Comparison of Three Different Doses of Esmolol to Attenuate Hemodynamic Stress Response During Laryngoscopy and Endotracheal Intubation

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ABSTRACT

Introduction: The hemodynamic stress can result from laryngoscopy and endotracheal intubation due to sympathoadrenal stimulation. Esmolol administered intravenously reduces the hemodynamic stress response. The lowest effective dose of esmolol for this purpose is still in debate, hence we chose to study three different doses. **Aims:** To evaluate various doses of esmolol administered intravenously in managing hemodynamic stress response in patients undergoing laryngoscopy and endotracheal intubation. **Methods**: This prospective and cross-sectional analytical study was conducted among 66 patients, administered 0.5 (Group A), 1 (Group B) and 1.5 mg/kg (Group C) doses of esmolol to 22 patients in each group undergoing laryngoscopy and endotracheal intubation, considering all inclusion and exclusion criteria. Parameters like heart rate, arterial blood pressure were all monitored before premdication, after premdication, before intubation, after intubation, till 7 minutes at different time intervals following laryngoscopy and intubation. **Results:** The heart rate data for Groups A, B, and C shows significant differences at various stages. For example, post succynylcholine Group data also showed significant differences, particularly at 3 and 4 minutes post-intubation ($p<0.001$). Mean arterial pressure (MAP) measurements further demonstrate significant differences at multiple stages (e.g., post-intubation MAP: Group A 115.5±8, Group B 108.2±7.2, Group C 109.2±8.9, $p<0.001$). **Conclusion**: The study has shown that it is better to choose 1.5 mg/kg to manage hemodynamic stress response during laryngoscopy and endotracheal intubation.

Keywords: Endotracheal intubation, Esmolol, Hemodynamic stress, Laryngoscopy

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INTRODUCTION

Laryngoscopy and tracheal intubation compromise hemodynamic responses, i.e. alteration of cardiovascular function including tachycardia, bradycardia, rise in arterial blood pressure, and various types of arrhythmias, maximum after intubation and lasting for 5-10 minutes. Laryngoscopy and endotracheal intubation stimulate sympathoadrenal receptors, releasing catecholamines in the stream. It is a somato-visceral type of reflex.[1] Perhaps this sympathoadrenal response is innocuous, transient and without sequelae in the average individual but is potentially dangerous and devastating for hypertensive patients, those with ischemic heart disease, cerebral pathology and susceptible respiratory tract.[2] This response can cause myocardial ischemia during the surgical period, cerebral vascular accident and acute heart failure.[3] There is an utmost requirement of hemodynamic stress response attenuator to compensate for the complication emerging during laryngoscopy and intubation. Various pharmacological as well as non-pharmacological techniques have been carried out, like lidocaine, opioids, barbiturates, benzodiazepines, beta-blockers, calcium channel blockers, magnesium sulphate, vasodilators and topical agents.[1] Esmolol, a cardio-selective beta-adrenergic receptor blocker, can be an ideal pharmacological agent for such cases because of its rapid onset of action, ultra-short duration, no rebound phenomenon on withdrawal and no life-threatening adverse effect. Esmolol has been proven efficacious clinically in providing hemodynamic control during laryngoscopy and intubation without fatal side effects.[2,3] In this study, we evaluated the efficacy of three doses of esmolol in attenuating hemodynamic response to laryngoscopy and endotracheal intubation. It allows for identifying the dose-response relationship, assessing the efficacy of each dose, and evaluating the safety profile to minimise adverse effects.

METHODS

This prospective, analytical, cross-sectional study was conducted in the Department of Anaesthesia and Critical Care at Nepalgunj Medical College after getting approval from the institutional review committee. The total durtation for study was 6 months from approval from IRC. A total of 66 patients with ASA grading 1 and 2 belonging to age group 20-50 years of both sexes undergoing elective surgeries under general anaesthesia requiring laryngoscopy and endotracheal intubation were included in this study. Pregnant, morbidly obese, patients with severe hypertension, diabetes, ischemic heart disease, emergency surgery, patients under medication like beta-blockers, ASA 3 or more, unwilling and uncooperative patients, and intubation time more than 30 seconds, which were not included in the study. All patients were admitted and a thorough pre-anesthetic evaluation was done. Informed consent was obtained from all patients. All patients were given anxiolytic diazepam oral 5mg the night before surgery and kept nil per oral from midnight. Induction of anaesthesia was standard for all patients. Patients were connected to baseline monitors in the operating room, IV access was opened with an 18 g cannula, and IV fluids were started. Baseline parameters like pulse rate, systolic, diastolic, MAP and SpO2 were recorded. Patients were randomly selected into three groups, with 22 in each group. For Group A, 0.5 mg/kg; Group B, 1mg/kg; and for Group C, 1.5 mg/kg of esmolol was given intravenously 2 mins before laryngoscopy and intubation.

Preoxygenation was done for 3 minutes with 100% oxygen. Fentanyl 2 mcg/kg was given 2 mins before induction. The study drug was prepared in a 10 ml syringe and given bolus over 15-25 seconds. Drugs were provided by an anaesthesiologist who was unaware of the study. No anticholinergic was given. The patient was induced with a titrating dose of propofol 2mg/kg and muscle relaxant succinylcholine 1.5mg/kg. After adequate muscle relaxation, direct laryngoscopy was done, and the patient was intubated with appropriate-sized cuffed endotracheal tubes within 15-30 seconds. Anaesthesia was maintained with oxygen, isoflurane, intermittent vecuronium bolus dose, and intermittent positive pressure ventilation. Heart rate, systolic BP, diastolic BP, and Mean arterial pressure were measured and recorded before premedication, after premedication, during intubation, after intubation and till 7 minutes after laryngoscopy and intubation. Bradycardia refers typically below 40 beats per minute. Hypotension was defined as fall in blood pressure by 30% from the baseline. Data entry was done in MS excel and SPSS version 28 was used for statistical analysis ANOVA test was utilised to determine the statistical analysis of data of three groups. The t-test is used to compare the mean values of continuous parameters like heart rate and blood pressure between groups. Demographic characteristics like gender was analyzed using Chi Square while age and BMI were compared using Kruskall Wallis test. P-value < 0.05 was considered statistically significant.

RESULTS

All three groups A, B and C, were comparable in terms of Age, Gender, and BMI. There was no statistically significant difference between the groups (p > 0.05).

Parameter		Group A	Group B	Group C	P-value
Gender	Male	12	14	11	0.078
	Female	10	8	11	
Age	20-30	7	6	9	0.088
	31-40	9	8	9	
BMI	19-24	18	20	16	0.068
	>24	4	4	8	

Table I: Demographic characteristics of the patients in each group

The heart rate recorded for Groups A, B, and C showed significant differences (p-values < 0.05) at various stages (Figure 1). Group A consistently had higher heart rates, peaking at 110.4 post-succinylcholine and during intubation. Groups B and C had lower heart rates during induction and subsequent minutes. The significant p-values highlight notable differences among the groups, especially post-choline and during intubation.

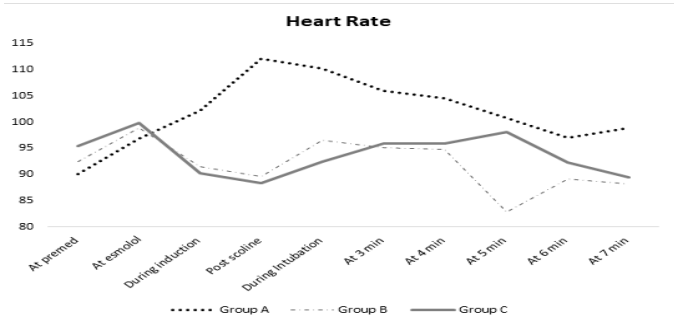

Figure 1: Variation of heart rate in each group at different stages

The systolic blood pressure data also demonstrated variations among the groups at different stages (Figure 2). Systolic pressure for Groups A, B, and C showed significant differences (p-values < 0.05). Group A consistently had higher systolic pressure, peaking at 155.5 at 3 minutes post-intubation. Groups B and C had lower pressure, particularly during induction and at subsequent minutes. Diastolic pressure also varied, with Group C showing significantly higher pressure post-choline and during intubation.

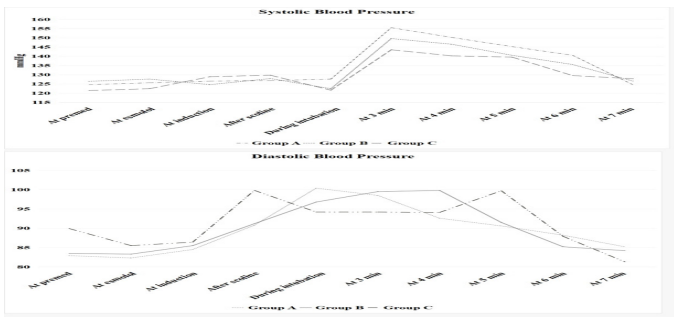

Figure 2: Variation of Systolic (above) and Diastolic Blood (below) Pressure in each group at different stage

Table II represents patients' mean arterial pressure (MAP) in Groups A, B, and C measured at various time periods. The MAP data showed significant differences among Groups A, B, and C at multiple stages. No significant differences were observed at administering esmolol and premedication (p-values 0.081 and 0.455). Significant differences were noted after choline (p=0.021) and post-intubation (p<0.001). At 3-7 minutes post-intubation, MAP differences remained substantial (p-values 0.003 to <0.001), with Group A consistently having higher MAP values.

Mean arterial pressure	Group A	Group B	Group C	P value
At esmolol	99.3±8.2	99.2±5.9	100.1±6.6	0.081
At premed	97.2±7.5	99.2±6.2	102.5±10.2	0.455
After Succinylcholine	103.6±7.2	98.6±8.9	96.2↑19.9	0.021
Post intubation	115.5±8	108.2±7.2	109.2±8.9	<0.001
During intubation	125.5±8.2	119.2±8.2	116.2±6.9	<0.001
At 3 min	121.5±8.2	119.2±6.9	111.2±5	0.003
At 4 min	117.2±7.1	115.2±8	110.25±5	<0.001
At 5 min	115.2±7	106.2±6.6	108.5±7	0.004
At 6 min	109.2±6.1	106.2±5.5	106.8±7.2	0.006
At 7 min	105.7±6.2	107.2±5.9	100.00±4	<0.001

Table II: Mean Arterial Pressure of the patients in each group

Table III represents the incidence of adverse events among patients in three groups. Adverse events included bradycardia (1 in Group C, p=0.527), hypotension (1 in Group C, p=0.871), nausea/vomiting (1 in Group B, 2 in Group C, p=0.812), headache (2 in Groups A and B, 1 in Group C, p=0.989), dizziness (1 in Groups A and B, 2 in Group C, p=0.726), and injection site reactions (1 in each group, p=0.613). No statistical significance among groups.

Adverse Event	Group A (n=22)	Group B (n=22)	Group C (n=22)	Total (n=66)	p-value
Bradycardia	0	0	1	1	0.527
Hypotension	0	0	1	1	0.871
Nausea/ Vomiting	0	1	2	3	0.812
Headache	2	2	1	5	0.989
Dizziness	1	1	2	4	0.726
Injection Site Reaction	1	1	1	3	0.613
Total	4	5	8	17	0.946

Table III: Adverse Events of the patients in each group

DISCUSSION

Laryngoscopy and surgical stimulation commonly cause alternation in cardiac rhythm and pulse rate during different stages of anaesthesia.[4] Laryngoscopy and intubation cause some physiological agitation, thus causing hypertension and tachycardia. This neuroendocrine reaction of the body can cause complications in patients with cardiac diseases like ST changes, ventricular arrhythmia, and pulmonary oedema because of a shift in the ratio between myocardial oxygen requirement and supply.[3,5] Within 2 mins of laryngoscopy and intubation the total autonomic balance (TAB) increases and usually returns to baseline within 5-10 mins.[6] To prevent increased blood pressure from direct laryngoscopy, the duration should be restricted to 15 seconds.[7] Nevertheless, the perfect inhibitor of this reflex is yet to be researched to suppress it completely. Strategies and chemicals have been applied in one way or another with different levels of effectiveness to the mentioned aim. The potential of esmolol for ultra-quick action to hinder hemodynamic stress responses is ideal for countering laryngoscopy and intubation complications. Feng et al explained the usefulness of esmolol bolus injection in preventing and limiting heart rate cardiac output, as well as systolic pressure increases.[8] Similarly, a study done by D Wiest on Esmolol's therapeutic efficacy and pharmacokinetic characteristics in obtunding stress response to laryngoscopy and intubation concluded that the pharmacokinetic profile of esmolol allows the drugs to provide rapid pharmacological control and minimize the potential for profound adverse effect. Bolus dose of 100-200mg effectively attenuates the adrenergic response associated with tracheal intubation.[9]

A study conducted by Vucovic et al for the efficacy of esmolol in attenuating cardiovascular response related to laryngoscopy and tracheal intubation discovered that patients who had esmolol administered 2 minutes before intubation exhibited a significantly decreased pressor response to laryngoscopy corresponding to our administration timing of drugs.[10] Similar studies done by Mulimani SM et al have shown that Inj. Esmolol given 2 min before intubation has a good response in attenuating the laryngoscopy response.[11] In this study, Groups A, B, and C were comparable in age, gender, and BMI with no significant differences ($p > 0.05$). However, significant differences were observed in cardiovascular responses, specifically heart rate, systolic blood pressure, and mean arterial pressure (MAP). Group A had higher heart rate and systolic blood pressure, particularly post-succinylcholine and during intubation, with significant differences at various stages ($p < 0.05$). Group A also had higher MAP post-intubation. No significant differences were found in adverse events such as bradycardia, hypotension, nausea, headache, dizziness, and injection site reactions across the groups ($p > 0.05$). The study demonstrated significant cardiovascular variations in response to esmolol doses, but adverse effects were similar across groups. The 1 mg/kg dose showed higher heart rate and blood pressure than the other doses, with post-intubation MAP of 115.5 ± 8 mmHg, indicating limited control of blood pressure. The 1 mg/kg dose was safe but less effective in controlling hemodynamic stress. The 1.5 mg/kg dose provided the most effective reduction in heart rate and blood pressure, with post-intubation MAP of 109.2 ± 8.9 mmHg, and minimal adverse effects, making it the most potent and safest option for hemodynamic control. A similar study by Rathore A et al concluded that to blunt both the pulse rate and systolic blood pressure response of laryn-

goscopy and intubation, a higher dose is used, where they used 50mgs,100mgs and 150mgs. However, they showed that higher doses tend to have adverse effects in a few individuals, so one must be cautious while using higher doses.[12]

Raghavan L and Basker N investigated how alternating doses of esmolol influence reduction in hemodynamic stress response during laryngoscopy plus endotracheal intubation; the finding showed that the ultimate dose of 1.5 mg/kg functioned effectively in mitigating hemodynamic response lacking significant adverse effect when compared to lower doses which are similar to our study.[5] Jagadeesh GM and. Dutta PK did a study in different centres, comparing three doses of esmolol. They concluded that Esmolol 1.5mg/kg as a safe dose of esmolol in obtunding the heart rate and blood pressure change to laryngoscopy; our result is similar to their result concerning heart rate, systolic blood pressure, diastolic pressure, mean arterial pressure. Still, neither of them compared the adverse effect, but we compared the adverse impact, which is insignificant.[13-14]

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. This study offers insight into the administration of esmolol in surgical patients requiring laryngoscopy and intubation, particularly its dosing regimen for managing hemodynamic response during crucial patients, which will be an addition to improving anaesthesia practice and patient safety.

LIMITATIONS

This study had a small sample size. Future studies should contain a larger sample size. For beat-to-beat blood pressure measurement, invasive blood pressure monitoring was not done.

CONCLUSION

This study showed that it is better to choose Esmolol 1.5 mg/kg in managing hemodynamic stress response during laryngoscopy and endotracheal intubation than the other two doses. Future research should explore the underlying mechanisms driving these cardiovascular responses and investigate the potential long-term effects of the interventions.

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