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A study to compare the efficacy of two different doses of esmolol to attenuate the hemodynamic response during laryngoscopy and endotracheal intubation

Dr. Sagana
MBBS 2nd year postgraduate, College - Vinayaka mission kirupanda variyar medical college and hospital, Department of anesthesiology
Email: dr.saganamahesh@gmail.com

Dr. Poorna Avadhani
MBBS MD, College - Vinayaka mission kirupanda variyar medical college and hospital, Department of anesthesiology
Corresponding author email: Poorna-puavadhani@gmail.com

Prof. Dr. Brindha
MBBS DA MD, College - Vinayaka mission kirupanda variyar medical college and hospital, Department of anesthesiology

***Abstract*---**Background: General anaesthesia is an altered physiological state characterized by reversible loss of consciousness, amnesia ,analgesia and some degree of muscle relaxation.no single agents can produce these desired effects.It involves inhalational anaesthetics,induction agents, opioids, neuromuscular blockers. Combination of all these drugs will produce the optimal anaesthesia which is known as balanced anaesthesia. Airway management is an integral part of general anaesthesia, which includes direct laryngoscopy and endotracheal intubation. Objective: To compare the efficacy of two different doses of esmolol to attenuate the hemodynamic response during laryngoscopy and endotracheal intubation. Methodology: The present comparative cross sectional study was conducted by the Department of Anaesthesia at Vinayaka Missions KirupanandaVariyar Medical College and Hospital, Salem from December 2019 – May 2021. The comparative study was done between two study groups with Group A receiving 50 mg of IV Esmolol and Group B Receiving 100 mg of IV Esmolol, A total of 60 study patients who met the inclusion criteria were included in the Study and divided into 30 subjects in each group. Results: The mean age of the patients in Group A was 37.3 (12.0) years with a minimum of 18 years

and a maximum of 60 years. The mean age of the patients in Group B was 36.0 (9.4) years with a minimum of 18 years and a maximum of 51 years. the patients were comparable by the gender distribution between the groups (p=0.602).It can be noted that the injection with Esmolol 100 mg provided better hemodynamic stability in terms of heart rate, Systolic and Diastolic Blood pressure over different time periods. Conclusion: From this study we conclude that Inj.Esmolol 100mg I.v given 2 minutes before intubation is comparatively better than Inj.Esmolol 50mg in attenuating the hemodynamic response of laryngoscopy and intubation.

***Keywords*---**Induction, Anaesthesia, Blood Pressure, Hemodynamic Stability.

Introduction

General anaesthesia is an altered physiological state characterized by reversible loss of consciousness,amnesia,analgesia and some degree of muscle relaxation no single agents can produce these desired effects.It involves inhalational anaesthetics,induction agents, opioids, neuromuscular blockers. Combination of all these drugs will produce the optimal anaesthesia which is known as balanced anaesthesia. Airway management is an integral part of general anaesthesia, which includes direct laryngoscopy and endotracheal intubation.[1]

Direct laryngoscopy allows the visualization of the vocal cords for endotracheal intubation. It is used during general anaesthesia, surgical procedures around larynx and resuscitation.Direct laryngoscopy and endotracheal intubation is the most important step of securing the airway comes with numerous complications. These complications can be classified in two categories- traumatic and non-traumatic. Traumatic injuries include direct blunt or penetrating trauma to the trachea, larynx, oropharynx, breaking of teeth, injury to lips, tongue, glottic trauma,dislocation of arytenoids. In rare instances extreme flexion or extension of the neck during direct laryngoscopy can cause cervical spinal cord injuries.[2,3]

Non traumatic complications include aspiration of gastric content, hypoxic brain damage from a prolonged attempt at intubation without adequate oxygenation, bronchospasm. Sympathetic surge causing tachycardia, dysrhythmias, myocardial ischemia or infraction, hypertension can occur as a result of stimulation of the highly innervated glottis by the laryngoscopy blade. These hemodynamical changes occur for a short duration without any sequel. But it can aggravate arrhythmias, myocardial ischemia, cerebralhaemorrhage in patients with coronary artery diseases and cerebrovascular diseases.[4,5,6]

Many drugs have been used to attenuate this pressor response of the laryngoscopy and intubation. Lidocaine, fentanyl, clonidine, dexmedetomidine. In this study we are using the short acting beta blocker esmolol to attenuate the laryngoscopy response. Esmolol is an ester and ultrashortacting cadioselective (beta 1) beta blocker with rapid onset of action. This drug does not possess membrane stabilizing activity or alpha adrenergic activity. Esmolol gets

metabolized by plasma esterases which accounts for the total body clearance of 285ml/kg/min and elimination halflife of 9.2 minutes.It produces average control of heart rate in an average effective dosage. In this study the efficacy of esmolol to attenuate the laryngoscopy response has been studied by using two different doses of the drug.[7,8]

Objectives

To compare the efficacy of two different doses of esmolol to attenuate the hemodynamic response during laryngoscopy and endotracheal intubation.

Materials and Methods

The presentcomparative cross sectional study was conducted by the Department of Anaesthesia at Vinayaka Missions KirupanandaVariyar Medical College and Hospital, Salem from December 2019 – May 2021.

The comparative study was done between two study groups with Group A receiving 50 mg of IV Esmolol and Group B Receiving 100 mg of IV Esmolol, A total of 60 study patients who met the inclusion criteria were included in the Study and divided into 30 subjects in each group.

Inclusion Criteria:
1. Patients undergoing elective surgeries under general anaesthesia.
2. Patients between the age group of 20 to 60yrs
3. American Society of Anesthesiologists physical status I or II

Exclusion criteria:
1. Patients not willing for the study
2. ASA III & ASA IV
3. Pregnant women
4. Patients with heart blocks
5. Patients with bronchial asthma
6. Patients with congestive cardiac failure
7. Patients with anticipated difficult airway for intubation
8. Patients on other beta-blockers.

Before data collection, informed written consent was obtained from all patients after explaining the procedure. All patients were interviewed during their first visit of the study, and their medical history was obtained using the proforma. Patients aged 20-60years assessed under ASA physical status I or II scheduled for elective surgeries under general anaesthesia was enrolled into the study. Study population was divided into 2 groups: Group A will receive Inj. Esmolol 50 mg and Group B will receive Inj. Esmolol 100mg.

Patients were examined preoperatively as well as a day before surgery. Patients were kept nil per oral for 8 hours duration T. Alprazolam 0.25 mg to be given a day prior to surgery. Inj.ondansetron 4mg iv and Inj.Glycopyrrolate 0.2mg was given before shifting the patient to theatre.

The anaesthesia machine was checked before shifting the patients, and all the airway gadgets like laryngoscope of appropriate size, endotracheal tube of appropriate size, oropharyngeal airway and suction apparatus was kept ready. Vasopressors and other drugs for emergency resuscitation was kept ready. 18G IV canula was secured to each patient and IV fluids was started. Patient shifted to operation theatre and placed in supine position. All standard monitors like pulse oximetry, NIBP, and electrocardiography was connected, and baseline heart rate, systolic blood pressure, diastolic blood pressure, and mean arterial pressure was recorded. Patient was preoxygenated with 100% oxygen for 3-5 minutes. The study group received either of the following 50 mg IV esmolol/100mg Iv esmolol will be diluted to 10 ml and given over 10-15 seconds.

Patient was induced with Inj. Propofol 1-2mg/kg, and Inj. succinyl choline 1mg/kg after giving Inj. fentanyl 1-2 mcg/kg. After abolition of fasciculation laryngoscopy will be done using Macintosh blade of appropriate size and patient was intubated using cuffed endotracheal tube of appropriate size. Heart rate, systolic blood pressure, diastolic blood pressure, and mean arterial pressure was recorded every 1 minute after intubation for 7 minutes. Anaesthesia was maintained with nitrous oxide:oxygen(3:2) and sevoflurane.Intermittent bolus doses of Inj.Vecuronium and Inj.Fentanyl was given to maintain the anaesthesia.

After the procedure, patient was extubated after giving reversal drug Inj. Neostigmine 0.05mg/kg and Inj. glycopyrrolate 0.01 mg/kg intravenously. Descriptive statistics is done for all data and reported in terms of mean values and percentages. The data will be analysed using SPSS software version 21.0. Quantitative variables will be analysed using Student's t test, and qualitative variables will be analysed using chi-square test. Level of significance will be estimated with 95% confidence interval and p value <0.05

Results

Out of the Total of 60 patients admitted for elective surgery under general anaesthesia were included in the study of which 30 patients were administered injection Esmolol 50 mg (Group A) and the remaining 30 patients were administered injection Esmolol 100 mg (Group B). The mean age of the patients in Group A was 37.3 (12.0) years with a minimum of 18 years and a maximum of 60 years. The mean age of the patients in Group B was 36.0 (9.4) years with a minimum of 18 years and a maximum of 51 years.

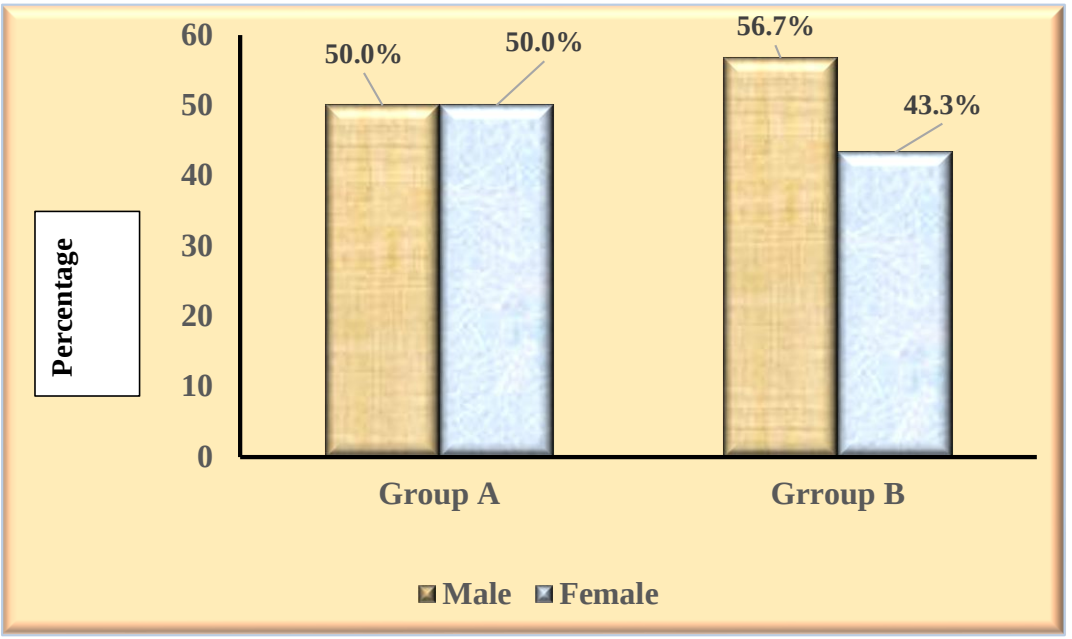

Figure 1. Graph wise Distribution of the patients by gender between the intervention arms

The Above Figure 1 shows that the patients were comparable by the gender distribution between the groups (p=0.602)

Table 1
Repeated-Measures ANOVA for mean difference in heart rate over time between the groups (N=60)

Group	Time (minutes)									Effect size	p value
	N	Base-line	At indu.	2	3	4	5	6	7		
Between groups (mean heart rate per minute)											
A	30	81.4	88.0	106.7	112.3	108.4	104.4	97.3	94.1	0.407	<0.001
B	30	78.8	82.6	89.1	89.9	88.7	87.3	83.8	80.0		
Within the subjects (mean heart rate per minute)											
	N	Base-line	At indu.	2	3	4	5	6	7	0.865	<0.001
	60	80.1	85.3	97.9	101.1	98.5	95.9	90.6	87.0		

The heart rate was relatively higher among the patients who were administered injection Esmolol 50 mg when compared to those who were given injection Esmolol 100 mg. The above shows the results of ANOVA with repeated measures. It can be seen that the effect size of change in mean heart rate over time between the two groups was 0.407 and was found to be statistically significant (p<0.001). The test for a difference in mean heart rate over time was also highly statistically significant (F=371.8; Effect size= 0.865; p<0.001).

Table 2
Repeated-Measures ANOVA for mean difference in systolic blood pressure over time between the groups (N=60)

Group	Time (minutes)									Effect size	p value
	N	Base-line	At indu.	2	3	4	5	6	7		
Between groups (systolic blood pressure[mm Hg])											
A	30	127.9	108.4	149.6	150.4	145.2	140.1	137.9	134.6	0.239	<0.001
B	30	127.4	122.5	134.3	133.1	130.3	129.2	129.1	127.7		
Within the subjects (systolic blood pressure[mm Hg])											
	N	Base-line	At indu.	2	3	4	5	6	7	0.839	<0.001
	60	127.6	115.5	141.9	141.7	137.7	134.6	133.5	131.2		

*A= Inj. Esmolol 50 mg B=Inj. Esmolol 100 mg

The systolic blood pressure was relatively higher among the patients who were administered injection Esmolol 50 mg when compared to those who were given injection Esmolol 100 mg. The Above shows that the effect size of change in mean systolic blood pressure over time between the two groups was 0.239 and was found to be statistically significant ($p<0.001$). The test for a difference in mean systolic BP over time was also highly statistically significant ($F=301.2$; Effect size= 0.839; $p<0.001$). The observations of the post-hoc analysis shows that significant difference in mean systolic BP was observed in almost all the time periods except between 2 min and 3 min.

Table 5a.
Repeated-Measures ANOVA for mean difference in diastolic blood pressure over time between the groups (N=60)

Group	Time (minutes)									Effect size	p value
	N	Base-line	At intubation	2	3	4	5	6	7		
Between groups (diastolic blood pressure[mm Hg])											
A	30	80.0	71.0	87.9	102.3	92.7	86.5	84.7	83.9	0.421	<0.001
B	30	78.2	74.0	81.1	79.3	77.1	76.4	76.6	76.3		
Within the subjects (diastolic blood pressure[mm Hg])											
	N	Base-line	At intubation	2	3	4	5	6	7	0.636	<0.001
	60	79.1	72.5	84.5	90.8	84.9	81.4	80.6	80.1		

*A= Inj. Esmolol 50 mg B=Inj. Esmolol 100 mg

The diastolic blood pressure was relatively higher among the patients who were administered injection Esmolol 50 mg when compared to those who were given injection Esmolol 100 mg. The above tableshows that the effect size of change in mean diastolic blood pressure over time between the two groups was 0.421 and

was found to be statistically significant ($p<0.001$). The test for a difference in mean diastolic BP over time was also highly statistically significant ($F=101.4$; Effect size= 0.636; $p<0.001$).

Discussion

Tachycardia and hypertension are the common response to the laryngoscopy and intubation.This hemodynamic changes were first described by the Reid and Brace[34].The hemodynamic response is initiated within seconds of direct laryngoscopy and further increases with the passage of the endotracheal tube. The response is initiated within 5 s of laryngoscopy, peaks in 1–2 min and returns to normal levels by 5 min[9].

Esmolol short-acting cardioselective β-adrenergic antagonist permits rapid titration to a desired level of β-blockade on administration; hence, it a suitable agent for the perioperative period. At therapeutic doses, it does not have intrinsic sympathetic activity or membrane-stabilizing activity. Esmolol gets metabolized by plasma esterases which accounts for the total body clearance of 285ml/kg/min and elimination halflife of 9.2 minutes.Hence esmolol will be an ideal drug to attenuate the hemodynamic response in terms of the duration of action. So usage appropriate dose of esmolol is necessary to avoid the side effects of the drugs and to achieve adequate hemodynamic stability.[10-13]

Studies done by Gupta et al[14] proved that Inj.Esmolol is better than inj.fentanyl in attenuating the pressor response of laryngoscopy and intubation.Many studies have proven that Esmolol is better than IVlignocaine in attenuating the laryngoscopy response.Mulimani et al [15]has proven that Inj.Esmolol given before 2 min of intubation have good response in attenuating the laryngoscopy response.so in our study we have given Esmolol bolus dose 2 min before the intubation.

Many studies have proven that Inj.Esmolol 100mg bolus dose 2 minutes before induction has given hemodynamical stability till 5 minutes after the intubation.As we are using Inj.Propofol (1-2mg/kg) and Inj.Fentanyl (1-2µg/ml) for induction which itself can lead to hypotension [12,16,17] we have included low doses of Inj.Esmolol (50mg and 100mg).

Conclusion

Using Inj.Esmolol 50 mg given 2 minutes prior to intubation has shown that there was decrease in the heart rate during the induction but after that heart rate was high compared to baseline heart rate in most of the individuals. Inj.Esmolol 100mg given 2 minutes before intubation showed decrease in the heart rate at induction and there was increase in heart rate after 2 minutes of induction.Increase in heart rate was relatively better with Inj.Esmolol 100mg when compared to Inj.Esmolol 50 mg.

Systolic blood pressure,diastolic blood pressure and mean arterial pressures were decreased at induction when Inj.Esmolol was given 2 minutes before the intubation.But there was increase in SBP,DBP and MAP after induction.Even with

Inj.Esmolol 100mg there was decrease in the blood pressure at induction and there was increase in SBP,DBP,MAP after induction which was relatively lower when compared to SBP,DBP,MAP with Inj.Esmolol 50 mg. From this study we conclude that Inj.Esmolol 100mg IV given 2 minutes before intubation is comparatively better than Inj.Esmolol 50mg in attenuating the hemodynamic response of laryngoscopy and intubation.

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