Section: Anesthesia

Original Research Article

A COMPARATIVE STUDY ON VARYING DOSES OF ESMOLOL IN ATTENUATING THE HEMODYNAMIC STRESS RESPONSE TO LARYNGOSCOPE AND ENDOTRACHEAL INTUBATION A PROSPECTIVE STUDY

G. M. Jagadeesh[1], A. Arunsundar[2], K.Venkatesan[3], P. Periasamy[4]

[1]Assistant Professor, Department of Anesthesia, Government Villupuram Medical College, Tamilnadu, India.
[2]Associate Professor, Department of Anesthesia, Government Villupuram Medical College, Tamilnadu, India.
[3]Assistant Professor, Department of Anesthesia, Government Villupuram Medical College, Tamilnadu, India.
[4]Assistant Surgeon, Department of Anesthesia, Government Hospital, Madukkarai, Coimbatore, Tamilnadu, India.

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Corresponding Author:
Dr. P. Periasamy
Email: drperiasamyp@gmail.com

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Abstract

Background: General anaesthesia is the most commonly used technique for major abdominal, cardiovascular thoracic and head and neck surgeries. Esmolol has the added advantage of attenuating heart rate and decreasing systolic, diastolic and mean arterial blood pressure. Aim: This study aimed to compare the efficacy of the Intravenous administration of Esmolol at varying doses in attenuating the intubation stress response and abolishing cardiovascular changes to maintain the myocardial oxygen demand and supply. **Materials and Methods:** This prospective randomized controlled study was conducted at the Department of Anesthesiology, Government Villupuram Medical College, Villupuram, from January 2020 to December 2020. All patients were randomly allocated into three groups where IV Esmolol was injected 2 minutes before intubation 30 patients in Group A (Esmolol - 0.5mg/kg), 30 patients in Group B (Esmolol 1mg/kg), and 30 patients in Group C (Esmolol 1.5mg/kg). **Result:** In the study, 46 males and 44 females were present. The gender was almost equally distributed, and there was no significant difference in the age and BMI of patients among the groups. Esmolol 1.5mg/kg IV significantly attenuated hemodynamic stress response more than Esmolol 1mg/kg IV and Esmolol 0.5mg/kg IV. It also produces side effects like bradycardia and hypotension. **Conclusion:** Esmolol 1.5mg/kg IV significantly attenuated hemodynamic stress response. Esmolol 1mg/kg IV and Esmolol 0.5mg/kg IV could be a choice.

INTRODUCTION

The hemodynamic response to laryngoscopy and endotracheal intubation was first described in 1940 by Reid and Brace.[1] During general anaesthesia, laryngoscopy and endotracheal intubation lead to hemodynamic stress response with remarkable cardiovascular changes such as hypertension and tachy/brady arrhythmias. These acute hemodynamic changes combined with surgical stimulation often evoke perioperative myocardial infarction, acute heart failure and cerebrovascular accident. The peak time for laryngoscopy to respond is around 2 minutes, and the time to return to normal is within 3-5 minutes. In healthy individuals, the sympathetic response may be of little importance.[2] The hazardous effect is exhibited in patients with hypertension, coronary artery disease, intracranial lesions and airways with an exaggerated response. In this scenario, intubation stress response must either be controlled or suppressed to avoid major adverse cardiac events. The use of systemic and topical agents leads to the suppression of hazardous hemodynamic response to laryngoscopy and intubation.[3] Narcotics, beta-blocking agents, calcium channel blockers, vasodilators, lignocaine and sympatholytics are the various intravenous drugs preferred to control the hemodynamic stress response. Topical techniques with a local anaesthetic solution can be an alternative, but it's of limited value. Due to its ultra-short-acting property, IV Esmolol seems to be the ideal agent to control

sympathetic response to laryngoscopy and intubation that is intense but brief.[4]

Aim

This study aimed to compare the efficacy of the Intravenous administration of Esmolol at varying doses in attenuating the intubation stress response and abolishing cardiovascular changes to maintain the myocardial oxygen demand and supply.

MATERIALS AND METHODS

This prospective randomized controlled study was conducted at the Department of Anesthesiology, Government Villupuram Medical College, Villupuram, from January 2020 to December 2020.

Ninety patients from both gender under the age group of 20 to 50 years, American Society of Anesthesiologists (ASA) physical status I and II patients and cases planned under General anaesthesia were included. The Ethics committee approval was obtained, and informed consent from the patient was obtained. All patients were randomly allocated into three groups where IV Esmolol was injected 2 minutes before intubation 30 patients in Group A (Esmolol - 0.5mg/kg), 30 patients in Group B (Esmolol 1mg/kg), and 30 patients in Group C (Esmolol 1.5mg/kg). Emergency surgeries, uncooperative and unwilling patients, difficult airway, contraindication to beta-blockers (e.g., Asthmatics, complete heart block), full stomach, and comorbidities – diabetes mellitus, systemic hypertension, coronary artery disease were excluded. Randomization was done by draw of lots. The follow-up of the patient and data analysis were done by personnel blinded to which group belonged. The drawing of lots for randomization and preparation of the study was prepared by a consultant who took no further part in the study. The rest of the study was conducted by an investigator blinded to the drug injected. Inj. Esmolol, Inj. Glycopyrrolate (Antisialogogue), Inj. Midazolam (Benzodiazepine), Inj. Fentanyl (opioids), Inj. Succinylcholine and Inj. Atracurium/Vecuronium, Inj. Neostigmine and Emergency drugs: Inj. Atropine and Inj. Adrenaline drugs were used.

Preoperative assessment was done in the assessment clinic. Informed and written anaesthetic consent was obtained. Preoperative investigations were complete blood count, coagulation profile, renal function test, random blood sugar, BT, CT, serum electrolytes, chest X-ray PA view, electrocardiogram, and echocardiogram. To alleviate the preoperative anxiety visit was done. Oral tablets of diazepam 5mg and antacid prophylaxis tablet ranitidine 150mg were given to all patients the night before surgery. Baseline pulse rate, blood pressure, and SpO2 were recorded. Forty-five minutes before surgery, Inj. Glycopyrrolate 5 mcg/kg IM was given. Intravenous access was obtained using 18G venflon. The patient was shifted to the operating room. NIBP, ECG, and pulse oximeter were connected. Three minutes of preoxygenation was done with 100% oxygen. Three minutes before induction, Inj. Fentanyl citrate two mcg/kg IV was given. The study drug was taken and diluted to 20 mL in a syringe, given as a bolus over 15-20 seconds two minutes before intubation. Induction was given using Inj. Thiopentone sodium 2.5% 5mg/kg IV. Inj. Succinylcholine 1mg/Kg IV was given. After doing direct laryngoscopy, the patient was intubated using an appropriate-size endotracheal tube, secured after confirming bilateral adequate air entry. Flow was maintained with 50% N2O and 50% O2. ETCO2 was connected and maintained at 35-45 mmHg. Intraoperative and postoperative events were uneventful. Heart rate, Systolic blood pressure, Diastolic blood pressure, and Mean arterial pressure. All recorded data were entered using MS Excel. ANOVA test was used to determine the significance among the three groups. Student's t-test was used to compare the two groups on mean values of various parameters. The p-value taken for significance is <0.05.

RESULTS

Table 1. Demographic data among the groups

		Group A	Group B	Group C	P-value
Gender	Male	17	15	14	0.732
	Female	13	15	16	
Age	20-30	6	11	9	0.708
	31-40	9	7	7	
	41-50	15	12	14	
BMI	19-24	29	29	22	0.004
	>24	1	1	8	

In the study, 46 males and 44 females were present. The gender was almost equally distributed, and there was no significant difference in the age and BMI of patients among the groups.

Heart rate among groups

There is no statistical significance among the mean value of heart rate at the pre-medication time ($p>0.05$). But it is significantly different during the administration of Esmolol bolus, induction, and intubation during and for about seven minutes following laryngoscopy and intubation. It was significantly lower in Group C than in Groups A and B ($p<0.001$). The initial fall in Group B is because of its direct action on the cardiac conducting system. There was no record of arrhythmias in any of the patients in any group. This is probably because all the

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patients are ASA Class I and II with no history of hypertension or other cardiac ailments [Figure 1].

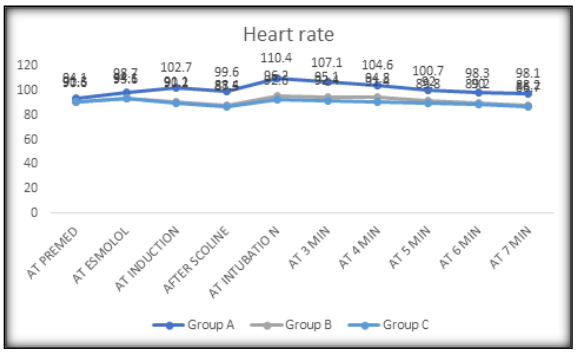

Figure 1: Distribution of heart rate

Systolic blood pressure among groups

There is no statistical significance on mean value among the three groups at pre-medication and during the administration of Esmolol bolus (p>0.05). But it is statistically significant in all other study periods (p<0.001) between the three groups. There was a 27% increase in systolic blood pressure from the baseline in Group A. There was a 21% increase in systolic blood pressure in Group B and a 12% increase in systolic blood pressure from the baseline. The rise in systolic blood pressure is comparatively less in Groups C than the Groups A and B. Higher mean value was reached at intubation in all three groups [Figure 2].

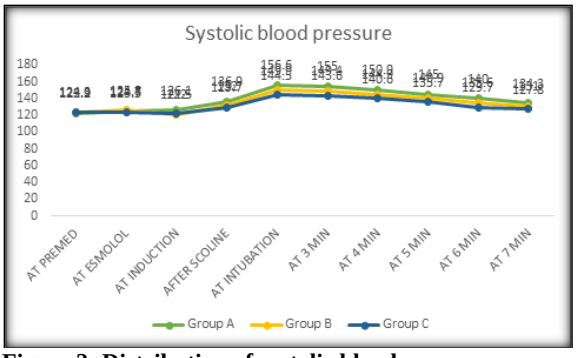

Figure 2: Distribution of systolic blood pressure

Diastolic blood pressure among groups

There is no statistical significance on the mean diastolic blood pressure at pre-medication and Esmolol (p>0.05). But it is statistically significant during induction (p<0.05). It is also statistically significant from the period of intubation to the end of the study period(p<0.001). There is up to 23% diastolic blood pressure in Group A, a 16% increase in diastolic blood pressure in Group B and a 12% increase in Group C from baseline. All the groups reached a higher mean value at intubation [Figure 3].

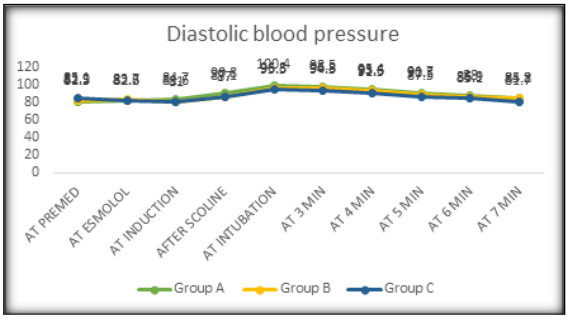

Figure 3: Distribution of diastolic blood pressure

Mean arterial pressure among groups

There is no statistical significance on the mean value of MAP up to induction during the study period (p>0.05). But it is statistically significant after the induction till the end of the study period (p<0.001). There is up to 25%, 18% and 14% increase from baseline during the operation in groups A, B and C, respectively. All three groups reached a higher mean value at intubation [Table 2] [Figure 4].

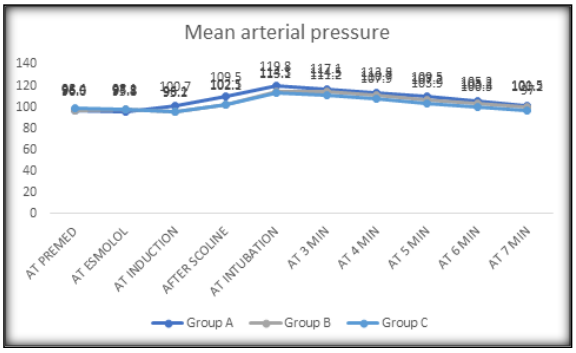

Figure 4: Distribution of mean arterial pressure

Table 2. Mean arterial pressure among groups

MAP	Group A		Group B		Group C		P value
	Mean	SD	Mean	SD	Mean	SD	
At premed	96.9	7.6	96.6	5.4	98.4	5.3	0.089
At esmolol	95.8	7.2	97.8	5.8	98.1	9.8	0.466
At induction	100.7	6.2	95.2	7.9	96.1	9.3	0.019
After scoline	109.5	6	102.1	6.5	102.5	8.8	<0.001
At intubation	119.8	7.8	114.3	6.5	113.1	6.5	<0.001
At 3 min	117.1	7.8	114.5	6.1	111.2	4.2	0.002
At 4 min	113.8	6.7	110.7	6	107.9	4.3	<0.001
At 5 min	109.5	6.4	107.2	6	103.9	6.4	0.003
At 6 min	105.2	5.7	103.2	5.2	100.3	6.1	0.005
At 7 min	101.5	5.2	100.2	4.1	97	3.6	<0.001

DISCUSSION

Endotracheal intubation using a laryngoscope is associated with a major hemodynamic stress response, which normal healthy patients will tolerate. However, those with high cardiovascular risk may experience major cardiovascular changes, such as tachycardia, hypertension, ST-T changes due to myocardial oxygen demand-supply imbalance, arrhythmias and pulmonary edema.

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Additionally, patients with cerebral and aortic aneurysms may experience transient cerebral perfusion impairment due to the stress response. An anesthesiologist is responsible for suppressing the hemodynamic stress response during intubation. This is done by restricting the laryngoscopy duration to 15 seconds and using systemic adjuncts such as beta-blockers and esmolol. However, studies comparing the efficacy of various doses of esmolol in attenuating the intubation stress response are lacking. In a study by Weist D et al.[5] Esmolol's therapeutic efficacy and pharmacokinetic characteristics in obtunding stress response to laryngoscopy and intubation were reviewed. A study by Kovac et al.[6] concluded that in an eye patient with coronary artery disease or in any patient whose increase in heart rate may be detrimental. Esmolol may be a useful adjunct with low-dose alfentanil to attenuate the increase in heart rate due to laryngoscopy and intubation. A study by Bensky et al.[7] concluded that a small dose of Esmolol effectively controlled heart rate and blood pressure during laryngoscopy and intubation. Feng CK et al.[8] compared and found that reliable control of heart rate and blood pressure changes was achieved by intravenous Esmolol, while low-dose fentanyl decreased heart rate. Still, no blood pressure changes or significant effect was noted with lignocaine. Hemodynamic stress responses to intubation were studied by Ebert et al.[9] using a single bolus dose of esmolol in healthy individuals. They concluded effective dose of Esmolol was 2mg/kg bolus in attenuating heart rate, systolic blood pressure, and diastolic blood pressure during endotracheal intubation. Sheppard et al.[10] studied the effectiveness of different doses of Esmolol as an intravenous bolus before intubation. This study concluded that 100mg intravenous bolus of esmolol is the effective dose for attenuating hemodynamic stress response to intubation. In a study done by Gomez et al.[11] who compared the efficacy of Lignocaine with Esmolol, it was observed that constant and reliable control in attenuating stress response was noted only with intravenous esmolol.

A Canadian multicentre trial done by Miller et al.[12] which included 548 patients, concluded that a 100mg bolus of Esmolol is safe and effective in controlling intubation stress response without clinically significant side effects. It was concluded by Vucovic M et al.[13] in a study evaluating the efficacy of Esmolol in managing cardiovascular responses to intubation that intravenous esmolol administered 2 minutes before intubation showed significant control of the pressor response to intubation. Our study also administered intravenous esmolol 2 minutes before laryngoscopy and intubation as per the above study. Yuan et al.[14] studied the efficiency of intravenous bolus 100 mg Esmolol versus 200 mg Esmolol in blunting the cardiovascular stress response to intubation. Their observation supported that a bolus dose of intravenous esmolol was effective and safe in attenuating intubation stress response. Furthermore, Esmolol 200 mg presented better hemodynamic stability than 100 mg Esmolol. In our study, Esmolol 1.5 mg/kg also provided better hemodynamic control than Esmolol 1mg/kg bolus. The effective dose of intravenous esmolol concluded by Sharma et al.[15] was 2mg/kg in adequate control of intubation stress response. In a study by Singh H et al.[16] observations were that Lignocaine 1.5 mg/kg IV and Nitroglycerine 2 mcg/kg IV effectively suppressed the hemodynamic stress response to intubation. But the efficacy of Esmolol 1.4 mg/kg was notably significant compared to Lignocaine or Nitroglycerine in controlling heart rate or mean arterial pressure increase during intubation. Sharma et al.[17] studied the efficacy of various doses of intravenous bolus Esmolol in blunting the intubation stress response in well-controlled hypertensive patients. It was witnessed that Esmolol 100 milligrams intravenous bolus dose was effective over and above safe in obtunding the intubation stress response. It was concluded that an effective and safe dose of intravenous esmolol was 1.2 mg/kg Wang et al.[18] Figueredo et al.[19] reviewed 38 RCTs' observations in controlling intubation stress response using various doses of Esmolol. It was concluded that the utmost effective intubation with a loading dose of 500 mcg per kg per min over 4 minutes followed by a continuous infusion dose of 200-300 mcg per kg per min. We also used Esmolol in the range of 0.5 mg/kg to 1.5 mg/kg, which was also safe with clinically insignificant side effects. In our study, the complete analysis revealed that intravenous Esmolol 1.5 mg/kg was more effective in attenuating the heart rate response and blood pressure changes accompanying laryngoscopy and intubation

CONCLUSION

We concluded, based on the hemodynamic control anticipated with intravenous esmolol bolus during laryngoscopy and endotracheal intubation. We observed an effective and safe dose of esmolol in obtunding the heart rate and blood pressure changes to laryngoscopy, and intubation was 1.5mg/kg.

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