Original Research Article

Alterations in Hemodynamic Response to Laryngoscopy and Intubation by Lidocaine, Esmolol, and Nitroglycerin-A comparative study

Author
Dr Ramesh Pendela
Assistant Professor, Prathima Institute of Medical Sciences, Karimnagar, Telangana
Corresponding Author
Dr Ramesh Pendela
Assistant Professor, Prathima Institute of Medical Sciences, Karimnagar, Telangana, India

Abstract
Background: The pressure response to laryngoscopy and endotracheal intubation has been recognized since long, resulting a rise in pulse and blood pressure.
Aims and Objectives: To compare the safety and efficacy of standard IV bolus doses of lidocaine, esmolol, and nitroglycerin in modifying the acute hemodynamic response to laryngoscopy and tracheal intubation.
Materials and Methods: The study sample of 60 normotensive patients were categorized in to 4 groups. Group 1 = saline 5 ml IV at time 0 minutes; Group 2 = lidocaine 1.5 mg/kg IV at time 1 minute; Group 3 = esmolol 1.4 mg/kg IV at time 2 minutes and Group 4 = nitroglycerin 2 µg/kg IV at time 3 minutes. The parameters measured were Mean arterial pressure and Heart Rate.
Results: MAP increased significantly following tracheal intubation in all four groups (control 47±20%, lidocaine 53% ± 27%, esmolol 24%±12%, nitroglycerin 43% ±22%) compared with preinduction baseline values. in the esmolol group, the increase in HR was significantly lower than in the other three groups.
Conclusion: Esmolol was significantly more effective than either lidocaine or nitroglycerin in controlling the increase in HR, and in minimizing the increase in MAP following tracheal intubation.
Keywords: Esmolol, Hemodynamic Response, Intubation, Laryngoscopy, Lidocaine, Nitroglycerin.

Introduction
Induction of general anaesthesia is known to induce clinically relevant changes in hemodynamic variables probably generated by direct laryngoscopy and endotracheal intubation. Although there are many new airway devices in common use but rigid laryngoscopy and tracheal intubation still remain the gold standard in airway management. The hemodynamic changes occurring from airway instrumentation are due to sympathoadrenal discharge caused by epipharyngeal and parapharyngeal stimulations. Anesthetic agents may display proarrhythmic and antiarrhythmic activity by inducing electrical activity through various mechanisms.1, 2
Several different cardiovascular drugs-including lidocaine, esmolol, nitroprusside, isosorbide, nitroglycerin, verapamil and clonidine have been
evaluated with respect to their ability to blunt the acute hemodynamic response to tracheal intubation.\(^3\)\(^,\)\(^4\) Hence we carried out a randomized, double-blind, placebo-controlled study to compare the safety and efficacy of standard IV bolus doses of lidocaine, esmolol, and nitroglycerin in modifying the acute hemodynamic response to laryngoscopy and tracheal intubation.

**Materials and Methods**

We carried a randomized double-blind, placebo-controlled study on patients undergoing elective surgery with general endotracheal anesthesia. The study was done in the department of anesthesia at Prathima Institute of Medical Sciences, Karimnagar, Telangana state, India, from March 2016 to March 2018. The study had institutional ethical clearance and informed consent from all the patients was obtained.

**Exclusion Criteria**

1. Patients with clinically significant cardiovascular disease.
2. Patients on whom follow-up was not possible.

The study sample of 60 normotensive patients were categorized in to 4 groups. Anesthesia was induced with propofol 2 mg/kg IV and vecuronium 0.15 mg/kg IV. Anesthesia was maintained with 0.5% to 1% isoflurane and 50% nitrous oxide in oxygen (O\(_2\)). Opioid analgesics and other adjunctive drugs were administered after the 20-minute study period.

We followed the procedure and parameters employed in previous similar studies.\(^1\)\(^-\)\(^4\) Laryngoscopy was initiated 3.5 minutes after the propofol induction by the same anesthesiologist, and tracheal intubation was accomplished within 30 seconds. The parameters measured were Mean arterial pressure (MAP) and Heart Rate (HR) recorded at 1 minute intervals for 20 minutes. In addition, hemoglobin O\(_2\) saturation and ECG were monitored continuously for 20 minutes.

**Statistical Analysis**

Data was analyzed by software SPSS Version 20 (IBM SPSS Statistics for Windows, IBM Corp., Armonk, NY: USA). Data were analyzed using repeated-measures of analysis of variance and Student’s paired t-test for evaluating changes within groups; an unpaired t-test with Bonferroni’s correction was used for comparisons between treatment groups. A p-value less than 0.05 was considered statistically significant.

**Results**

Demographic variables like age, weight, and ASA physical status were comparable in the 4 groups (Table 1 and Graph 1).

| Parameter | Saline | Lidocaine | Esmolol | Nitroglycerin |
|-----------|--------|-----------|---------|--------------|
| Age in years | 51±12 | 46±17 | 52±15 | 54±16 |
| Weight in Kgs | 76±9 | 80±15 | 83±19 | 89±15 |
| ASA-I (n=33) | 8 | 7 | 9 | 9 |
| ASA-II (n=27) | 7 | 8 | 6 | 6 |
We observed that MAP increased significantly following tracheal intubation in all four groups (control 47%±20%, lidocaine 53% ± 27%, esmolol 24%±12%, nitroglycerin 43% ±22%) compared with preinduction baseline values.

In the saline (control) group, the maximum pressor response was observed 1 minute following intubation, with the value returning to baseline 6 minutes later. In the esmolol, nitroglycerin, and lidocaine groups, the maximum pressor response was observed at the time of tracheal intubation, with the values returning to baseline 3, 6 and 7 minutes respectively, after intubation.

Heart rate increased significantly in the control (30% ± 5%), nitroglycerin (39% ± 7%), and lidocaine (50% ± 9%) groups. Whereas in the esmolol group, the increase in HR was significantly lower than in the other three groups (22% ± 2%). The maximum increase in HR occurred 2 minutes, 1 minute, 0 minutes, and 2 minutes after intubation and returned to preinduction baseline by 9 minutes, 7 minutes, 9 minutes, and 8 minutes following tracheal intubation in the control, lidocaine, itroglycerin, and esmolol groups, respectively.

During the study period, no patient developed cardiac arrhythmias or evidence of ischemic changes on ECG.

**Discussion**

Important increases can occur in arterial blood pressure, HR, and plasma catecholamine concentrations during laryngoscopy and endotracheal intubation. Increase in hemodynamic parameters may lead to myocardial ischemia, infarction, arrhythmia and cerebral hemorrhage in patients with coronary heart disease, hypertension or cerebrovascular disease.\(^5,6\)

Prasad SR et al in their study gave 1.5 mg/kg IV lidocaine 3 minutes before intubation. They observed that lignocaine did not effectively attenuate hemodynamic response to laryngoscopy and intubation.\(^7\)

Few authors reported that the lignocaine fails to attenuate hemodynamic response, and our observations are in accordance with them.\(^8,9\)

However several authors have concluded that 1.5 mg/kg of lignocaine suppresses stress response to intubation when given 3 min before intubation.\(^10,12\)

These investigators suggested that topical analgesia, rather than a central action of lidocaine, was responsible for attenuating the hemodynamic response.

Longmire et al carried out a study to find out the effectiveness of intravenous nitroglycerin infusion in lowering maternal blood pressure and in blunting the hemodynamic responses to endotracheal intubation was evaluated in six
primigravid women with severe preeclampsia. The hemodynamic effects associated with endotracheal intubation revealed a change in the heart rate from 104 ± 10 to 133 ± 17 beats/min, an increase in mean arterial pressure from 134 ± 12 to 164 ± 32 mm Hg, and an increase in systemic vascular resistance from 1262 ± 342 to 1351 ± 259 dynes-sec-cm−5 that was accompanied by a small change in the cardiac index from 4.5 ± 1.2 to 4.5 ± 0.9 L · min−1 · m−2.13 Mikawa et al evaluated the efficacy and safety of intravenous (IV) nitroglycerin in attenuating the hypertensive response to laryngoscopy and intubation. They concluded that a single, rapid IV dose of nitroglycerin is a simple, practical, effective, and safe method to attenuate the hypertensive response to laryngoscopy and tracheal intubation.14 In our study When nitroglycerin 2 µg/kg IV was administered 30 seconds prior to laryngoscopy, we found it to be ineffective in preventing the hyperdynamic response to tracheal intubation. This finding could be due to the shorter duration of action of nitroglycerin compared with the untreated hyperdynamic response (1 to 2 minutes vs. 6 to 10 minutes). The pharmacokinetic profile of esmolol makes it well suited for controlling the cardiovascular response to tracheal intubation when it is administered as a continuous infusion. Vucevic et al in a double-blind, randomized, controlled prospective study, found that the heart rate decreased in the esmolol group before induction of anaesthesia. The pressor response to laryngoscopy was significantly less marked in the esmolol group.15 Parnass et al studied the efficacy of a single bolus dose of esmolol in the prevention of intubation-induced tachycardia and hypertension in a double-blind manner. They found that esmolol 100 mg (1.4 +/- 0.3 mg/kg) and 200 mg (2.6 +/- 0.7 mg/kg) significantly (p less than 0.05) blunted the maximum increases in HR and BP following intubation. The average maximum HR increase in the placebo group was 40% as opposed to 16% in the esmolol 100 mg group and 14% in the esmolol 200 mg group. Both esmolol groups blunted the tachycardic response over a 4-minute postintubation time period. The average maximum BP increase was 47% in the placebo group versus 22% and 19% in the esmolol 100 mg and esmolol 200 mg groups, respectively. There were no significant differences between the two esmolol groups. Their study demonstrated the efficacy of a single bolus dose of esmolol in blunting the tachycardic and hypertensive responses to laryngoscopy and intubation in an ambulatory surgery setting.16 Miller et al carried out a multicentre trial to determine the dose-response and side-effects of esmolol when administered as a single iv bolus prior to induction of anaesthesia for controlling the haemodynamic response to tracheal intubation. Patients who received placebo and no narcotic had greater HR and SBP values after tracheal intubation than patients who received either E100 or E200 (P < 0.005). The proportion of patients whose maximum HR exceeded 110 min−1 was also greater in the placebo group (22/180) than in either the E100 (10/187) or E200 (9/181) groups (P < 0.05), but was not different when comparing E100 with E200. They concluded that esmolol was less effective in controlling blood pressure, but, in combination with low-dose narcotic, esmolol suppressed the SBP response to tracheal intubation and suggested that a 100 mg bolus of esmolol is safe and effective for controlling the haemodynamic response to tracheal intubation.17 Limitation of our study was that the effect was not seen in hypertensive and cardiac patients. It will be more useful to study in high-risk hypertensive and cardiac patients.

Conclusion
Esmolol was significantly more effective than either lidocaine or nitroglycerin in controlling the increase in HR, and in minimizing the increase in MAP following tracheal intubation. Lidocaine and nitroglycerin were ineffective in controlling the acute hemodynamic response following laryngoscopy and intubation. In situations where
opioid analgesics are contraindicated, esmolol would appear to be the cardiovascular drug of choice in maintaining hemodynamic stability during laryngoscopy and intubation.

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