Original Research Article

Attenuation of cardiovascular responses to laryngoscopy and intubation - A comparative study between IV bolus esmolol and lignocaine

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Abstract

Background: Endotracheal intubation is the translaryngeal placement of endotracheal tube into the trachea, via the nose or mouth. Laryngoscopy, tracheal intubation and subsequent extubation are often associated with an increase in arterial Blood pressure, Heart Rate, arrhythmias and raised Intracranial Pressure and Intra ocular Pressure. General Anaesthesia procedures provokes autonomic response at various stages. The most stressful situations are seen during the period of induction, intubation and extubation. Since 1950's, Hypertension and tachycardia have been recognized as commonly associated with intubation under light anaesthesia. The mechanical stimulation of four areas of upper respiratory tract – the nose, the epipharynx, the laryngopharynx and tracheobronchial tree induces reflex cardiovascular response which is associated with enhanced neuronal activity in cervical sympathetic fibres. Laryngoscopy and tracheal intubation induces cardiovascular stress response characterized by tachycardia and hypertension, which are well tolerated in normotensive individuals but are of greater significance in patients with cardiovascular and cerebrovascular disorders. The quest for an effective suppression of these responses continues. **Materials and Methodology:** A randomized, prospective, double-blind study was conducted in which the efficacy of Lignocaine 1.5 mg/kg and Esmolol 1.5 mg/kg were compared in attenuating the cardiovascular response to laryngoscopy and tracheal intubation in sixty patients undergoing elective surgery under general endotracheal anaesthesia. Patients were divided into two groups receiving Lignocaine or Esmolol Anaesthesia was induced with intravenous Thiopental Sodium 5 mg/kg and intubation was facilitated with Vecuronium 0.12 mg/kg after administering the study drug. Blood pressure and heart rate were compared among the two groups. Statistical Analysis**:** The data was subjected to statistical computation with percentage, mean, standard deviation, Chi-square and Independent test were calculated. **Results:** Systolic, Diastolic and Mean Arterial Pressures increased significantly in lignocaine group whereas it was attenuated more effectively in Esmolol group ($p<0.05$). The increase in HR was significantly lower ($p<0.05$) in esmolol group compared with lignocaine group. **Conclusion:** Esmolol is more effective than lignocaine in attenuating cardiovascular response to laryngoscopy and tracheal intubation.

Keywords: cardiovascular response, Laryngoscopy, IV bolus Esmolol and Lignocaine.

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INTRODUCTION

Endotracheal intubation is the translaryngeal placement of endotracheal tube into the trachea, via the nose or mouth. Laryngoscopy, tracheal intubation and subsequent extubation are often associated with an increase in arterial Blood pressure, Heart Rate, arrhythmias and raised Intracranial Pressure and Intra ocular Pressure. General Anaesthesia procedures provokes autonomic response at various stages. The most stressful situations are seen during the period of induction, intubation and extubation. Since 1950's, Hypertension and tachycardia have been

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recognized as commonly associated with intubation under light anaesthesia [1] The mechanical stimulation of four areas of upper respiratory tract – the nose, the epipharynx, the laryngopharynx and tracheobronchial tree induces reflex cardiovascular response which is associated with enhanced neuronal activity in cervical sympathetic fibres. A 25-50% increase in Mean Arterial Pressure and Heart Rate is seen during induction followed by laryngoscopy and intubation peaking at 1-2 min and returning to baseline within 10-15 min. This response is accompanied by raised plasma adrenaline concentration. These changes are probably of little consequence in healthy patients. But this cardiovascular response to intubation is of a serious concern in patients with hypertension, raised ICP, diseased cerebral vasculature or with ischemic heart disease where increase in myocardial oxygen consumption can lead to Myocardial Infarction [2]. Failure to blunt the responses to intubation may have disastrous consequences like acute Left Ventricular Failure, intracranial haemorrhage and pulmonary edema. Convulsions may be precipitated in eclamptic patients. Herniation of intracranial contents and cerebral ischemia can occur in patients with raised intracranial pressure. Arrhythmias (sinus tachycardia and sinus bradycardia, atrial and ventricular extra systoles and pulsus alternans, less commonly multifocal extra systoles, pulsus bigeminy and atrial fibrillation) are reported. Heart block, ventricular tachycardia and ventricular fibrillation are rare. Till date, the exact mechanism of hemodynamic response to laryngoscopy and intubation is not clear. The principle mechanism behind hypertension and tachycardia is an exaggerated sympathetic action[3,4] due to increased catecholamine release. [5] The raise in the pulse and blood pressure is usually transient, variable and unpredictable. This may not be of much significance in healthy individuals but can be hazardous in those with hypertension, cardiac dysfunction, coronary artery disease or cerebrovascular disease.[5] Laryngoscopic response in such individuals can precipitate myocardial insufficiency, pulmonary edema, arrhythmias, left ventricular failure, and cerebrovascular hemorrage[6], Various pharmacological and non-pharmacological methods have been used to attenuate the hemodynamic response to laryngoscopy and endotracheal intubation.

The non pharmacological methods include:-

1. Smooth and Gentle intubation with a shorter duration of laryngoscopy.
2. Insertion of LMA in place of endotracheal intubation. [8]
3. Blocking glossopharyngeal and superior laryngeal nerves.

Pharmacological methods like inhalational anesthetics,[9] intravenous lidocaine[10,11,12], narcotics,[13,14,15] topical anesthesia, beta blockers,[16,17,18] calcium channel blockers[19,20,21] ACE inhibitors, vasodilators like nitroglycerine and sodium nitroprusside[22] etc were tried by various authors. Lignocaine is an easily available drug used for pressor response, and also has analgesic properties. Esmolol is a beta – selective (cardio selective) adrenergic receptor blocking agent with a short duration of action(ultra short acting). It has predominant action on beta receptors and possess no significant membrane stabilizing activity. It has rapid onset and ultra short acting duration of action (10-15 min)[23], as it is metabolised by plasma esterases. Peak effects with bolus injection of esmolol are seen in one or two minutes[24] Esmolol is being used since many years as a pre- medication agent. Lignocaine given as bolus dose just prior to tracheal intubation [25] or extubation[26] has been effectively used to decrease haemodynamic responses associated with them. In addition, perioperative intravenous (IV) infusion of lignocaine has been used as a method to control post-operative pain. Hence, the primary objective of the present study is to observe whether a regimen of I.V Lignocaine versus I.V Esmolol of pre-operative bolus doses can reduce the hemodynamic changes during tracheal intubation following elective surgeries.

Objective:

To compare the efficacy of Esmolol and Lignocaine in attenuating the hemodynamic responses after direct laryngoscopy and endotracheal intubation.

MATERIALS AND METHODS

After taking the approval from institutional ethics committee, the present study was conducted in a total of 60 patients over a period of 2 years. All the patients were randomized and divided into two groups such that each group consists of 30 patients (n=30) using a 'sealed envelope method':

Group E received intravenous esmolol 1.5mg / kg body weight. Group L received intravenous lignocaine 1.5mg / kg body weight.

Inclusion Criteria: Patients with ASA physical status I and II. Patients of age between 18-65years of either sex. Patients posted for elective surgeries under general anesthesia requiring endotracheal intubation.

Exclusion Criteria: Patients with anticipated difficult intubation. Patients with ASA physical status III and more. Patients with history of Hypertension, Asthma, Chronic obstructive pulmonary disease, Sinus bradycardia, Heart block greater than first degree, Arrhythmias, Overt heart failure, Cardiogenic shock, Pregnant patients, Patients requiring laryngoscopy for duration longer than 15 seconds and with multiple attempts.

All the patients included in the study were admitted to hospital a day or two before surgery and were assessed as per the routine pre-anaesthetic check up protocol. After

taking informed written consent, all patients included were kept nil per oral since midnight day before surgery. After shifting the patient to operating room all the monitors were connected and the base line SBP, DBP, MAP, HR, SpO_2 and ECG were recorded. Subsequently, an 18G intravenous access was secured and Ringers lactate @ 15ml/kg body weight was started. All the patients were premedicated with intravenous glycopyrrolate 5µ/kg body weight, midazolam 0.02mg/kg body weight and fentanyl 2µ/kg body weight were given. Anaesthesia was induced with intravenous Thiopental sodium 5mg/kg body weight given over 30 seconds, effects confirmed by loss of eyelash reflexes. Then manual ventilation was checked and if adequate, intravenous vecuronium bromide 0.12mg/kg was given for muscle relaxation. The patients were then ventilated by mask with 100% oxygen.

After 2minutes of giving vecuronium vital parameters were once again recorded just before administering the study drug. After recording the vital parameters the study drug was administered:

1. Group E received intravenous Esmolol 1.5mg/kg as a bolus diluted to a total volume of 10ml with normal saline.
2. Group L received intravenous Lignocaine 1.5mg/kg as a bolus diluted to a total volume of 10ml with normal saline.

The study drugs were prepared and administered by the anaesthesia assistant who was not involved in the study. The observer was unaware of the drugs administered.

Exactly three minutes after the administration of the study drug, direct laryngoscopy was attempted and trachea was then intubated with cuffed endotracheal tube. The same anesthesiologist performed all the intubations.

After intubation patients were maintained with sevoflurane (1%) + N_2O (50%) + O_2 (50%) and controlled mechanical ventilation. Non-depolarizing muscle relaxant vecuronium bromide 0.02mg/kg body weight was given intermittently.

The immediate time after endotracheal intubation was considered as '0' minute./ Systolic blood pressure (SBP), diastolic blood pressure (DBP), mean arterial blood pressure (MAP) and heart rate (HR) were recorded at 0min, 1min, 3min and 5min time intervals after the endotracheal intubation. Surgical incision was allowed only after 5min of endotracheal intubation. The raise in blood pressure or heart rate by more than 20% of base line value was considered significant. The heart rate below 50 bpm was treated with intravenous gylcopyrrolate 0.2mg and fall in systolic blood pressure 20% below the base line was treated with intravenous mephentermine 6mg bolus. If the blood pressure and heart rate was >20% of the baseline value sevoflurane was increased to 2% or 2.5% till the blood pressure was controlled. At the end of the surgical procedure, the residual neuromuscular blockade was antagonized with intravenous neostigmine 0.05mg/kg and glycopyrrolate 10µ/kg and extubation was performed after fulfilling the criteria for routine 'awake extubation'. Patients were observed for few minutes in the operating room and then shifted to post anesthesia care unit where they were monitored for the next 24 hours.

Statistical Analysis: Data were entered in MS-Excel and analyzed in SPSS V21. Descriptive statistics were represented with percentages, Mean with SD. Shapiro wilk test was applied to find normality. Chi-square test, Independent t-test were calculated. $P<0.05$ was considered as statistically significant.

OBSERVATIONS AND RESULTS

In group E, the mean of age is 41.17 and SD is 12.77. In group L, the mean of age is 41.33 and SD is 12.64.

In group E, the mean of weight is 65.77 and SD is 14.18. In group L, the mean of weight is 60.07 and SD is 9.22. Both the groups were comparable in terms of age and weight but was not statistically significant.

The total number of female patients in group E and group L were 12(40%) and 19(63%) respectively.

The total number of male patients in group E and group L were 18(60%) and 11(36%) respectively.

Both the groups were comparable in terms of gender, but was not statistically significant.

Table 1: Depicts the changes in mean and SD of SBP at different time intervals in group E and group L.

Time	N	ESMOLOL		LIGNOCAINE		t value	*P value*
		Mean	SD	Mean	SD		
Base line	30	124.37	8.03	126.50	10.46	0.88	0.38
Pre-intubation	30	106.80	9.84	113.97	11.07	2.65	**0.01**
After intubation 0 min	30	119.30	12.28	114.03	10.54	1.78	**0.07**
1 min	30	119.53	7.92	141.07	8.26	10.3	**0.0001**
3 min	30	116.43	8.29	138.00	8.6	9.88	**0.0001**
5 min	30	111.63	7.83	132.57	6.67	10.19	**0.0001**

From table-1: The change in mean and SD of SBP at baseline and immediately after intubation at 0 min were not statistically significant. The change in mean and SD of SBP before intubation or before the administration of the study drug is statistically significant ($p<0.05$) between the two groups. The change in mean and SD of SBP after intubation at

1min, 3min and 5min is statistically significant between the two groups. During the study it was observed that the SBP decreases from baseline values before the study drug administration in both the groups. But SBP increases to the highest degree at 1min (>20% from the baseline) after intubation in group L. The SBP remained above the baseline till 5 min after intubation in group L. The SBP increases to the highest value at 1 min after intubation but being less than the baseline value. The SBP remained below the baseline till 5min after intubation in group E.

Table 2: Depicts the changes in mean diastolic blood pressure at different time intervals between group E and group L.

Time	N	ESMOLOL		LIGNOCAINE		t value	*P value*
		Mean	SD	Mean	SD		
Base line	30	79.67	7.74	78.57	7.29	0.56	0.57
Pre-intubation	30	69.73	9.73	79.03	7.82	4.08	**0.0001**
After intubation 0min	30	76.17	8.95	78.40	8.04	1.01	0.31
1 min	30	73.23	7.91	88.37	4.66	9.03	**0.0001**
3 min	30	76.27	10.64	86.00	6.17	4.33	**0.0001**
5 min	30	72.73	8.67	82.00	5.93	4.38	**0.0001**

The change in mean and SD of DBP at baseline and immediately after intubation at 0min were not statistically significant. The change in mean and SD of DBP before intubation or before the administration of the study drug is statistically significant ($p<0.05$) between the two groups. The change in the mean and SD of DBP after intubation at 1min, 3min and 5min is statistically highly significant between the two groups ($p<0.05$). During the study it was observed that in group E the DBP decreases from baseline values before the study drug administration, but there was an increase in DBP to the highest degree immediately after intubation at 0 and 3min, the increase being below the baseline values. In group L, it was observed that the DBP was near the baseline value before and after intubation at 0min, but the highest degree being at 1min and the increase in DBP remained above the baseline values till 5min after intubation in group L.

Table 3: Depicts the changes in mean arterial blood pressure at different time intervals between group E and group L.

Time	N	ESMOLOL		LIGNOCAINE		t value	*P value*
		Mean	SD	Mean	SD		
Base line	30	94.50	6.73	94.30	6.69	0.11	0.90
Pre-intubation	30	82.07	9.31	90.67	6.32	4.18	**0.0001**
After intubation 0min	30	90.43	8.14	90.37	6.71	0.03	0.97
1 min	30	88.60	6.11	106.03	5.26	11.84	**0.0001**
3 min	30	89.63	8.56	103.37	6.55	6.98	**0.0001**
5 min	30	85.73	7.63	98.80	5.23	7.73	**0.0001**

From table-3: The mean and SD of mean arterial blood pressure at baseline and after intubation at 0 min compared between group E and L is not statistically significant. The mean and SD of mean arterial blood pressure before intubation or before the administration of the study drug is statistically highly significant ($p<0.05$). The mean and SD of mean arterial blood pressure after intubation at 1min, 3min and 5min after intubation is statistically significant ($p<0.005$). During the study it was observed that there was a decrease in MAP from baseline values in both the groups before the study drug was administered. In group E the MAP increased with a highest degree at 0 min after intubation, but the increase being less than the baseline value and it remained decreased even at 5 mins after intubation. In group L, MAP increased above the baseline value with a highest degree observed at 1 min after intubation and decreased gradually but it remained above the baseline at 5 mins after intubation.

Table 4: Depicts the comparision of changes in mean heart rate at different time intervals between group E and group L.

Time	N	ESMOLOL		LIGNOCAINE		t value	*P value*
		Mean	SD	Mean	SD		
Base line	30	85.27	8.61	86.90	7.85	0.76	0.44
Pre-intubation	30	80.01	9.22	80.97	8.01	0.39	0.6900
After intubation 0min	30	84.23	9.07	82.93	6.88	0.62	0.53
1 min	30	81.93	8.96	104.00	10.67	8.67	**0.0001**
3 min	30	79.27	8.04	100.60	11.74	8.21	**0.0001**
5 min	30	77.73	9.65	97.57	11.88	6.38	**0.0001**

From table-4: The change in mean and SD of heart rate between group E and group L at base line, before the study drug administration and at 0 mins after intubation is not statistically significant. The change in mean heart rate compared between group E and group L after intubation at 1min, 3min and 5min is statistically highly significant ($p<0.05$). During the study the change in mean HR was observed to be decreased before the study drug administration in both the groups. In

group E the mean HR remained below the baseline value even at 5min after intubation. In group L the mean HR increased >20% from the baseline value at 1 and 3 mins after intubation and remained increased even at 5 mins after intubation.

DISCUSSION

From the present study, observed a slight increase in SBP, DBP, and MAP before study drug administration or pre intubation. The change in SBP, DBP, and MAP was slightly increased in both the groups after 1min, 3min, 5min above the baseline. This might be due to intubation response. Among the two groups E and L the increase was attenuated significantly in esmolol than lignocaine. 5min after intubation HR, SBP, DBP and MAP returned to almost baseline value in esmolol group. These findings are in agreement with that of UGUR B , OGURULU M , *et al.*[27] who showed attenuated hemodynamic response due to sympathetic stimulation associated with endotracheal intubation. Stanley Tam, Frances Chung, Michael Campbell [28] made a study for determining optimal time of injection of IV lignocaine for the attenuation of circulatory responses secondary to endotracheal intubation. Four groups received lignocaine 1.5 mg/kg IV single bolus over a period of less than 5 seconds 1, 2, 3 and 5min before intubation. Fifth group served as the control and received no IV lignocaine. They observed that cardiovascular responses were significantly above base line levels in patients given lignocaine 1min group ($p < 0.05$), 2min group ($p < 0.05$), and 5min group($p < 0.05$) before intubation or in controls ($p < 0.05$) compared to IV lignocaine 3min before intubation group. In our study Plain preservative free Lignocaine 2%, 1.5 mg/kg IV bolus was given 3minutes prior to direct laryngoscopy. The results were in accordance to 1min, 3min and 5min group of Stanley Tam *et al.* study i.e, cardiovascular responses were significantly above baseline levels. Aleem *et al.* [29] compared the effects of lignocaine and fentanyl in attenuation of pressor response to laryngoscopy and tracheal intubation. After endotracheal intubation incidence of tachycardia (HR>100/min) was significantly greater in lignocaine group than in fentanyl group ($p<0.05$). Rise in SBP and DBP were also statistically significant in lignocaine group than in fentanyl group ($p<0.05$). Attenuation of pressor response is seen both with lignocaine and fentanyl. Of the two drugs fentanyl 4 microgram/kg IV bolus provides a consistent, reliable and effective attenuation as compared to lignocaine 1.5 mg/kg IV bolus. In our study Plain preservative free Lignocaine 2%, 1.5 mg/kg IV bolus was given 3min prior to direct laryngoscopy.The results were similar to that of the study conducted by Aleem *et al.* Abou - Modi, Keszer and Yacoub[30] *et al.* who had used intravenous lignocaine in 1.5mg / kg and 0.7 mg/kg doses and found that intravenous lignocaine in 1.5mg/kg dose provided complete protection against arrhythmias, but only a borderline protection against increase in blood pressure and heart rate, while the dose 0.7mg/kg was inadequate in providing protection against arrhythmias, only preventing blood pressure elevation. They have described the possible mechanisms of action of lignocaine as – direct myocardial depressant effect, peripheral vasodilating effect and effect of synaptic transmission. Robert Stoelting[31] found that lignocaine in 1.5mg/kg intravenously can attenuate the pressor response effectively in a study conducted on 36 known heart disease patients scheduled for non – cardiac major surgeries. D.G. Clayton *et al.*[32] studied effects of pre - treatment with intravenous lignocaine 1.5mg/kg given 1min prior to induction of anaesthesia. It was shown to reduce significantly, the incidence of dysrhythmias during dental anaesthesia and also to reduce the rise in blood pressure associated with endotracheal intubation. Gupta *et al.*[33] compared effectiveness of intravenous esmolol and lignocaine in suppressing the cardiovascular stress response. Patients were divided into three groups of 20patients each. Group - L received lignocaine and Group – E received esmolol three minutes before intubation, Group-C did not receive any drug under study. It was found that patients given esmolol had better attenuation of stress response to laryngoscopy and intubation than patients given lignocaine. Our results were similar to that of above study.

Nooraei *et al.*[34] compared the effects of intravenous administration of lignocaine and magnesium sulphate on unwanted hemodynamic responses following laryngoscopy and intubation in elective surgery candidates. This randomized doubleblind clinical trial concluded that Magnesium sulphate is more effective than lignocaine in controlling hemodynamics, although it may increase the heart rate. The results of our study were similar to that of above study. Esmolol, a water - soluble, cardioselective, and ultrashort – acting ß - adrenergic antagonist, has also been shown to be effective in controlling both the HR and BP responses to intubation, but only in patients undergoing elective surgery studied by Helfman SM[35] Kindler CH *et al.*[36] Kampine JP *et al.*[37] Parnass SM *et al.*[38] found in patients undergoing general anesthesia for elective surgery, that esmolol (loading dose of 500 µg/kg/min for 4 minutes, followed by a maintenance infusion of 300 µg/kg/min for 11minutes) significantly attenuated the maximum increases in HR and BP when compared with placebo. Another study found that a single bolus dose of 100 or 200 mg was able to attenuate the hypertensive and tachycardic responses to laryngoscopy and intubation (Parnass *et al.* Bostana and Eroglu reported that IV esmolol in dose of 1mg/kg before intubation was effective in suppressing the HR and arterial BP[39] which are similar to the present study. Kindler *et al.*[40]

found that esmolol administration before laryngoscopy was sufficient to control HR after intubation, but it did not affect systolic arterial pressure (SAP) .In this study, esmolol 2 mg/kg was found to be quite effective in attenuating the hypertensive response (MAP) as well as the HR during laryngoscopy and tracheal intubation till 5 min. In this present study the change in mean and SD of HR, SBP, DBP, MAP during 1min, 3min and 5 min is statistically highly significant between the two groups ($p<0.05$). S. Sharma, *et al.*[41] obtained similar result by comparing the ability of different bolus doses of esmolol to blunt the haemodynamic effects of laryngoscopy and tracheal intubation in treated hypertensive patients. Esmolol 100 mg given as bolus, is effective as well as safe in blunting the haemodynamic responses to laryngoscopy and tracheal intubation in treated hypertensive patient. Similar results were obtained by Bensky KP, *et al.*[42] This study shows that small doses of esmolol may block the increase in heart rate and blood pressure resulting from laryngoscopy and intubation. Recently, anesthesia research has began to compare the efficacies of several drugs against each other, rather than relying on studies that isolate a single drug's effect vs a placebo intervention. The ability of esmolol vs lidocaine to attenuate the hemodynamic response to intubation was first studied by Helfman *et al.* in 1990. The present study compared the efficacy of IV esmolol, and IV lignocaine in determining which is best in preventing tachycardia and hypertension secondary to endotracheal intubation. The result obtained from this study found that both I.V esmolol and I.V lignocaine are effective in controlling SBP, DBP, HR, and MAP. Esmolol is more effective than I.V lignocaine in attenuating both SBP and DBP. Esmolol, at an intravenous bolus dose of 1.5mg/kg, "provided consistent and reliable protection against increases in both HR and BP accompanying laryngoscopy and Intubation. The Observations are also in close agreement with other studies who used this drug to achieve attenuation of pressor respose to direct laryngoscopy and endotracheal intubation.

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