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EFFECTS OF ESMOLOL ON HAEMODYNAMIC RESPONSE TO TRACHEAL EXTUBATION IN DIABETIC AND NON- DIABETIC PATIENTS, COMPARATIVE, RANDOMIZED, PROSPECTIVE, OBSERVATIONAL STUDY

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Abstract

Background and aims: Extubation after an elective intubation for GA depends on patients preoperative status, the intraoperative course and expected post operative recovery. Increased cardiovascular instability during anaesthesia and abnormal cardiovascular responses to intubation and extubation have been described in patients with diabetic autonomic neuropathy. **Aim:** To assess the effectiveness of esmolol on blocking the hemodynamic response to extubation in diabetic and non-diabetic patients. **Methodology:** It is a comparative, randomized, prospective, observational study. A total of 42 patients of ASA grade 1 and 2 of either sex, aged 30 to 80 years, scheduled for elective surgeries under General Anaesthesia (GA) were randomly allocated into two groups of 21 each – Group A- Non-Diabetic, Esmolol received 1.5mg/kg IV 2 minutes before extubation Group B- Diabetic, Esmolol received 1.5mg/kg IV 2 minutes before extubation. Heart rate (HR), Systolic arterial pressure (SAP), Diastolic arterial pressure (DAP), and mean arterial pressure (MAP) were recorded 1 minute before IV administration, during extubation at 1, 3, 5, and 10 minutes after extubation. Data analysis done using standard statistical tests and SPSS for windows software. **Results:** HR and BP values of the diabetic esmolol group were significantly lower as compared to the non-diabetic esmolol group. In group 1, HR at administration of drug, at extubation after 1,5 and 10 minutes was higher. In group 1, SAP at administration of drug, extubation after 1,3, 5 minutes was higher. DAP was higher in group 1. MAP was not statistically significant between two groups.

Conclusion: Use of esmolol 1.5mg/kg dose 2 minutes before extubation is effective in diabetic and non-diabetic patients in preventing tachycardia and hypertension without any serious side effects.

Keywords: Cardiovascular, Diabetic, Esmolol, Extubation

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Introduction

Extubation after an elective intubation for GA depends on patients preoperative status, the intraoperative course and expected post operative recovery. It is known that on tracheal intubation there is an increase in heart rate and arterial pressure associated with increase in plasma concentration of both noradrenaline and adrenaline, and this response also occurs on tracheal extubation due to sympathetic discharge caused by epilaryngeal and laryngopharyngeal stimulation. [1,2]

This increase in heart rate and arterial pressure are usually transitory, variable and unpredictable. [3,4] Smooth tracheal extubation requires the absence of straining, movement, coughing, breath holding or laryngospasm. [5] Although various techniques and antihypertensives drugs are available to attenuate the hemodynamic response during extubation, none have been completely successful. Attempts have been made to attenuate the pressor response by the use of drugs such as narcotics analgesics, deep anaesthesia induced by inhalational anaesthetics, local anaesthetics, adrenoceptors blockers and vasodilator agents. [6] Studies have been carried out with use of diltiazem, [7,8] lignocaine [9,10,11], esmolol [12], labetalol[12] , nicardipine[13] and opiods[14] as sole agents or in comparison with each other.

The increased anaesthetic risk for patients with aging and diabetes occurs due to autonomic dysfunction. Among autonomic neuropathies, diabetic neuropathy is most common. It occurs in 20% to 40% of all insulin dependent diabetic patients.[26] Increased cardiovascular instability during anaesthesia and abnormal cardiovascular responses to intubation and extubation of anaesthesia have been described in patients with diabetic autonomic neuropathy.[15,16]. Both attenuated and enhanced pressure response have been reported. These altered responses have been attributed directly to autonomic neuropathy.[15-18]

Clinical symptoms of autonomic neuropathy generally do not occur until long after the onset of diabetes. Subclinical autonomic dysfunction can, however, occur within a year of diagnosis in type 2 diabetes patients and within two years in type 1 diabetes patients.[25] In autonomic dysfunction there is loss of adrenergic control through the reduction of alpha 2 and beta receptor mediated responses causing a decrease in the sympathetic nervous system's ability to maintain cardiovascular homeostasis. Diabetic patients with autonomic dysfunction may have a significantly greater decline in blood pressure with induction and a greater need for vasopressors than non-diabetic patients.[26]

The purpose of this study is to show the effectiveness of esmolol (1.5mg/kg I.V 2 minutes before extubation), an ultra-short acting beta 1 cardio-selective beta blocker agent (with half-life 9 minutes) which is used to prevent or treat hypertension and tachycardia during intraoperative and postoperative periods and has been reported to decrease plasma catecholamine levels, on blocking the hemodynamic response to extubation in diabetic versus non-diabetic patients.

Methodology

Source of data: Patients aged between 30-80 years, scheduled for elective surgery under general anaesthesia with endotracheal intubation admitted in A.J.Institute of Medical Sciences and Research Centre, Mangalore.

Study site: Department of Anaesthesia, A.J Institute of Medical Sciences and Research Centre, Mangalore.

Study design: Comparative, randomized, prospective, observational study.

Study duration: One year

Study period: November 2019 to November 2020.

Sampling method: To detect approximate mean difference of systolic blood pressure of 15 mmHg after intubation, response when checked at 2nd minute, between the non-diabetics with esmolol use versus diabetic patients after use of esmolol for suppression of laryngoscopic

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response was used to as the base to calculate the sample size for this study. A minimum number of 17 patients were required in each group to detect a mean SBP difference of 15mmHg (power,1-β,80%, α=0.05 with standard deviation (SD) of 15 mmHg in each group) assuming with differences of <15mmHg would not be clinically significant. However, with an assumption of 15% dropouts during the study, we planned to include 42 patients (17+17+4+4=42) for our study.

Inclusion criteria

1. All patients scheduled for various elective surgical procedures belonging to patients physical status American Society of Anesthesiologists (ASA) classes 1 and 2
2. All patients with controlled diabetes (HbA1c<-7.5 on insulin or oral hypoglycemic drugs) or non-diabetic patients who were scheduled to undergo elective operations under general anaesthesia.

Exclusion criteria

1. Those with significant cardiopulmonary disease
2. Patients whose blood pressure not between 100/50-150/100mmhg,
3. Patients with difficult airway
4. Patients with severe liver and renal insufficiency
5. Patients who refused, posted for emergency surgery, physical status ASA Class 3 or more
6. Patients who are on beta blockers.

Methods of collection of data

After obtaining approval from institutional ethics committee a comparative, randomized two group clinical study was conducted.

A total of 42 patients of ASA 1 and ASA 2 of either sex, aged 30 to 80 years, scheduled for various elective surgeries under general anaesthesia were included in the study. All the patients who required oro-tracheal intubation as part of their anaesthetic management and have given informed written consent to participate in the study were randomly allocated into two groups of 21 each and were subjected to the following regimen-

Group A: Non-Diabetic Esmolol (NDE), patients who are non-diabetic received 1.5mg/kg esmolol I.V 2 minutes before extubation (n=21)

Group B: Diabetic Esmolol (DE), patients with known history of diabetic received 1.5mg/kg esmolol I.V. 2 minutes before extubation (n= 21)

Method of study

All patients were assessed pre-operatively by history, physical examination, routine laboratory tests, chest x-ray and electrocardiogram.

Patients were nil per oral for 8 hours prior to the procedure. Anti-hypertensives were continued until the morning of surgery. Oral hypoglycemic drugs and insulin were withheld on the morning of surgery.

Pre-anaesthetic medication was Tablet Ranitidine 150mg BD and Tablet Diazepam 5mg HS.

After arrival to the anaesthetic room, pre-induction monitors were connected, ECG (5 lead) with automated ST segment analysis, pulse oximetry, non-invasive blood pressure, temperature probe and basal reading noted.

Following pre-medications were given: Inj. Fentanyl 2 µg/kg, Inj. Glycopyrrolate 0.005mg/kg. All the patients were preoxygenated for 3 minutes. Induced with 5mg/kg dose of Inj. Thiopentone. Intubated with appropriate size cuffed, portex endotracheal tube after administration of Inj. Vecuronium 0.15 mg/kg

Mechanical ventilation was initiated. Anaesthesia was maintained with isoflurane, O2:N2O=40%:60%.

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Low-flow technique (fresh gas flow of 1 L/min) using anaesthesia machine to achieve end-tidal carbon-dioxide tensions of 35 ± 3 mm Hg was used. Inspired and expired gas concentration of O_2, carbon dioxide (CO_2) and isoflurane was measured using smart anaesthetic gas monitoring system. Haemodynamic parameters were maintained within 20% of the basal values. Intraoperative hypothermia was prevented by the use of warm airflow, warming blanket and warm intravenous fluids.

After completion of surgery, neuromuscular blockade was reversed with Inj. Neostigmine 0.05mg/kg and Inj. Glycopyrrolate 0.01mg/kg intravenously.

Group A: Non-Diabetic Esmolol (NDE) in this group, patients received esmolol 1.5mg/kg I.V 2 minutes before extubation.

Group B: Diabetic Esmolol (DE) in this group, patients with known history of diabetic received esmolol 1.5mg/kg I.V 2 mins before extubation.

The attending anaesthesiologist recording the data was blinded to the group. The drug was given 2 minutes prior to extubation. Patients were given 100% Oxygen between injections of drug and tracheal extubation. When spontaneous breathing began, the patients were extubated after aspiration of oropharyngeal secretions.

The quality of extubation was assessed with a 5-point rating scale:

1: no cough and normal breathing
2: mild cough
3: moderate cough
4: severe cough and difficulty in breathing
5: laryngospasm with severe cough and forced breathing [19].

After extubation, the patients inhaled 100% oxygen with an oxygen mask for 5 min.

Heart rate, SAP, DAP, and MAP were recorded 1 min before intravenous administration, during extubation, and at 1, 3, 5, and 10 min after extubation.

The following treatments were provided: 0.5 mg Atropine sulphate was administered for bradycardia (HR <50 beat min-1), 5 mg Ephedrine was administered for hypotension (systolic arterial pressure <100 mmHg), and 0.02 mg Nitroglycerine iv was given for hypertension (systolic arterial pressure >180 mmHg) as and when required.

Various complications such as desaturation, breathe holding, laryngospasm, bronchospasm, bradycardia, hypotension, nausea, vomiting, restlessness, etc., were noted

Statistical Analysis

All data collected was entered in Microsoft Excel sheet and analysis was done using Social Sciences (SPSS) for windows software (Version 22: SPSS)

Standard statistical tests (ANOVA, Paired t-test, Student's *t*-test, chi-squared test, and Wilcoxon-Mann-Whitney *U* test) was used to analyze the data. The results so obtained with a 5% level of significance (p value < 0.05) were considered significant.

Results

Half of the patients included in the study were within the age group 41-50 years with the age distribution being comparable between the two groups.76.2% of the study subjects were male with the ratio of females to males not being statistically significant between both groups.

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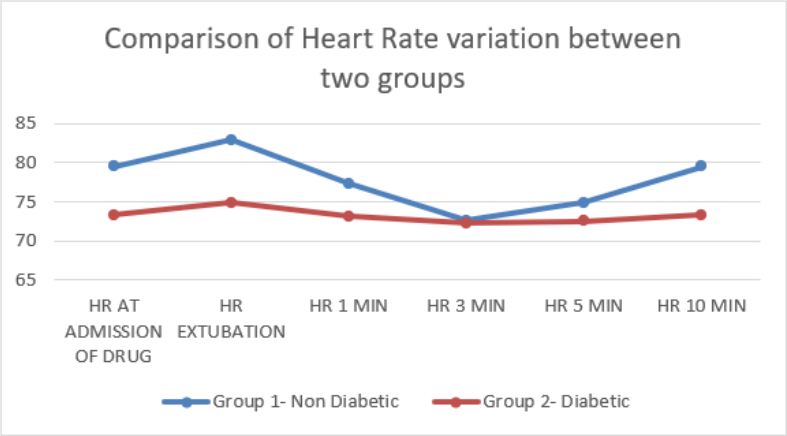

Chart 1: Comparison of the HR between the two groups

Chart 1 shows the comparison of heart rate between the two groups. The heart rate was noted to be higher in Group 1 – Non-diabetic esmolol group in our study at the time of admission of the drug, at extubation, after 1 minute, 5 minutes and 10 minutes as compared to Group 2 with the result being statistically significant ($p<0.001$, except at after 5 minutes with $p=0.038$). At after 3 minutes from extubation, the heart rate between the two groups was not statistically significant for comparison ($p=0.625$).

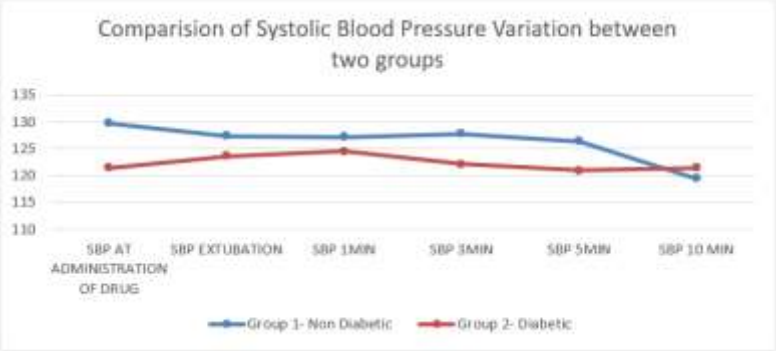

Chart 2: Comparison of the SBP between two groups

Chart 2 shows the comparison of systolic blood pressure between the two groups. At the time of administration of drug, comparison between the two groups shows that SBP is higher in Group 1- Non-Diabetic group and also, comparison of the SBP at extubation, after 1min, 3minutes, 5minutes of extubation reveals that SBP is higher in Group 1- Non-Diabetic group. All were statistically significant with a p value of <0.001, p=0.028, p <0.001 and p <0.001 respectively.

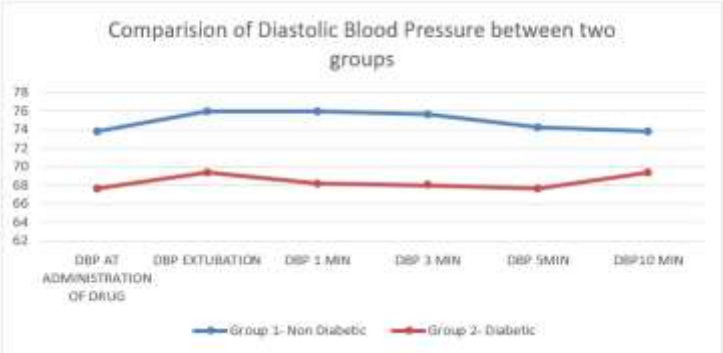

Chart 3: Comparison of the DBP between two groups

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Chart 3 shows the comparison of diastolic blood pressure between the two groups. In this study, we found that the DBP was higher in Group 1 throughout the evaluation period as compared to Group 2 and was statistically significant with p<0.001.

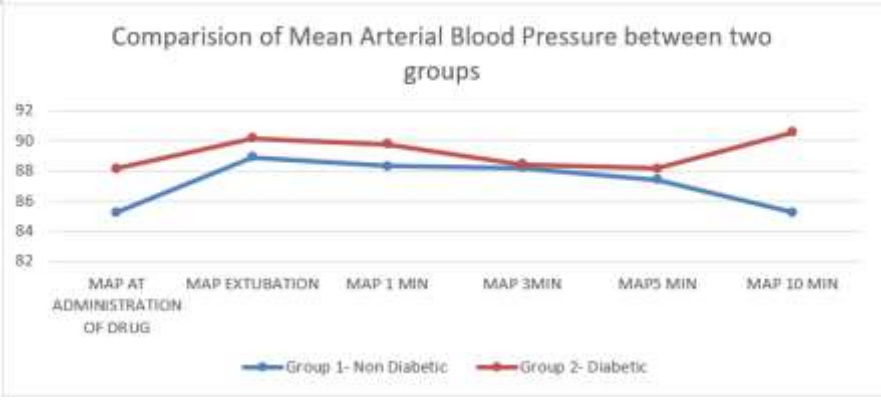

Chart 4: Comparison of the MAP between two groups

Chart 4 shows the comparison of mean arterial pressure between the two groups. The comparison of the MAP at the time of administration of the drug and at after 10 mins of extubation between the two groups showed that MAP is higher in Group 2- Diabetic group and was statistically significant with a p value of 0.005 and p<0.001 respectively. At other points of evaluation, MAP was higher in Group 2 but was not statistically significant.

There was no statistically significant difference between the two groups regarding quality of extubation based on cough score in our study.

Discussion

Emergence from general anesthesia and post-extubation phase are the stages associated with cardiovascular hyperdynamic status leading to increase in oxygen consumption and catecholamine release. This phase lasts for 5-15 minutes and could frequently be accompanied by reflex tachycardia and hypertension. Most patients endure this temporary situation appropriately however, patients with autonomic dysfunction could be affected by severe cardiac and cerebral complications.

Several drugs and technique have been tried to attenuate hyperactive sympatho-adrenal pressor response, but few have been tried to compare between diabetic and non-diabetic subject in context of diabetic autonomic neuropathy.

In our study, we compared efficacy of Esmolol 1.5 milligrams per kilograms, single intravenous dose to attenuate pressor response to extubation in diabetic and non-diabetic patients.

We observed that HR and BP values of the diabetic esmolol group were significantly low compared non-diabetic esmolol group. This attenuated response post neuromuscular reversal can be attributed to autonomic neuropathy.

Heart rate was lower in diabetic esmolol group at extubation,1minute, 5minutes and 10 minutes post-extubation. This result was similar to the study conducted by Murat Alp Alkaya *et al.* [23] They observed that the HR was significantly lower in the esmolol group at extubation and 1, 3, 5, and 10 min after extubation when compared to control group.

The Systolic blood pressure was significantly lower in diabetic esmolol group at drug administration, 1minute, 3minutes and at 5th minute post-extubation. In the study conducted by H. S. Prajwal Patel *et al.*, [20] esmolol group was more effective in controlling systolic blood pressure at 1 minute and 2 minutes post-extubation, which was statistically significant.

Diastolic blood pressure was lower in diabetic esmolol group at drug administration, at extubation, 1minute, 3 minutes, 5 minutes and 10 minutes post-extubation in our study. In the

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study conducted Murat Alp Alkaya *et al.*, [23] the DBP was significantly lower in the esmolol group when compared to the control group at extubation, and 3 and 5 min after extubation.

Mean arterial blood pressure was not statistically significant between two groups in this study. During the 24 hours observation period, there were no other side effects like ventilatory depression, bradycardia, tachycardia, hypotension, hypertension, nausea and vomiting.

Though the study produced several statistically significant results, it has its own shortcomings. There was no control diabetic group to compare the extubation response and the duration of diabetes mellitus was not considered to corelate with extubation response. No autonomic function testing was conducted to assess the autonomic function before the surgery. Further categorization based on diabetic treatment; insulin or oral hypoglycemic medications was not done and blood glucose level was not checked after esmolol administration. Hence, an extension of the study can be done with provisions for the above-mentioned drawbacks.

Conclusion

Our findings suggest that use of esmolol 1.5mg/kg dose 2 mins before extubation is effective in diabetic and non-diabetic in preventing tachycardia and hypertension without any serious side effects during and after extubation. The quality of extubation is comparable between the groups.

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