SUPPRESSION OF PRESSOR RESPONSE DURING LARYNGOSCOPY AND ENDOTRACHEAL INTUBATION BY ESMOLOL ADMINISTERED IN DOSES OF 1.5 mg/kg, 2.25 mg/kg: A COMPARATIVE CLINICAL STUDY

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ABSTRACT

BACKGROUND

Laryngoscopy and endotracheal intubation results in physiological changes of various body systems like heart rate and blood pressure in cardiovascular system. For attenuating the hyperdynamic cardiovascular response to tracheal intubation, numerous trials with many drugs were undertaken.

AIM

Of our study is to find out the safety and efficacy of attenuation of pressor response during laryngoscopy and tracheal intubation using Esmolol, administered as single intravenous bolus prior to induction of anaesthesia in two different doses of 1.5 mg/kg and 2.25 mg/kg. Control group was considered in our previous study using the same drug with different dosage, i.e. a dose of 0.75 mg/kg was compared with a placebo. We would like to go ahead with further increase in the dosage per kg body weight to get an ideal suppression of the pressor responses.

MATERIALS AND METHODS

The study was conducted in 50 patients, who were randomly assigned into 2 groups of 25 each. Group A (25) received Inj. Esmolol 1.5 mg/kg and Group B (25) received Inj. Esmolol 2.25 mg/kg IV before induction.

RESULTS

Heart rate and blood pressures were well maintained within physiological range in Group A, whereas there was a decrease in blood pressure and heart rate in the Group B immediately after intubation and at the end of 4th min.

CONCLUSION

In this study, the Group B showed an inappropriate decrease in mean values of Heart Rate, Blood Pressure immediately after administration.

KEYWORDS

Endotracheal Intubation, Laryngoscopy, Pressor Response.

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INTRODUCTION

Endotracheal intubation as well as laryngoscopy, both disturbs the patient's protective airway reflexes and thus results in physiological changes of various body systems. Laryngoscopy and intubation results in marked reflex changes in cardiovascular system that leads to a mean rise in heart rate by 20% and blood pressure by 50%.[1]

To seek the effective blockade of these responses involves topical or intravenous lignocaine or.[2,3] sympathetic blockers, vasodilators, inhalational anaesthetics and analgesics of opioid family.[4] Fentanyl is one of the narcotic drugs which affects both blood pressure and ventricular rate responses, but it has its own side effects like truncal rigidity, severe respiratory depression, etc.

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Some drugs like lignocaine and vasodilators give an incomplete solution by regulating mean arterial blood pressure, but do not affect ventricular heart rate. Beta blocker namely propranolol gives effects, which outlasted the stressful interval by several hours and did not usually include an increase in bronchomotor tone.

Esmolol (Methyl 3-[4-(2-hydroxy-3- [Isopropyl] proxy) phenyl] propionate) is an ultra-short acting beta-adrenergic blocking drug. It is a preferred drug as it exhibits properties of rapid onset of action, cardio selectivity and extremely short elimination half-life of 9.2±2 min.

Esmolol has an apparent volume of distribution of 3.4±1.4 L/kg and a distribution half-life of 2.0±0.5.[5] The drug is metabolized very rapidly as a result of hydrolysis by red blood cell esterases to form methanol and an inactive metabolite. The peak effect of intravenous injection of esmolol on heart rate is observed within one minute, whereas that on blood pressure within two minutes.

Esmolol is suitable for administration by either continuous infusion or bolus injection because of its pharmacokinetic and pharmacodynamic properties. Few studies in the past have revealed that tachycardia, increase in mean arterial blood pressure and increase incidence of myocardial ischemia during the pre-bypass period in patients

undergoing coronary artery bypass can be effectively prevented by infusion of esmolol.[6] It was recognized however that because of esmolol's rapid onset and short duration of action bolus injection might be a simple and effective alternative to infusion of this drug in situations involving transient hyperdynamic cardiovascular events. Therefore, for attenuating the hyperdynamic cardiovascular response to tracheal intubation, trials are undertaken to determine the safety and efficacy of bolus administration of esmolol.

AIM OF STUDY

To study the safety and efficacy of attenuation of pressor response during laryngoscopy and tracheal intubation using esmolol, administered as single intravenous bolus prior to induction of anaesthesia in two different doses of 1.5 mg/kg and 2.25 mg/kg.

MATERIALS AND METHODS

This study was undertaken for duration of two years, i.e. from 2006 June - 2008 June in Kamineni Hospitals, after obtaining permission from the Hospital Ethical Committee.

The study included 50 patients who were randomly divided into 2 groups of 25 each, namely Group A (n=25) Inj. Esmolol 1.5 mg/kg IV and Group B (n=25) Inj. Esmolol 2.25 mg/kg IV. Informed consent was taken after explaining them about this study in their vernacular language from each patient involved in our study. Inclusion criteria includes patients aged 18-60 years of both sexes, normotensive or controlled hypertensive patients as well as ASA I and II grade and patients undergoing non-cardiac surgery. Exclusion criteria includes baseline heart rate of less than 70 beats per minute, right ventricular or left ventricular failure, heart blocks, arrhythmias, myocardial infarction in the past 3 months, uncontrolled hypertension, hyper-reactive airway disease, patients on treatment with either sympathetic augmenting or depleting drugs and other experimental drugs within the last 14 days.

Patients were pre-medicated the night before surgery with Tab. Alprazolam 0.5 mg and Cap. Omeprazole 40 mg. One hour before surgery Inj. Promethazine hydrochloride 0.5 mg/kg and Inj. Tramadol 1 mg/kg was given. A good IV line was secured on arrival in the operation theatre. Monitors like Pulse Oximetry, ECG and NIBP-Philips, IntelliVue, MP 40 were attached to note the baseline reading of Heart Rate (HR), Systolic Blood Pressures (SBP), Diastolic Blood Pressure (DBP). Inj. Esmolol dose of 1.50 mg/kg in 20 mL Normal saline was administered to Group A and Group B received a dose of Inj. Esmolol 2.25 mg/kg in 20 mL Normal saline over 15 seconds. Later Inj. Midazolam 0.04 mg/kg and Inj. Fentanyl 1-2 pg/kg was administered prior to induction.

Patient was induced with Inj. Thiopentone 3-5 mg/kg. Laryngoscopy and tracheal intubation was done 45-60 seconds after administering Inj. Succinylcholine. Anaesthesia was maintained with 50% N_20, 50% 02, 0.2% to 0.4% Isoflurane and Inj. Pancuronium 0.08 mg/kg (Loading dose). Haemodynamic changes were monitored and baseline readings recorded. Readings were immediately noted after 4 min. and 8 min. after intubation.

STATISTICS

Medical statistical 8.2 Version was used for statistical analysis.

RESULTS

The results of our study done on 50 patients are explained in tables.

The age range was 18-60 years in both groups. The mean values of age with standard deviation are 34.36±8.24, 37.0±12.8 for Groups A and B respectively. There was no significant difference between the two (P=0.466). In Groups A and B, weight ranged between 48 and 110, 44-98 Kgs respectively. Mean values and standard deviation of weight for Groups A and B are 68.44±15.5 and 67.68±14.21 respectively.

	Group A		Group B	
Age (years)	18-60	34.36±.24	18-60	37.00±12.8
Weight (Kgs)	48-110	68.44±15.5	44-98	67.68±14.21

Table 1: Distribution according to Age and Weight

In Group A 68% patients are males, 32% were females and Group B 64% patients are males and 36% were females. No significant difference was observed in Sex wise distribution of the cases in between the two groups (P=0.504).

Sex	Group A	Group B
Male	17	16
Female	8	9
Total	**25**	**25**

Table 2: Sex Distribution

The Group A baseline readings of HR was 86.76±8.39 [Mean±SD]. There was a 4.01% decrease in HR after induction with a Mean±SD of 83.28±11.90. A 54% decrease of HR was noticed immediately after intubation with a Mean±SD of 82.04±9.55. An increase in HR of only 0.41% was noted at the end of 4th min. Further increase by 4.43% was noticed at the end of 8th min with a Mean±SD of 90.60±8.587. There was a significant variation in HR before and after induction and at the intervals of 4th and 8th min. following intubation (P<0.001, P<0.01 respectively).

In Group B, the Mean±SD value of HR at baseline was 84.16±11.45. There was a 26.33% decrease in HR with induction with a Mean±SD of 62.00±6.81 and a further decrease was noted with laryngoscopy and intubation by 19.63% with a Mean±SD of 67.64±6.71. The HR at the end of 8th min. was 69.56±10.14, which amounted to a 17.35% decrease in comparison to the baseline value. This difference in Group B was statistically highly significant at all times of assessment compared to the values in the other groups (P<0.00l).

Time of Assessment	Group A		Group B	
	Mean ± SD	% Differences	Mean ± SD	% Difference
Baseline readings	86.76±8.39	-	84.16±11.45	-
0 min : study drug	83.28±11.91	-4.01	62.00±6.82	-26.33
Immediately after intubation	82.04±9.56	-5.44	67.64±6.72	-19.63
4 min after intubation	87.12±9.51	0.41	65.84±8.12	21.77
8 min after intubation	90.60±8.59	4.43	69.56±10.14	-17.35

Table 3: Comparison of Changes in Heart Rate

This table shows decrease in both systolic and diastolic blood pressures in Group B. The blood pressures were very much lowered immediately after intubation in both Groups A and B.

Time of Assessment	Group A [Mean±SD]		Group B [Mean±SD]	
	SBP	DBP	SBP	DBP
Baseline readings	131.20±11.89	86.88±10.37	129.4±8.61	82.01±8.42
0 min : study drug	127.12±12.00	81.48±10.19	123.84±9.32	71.36±9.22
Immediately after intubation	125.80±12.71	79.40±11.97	103.00±6.47	66.60±8.01
4 min after intubation	129.68±10.08	86.44±10.48	104.24±8.56	72.74±7.08
8 min after intubation	134.56±10.26	88.68±10.16	112.40±7.06	74.56±9.41

Table 4: Comparison of Changes in Blood Pressure

DISCUSSION

Our study was done on 50 patients to compare the efficacy and safety of attenuation of pressor response during laryngoscopy and tracheal intubation using esmolol, administered in dose of 1.5 mg/kg or 2.25 mg/kg single IV bolus prior to induction of anaesthesia. Circulatory disturbances are reflexly provoked by sympathetic stimulation during laryngoscopy and endotracheal intubation, which is associated with rise in plasma norepinephrine.[7] These changes are marked by increase in blood pressure and heart rate and occasionally arrhythmias. Less commonly bradycardia may occur as a result of vagal stimulation.[8]

Many studies were conducted in the past regarding the efficacy of esmolol administration during laryngoscopy and tracheal intubation.

Menkhaus studied the effectiveness of esmolol infusion. They showed that unique pharmacokinetic behaviour of esmolol makes it well suited for controlling the cardiovascular responses to tracheal intubation when used as a continuous infusion technique.[9] Newsome LR demonstrated that esmolol was effective in attenuating the haemodynamic responses during anaesthesia.[10] Sheppard et al. (1990) observed that Esmolol 200 mg was effective in attenuating the pressor response to intubation after tracheal intubation.[7] Oxorn et al. commented that hypotension on induction was observed with higher doses of esmolol.[11] Helfman et al. concluded that esmolol was more effective than lignocaine and fentanyl for HR control, timing of doses was an issue.[12]

Kindler CH, concluded that Esmolol 1-2 mg/kg is not reliably effective in attenuating the heart rate response to intubation; neither of the two doses of esmolol tested nor the lidocaine affected the blood pressure response. Combination of esmolol and lidocaine attenuated both the heart rate and the blood pressure response to intubation.[13]

Bensky et al. carried out a study using small doses of Esmolol 0.2 mg/kg and 0.4 mg/kg to find out the dose related effects of bolus esmolol on heart rate and blood pressure following laryngoscopy and intubation. Patients received 0.2 mg/kg or 0.4 mg/kg or placebo. It was shown that esmolol group had very small increase in heart rate when compared to placebo group and in Esmolol 0.4 mg/kg, the systolic blood pressure was significantly blunted.[14]

J Agarwal (2002) concluded that esmolol, is a suitable drug to attenuate the haemodynamic response to laryngoscopy and intubation with an effective control of arrhythmia by its infusion and no evidence of hypersensitivity reactions.[15]

CONCLUSION

In this study, both the groups in which esmolol was used showed a decrease in mean values of HR, SBP and DBP immediately after administration of the study drug. The reductions were marked with dose of 2.25 mg/kg in comparison to dose of 1.5 mg/kg.

Thus Esmolol in dose of 1.5 mg/kg given at induction of general anaesthesia, also in comparison with a dose of 0.75 mg/kg which was used in similar situations and was compared to placebo in our previous study it can be concluded that:

- Effectively attenuates HR response to laryngoscopy and endotracheal intubation.
- Prevents hypertensive response to laryngoscopy and endotracheal intubation. The effect is more marked on systolic blood pressure than diastolic blood pressure.
- Does not cause ischemic changes.
- Produces effects, which last for at least 5 mins. after administration.
- Does not produce serious effects such as bronchospasm, hypotension, bradycardia, conduction blocks and phlebitis.
- The drug has also been studied in corroboration with a control group in my previous study and has been published.

Our Present Clinical Study however has a Few Limitations:

- Adequate depth of anaesthesia and skeletal muscle relaxation was monitored only by clinical observations.
- Various drugs used in the present study are known to influence the haemodynamic changes, which was not evaluated.
- Variations in parameters can occur as the patient starts to come out of succinylcholine and before the action of supplemented pancuronium sets in.
- Haemodynamic changes associated with two stages, i.e. direct laryngoscopy and passage of the tracheal tube into the trachea were not studied separately.
- Some patients did develop bradycardia and hypotension, which was attended efficiently.

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