Original Research Paper

Volume - 13 | Issue - 09 | September - 2023 | PRINT ISSN No. 2249 - 555X | DOI : 10.36106/ijar

Anaesthesiology

# A COMPARATIVE STUDY ON HEMODYNAMIC STRESS RESPONSE BETWEEN 1 mg/kg AND 1.5 mg/kg OF ESMOLOL BOLUS AMONG THE PATIENTS UNDERGOING ENDOTRACHEAL INTUBATION

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**ABSTRACT** **Background:** When giving general anaesthesia, direct laryngoscopy is followed by endotracheal intubation which often precipitate the pressor response. Esmolol is a cardio-selective drug, which alleviates the pressor response during direct laryngoscopy and endotracheal intubation. It achieves peak effect on heart rate within one minute, and on blood pressure within two minutes of intravenous injection. These properties make esmolol suitable for administration by bolus injection. Our study aimed to compare the hemodynamic stress response between 1 mg/kg and 1.5 mg/kg of esmolol bolus among the patients undergoing endotracheal intubation. **Methods:** Our study was conducted on 60 patients scheduled for elective surgery under general anesthesia. After random allocation, about 30 patients in Group A received injection Esmolol 1 mg/kg as a bolus dose, while remaining 30 patients in Group B received 1.5 mg/kg as bolus, both over 30 seconds and endotracheal intubation after 3 minutes. All the vital parameters recorded at baseline followed by 2 minutes, 1 minute before direct laryngoscopy and then at 1 minute interval post endotracheal intubation for next 5 minutes, and final reading at 10 minutes; were compared with respect to different doses of Esmolol. **Results:** In our study, the mean ages of the subjects were 42.75 ± 8.96 years and 44.17 ± 9.31 years in Groups A and B respectively. Majority were males, and belonged to ASA Grade II, in both the groups. On analysis, Esmolol 1.5 mg/kg significantly attenuated hemodynamic stress response better than Esmolol 1 mg/kg, both in terms of HR and MAP. Although side effects like bradycardia and hypotension were evident comparatively more with Esmolol 1.5 mg/kg IV, the proportion was very minimal. **Conclusion:** Esmolol 1.5mg/kg was observed to be better than that of 1mg/kg, in attenuating hemodynamic stress response among the patients undergoing endotracheal intubation.

**KEYWORDS :** Comparative study, Esmolol, Hemodynamic stress response, Endotracheal intubation

## INTRODUCTION:

When administering general anesthesia, the process of direct laryngoscopy followed by endotracheal intubation can often trigger a pressor response. This response is characterized by an increase in heart rate and elevated blood pressure due to heightened sympathetic activity. Typically, this response is of short duration, lasting less than 10 minutes. While it may be well tolerated by healthy individuals, it can pose a health risk for patients with underlying cardiac issues.[1]

Various agents, including magnesium sulfate, beta blockers, lignocaine, gabapentin, pregabalin, and others, have been used to mitigate the pressor response during direct laryngoscopy and endotracheal intubation.[2] Among these, esmolol stands out due to its cardioselectivity, rapid onset of action, and an extremely short elimination half-life of 9.2 ± 2.0 minutes.[3] Esmolol has an apparent volume of distribution of 3.4 ± 1.4 L/kg and a distribution half-life of 2.0 ± 0.5 minutes. It undergoes rapid metabolism through hydrolysis by red blood cell esterases, leading to the formation of methanol and an inactive metabolite.[4]

Esmolol achieves peak effect on heart rate within one minute, and on blood pressure within two minutes of intravenous injection. These pharmacokinetic and pharmacodynamic properties make esmolol suitable for administration by bolus injection.[5] However, due to its rapid onset and short duration of action, the effectiveness of bolus injection can vary with different doses. Hence, the exploration of the optimal esmolol dosage is of utmost importance.

Thus our study was conducted with the objectives of comparing the hemodynamic stress response between two different doses of esmolol bolus i.e., 1 mg/kg and 1.5 mg/kg, among the patients undergoing endotracheal intubation.

## METHODOLOGY:

The present randomized controlled study was carried out on 60 patients who got posted for elective non-cardiac surgery under general anaesthesia at Shridevi Institute of Medical Sciences and Research Hospital, Tumkur. Our study included patients aged between 18 and 60 years, with ASA grading I and II. Patients under 18 years old, those with BMI higher than 35 kg/m$^2$, Mallampati Grade III and IV, with bradycardia or hypotension, or those already on beta blockers or allergic to beta blockers, were excluded from the study. With the help of random sampling method, eligible patients were allocated to two groups, Group A and Group B, each comprising 30 patients.

All the necessary emergency drugs were kept on standby inside the operation theatre. We initiated the process by inserting an 18-gauge IV cannula in the pre-operative ward. After shifting the patient to the operation theater, we connected them to a monitor for non-invasive blood pressure monitoring, oxygen saturation, and ECG, recording all baseline parameters. Each patient was provided with injection midazolam 0.02 mg/kg, injection glycopyrrolate 0.01 mg/kg and injection ondansetron, 0.15 mg/kg as part of regular premedication. All the patients were preoxygenated with 100% oxygen for 3 minutes prior to direct laryngoscopy.

Randomization was accomplished using a random number generator, with the allocated group mentioned in a sealed envelope attached to each patient's case sheet upon transfer to the operation theater. The allocation sequence was concealed from those responsible for assigning patients to intervention groups, mitigating selection bias. However, blinding was not maintained throughout the study due to its short duration and the absence of subjectivity. Patients in Groups A and B received an injection of esmolol bolus at 1 mg/kg and 1.5 mg/kg, respectively, administered over a 30-second period. Following the completion of the esmolol bolus dose, injection succinylcholine 2 mg/kg was administered at 2-minute intervals, and intubation occurred 1 minute thereafter.

The induction was carried out with intravenous injection of propofol (2 mg/kg), followed by endotracheal intubation facilitated by injection succinylcholine (2 mg/kg). Direct laryngoscopy was conducted by a single investigator for all patients after a 3-minute interval. A rigid Macintosh blade of appropriate size was used for laryngoscopy, and intubation was performed using an appropriately sized disposable high volume low-pressure cuffed endotracheal tube. The entire process of endotracheal intubation, including direct laryngoscopy, was completed within 15 to 20 seconds and documented by an assistant.

All the vital parameters (Heart rate, systolic and diastolic blood pressure, and mean arterial pressure) were recorded at baseline (before giving the pre medication) followed by 2 minutes, 1 minute before direct laryngoscopy and then at 1 minute interval post endotracheal intubation for next 5 minutes. The final reading was taken at 10 minutes post intubation. As esmolol, the intervention agent, could potentially lead to adverse effects such as bradycardia and hypotension, we managed these issues by administering atropine (0.6 mg as needed) and mephentermine (6 mg as needed), respectively.

We compiled and documented the data obtained from the selected cases in Microsoft Excel. Descriptive statistics, such as means and standard deviations, were used to represent continuous data, while categorical data were expressed in frequencies and proportions. Statistical analysis was conducted using SPSS version 26, applying appropriate tests of significance based on the nature of the data. A p-value below 0.05 was considered statistically significant, adhering to all relevant rules governing statistical tests.

## RESULTS:

In the study, the mean age of 42.75 ± 8.96 years and 44.17 ± 9.31 years in Group A and Group B respectively. Majority were males, and belonged to ASA Grade II, with no significant difference between the groups. (Table 1)

**Table 1: Characteristics Of The Study Subjects**

| | | Group A (N=30) | | Group B (N=30) | | p-value[#] |
|---|---|---|---|---|---|---|
| | | N | % | N | % | |
| Age group | ≤30 years | 3 | 10.0% | 4 | 13.3% | 0.954 |
| | 31-40 years | 10 | 33.3% | 9 | 30.0% | |
| | 41-50 years | 12 | 40.0% | 11 | 36.7% | |
| | 51-60 years | 5 | 16.7% | 6 | 20.0% | |
| Gender | Male | 17 | 56.7% | 19 | 63.3% | 0.598 |
| | Female | 13 | 43.3% | 11 | 36.7% | |
| ASA | Grade I | 14 | 46.7% | 12 | 40.0% | 0.602 |
| | Grade II | 16 | 53.3% | 18 | 60.0% | |

# Chi-square test

Heart rate (HR) being one of the vital hemodynamic parameters, was monitored among the subjects, and the study found that both the doses of interventions were successful in maintaining the HR throughout the follow-up. Even, on comparing the variation in HR, initially, there exists no significant difference between the groups till 1 minute after intubation. However, the study later recorded statistically significant difference between the groups, thereby implying that the dose of 1.5 mg/kg of Esmolol was more effective than 1 mg/kg of Esmolol comparatively, in controlling the HR to the baseline level. (Figure 1)

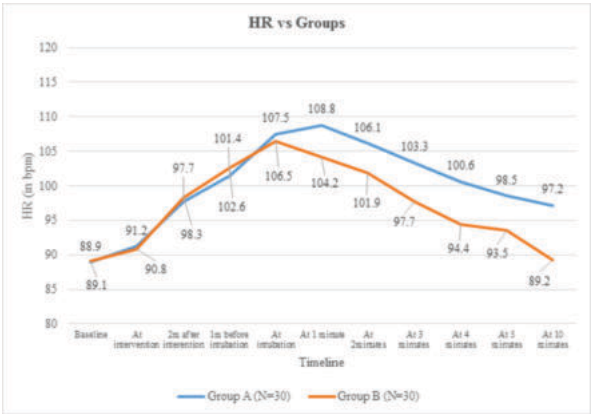


**Figure 1:** Line Diagram Comparing The Variation Of HR Between The Groups, Over The Period Of Follow-up

Mean arterial pressure (MAP) was estimated at specific intervals using systolic and diastolic blood pressure readings. Upon analyzing the MAP in the study subjects, both doses of interventions effectively maintained MAP throughout the follow-up period. Furthermore, when comparing MAP variations, initially, no significant differences were noted between the groups until the point of intubation. However, as the study progressed, statistically significant differences emerged between the groups, indicating that the 1.5 mg/kg esmolol dosage was more effective than the 1 mg/kg esmolol dosage in returning MAP to baseline levels and attenuating its fluctuations. (Figure 2)

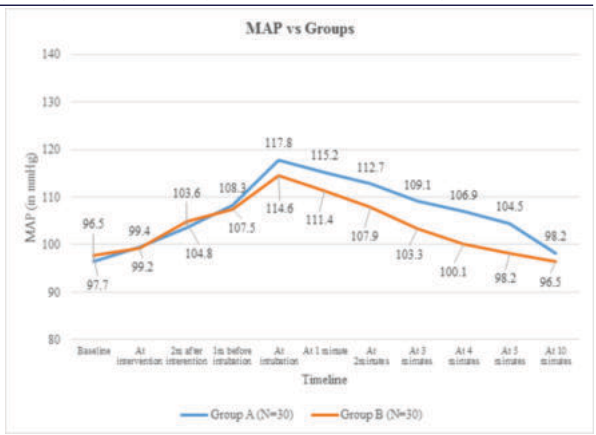


**Figure 1:** Line Diagram Comparing The Variation Of MAP Between The Groups, Over The Period Of Follow-up

In the study, the adverse effects experienced by the subjects were very mild and lesser in proportions in both the groups. Although, more subjects with 1.5 mg/kg dose of Esmolol complained of adverse effects comparatively, the study found no significant difference between the groups in these aspects. (Table 2)

**Table 2: Adverse Effects Among The Study Subjects**

| | | Group A (N=30) | | Group B (N=30) | | p-value[#] |
|---|---|---|---|---|---|---|
| | | N | % | N | % | |
| Bradycardia | Yes | 6 | 20.0% | 7 | 23.3% | 0.754 |
| | No | 24 | 80.0% | 23 | 76.7% | |
| Hypotension | Yes | 5 | 16.7% | 8 | 26.7% | 0.347 |
| | No | 25 | 83.3% | 22 | 73.3% | |

# Chi-square test

## DISCUSSION:

Endotracheal intubation using a laryngoscope is known to induce a significant hemodynamic stress response, necessitating mitigation by anesthesiologists during the intubation process. This strategy typically involves minimizing the duration of laryngoscopy and employing systemic adjuncts like beta-blockers and esmolol. However, there is a dearth of studies comparing the effectiveness of varying esmolol dosages in reducing the stress response associated with intubation. In this context, our randomized controlled study was conducted to compare the hemodynamic stress response in patients scheduled for elective surgery, all of whom underwent endotracheal intubation for general anesthesia, with two distinct esmolol bolus dosages: 1 mg/kg and 1.5 mg/kg.

The mean age of the participants in our study was 42.75 ± 8.96 years in Group A and 44.17 ± 9.31 years in Group B, which aligns with the demographics of previous studies, including those by Ugur B et al[6], Kindler CH et al[7], and Selvaraj V et al[8], where the majority of participants fell within the adult age group. Our study population was predominantly male and classified as ASA-II, resembling the gender distribution and health status observed in prior studies with similar objectives, such as those by Sharma S et al[9], Sheppard S et al[10], and Kumar BS et al[11].

Our study yielded statistically significant difference between the groups with respect to hemodynamic variation, indicating that the 1.5 mg/kg esmolol dose was more effective in reducing both mean arterial pressure (MAP) and heart rate (HR) to baseline levels compared to the 1 mg/kg dose. This finding is consistent with results from previous studies, including those by Ebert et al[12], Gomez et al[13], Miller et al[14], Vukovic M et al[15], and Yuan et al[16].

Studies by Sheppard S et al[10] and Kumar BS et al[11] also reported that a 200 mg esmolol dose was superior to a 100 mg dose in hemodynamic control. Furthermore, research by Jagadeesh GM et al[12] demonstrated that both 1.5 mg/kg and 1 mg/kg doses of esmolol were similarly effective, surpassing the 0.5 mg/kg dose in attenuating the hemodynamic response. Notably, adverse effects experienced by participants in our study were generally mild and exhibited similar proportions in both dosage groups. Although a slightly higher number of subjects in the 1.5 mg/kg esmolol group reported adverse effects, our study did not detect any significant intergroup differences in this

regard. Thus our study was successful in determining the effective minimal dose of Esmolol capable of attenuating the hemodynamic response to endotracheal intubation.

## CONCLUSION:

In our study, both the doses of esmolol resulted in decrease in mean heart rate and mean arterial pressure following drug administration. Nevertheless, it was observed that the 1.5 mg/kg esmolol dose was more effective and demonstrated safety when compared to the 1 mg/kg dose in mitigating the hemodynamic stress response in patients undergoing endotracheal intubation.

**Acknowledgement:**
We extend our sincere gratitude to the study participants for their invaluable contributions and participation in this research.

**Declarations**
**Funding:** None

**Conflict of interest:** None declared

**Ethical approval:** The study was approved by the Institutional Ethics Committee

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