

## Comparison of Esmolol and Lidocaine for Attenuating Cardiovascular Stress Response to Direct Laryngoscopy and Endotracheal Intubation

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### Abstract

**Aims:** Cardiovascular response was increase by direct laryngoscopy and endotracheal intubation. The aims of this study the hemodynamic change and compare the best among the two drugs in prevention of cardiovascular response to direct laryngoscopy and Endotracheal intubation. **Background:** This study also evaluates the efficacy of intravenous Esmolol (1 mg/kg) and intravenous Lidocaine (1.5 mg/kg) in attenuating cardiovascular stress response during direct laryngoscopy and endotracheal intubation in normotensive patients undergoing plan routine surgeries. **Materials and Methods:** This prospective study was conducted from June 2017 to May 2019 after informed consent was obtained from 120 patients. The study population consisted of ASA physical status I or II, and Mallampatti Score 1 or 2. All patients had enrolled our study are between the age of 20 years and 65 years and are scheduled for various elective surgical procedures. This study was a prospective, randomized, and clinical comparison study in rural tertiary referral health center. The Sample size for the study was 120 generated using a sample size calculator. The study participants were divided into Three Groups. A study patient (Group A) who was received intravenous esmolol 1 mg/kg two minutes before intubation. In Group B, who was received intravenous Lidocaine 1.5 mg/kg, two minutes before intubation and Group C, who received only prescribed premedication and listed in Control Group. All drugs were diluted in 10 milliliters of distilled water. All patients were monitored Heart Rate (HR), Systolic Blood Pressure (SBP), Diastolic Blood Pressure (DBP), and Mean Arterial Pressure (MAP) with respect to time. All patients were kept unaware of the drug injected to enable double-blinding. **Results:** Group C had statistically highly significant ( $p \leq 0.0001$ ) value of HR, SBP, DBP, and MAP at all time interval after intubation when compared to Group B and Group C had statistically significant ( $p \leq 0.05$ ) higher values of hemodynamic variable at all time interval when compared to Group A. **Conclusions:** Intravenous lidocaine (1.5 mg/kg) and esmolol (1 mg/kg) are effective agents in suppressing the hemodynamic response to laryngoscopy and intubation without any deleterious effect. Esmolol 1 mg/kg appears to be very effective and should be viewed as potential treatment strategy for attenuating hemodynamic changes during induction of anesthesia.

**Keywords:** Direct Laryngoscopy; Intubation; Esmolol; Lidocaine; Cardiovascular response.

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## Introduction

Direct laryngoscopy and endotracheal intubation is not only an integral part of modern day balanced anesthesia but is also the most delicate phase in general anesthesia. Cardiovascular complications are one of the most common causes of anesthesia-related morbidity and mortality.<sup>1</sup> Direct laryngoscopy and endotracheal intubation frequently induces a cardiovascular stress response characterized by hypertension and tachycardia due to reflex sympathetic stimulation. The response is transient occurring 30 sec after intubation and lasting for less than 10 min.<sup>2</sup> It may be well-tolerated in healthy people, but may be hazardous in patients with hypertension, tachycardia, myocardial infarction, and other complications.<sup>3</sup> Various pharmacological approaches have been used to attenuate the pressure responses to direct laryngoscopy and endotracheal intubation.<sup>4</sup> Direct laryngoscopy and endotracheal intubation causes mechanical stimulation to the oropharynx, laryngopharynx and the tracheobronchial tree causing increased reflex sympathetic activity and it's hence increase in blood pressure and heart rate, as reflected by an increase in the level of circulating catecholamine's and stress hormone. Direct laryngoscopy was a more potent stimulus to develop hypertension than the endotracheal intubation. The stimulation of the sympathetic system occurs as a result of the direct laryngoscope pressing on the base of tongue and lifting the epiglottis thus, stimulation the mechanoreceptors concentrated in the proximal portion of the trachea-bronchial tree. The stimulation of Sympathetic system lead to a transient rise in systolic arterial blood pressure of approximately 20–25 mm Hg and peaks up to 30–45 seconds after direct laryngoscopy. The degree of reflex response to laryngeal stimulation appears to vary with the depth of anesthesia, duration and difficulties encountered during endotracheal intubation as well as on patients dependent variables, including age and chronic diseases.

Expertise in establishing a definitive airway is not limited to being able to successfully intubation but also in a manner that does not significantly alters the vital parameters or increases the myocardial oxygen demand of patients. These techniques for attenuation of intubation related stress response depend on reduction input of stimuli or the blockage of the adrenergic responses. It can be achieved by minimizing the duration of direct laryngoscopy to less than 15 seconds, deep inhalation anesthesia, antihypertensive drugs,

use large dose of opiates and alpha-2-agonists. Lidocaine is the oldest and most widely use drugs for the purpose of attenuating oropharyngeal and laryngopharyngeal reflexes.

Perioperative myocardial infarction is a leading cause of postoperative morbidity and mortality due to hypertension and tachycardia. Such anesthesia-related deaths could be reduced by controlling the hemodynamic changes that occur due to myocardial ischemia. There is increasing evidence that the control of the heart rate and blood pressure response to direct laryngoscopy and endotracheal intubation is essential in preventing adverse cardiovascular outcomes, as Rate Pressure Product (RPP) acts as an indicator of oxygen demand by the heart at the onset of ischemia,<sup>9</sup> there is therefore, a need for assessment in this direction as.

The present study, is designed to compare and select the best among the two drugs in prevention of cardiovascular response to direct laryngoscope and endotracheal intubation. To evaluate the efficacy of intravenous Esmolol (1 mg/kg) and intravenous Lidocaine (1.5 mg/kg) in attenuating stress response during direct laryngoscopy and endotracheal intubation, both above mentioned drugs are given two minutes before induction of general anesthesia. The hemodynamic status and electrocardiographic assessment are monitoring of all normotensive patients. Efforts are being made in practice safe anesthesia and reduce perioperative complication and mortality during anesthesia.

## Aims and Objectives

Cardiovascular response was increase by direct laryngoscopy and endotracheal intubation. The aims of this study the hemodynamic change and compare the best among the two drugs in prevention of cardiovascular response to Direct laryngoscopy and Endotracheal intubation. This study also evaluates the efficacy of intravenous Esmolol (1 mg/kg) and intravenous Lidocaine (1.5 mg/kg) in attenuating cardiovascular stress response during direct laryngoscopy and endotracheal intubation in normotensive patients undergoing plan routine surgeries.

## Materials and Methods

This prospective study was conducted from June 2017 to May 2019 after informed consent was obtained from 120 patients. The study population consisted of ASA physical status I or II, and Mallampatti Score 1 or 2. All patients had enrolled

our study are between the age of 20 years and 65 years and are scheduled for various elective surgical procedures.

### **Study Design**

This study was a prospective, randomized, and clinical comparison study in rural tertiary referral health center. The Sample size for the study was 120 generated using a sample size calculator. The study participants were divided into Three Groups. A study patient (Group A) who was received intravenous esmolol 1 mg/kg two minutes before intubation. In Group B, who was received intravenous Lidocaine 1.5 mg/kg, two minutes before intubation and Group C, who received only prescribed premedication and listed in Control Group. All drugs were diluted in 10 milliliters of distilled water. All patients were monitored Heart Rate (HR), Systolic Blood Pressure (SBP), Diastolic Blood Pressure (DBP), and Mean Arterial Pressure (MAP) with respect to time. All patients were kept unaware of the drug injected to enable double-blinding.

### **Inclusion Criteria**

For the study was ASA Class I or II, age range 20-65, oropharyngeal anatomy of Mallampati Class I or II and elective operation other than cardiac and neurosurgery performed under general anesthesia with direct laryngoscopy followed by endotracheal intubation.

### **Exclusion Criteria**

For the study included patients who were morbidly obese, patients with cardiovascular disease, heart rate < 60 beats per minute (bpm), basal SBP < 100 mm Hg and other conditions such as bronchial asthma, diabetes mellitus, chronic kidney diseases, liver diseases, cardiovascular diseases, drug allergies, and total duration of Direct laryngoscopy was noted and in cases where duration exceeded 15 sec, and patients refuse was excluded from study.

### **Presurgical protocol**

All selected patients underwent a preanesthetic evaluation with special consideration to elicit a history of hypertension, dyspnoea, chest-pain, cough, wheezing, convulsions, and diabetes mellitus as well as previous anesthetic history and drug sensitivity prior to surgery. Information collected also included weight, nutritional status, and airway assessment by the Mallampatti scoring system, a detailed examination of the respiratory, cardiovascular, and central nervous system. A preoperative routine investigations such as

hemoglobin, hematocrit, total lymphocyte count, differential lymphocyte count, serum electrolytes, blood group/Rh typing, blood urea nitrogen, serum creatinine, fasting blood sugar, chest radiography, and electro-cardiogram in all patients. Patients were advised to fast the night prior to surgery. All selected patients were given uniformly premedication on tablet diazepam 5 mg at night before surgery and same dose at 6 a.m. on day of surgery with sip of water and with Inj. pethidine 1 mg /kg, Inj. Phenergan 0.5 mg/kg I.M. 45 min. before induction of general anesthesia.

### **Surgical protocol**

All selected patient identification a short preoperative history was taken; clinical examination and routine investigations were rechecked in all patients. Study objective and procedure were explained to the participant's patients and a written informed consent was obtained from each participant patients.

In all the groups, after shifting the patients to Operation Theater base line parameters were recorded. All the patients were pre oxygenated for 3 minutes with 100% oxygen and intravenous access was secured and infusion of Ringer's lactate solution started. All patients were then shifted to the operating room after which routine noninvasive monitor was applied and vital signs monitored. The patient was preoxygenated for 3 minutes with 100% oxygen. All the patients were induced with 5 mg kg<sup>-1</sup> IV thiopentone sodium in incremental doses until loss of eyelash reflex occurred, then Injection succinylcholine 1.5 mg/kg IV after check ventilation, followed up by administering the study drugs (normal saline, esmolol, or lidocaine) 2 min before laryngoscopy and intubation. The study drug was randomly allocated to patients in a double blinded manner. General anesthesia was maintained with oxygen 40%, Nitrous oxide 60%, Isoflorane, Vecuronium 0.10 mg/kg/ IV and supplemented as needed, Controlled ventilation was employed using Bains circuit system. At the end of surgery action of muscles relaxant was reversed with Injection Neostigmine 0.05 mg/kg and Injection atropine 0.02 mg/kg/IV.

All parameter were monitored and recorded like HR, SBP, DBP, MAP, RPP (rate pressure product), SpO<sub>2</sub> (oxygen saturation), and ECG (electrocardiogram) before induction (Basal) and after tracheal intubation at 1, 3, 5,10, 15 and 30 minutes for the purpose of this study. No manipulation like painting and draping the area of operation was allowed till 10 min after the study drug administration.

### Parameters and statistical analysis

Summary statistics of patient gender, age, and weight for all three groups were reported as means  $\pm$  standard deviation. HR, SBP, DBP, and MAP were recorded before induction (Baseline), after tracheal intubation at 1, 3, 5, 10, 15, and 30 minutes during monitoring. From the data RPP was calculated by multiplying heart rate with systolic blood pressure. Patients were also observed for complications like hypotension, hypertension, arrhythmias, and hypoxemia. Statistical analysis was done by student *t*-test and *P*-values were calculated. Hemodynamic variables were represented by mean  $\pm$  SD. ANOVA with repeated measures was used to compare the changes in HR, MAP, and RPP values. Bonferroni's multiple comparison tests were applied to evaluate intragroup comparisons. The statistical package SPSS® 17.0 and Graph pad prism 5 was used.  $p < 0.05$ ,  $p < 0.001$  were considered significant and highly significant, respectively, for the study.

### Results

The present study is designed to compare and select the best among the two drugs in prevention of cardiovascular response to direct laryngoscope and endotracheal intubation. To evaluate the efficacy of intravenous Esmolol (1 mg/kg) and intravenous Lidocaine (1.5 mg/kg) in attenuating stress response during direct laryngoscopy and endotracheal intubation, both above mentioned drugs are given two minutes before induction of

general anesthesia. A study patient (Group A) who was received intravenous esmolol 1 mg/kg two minutes before intubation. In Group B, who was received intravenous Lidocaine 1.5 mg/kg, two minutes before intubation and Group C, who received only prescribed premedication and listed in control group. All drugs were diluted in 10 milliliters of distilled water. All patients were monitored Heart Rate (HR), Systolic Blood Pressure (SBP), Diastolic Blood Pressure (DBP), and Mean Arterial Pressure (MAP) with respect to time. All patients were kept unaware of the drug Injected to enable double-blinding.

All the demographic profiles in the Group C-control, Group-B-lidocaine, and Group-A-esmolol were comparable shown in Table 1. The mean age of patients in group A is 34.15 years. There was no significant difference in mean age among the groups ( $p < 0.05$ ). In Group A and Group C there were 14 male and 26 female and Group B there were 18 male and 22 female patients. Overall there was no significant difference in the sex distribution of the Groups ( $p < 0.05$ ). In Groups A and B 36 patients were of ASA Grade 1 and 4 patients were Grade ASA 2. In Group C-32 and 8 patients belonged to ASA Grades 1 and 2 respectively ( $p < 0.05$ ).

An increase in HR, MAP, and RPP from the base line and maximum at 1 min after intubation was observed in Group-C, however in the Groups-L and E there was no significant variation of HR, MAP, and RPP from the base line after 1 min of intubation, (Table 2).

**Table 1:** Distribution of patient's demographic profile

Parameters	Group A (Esmolol)	Group B (Lidocaine)	Group C (Control)	<i>p</i> - Value (A/B, A/C, B/C)
Age	34.15 $\pm$ 7.3	34.05 $\pm$ 9.63	36.8 $\pm$ 9.8	0.97, 0.34, 0.38
Sex	Male	14	18	14
	Female	26	22	26
ASA	1	36	36	32
	11	4	4	8

( $p < 0.05$  is significant)

**Table 2:** Baseline hemodynamic parameters

Parameters	Group A (Esmolol)	Group B (Lidocaine)	Group C (Control)	<i>p</i> - Value (A/B, A/C, B/C)
HR	92 $\pm$ 11	97 $\pm$ 16	90 $\pm$ 12	0.2, 0.28, 0.15
SBP	131 $\pm$ 5	134 $\pm$ 6	130 $\pm$ 12	0.1, 0.53, 0.11
DBP	83 $\pm$ 12	86 $\pm$ 5	82 $\pm$ 9	0.32, 0.32, 0.31
MAP	99 $\pm$ 10	100 $\pm$ 5	97 $\pm$ 9	0.17, 0.45, 0.19
RPP	11641 $\pm$ 1663	12731 $\pm$ 2100	11751 $\pm$ 2269	0.13, 0.52, 0.17
Spo <sub>2</sub>	100 $\pm$ 1	100 $\pm$ 1	100 $\pm$ 1	0.41, 0.19, 0.62

Data are presented as means standard deviation. HR = Heart Rates, SBP = Systolic Blood Pressure, DBP = Diastolic Blood Pressure, MAP = Mean Arterial Pressure, RPP = Rate Pressure Product. ( $p < 0.05$  is significant)

**Table 3:** Hemodynamic parameters after administering the drugs (esmolol and lidocaine) two minutes before and during induction

Parameters of study drugs	Group A (Esmolol)		Group B (Lidocaine)		Group C (Control)		p - Value (A/B, A/C, B/C)	
	2 Minutes before induction	During induction	2 Minutes before induction	During Induction	2 Minutes before induction	During Induction	2 Minutes before induction	During induction
HR	78 ± 10	80 ± 12	94 ± 18	95 ± 13	94 ± 14	98 ± 13	< 0.001, < 0.001, < 87	< 0.001, < 0.001, 0.42
SBP	122 ± 7	122 ± 9	131 ± 5	128 ± 8	129 ± 11	125 ± 11	< 0.001, 0.03, 0.48	0.043, 0.38, 0.38
DBP	77 ± 9	77 ± 10	85 ± 6	85 ± 8	82 ± 10	80 ± 15	< 0.001, 0.11, 0.19	0.008, 0.445, 0.2
MAP	92 ± 7	92 ± 8	101 ± 5	100 ± 7	97 ± 9	94 ± 13	< 0.001, 0.05, 0.12	0.002, 0.53, 0.08
RPP	9475 ± 1545	9791 ± 1980	12292 ± 2086	12177 ± 1991	12071 ± 2350	12358 ± 2259	< 0.001, < 0.001, 0.75	0.001, < 0.001, 0.79
SpO <sub>2</sub>	99 ± 1	99 ± 1	99 ± 1	99 ± 1	99 ± 1	99 ± 1	0.28, 0.23, 0.2	0.4, 0.08, 0.09

Data are presented as means standard deviation. HR = Heart Rates, SBP = Systolic Blood Pressure, DBP = Diastolic Blood Pressure, MAP = Mean Arterial Pressure, RPP = Rate Pressure Product. (p < 0.05 is significant)

**Table 4:** Hemodynamic parameters immediately after Intubation

Intubation	Group A (Esmolol)	Group B (Lidocaine)	Group C (Control)	p - Value (A/B, A/C, B/C)
Heart Rate	98 ± 11	116 ± 15	129 ± 14	< 0.001, < 0.001, 0.01
SBP	140 ± 5	149 ± 9	161 ± 16	< 0.001, < 0.001, 0.01
DBP	88 ± 11	97 ± 8	105 ± 12	0.006, < 0.001, 0.01
MAP	106 ± 8	114 ± 7	123 ± 12	< 0.001, < 0.001, 0.022
RPP	13680 ± 1770	17483 ± 2788	20801 ± 3625	< 0.001, < 0.001, 0.01
SpO <sub>2</sub>	99 ± 1	99 ± 1	99 ± 1	0.83, 0.12, 0.14

Data are presented as means standard deviation. SBP = Systolic Blood Pressure, DBP = Diastolic Blood Pressure, MAP = Mean Arterial Pressure, RPP = Rate Pressure Product. (p < 0.05 is significant)

**Table 5-A:** Percentage change in Hemodynamic parameters, Percentage change in Heart Rate (HR)

Percentage change in Heart Rate	Baseline Vs Study drugs (p - Value)	Baseline Vs Induction (p - Value)	Baseline Vs Intubation (p - Value)
Group A (Esmolol)	↓ 9.7 (0.023 A/B)	↓ 7.5 (0.102 A/B)	↑ 13.71 (0.112 A/C)
Group B (Lidocaine)	↓ 2.4 (< 0.001 A/C)	↓ 0.86 (< 0.001 A/C)	↑ 21.53 (< 0.001 A/C)
Group C (Control)	↑ 3.44 (0.008 B/C)	↑ 9.23 (0.003 B/C)	↑ 44 (< 0.001 B/C)

(p < 0.05 is significant)

All hemodynamic parameters were recorded at specified intervals in each of the group and tabulated as follows:

$p$  - value between Group A and B, A and C, and B and C were more than 0.05, i.e. there were no significant difference in the hemodynamic parameters of patients between any two groups at the baseline. SpO<sub>2</sub> was similar among all the groups at the intervals (Table 3).

A Significant decrease in heart rate, systolic blood pressure, diastolic blood pressure and mean arterial pressure was noted after administration of esmolol as compared to lidocaine ( $p < 0.05$ ). ON calculation, rate pressure product was found to be significantly low in Esmolol Group as compared to Lidocaine Group ( $p < 0.05$ ). There was a significant fall in heart rate, SBP, RPP ( $p < 0.05$ ) in Esmolol Group as compared to control group.

All the vital parameters noted were significantly lower in the Esmolol Group compared to Lidocaine Group ( $p < 0.05$ ) and heart rate and rate pressure product ( $p < 0.05$ ) was statistical significance decrease as compared to the control group. No statistical significance was found in parameters with compare to Control Group ( $p < 0.05$ ).

All the parameters were increase at intubation in all three groups. The percentage increases was significantly higher in the control group as compared to esmolol and Lidocaine Groups ( $p < 0.05$ ). All the parameters were increase minimum in Esmolol Group, shown as in Table 4. In Lidocaine Group, all the parameters were significantly higher than in Esmolol Group ( $< 0.05$ ).

We noted a decrease in heart rate after giving the study drugs and after induction in groups receiving Esmolol (Group A) and Lidocaine (Group B). After

**Table 5-B:** Percentage change in Systolic Blood Pressure (SBP)

Parameters	Baseline Vs Study drugs ( $p$ - Value)	Baseline Vs Induction ( $p$ - Value)	Baseline Vs Intubation ( $p$ - Value)
Group A (Esmolol)	↓ 7.14 (0.009 A/B)	↓ 6.7 (0.333 A/B)	↑ 6.7 (0.048 A/B)
Group B (Lidocaine)	↓ 2.6 (<0.001 A/C)	↓ 4.55 (0.048 A/C)	↑ 11 (<0.001 A/C)
Group C (Control)	↓ 0.56 (0.150 B/C)	↓ 3.16 (0.429 B/C)	↑ 24 (<0.001 B/C)

( $p < 0.05$  is significant)

**Table 5-C:** Percentage change in Diastolic Blood Pressure (DBP)

Parameters	Baseline Vs Study drugs ( $p$ - Value)	Baseline Vs Induction ( $p$ - Value)	Baseline Vs Intubation ( $p$ - Value)
Group A (Esmolol)	↓ 6.9 (0.004 A/B)	↓ 6.97 (0.034 A/B)	↑ 7.28 (0.128A/B)
Group B (Lidocaine)	↓ 0.87 (<0.001 A/C)	↓ 1.39 (0.026 A/C)	↑ 13 (<0.001 A/C)
Group C (Control)	↑ 2.33 (0.08 B/C)	↓ 0.27 (0.703 B/C)	↑ 31 (<0.001 B/C)

( $p < 0.05$  is significant)

**Table 5-D:** Percentage change in Mean Arterial Pressure (MAP)

Parameters	Baseline Vs Study drugs ( $p$ - Value)	Baseline Vs Induction ( $p$ - Value)	Baseline Vs Intubation ( $p$ - Value)
Group A (Esmolol)	↓ 6.5 (0.006 A/B)	↓ 6.4 (0.066 A/B)	↑ 7.5 (0.098 A/B)
Group B (Lidocaine)	↓ 1.3 (<0.001 A/C)	↓ 2.1 (0.083 A/C)	↑ 12 (<0.001 A/C)
Group C (Control)	↑ 0.6 (0.10 B/C)	↓ 2.4 (0.878 B/C)	↑ 28 (<0.001 B/C)

( $p < 0.05$  is significant)

**Table 5-E:** Percentage change in Rate Pressure Product (RPP = HR × SBP)

Parameters	Baseline Vs Study drugs ( $p$ - Value)	Baseline Vs Induction ( $p$ - Value)	Baseline Vs Intubation ( $p$ - Value)
Group A (Esmolol)	↓ 15.66 (0.007 A/B)	↓ 13.0 (0.069 A/B)	↑ 22 (0.005 A/B)
Group B (Lidocaine)	↓ 2.28 (<0.001 A/C)	↓ 2.64 (<0.001 A/C)	↑ 39 (<0.001 A/C)
Group C (Control)	↑ 3.0 (0.194 B/C)	↑ 5.67 (0.082 B/C)	↑ 79 (<0.001 B/C)

( $p < 0.05$  is significant)

administration of study drugs, both Esmolol and Lidocaine Groups showed significant decreases in heart rate, with fall in esmolol group being significantly more than in lidocaine group. In the control group there was a significant increase in heart rate after induction as compared to study drugs. After intubation all groups showed an increase in heart rate but the less increase in esmolol group as comparable between Esmolol (13.7%), Lidocaine (21.53%) and Control group (44%) but each of these groups showed a statistically significant difference from control group, shown in (Table 5-A).

Systolic blood pressure decreased after administration of study drugs in the entire group, but significantly maximum fall systolic blood pressure was seen after Esmolol (7.14%). After induction fall in systolic blood pressure was comparable between esmolol and lidocaine group and lidocaine and control groups, but significant fall in systolic blood pressure was seen in esmolol group as compared to control group. After intubation all patients had a rise in systolic blood pressure but Control Group (24%) has highly significant as compared to study drugs. The rise in systolic blood pressure was significantly in Esmolol Group (6.7%) as compared to Lidocaine Group (11%), shown in (Table 5-B).

Diastolic blood pressure decreased significantly after administration of study drugs as compared to Control Group. Esmolol showed significantly highest fall among the Group (6.9%). Whereas no statistically significant drop diastolic blood pressure was seen in Lidocaine Group as compared to Control Group. After induction Diastolic Blood Pressure (DBP) fall in the entire group; Esmolol Group showed significant DBP drop as compared to the Lidocaine and Control Group, though no significant difference in DBP was seen in control and Lidocaine Group. After intubation the entire three groups showed increase in DBP, but this rise was comparable between Esmolol (7.28%) and Lidocaine (13%) Groups and each of these groups showed statistically significant lower rise in DBP as compared to Control Group (31%), shown in (Table 5-C).

Mean arterial pressure showed significant drop after administration of Esmolol (6.5%) as compared to Lidocaine and Control Groups, though it increased in the control group. After induction, the MAP fell in all groups but this was statistically insignificant even after Esmolol (6.4%) administration. After intubation, MAP was increased in the entire group, but significantly higher in Control Group (28%) as compared to study group, shown in (Table 5-D).

Increase in rate pressure product after intubation was significant in all the groups but it was significantly lower in Esmolol Group (22%) as compared to Lidocaine (39%) and Controls (79%) Groups. Lidocaine Group showed significantly lower rise in RRP as compared to Control Group, shown in (Table 5-E).

All the parameters were recorded in 1 min., 3 min., 5 min., 10 min., 15 min., and 30 minute after intubation they were significantly lower in the esmolol group as compared to the lidocaine and control groups. Heart rate and rate pressure product were significantly lower in esmolol compared with lidocaine and control groups ( $p < 0.05$ ), (Table 6).

In Groups C, B, and A maximum increase in mean heart rate over the baseline values were  $90.00 \pm 12$ ,  $97.00 \pm 16$ , and  $92.00 \pm 11$ , respectively, and at 1 minute was  $119.00 \pm 14$ ,  $110.00 \pm 16$ , and  $91 \pm 12$  after intubation, respectively. The difference between means from baseline value and 1 minute were 30.00 bpm, 13.00 bpm, and 0.40 bpm in Groups-C, B, and A, respectively. The mean difference in the heart rate between Groups C-B, C-A, and B-A recorded at 1 minute were 7.00, 29.60, and 12.60 bpm [ $p < 0.0001$ ], (Table 6).

In all Three Groups the vitals remained attenuated for 5 min after intubation; however, the vitals returned to baseline values after 15 to 30 minute. Control Group patients undergoing laryngoscopy and intubation showed an incidence of 8% ventricular ectopics and 5% dropped beats however no such findings were recorded in the lidocaine and esmolol groups.

**Table 5-F:** Percentage change in SpO<sub>2</sub>

Parameters	Baseline Vs Study Drugs ( <i>p</i> - Value)	Baseline Vs Induction ( <i>p</i> - Value)	Baseline Vs Intubation ( <i>p</i> - Value)
Group A (Esmolol)	↓ 0.5	↓ 0.02	↓ 0.24
Group B (Lidocaine)	↓ 0.35	↓ 0.5	↓ 0.5
Group C (Control)	↓ 1.0	↓ 1.0	↓ 1.26

Over all, there was no significant change in the peripheral oxygen saturation at any time in any of the groups *p* - value was between any two groups  $< 0.05$ , (Table 5-F)

Table 6: Hemodynamic change were significantly lower in esmolol compared with lidocaine and control groups.

Parameter	Basal	1 Min. After Intubation	3 Min. After Intubation	5 Min. After Intubation	10 Min. After Intubation	15 Min. After Intubation	30 Min. After Intubation	p Value
<b>A. heart Rate</b>								
1. Group A. (Esmolol)	91 ± 11	91 ± 12	88 ± 10	84 ± 14	77 ± 13	75 ± 9	75 ± 6	<0.001
2. Group B. (Lidocaine)	97 ± 16	110 ± 16	102 ± 13	97 ± 14	91 ± 11	89 ± 13	86 ± 11	<0.001
3. Group C. (control)	90 ± 12	119 ± 14	115 ± 14	108 ± 16	104 ± 15	101 ± 15	96 ± 13	<0.001
<b>B. SBP</b>								
1. Group A. (Esmolol)	131 ± 5	128 ± 10	123 ± 10	121 ± 10	123 ± 10	125 ± 9	126 ± 9	<0.001
2. Group B. (Lidocaine)	134 ± 6	144 ± 12	139 ± 9	133 ± 12	134 ± 9	132 ± 9	130 ± 23	<0.001
3. Group C. (control)	130 ± 12	147 ± 15	138 ± 12	135 ± 14	134 ± 11	131 ± 11	130 ± 10	<0.001
<b>C. DBP</b>								
1. Group A. (Esmolol)	83 ± 12	95 ± 10	83 ± 9	83 ± 10	83 ± 11	83 ± 10	83 ± 12	<0.001
2. Group B. (Lidocaine)	86 ± 5	99 ± 10	94 ± 8	91 ± 9	92 ± 10	89 ± 8	88 ± 10	<0.001
3. Group C. (control)	82 ± 9	95 ± 9	92 ± 11	89 ± 10	91 ± 10	86 ± 10	83 ± 10	<0.001
<b>D. MAP</b>								
1. Group A. (Esmolol)	99 ± 10	100 ± 10	96 ± 8	95 ± 9	97 ± 10	97 ± 9	97 ± 10	<0.001
2. Group B. (Lidocaine)	100 ± 5	114 ± 10	109 ± 6	105 ± 9	106 ± 9	103 ± 8	104 ± 9	<0.001
3. Group C. (control)	970 ± 9	112 ± 11	107 ± 10	104 ± 10	105 ± 9	101 ± 9	99 ± 9	<0.001
<b>E. RPP</b>								
1. Group A. (Esmolol)	11641 ± 1663	11765 ± 2224	11013 ± 1839	10290 ± 2205	9645 ± 1709	9539 ± 1394	9571 ± 1229	<0.001
2. Group B. (Lidocaine)	12731 ± 2160	15891 ± 2482	14115 ± 1677	12840 ± 2025	12204 ± 1576	11744 ± 1948	11642 ± 1877	<0.001
3. Group C. (control)	11751 ± 2269	17577 ± 2974	15908 ± 2610	14632 ± 2930	13943 ± 2649	13233 ± 2370	12425 ± 1941	<0.001
<b>Spo2</b>								
1. Group A. (Esmolol)	100 ± 1	99 ± 1	99 ± 1	99 ± 1	99 ± 1	99 ± 1	99 ± 1	<0.001
2. Group B. (Lidocaine)	100 ± 1	99 ± 1	99 ± 1	99 ± 1	99 ± 1	99 ± 1	99 ± 1	<0.001
3. Group C. (control)	100 ± 1	99 ± 1	99 ± 1	99 ± 1	99 ± 1	99 ± 1	99 ± 1	<0.001

Data are presented as means standard deviation. SBP = Systolic Blood Pressure, DBP = Diastolic Blood Pressure, MAP = Mean Arterial Pressure, RPP = Rate Pressure Product. ( $p < 0.05$  is significant)



## Discussion

So, far we have come to know that direct laryngoscopy and intubation evokes stress response in all individuals, and various study have come up to establish one maneuver or one drug over the other for prevention of this response. King et al. described the hemodynamic stress response due to laryngoscope and intubation more than 60 years ago.<sup>23</sup> Orotracheal intubation consists of two phases: Direct Laryngoscopy and passing of endotracheal tube through the vocal cords and trachea.<sup>24</sup> It has been seen in various studies that increase in HR occurs during endotracheal intubation whereas the greatest increase in BP occurs during laryngoscopy.<sup>25</sup> Both sympathetic and parasympathetic element has been found as a mechanism to this intubation response. The sympathetic response is a polysynaptic pathway due to glossopharyngeal and vagus nerve forming the afferent arc to the sympathetic nervous system through the brain stem and spinal cord causing increased firing of the cardio-accelerator fibers and release of adrenergic mediators including norepinephrine, epinephrine, and vasopressin. The net effect of this autonomic surge is an increased BP, HR, pulmonary artery wedge pressure, and decreased ejection fraction. On the other hand, the parasympathetic reflex is monosynaptic, more common in children but can occur in some adults. The reflex is mediated by the increased vagal tone at the SA node.<sup>26</sup> Lidocaine is the oldest among this list of drugs and esmolol is a relatively new drug. The present study was designed to compare the efficacy of these two drugs in maintaining the prelaryngoscopy and intubation hemodynamic after these most critical events during general anesthesia.

Lidocaine is a sodium channel blocker in the nerve cell membrane and on the myocardial cell membrane. This explains its local anesthetic. Myocardial depressant, Peripheral Vasodilator,<sup>16</sup> and antiarrhythmic action, and is also the proposed mechanism for its role in prevention of adverse effects of the stress response generated upon direct laryngoscope and intubation<sup>17-19</sup>.

Beta-blockers are generally less effective in hypertensive as a result of the tendency toward a low-renin state and with increased peripheral resistance. Higher doses of beta-blockers are therefore, required to achieve target blood pressures.<sup>10</sup> Esmolol is an ultra short acting  $\beta_1$ -blocker, its possesses several properties which make it a valuable agent to obtund the cardiovascular

response by prevent the hemodynamic change. Firstly, it is a cardio selective agent, and secondly it has ultra short duration of action (9 min)<sup>11</sup> and finally, significant drug interaction with commonly used anesthetics has not been reported.<sup>12</sup> Korpinen *et al.* (1998) reported that the administration of esmolol bolus 2 mg kg<sup>-1</sup> IV 2 min before laryngoscopy and intubation suppressed the increase in the heart rate rather than arterial blood pressures.<sup>11</sup> Bostana and Eroglu (2012) reported that IV esmolol in dose of 1 mg kg<sup>-1</sup> before intubation was effective in suppressing the heart rate and arterial blood pressure.<sup>14</sup> Kumar *et al.* (2003) have also claimed optimal results while using higher doses of esmolol in Asian population, i.e., 2 mg kg<sup>-1</sup> without any incidence of unplanned hypotension or bradycardia. However, no consensus has been reached regarding the optimum dose and timing of its delivery.<sup>15</sup> The hemodynamic changes in HR, MAP, and RPP from baseline values 1 min after tracheal intubation, in esmolol group were highly significantly less than those in lidocaine. Our failure to detect any significant effect of lidocaine as compared to esmolol on stress response could be due to the fact that we performed this study in patients without heart disease while Stoelting *et al.* included patients with heart disease and reported a favorable response.<sup>20</sup> Studies have shown that there is increased incidence of myocardial infarction when intraoperative heart rates are more than 110 beats min<sup>-1</sup>.<sup>21</sup> In our study, none of the patients in study groups showed heart rate > 110 beats min<sup>-1</sup>. Heart rate, Systolic blood pressure and Rate Pressure Product (RPP) found fall after intubation.<sup>27</sup> Blood Pressure and Heart rate was found decrease in patients pretreated with intravenous lidocaine prior to induction and overall decreases in cardiovascular complications.<sup>28</sup> RPP is a good estimate of myocardial oxygen requirement. The RPP levels close to 20,000 are normally associated with angina and myocardial ischemia.<sup>22</sup> RPP 1 min after intubation remained less than 20,000 in study drug groups. This finding confirms the cardio-protective effect of study drugs during laryngoscopy and intubation. Rate Pressure Product (RPP) was significantly lower after intubation in esmolol group as compared to lidocaine group with same dose of both intravenous lidocaine and esmolol are 1.5 mg/kg. These results are similar to the finding of our study; we have also found that the maximal difference in percent rise of parameters when esmolol was compared to lidocaine or the control group was in term of SBP and RPP, Table 5-E.<sup>29</sup> Lidocaine and Esmolol, both in the dose of 2 mg/kg intravenous showed that both were efficacious in attenuation of moderate

hemodynamic response to intubation,<sup>30</sup> which are same in our study. Intravenous lidocaine (1.5 mg/kg) and esmolol (2 mg/kg) are effective agents in suppressing the hemodynamic response to laryngoscopy and intubation without any deleterious effect.<sup>31</sup> In conclusion, the present our data suggest that lidocaine 1.5 mg kg<sup>-1</sup> when injected 2 min before intubation can blunt the cardiovascular responses to laryngoscopy and tracheal intubation successfully. However, the prophylactic therapy with esmolol 1 mg kg<sup>-1</sup> when injected 2 min before intubation is significantly more effective than lidocaine in suppressing hemodynamic changes to laryngoscopy and tracheal intubation in normotensive patients. The dosage and timing of administration of drugs are important factors that determine whether they will have beneficial effect on the laryngoscopy and tracheal intubation, therefore further research is necessary to elucidate the effects of different doses of esmolol in black population.

### Conclusion

Intravenous lidocaine (1.5 mg/kg) and esmolol (1 mg/kg) are effective agents in suppressing the hemodynamic response to laryngoscopy and intubation without any deleterious effect. Esmolol 1 mg/kg appears to be very effective and should be viewed as potential treatment strategy for attenuating hemodynamic changes during induction of anesthesia.

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