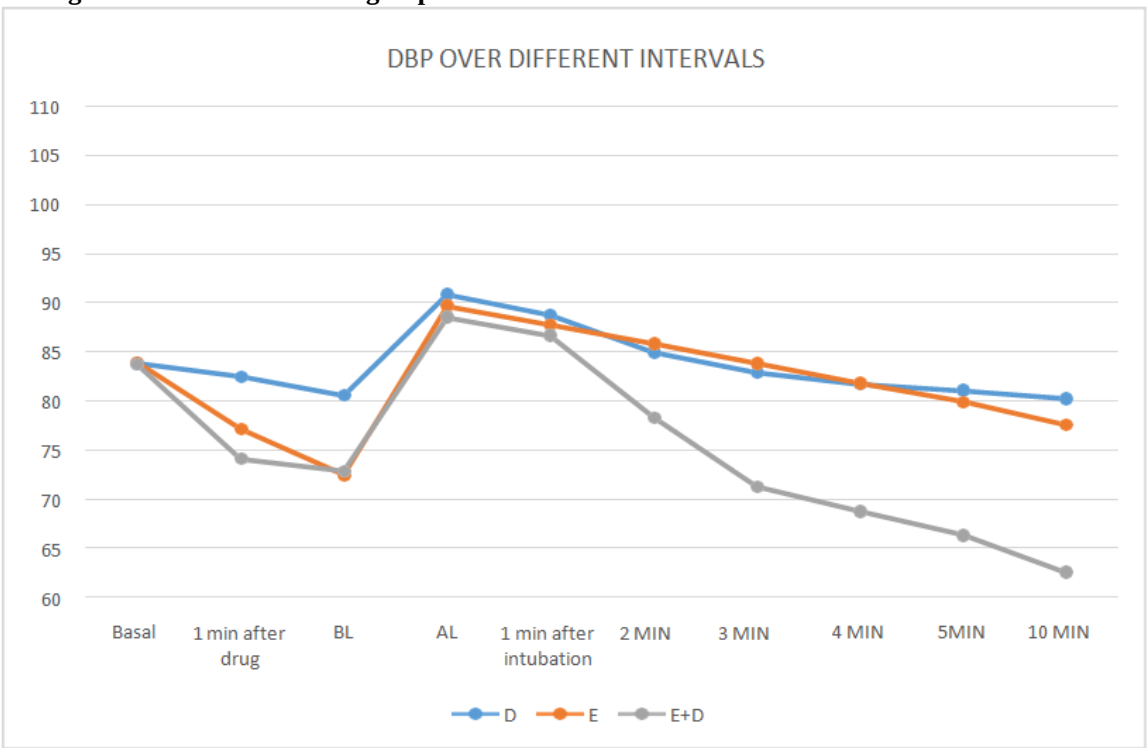
Shows comparison of heart rate between diltiazem, esmolol and combination groups it was found that there was significant difference ($p < 0.05$) in heart rate at all intervals of time except for the base line values.

Line diagram 2: SBP of all three groups over different time intervals



Shows comparison of Systolic BP between diltiazem, esmolol and combination groups it was found that there was significant difference ($p < 0.05$) in systolic BP at all intervals of time except for the base line values.

Line diagram 3: **DBP of all three groups overdifferent time intervals**



Shows that except for baseline diastolic blood pressure values, all other interval of time had a statistically significant association between all three groups. It clearly shows a reduced diastolic BP in Combination group compared to the diltiazem and esmolol group after laryngoscopy which is denoted by a significant p value ($p < 0.05$).

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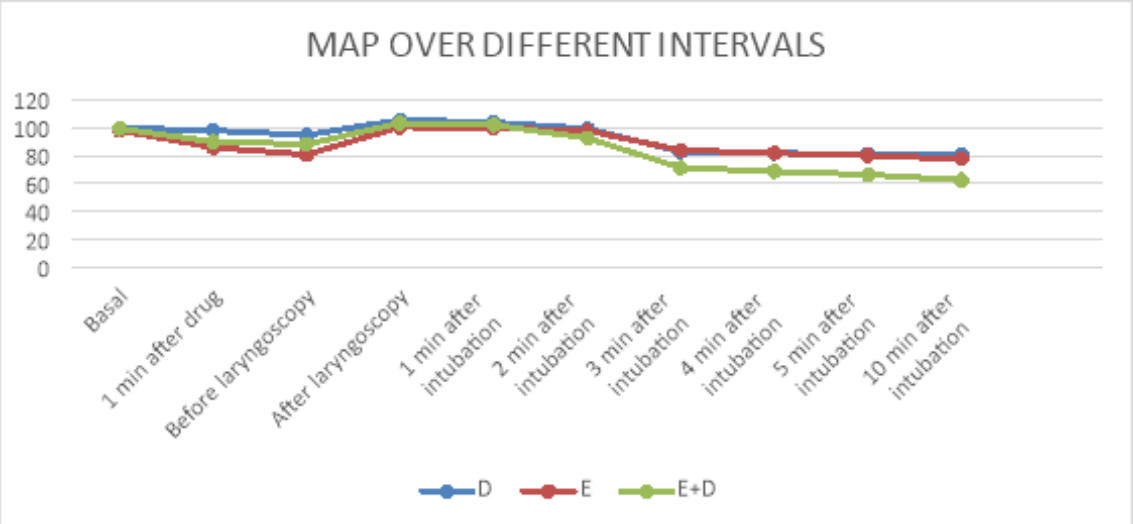
Line diagram 3: MAP over different time intervals



DISCUSSION

Transitory and self- limiting upsurge of basic hemodynamic parameters are common sequalae of direct laryngoscopy and endotracheal intubation. Esmolol and Diltiazem have systematically been shown to abate hemodynamic responses to laryngoscopy and intubation.[8,9,10] Thus a mixture of both might, therefore, be able to cater better efficacious suppression of hemodynamic sequelae as compared to either drug alone. Hence both the drugs have been included in our study in attenuating the hemodynamic response to intubation and have shown promising results.

We have studied ninety patients of both sex aged between 20 and 60 years with ASA physical status grade I and II. There was no significant distinction among the groups with respect to demographic parameters. During a study on the efficacy of Esmolol, Singh et al. deduced that prophylactic treatment with beta-adrenergic blocker (2 mg/kg) is most effective in blunting heart rate in response to laryngoscopy and intubation that was in concordance with our study.[4]Studies done by Nazir M et al additionally showed that beta-adrenergic blocker (2 mg/kg) given ninety seconds and three min before induction, severely, prevents an increase in heart rate .[5]

Diltiazem was related to a significant rise in heart rate until two min after laryngoscopy (Line diagram 1). Singh et al[4] found that Diltiazem (0.3 mg/kg) failed to dampen the rise in heart rate, once administered alone that is in concordance to the present study. This was in distinction to a study by Sarkar et al[1] that explained attenuation in heart rate response to laryngoscopy when compared between Diltiazem and Esmolol. Maybe, this can be applied to the actual fact that they had administered Diltiazem (0.2 mg/kg) one min before laryngoscopy and intubation, in contrast to our study, where we have administered Diltiazem 2 min before.

All groups were related to a significant fall in SBP, DBP, and MAP when induction was done as compared to the baseline. Esmolol and also the combination groups were effective in preventing an increase in SBP until 10 min and also the Diltiazem group until 2 min when LTI (line diagram 2). However, no distinction was found between Esmolol and combination drug groups. This is in unison to studies done by Singh et al[4] and Kumar et al[12], United Nations agency which showed that esmolol during a dose of 2 mg/kg, blunts the SBP response post intubation. Mikawa et al[13] showed that Diltiazem during a dose of 0.2-0.3 mg/kg, successfully suppresses the pressure response to intubation, and its action is fast and short. Fujii et al[14] equally showed that beta- adrenergic blocker and Diltiazem attenuate the increase in SBP when laryngoscopy, as compared to control group. All groups were associated with a significant rise in DBP and MAP immediately after laryngoscopy, as compared to the baseline. Atlee et al.[15]concluded that a combination of esmolol and nicardipine (one-half dose each) was effective in controlling rise in SBP, DBP, and MAP. We did not find any difference between diltiazem and esmolol for preventing rise in DBP after LTI. MAP in the groups getting Diltiazem and esmolol, there was no significant difference between the two at 3 minutes after LTI. To the best of our knowledge, till date, very few studies have been done using a combination of esmolol and diltiazem to blunt pressor response to laryngoscopy and intubation. Kumar et al.[12] showed that both diltiazem and esmolol were effective in controlling DBP after laryngoscopy and intubation; however, they did not record the effect on MAP. In a study done by Parvez et al.[11], it was concluded that esmolol is a better agent than diltiazem for attenuating pressor response to laryngoscopy and intubation (HR, DBP, and rate pressure product) in controlled hypertensives. No ECG abnormalities, cardiovascular disease, spasm or cardiac arrhythmia that shows notable effects of the study drugs which were discovered in either groups.

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CONCLUSION

In this study the combination group was found to be effective in preventing a rise in HR, SBP, DBP and MAP. A combination of drug offers the advantage of both the drugs while at the same time reduces there side effects due to relatively lesser dose of the drugs. We therefore conclude that a combination for drug esmolol and diltiazem in minimal effective doses can be used safely for attenuating hemodynamic responses during laryngotracheal intubation.

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