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Original Research Article

# Attenuation of Stress Response during Laryngoscopy and Endotracheal Intubation using Esmolol and Fentanyl - A Comparative Study

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**Abstract**

**Background:** Laryngoscopy and endotracheal intubation are noxious stimuli, that can evoke detrimental hemodynamic consequences in patients with coronary artery and cerebrovascular disease. Hence there is a need to suppress these hemodynamic effects. Various group of drugs are administered prior to laryngoscopy for suppression of these hemodynamic effects. Esmolol, Fentanyl, Clonidine and Lignocaine are commonly used in anaesthetic practise for stress response attenuation prior to laryngoscopy. In our study we compared the efficacy of Esmolol and Fentanyl in attenuating various hemodynamic variables during laryngoscopy, intubation and in the immediate post intubation phase.

**Methods:** A prospective randomized comparative observational study was conducted in 100 patients belonging to ASA I and II categories during the study period from December 2018 to June 2020.They were divided into two groups containing fifty subjects each, after satisfying the inclusion and exclusion criteria and randomization. After obtaining informed consent, each group received either of the study drug 3 minutes prior to laryngoscopy, followed by induction with IV Propofol and neuromuscular blockade with IV Vecuronium. Hemodynamic variables like HR, SBP, DBP and MAP were recorded at fixed time intervals and data sheet prepared in MS excel format. Any adverse events which occurred during the study were also recorded. A p-value of less than 0.05 was considered as statistically significant.

**Results:** Both groups were comparable in terms of demographic variables, ASA class and Mallampati grades.

Tachycardia was lower in Esmolol group. Systolic BP, Diastolic BP and Mean Arterial Pressure were increased in both groups after laryngoscopy and intubation and at different time intervals. There was no significant difference in mean Systolic BP & Diastolic BP between 2 groups. There was significant difference in Rate Pressure Product between 2 groups, after drug administration to 10 minutes after intubation, with Esmolol group having lower mean Rate Pressure Product compared to Fentanyl group. There was no ST- T segment changes in both the groups.

**Conclusions:** Esmolol was found to be a better drug in attenuating the stress response to laryngoscopy and intubation in terms of Heart rate. The blunted effect of Esmolol to laryngoscopy and intubation stress response may be due to the time lag between bolus dose and timing of intubation which requires more studies for confirmation.

**Keywords:** Laryngoscopy, intubation, attenuation, cardiovascular response, Fentanyl, Esmolol.



## Introduction

Laryngoscopy and endotracheal intubation are important steps in the process of securing a patient's airway. During this process, the oropharyngeal and laryngeal structures, which are richly supplied by sympathetic nerves get stimulated, producing sympathoadrenal responses in the form of tachycardia, hypertension and dysrhythmias [1]. The extent of hemodynamic response to direct laryngoscopy by Macintosh laryngoscope and endotracheal intubation depends upon factors such as distortion of the airway or the type and duration of physical stimulus to the oropharyngeal structures [2].

Laryngoscopy and endotracheal intubation come in the category of noxious stimuli which evokes tachycardia and hypertension. Patients can go for myocardial ischemia, infarction and cerebrovascular accidents during intubation and in the immediate post intubation phase. About half of the patients with coronary artery disease experience episodes of myocardial ischemia during intubation when no specific prevention is undertaken [3]. Perioperative myocardial infarction is a leading cause of postoperative morbidity and mortality due to hypertension and tachycardia [4].

To prevent the adverse hemodynamic consequences during laryngoscopy and intubation it is important to attenuate the sympathoadrenal stress responses during this period. In contrast to topical anaesthesia which appears to provide inconsistent benefits, nerve blocks prevent hemodynamic responses to intubation [5].

Intravenous pharmacological agents are easy to administer and can also be used in any emergency scenario and a wide range of drugs belonging to different classes are available for routine use. Studies have been conducted with various drugs like Lignocaine, Fentanyl, Beta blockers, Calcium channel blockers, sympatholytics like Clonidine, Dexmedetomidine, Volatile anaesthetics and vasodilators. But none of them proved to be ideal to attenuate these responses [2].

This study is designed to evaluate the attenuation of hemodynamic response to laryngoscopy and endotracheal intubation with available cost-effective intravenous drugs like Esmolol and Fentanyl.

Esmolol is a striking option among the various Beta blockers, because of its cardio-selectivity and ultra-short duration of action, but it can be administered only intravenously. Esmolol at doses of 100-200mg suppressed the hemodynamic response to intubation, particularly when combined with a moderate dose of opioid [6].

### Intubation in the Presence of Cardiovascular Diseases [7]

Myocardial ischemia results when there is an imbalance between myocardial O2 supply and demand. In the presence of a stable O2 content of whole blood (the product of hemoglobin concentration and saturation, with a minor contribution from dissolved O2), the myocardial O2 supply is almost entirely determined by coronary blood flow and distribution, because O2 extraction at the cellular level is at or near maximum even under resting conditions.

This set of circumstances is responsible for episodes of ischemic electrocardiographic ST segment depression and increased pulmonary artery diastolic blood pressure

that may be seen when intubation is performed in patients with arteriosclerosis.

Patients with aneurysmal disease of the cerebral and aortic circulation may also be at particular risk of complications related to a sudden increase in BP during airway instrumentation. Laplace's law defines the transmural wall tension of a blood vessel as the product of the pressure inside the vessel and its radius divided by the wall thickness. The presence of a thin-walled vascular aneurysm (higher transmural wall tension at baseline) combined with a sudden increase in intraluminal pressure can lead to rupture of the affected vessel and abrupt deterioration in the patient's status.

## Objectives

1. To compare the efficacy of Fentanyl and Esmolol in attenuating the cardiovascular response during endotracheal intubation.
2. To compare the ST-T changes produced by the two drugs.

## Study Method and Procedure

After getting approval from Institutional Research Committee and Ethics Committee, the study population were randomly allocated into one of the two groups (Group 1 and 2), with each group having 50 subjects each, by picking lots as a means of simple randomization.

## Methodology

### Study Design

This study conducted was a prospective observational study.

### Study Population

American Society of Anesthesiologist (ASA) physical status I and II patients of either sex, aged 30-60 years, who consented for elective non-cardiac surgery under General anesthesia (GA) requiring endotracheal (ET) intubation were studied.

### Study Setting and Duration

Study was conducted in the Department of Anesthesiology, Government T.D Medical College, Alappuzha during the period of 18 months after obtaining clearance from Institutional Research Committee and Ethical Committee.

### Sample Size

As per the study by Gupta et al, mean Heart rate at 1 min after intubation was found to be 88 in Esmolol group and 92 in Fentanyl group. Using this, sample size calculated using the formula,

$$n = \frac{(Z_a + Z_{1-B})^2 * [SD_1^2 + SD_2^2],}{(m1-m2)2}$$

where SD= standard deviation and m= mean

Where $Za_{=}$ 2.56 for 1% significance level & $Z_{1-B}$= 1.28 for 90% power

SD1=5.28 and SD2=3.95

By substituting variables, n= 50 per group

### Inclusion Criteria

- American Society of Anaesthesiologist (ASA) I & II patients of either sex who consented for the study.
- Age between 30-60y
- Elective non cardiac surgery

### Exclusion Criteria

- Anticipated difficult airway
- Hypertension, cardiovascular, neurological or renal impairment
- Heart rate<60 per min & systolic BP<100
- Heart block
- History of Drug allergy
- Pregnant & lactating women
- Patients on beta blockers.

### Preanesthetic Preparation

All patients underwent a pre-anesthetic evaluation with proper history-taking and physical examination of all the systems

and airway. Pre-operative routine investigations such as hemoglobin, platelet count, total and differential count, Serum electrolytes, Renal function tests, Random blood sugar, blood grouping and Rh typing, chest radiography and electrocardiogram were done. Patients were advised to fast for 8 hours before surgery. Tablet Alprazolam 0.25mg was given the night before surgery to allay anxiety.

**Anesthetic Technique**

Patient identification was done following which a short preoperative history was taken. Then, clinical examinations and routine investigations were rechecked in all patients. Study objective and procedure was explained, and informed written consent was taken from each patient. Patients who received one of the two drugs either Esmolol or Fentanyl were observed and were included into two groups.

Intravenous access was secured, and Ringer Lactate infusion started. All the patients were uniformly premedicated with intravenous Ondansetron 0.08 mg/kg, and intravenous Midazolam 0.02mg/kg, 10 min before induction. Then, the patient was shifted to the operating room after which routine non-invasive monitors pulse oximetry, Elecrocardiography and Non-invasive BP were attached, and vital signs monitored. Patients were preoxygenated for 3 minutes with 100% oxygen. Drugs were loaded in 10ml syringes by a Senior Resident and administered by a qualified Anaesthesiologist. Patients who received Fentanyl (2microgram/kg) were observed as Group 1 and patients who received Esmolol (1 mg/kg) were observed as Group 2. Hemodynamic changes associated were observed and recorded by the investigator who was blinded to the drug.

Patients received either Esmolol (1mg/kg) iv or Fentanyl (2 microgram/kg) iv, which was administered by a qualified Anaesthesiologist 3 minutes prior to intubation and then induced with 2 mg/kg propofol intravenously in incremental doses. After checking the adequacy of mask ventilation, Inj Succinylcholine 1.5mg/kg was given. Patient was ventilated with oxygen using IPPV with a fresh gas flow of 6 L/minute until intubation. Laryngoscopy and endotracheal intubation was done with Macintosh curved blade. The trachea was intubated with appropriate size cuffed endotracheal tube. Laryngoscopy and intubation were limited to 20 seconds, failure to intubate within this period was excluded from this study. After confirmation of the endotracheal tube placement, anesthesia was maintained with 66 % N20 & 33% Oxygen and Isoflurane 0.4%. Inj. Vecuronium 0.1 mg/kg was given as muscle relaxant.

Heart rate, systolic blood pressure, diastolic blood pressure, mean arterial pressure changes were recorded before induction(baseline), after study drug administration, after induction, after tracheal intubation & at 1, 3, 5 and 10 minutes after intubation using multiparameter monitor. Continuous ECG monitoring was done to detect any associated ST-T changes. No surgical intervention was allowed throughout the study period of 10 min. Intravenous Paracetamol infusion was given for analgesia in both groups.

The hemodynamic alterations like fall in Mean arterial pressure to an extent greater than 20% below the baseline value or Systolic blood pressure less than 90 mm of Hg was treated primarily by increasing the IV fluid infusion rate and then lowering Isoflurane concentration or incremental doses of Mephenteramine 6 mg bolus IV. Decrease in heart rate (<50 beats/min) was treated with Atropine 0.6 mg IV and such patients were excluded from study.

Anaesthesia was maintained using Nitrous oxide, Oxygen, Isoflurane and Vecuronium at intervals. Patients were

extubated after adequate recovery. In recovery room they were monitored for complications such as pain, respiratory depression, hypertension, hypotension, bradycardia, drowsiness, nausea or vomiting.

**Methods of Data Collection**

Data collected from patients and were entered in excel sheet. The study variables included:

- Heart rate
- Systolic BP
- Diastolic BP
- Mean arterial pressure
- Rate pressure product
- ST- T changes

**Statistical Analysis:**

Data was entered into Microsoft excel data sheet and was analyzed using SPSS 22 version software. Categorical data was represented in the form of Frequencies and proportions. Chi-square test was used as test of significance for qualitative data.

Continuous data was represented as mean and standard deviation. Independent t test was used as test of significance to identify the mean difference between two quantitative variables.

**Graphical representation of data:** MS Excel and MS word were used to obtain various types of graphs such as bar diagram.

**p value** (Probability that the result is true) of <0.05 was considered as statistically significant after assuming all the rules of statistical tests.

**Statistical software:** MS Excel**,** SPSS version 22 **(**IBM SPSS Statistics, Somers NY, USA) was used to analyze data.

**Results**

**Table 1: Age Distribution between two groups**

| | | Group | | | |
|---|---|---|---|---|---|
| | | Fentanyl | | Esmolol | |
| | | Number | % | Number | % |
| Age Group | <= 30 years | 4 | 8.00% | 4 | 8.00% |
| | 31 - 40 years | 14 | 28.00% | 17 | 34.00% |
| | 41 - 50 years | 20 | 40.00% | 13 | 26.00% |
| | > 50 years | 12 | 24.00% | 16 | 32.00% |

$\chi 2 = 2.347$, df = 3, p = 0.504

In Fentanyl, 8% were <= 30 years, 28% were in 31 – 40 years, 40% were 41 – 50 years and 24% were >50 years.

In Esmolol, 8% were <= 30 years, 34% were in 31 – 40 years, 26% were 41 – 50 years and 32% were >50 years.

There was no significant difference in age distribution between two groups.

**Table 2: Mean Age Comparison between two groups**

| | Group | | | | p value |
|---|---|---|---|---|---|
| | Fentanyl | | Esmolol | | |
| | Mean | SD | Mean | SD | |
| Age | 44.44 | 9.64 | 43.86 | 10.25 | 0.771 |

Mean age in Fentanyl Group was 44.44 ± 9.64 years and in Esmolol Group was 43.86 ± 10.25. There was no significant difference in the mean age comparison between two groups.

**Table 3: Gender Distribution between two groups**

| | **Group** | | | |
|---|---|---|---|---|
| | **Fentanyl** | | **Esmolol** | |
| Gender | **Count** | **%** | **Count** | **%** |
| Female | 31 | 62.00% | 28 | 56.00% |
| Male | 19 | 38.00% | 22 | 44.00% |

$\chi 2 = 0.372$, df = 1, p = 0.542

In Fentanyl Group, 62% were female and 38% were male.

In Esmolol Group, 56% were female and 44% were male. There was no significant difference in gender distribution between two groups

**Table 4: ASA Distribution between two groups**

| | **Group** | **Fentanyl** | | **Esmolol** | |
|---|---|---|---|---|---|
| | | **Number** | **%** | **Number** | **%** |
| ASA | 1 | 36 | 72.00% | 33 | 66.00% |
| | 2 | 14 | 28.00% | 17 | 34.00% |

$\chi 2 = 0.421$, df = 1, p = 0.517

In Fentanyl Group, 72% were ASA 1 and 28% were ASA 2.

In Esmolol Group, 66% were ASA 1 and 34% were ASA 2. There was no significant difference in ASA distribution between two groups.

**Table 5: Mallampati distribution between two groups**

| | **Group** | **Fentanyl** | | **Esmolol** | |
|---|---|---|---|---|---|
| | | **Count** | **%** | **Count** | **%** |
| MP | 1 | 38 | 76.00% | 30 | 60.00% |
| | 2 | 12 | 24.00% | 20 | 40.00% |

$\chi 2 = 2.941$, df = 1, p = 0.086

In Fentanyl Group, 76% were Mallampati 1 and 24% were Mallampati 2.

In Esmolol Group, 60% were Mallampati 1 and 40% were Mallampati 2.

There was no statistically significant difference in Mallampati distribution between two groups.

**Table 6: Mean Heart Rate Comparison between two groups at different intervals of time**

| | **Group** | | | | **p value** |
|---|---|---|---|---|---|
| | **Fentanyl** | | **Esmolol** | | |
| | **Mean** | **SD** | **Mean** | **SD** | |

| | | | | | |
|---|---|---|---|---|---|
| Baseline | 79 | 3.71 | 79.88 | 7.08 | 0.438 |
| After Study Drug Administration | 73.24 | 3.89 | 76.16 | 6.61 | 0.008* |
| Induction | 72.92 | 6.1 | 73.12 | 7.09 | 0.88 |
| Laryngoscopy & Intubation | 90.72 | 3.91 | 82.74 | 4.65 | < 0.001* |
| 1 Min | 87.66 | 4.63 | 80.08 | 4.7 | < 0.001* |
| 3 Min | 84.5 | 4.99 | 76.94 | 5.03 | < 0.001* |
| 5 Min | 81.94 | 5 | 74.38 | 5.51 | < 0.001* |
| 10 Min | 80.8 | 5.78 | 72.5 | 5.35 | < 0.001* |

In the study there was no significant difference in mean HR at baseline between two groups.

There was statistically significant difference in mean heart rate immediately after study drug administration with mean heart rate lower in Fentanyl group immediately after study drug administration. But later heart rate was lower in Esmolol group compared to Fentanyl group upto after 10 minutes after intubation.

**Table 7: Mean Systolic BP Comparison between two groups at different intervals of time**

| | **Group** | | | | **p value** |
|---|---|---|---|---|---|
| | **Fentanyl** | | **Esmolol** | | |
| | **Mean** | **SD** | **Mean** | **SD** | |
| Baseline | 123.68 | 9.03 | 122.42 | 9.29 | 0.493 |
| After Study Drug Administration | 115.08 | 10.04 | 117.32 | 9.16 | 0.247 |
| Induction | 114.16 | 10.01 | 116.2 | 10.59 | 0.325 |
| Laryngoscopy & Intubation | 143.14 | 8.3 | 139.96 | 14.45 | 0.180 |
| 1 Min | 140.5 | 9.5 | 142.4 | 16.34 | 0.479 |
| 3 Min | 135.96 | 8.89 | 137.38 | 14.91 | 0.564 |
| 5 Min | 130.48 | 8.59 | 132.1 | 15.5 | 0.520 |
| 10 Min | 126.3 | 8.89 | 128.36 | 14.61 | 0.396 |

In the study there was no significant difference in mean SBP between two groups from baseline to 10 min after drug administration.

**Table 8: Mean Diastolic BP Comparison between two groups at different intervals of time**

| | **Group** | | | | **p value** |
|---|---|---|---|---|---|
| | **Fentanyl** | | **Esmolol** | | |
| | **Mean** | **SD** | **Mean** | **SD** | |
| Baseline | 76.08 | 7.65 | 76.5 | 8.16 | 0.791 |
| After Study Drug Administration | 73.04 | 6.88 | 73.7 | 8.15 | 0.663 |
| Induction | 71.98 | 8.06 | 72.42 | 8.02 | 0.785 |
| Laryngoscopy & Intubation | 90.12 | 6.36 | 85.68 | 9 | 0.005* |

| | | | | | |
|---|---|---|---|---|---|
| 1 Min | 88.4 | 7.25 | 87.74 | 10.44 | 0.714 |
| 3 Min | 85.06 | 6.73 | 85.14 | 9.88 | 0.962 |
| 5 Min | 80.74 | 7.3 | 81.04 | 9.22 | 0.857 |
| 10 Min | 78.24 | 7.28 | 78.12 | 9.29 | 0.943 |

In the study there was no statistically significant difference in mean DBP between two groups from baseline to 10 min after drug, except at Laryngoscopy &

Intubation, where in mean DBP was lower in Esmolol group compared to Fentanyl group and it was statistically significant.

**Table 9: Mean MAP Comparison between two groups at different intervals of time**

| | **Group** | | | | **p value** |
|---|---|---|---|---|---|
| | **Fentanyl** | | **Esmolol** | | |
| | **Mean** | **SD** | **Mean** | **SD** | |
| Baseline | 91.94 | 6.81 | 91.9 | 7.99 | 0.979 |
| After Study Drug Administration | 86.98 | 6.47 | 88.22 | 8.17 | 0.402 |
| Induction | 86.04 | 6.28 | 86.8 | 8.05 | 0.600 |
| Laryngoscopy & Intubation | 107 | 5.25 | 99.36 | 9.35 | < 0.001* |
| 1 Min | 105.4 | 6.64 | 98.56 | 9.61 | < 0.001* |
| 3 Min | 101.06 | 4.95 | 98.3 | 9.32 | 0.067 |
| 5 Min | 96.7 | 5.78 | 92.08 | 7.83 | 0.001* |
| 10 Min | 93.68 | 6.04 | 89.4 | 9.31 | 0.008* |

In the study there was statistically significant difference in mean MAP between two groups at Laryngoscopy & Intubation, 1 min, 5 min and 10 min. At these intervals, mean MAP was lower in Esmolol group compared to Fentanyl group.

**Table 10: Mean Rate Pressure Product Comparison between two groups at different intervals of time**

| | **Group** | | | | **p value** |
|---|---|---|---|---|---|
| | **Fentanyl** | | **Esmolol** | | |
| | **Mean** | **SD** | **Mean** | **SD** | |
| Baseline | 9,760.58 | 713.72 | 9,757.48 | 946.33 | 0.985 |
| After Study Drug Administration | 8,420.72 | 776.55 | 8,916.96 | 864.83 | 0.003* |
| Induction | 8,320.52 | 978.46 | 8,485.08 | 1,035.90 | 0.416 |
| Laryngoscopy & Intubation | 12,988.62 | 988.34 | 11,570.16 | 1,246.19 | < 0.001* |
| 1 Min | 12,324.42 | 1,178.81 | 11,397.30 | 1,393.04 | 0.001* |
| 3 Min | 11,485.36 | 976.6 | 10,557.36 | 1,220.86 | < 0.001* |
| 5 Min | 10,686.48 | 922.3 | 9,811.46 | 1,249.13 | < 0.001* |
| 10 Min | 10,198.76 | 955.81 | 9,284.54 | 1,077.86 | < 0.001* |

In the study there was statistically significant difference in mean Rate pressure product between two groups after Drug administration to 10 min after drug administration. Mean RPP was lower in Esmolol group compared to Fentanyl group at these intervals.

**Table 11: ST -T Change Distribution between two groups**

| | | Group | | | |
|---|---|---|---|---|---|
| | | Fentanyl | | Esmolol | |
| | | Number | % | Number | % |
| ST -T Change | No | 50 | 100% | 50 | 100% |

In both the groups, none of the subjects had ST-T change

## Discussion

Orotracheal intubation consists of two phases: Direct laryngoscopy and passing of endotracheal tube through the vocal cords and trachea. It has been seen in various studies that increase in Heart Rate occurs during endotracheal intubation whereas the greatest increase in BP occurs during laryngoscopy. 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 cardioaccelerator fibers and release of adrenergic mediators including norepinephrine, epinephrine, and vasopressin. The net effect of this autonomic surge is an increased Blood pressure, Heart rate, 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 Sinoatrial node [8].

In 1981, Russell et al monitored the changes in arterial pressure and arterial concentrations of noradrenaline, adrenaline and dopamine were monitored in 16 patients undergoing endotracheal intubation. Significant increases in mean arterial pressure and plasma noradrenaline were noted. The increases in arterial pressure were associated with increases in noradrenaline concentrations. Adrenaline and dopamine concentrations did not change significantly following intubation. The results suggest a predominantly sympathetic response during intubation and the need for prophylaxis in patients at risk [9]. In 1983, Derbyshire et al measured the plasma adrenaline and noradrenaline concentrations in 24 patients during the induction of anaesthesia and the subsequent tracheal intubation. The patients received either suxamethonium 1 mg kg−1 or pancuronium 0.1 mg kg−1 to facilitate tracheal intubation. Mean arterial pressure (MAP) increased in both groups following laryngoscopy and tracheal intubation and there were concomitant increases in the plasma catecholamine concentrations, the changes being more marked in the suxamethonium group. There was a significant correlation between Mean arterial pressure and plasma catecholamine concentrations in the suxamethonium group. Measurement of plasma catecholamine concentrations in samples obtained simultaneously from central venous, peripheral venous and arterial sites were in broad agreement; the greatest changes occurred in central venous samples [10].

Both Heart rate and Blood pressure are determinants of oxygen delivery and demand. An increase in Heart Rate deleteriously affects both supply and demand of oxygen. BP is related to cardiac output (CO) and systemic vascular

resistance (SVR). A change in either CO or SVR will result in a compensatory change in the other. Hypertension can, therefore, also affect both supply and demand [11]. The strict control of hemodynamic variables has reduced myocardial ischemia, while hemodynamic aberrations, such as tachycardia, systolic hypertension and hypotension, elevated Rate pressure product and Mean blood pressure/Heart rate ratio of less than one may cause ischemia, Rate pressure product is correlated with myocardial oxygen demand and a threshold value of Rate pressure product had been correlated with the onset of angina. During anaesthesia, myocardial ischemia is poorly correlated with Rate pressure product.

Suctioning, similar to laryngoscopy and intubation, seems to induce a comparable hemodynamic response. Endotracheal suctioning has also been shown to stimulate the cough reflex [12]. Esmolol appears to be an appropriate choice of agent for attenuating the hemodynamic response to laryngoscopy and tracheal intubation, due to its β 1cardioselective property, rapid onset of action and short elimination halflife (9 min) along with no significant drug interaction with commonly used anesthetics. Esmolol decreases the force of contraction and heart rate by blocking β adrenergic receptors of the sympathetic nervous system which are found in the heart, blood vessels, and other organs of the body. Esmolol prevents the action of two naturally occurring neurotransmitters epinephrine and norepinephrine, thereby attenuates the tachycardia and hypertensive responses to laryngoscopy and tracheal intubation [13]. Esmolol (adrenergic receptor antagonist + ultra-short-acting) provides hemodynamic stability during laryngoscopy and tracheal intubation without side effects [14].

Gupta et al in their study to compare the effectiveness of Esmolol and Fentanyl in attenuating stress response during laryngoscopy and endotracheal intubation, administered Esmolol 2mg/kg iv in one group and Fentanyl 2 microgram/kg in other group, 3 min before induction of anesthesia. Heart rate, blood pressure and rate pressure product were compared with baseline in each group. Both esmolol in a bolus dose of 2mg/kg and fentanyl in bolus dose of 2 μg/kg before induction of anesthesia are effective in attenuating the hemodynamic responses to laryngoscopy and endotracheal intubation like heart rate and rate pressure product. But only esmolol provided consistent and reliable protection against increases in both heart rate and systolic blood pressure accompanying laryngoscopy and endotracheal intubation. Esmolol group did not reveal any rhythm abnormality. No ST-T segment changes were seen in any patients.

They found that rise in heart rate was minimal in Esmolol group and was highly significant [1].

In our study also rise in heart rate was lower in Esmolol group compared to Fentanyl group. In our study also none of the patients developed any ST-T segment changes.

Parth Shah et al in their study for comparison of Fentanyl, Esmolol and their combination for attenuation of stress response found that there was a significant increase in the heart rate during laryngoscopy and post endotracheal intubation in all the groups. The heart rate returned to pre induction values only in group who received both Esmolol and Fentanyl. The combination of Fentanyl and Esmolol significantly attenuated the rise in heart rate and a more significant attenuation of rise in systolic blood pressure compared to Fentanyl and Esmolol alone.

In majority of previous studies, Esmolol was administered by infusion prior to

induction and was found to protect patients from hypertension and tachycardia. But in emergency cases, the preparation and administration of an infusion is time consuming and cumbersome. In such cases, it would be very helpful if Esmolol could be administered as a single bolus in rather than an infusion prior to intubation. We used Esmolol as a single bolus dose rather than infusion in our study.

Chung et al in their study found that combination of low dose Fentanyl and Esmolol is more effective than same dose of either agent alone in blunting tachycardia and hypertensive responses to laryngoscopy and intubation following rapid sequence induction. It is more effective in blunting the Heart rate but was less effective in blunting the BP response than Fentanyl. The combination thus provides an alternative to a higher dose of Fentanyl for blunting the hemodynamic responses to laryngoscopy and intubation during rapid sequence induction in healthy patients [15]

Ebert et al in their study found that Esmolol blunted the HR response, while Fentanyl decreased it below the baseline and maintained it there, in spite of laryngoscopy. They also concluded that Fentanyl decreased the systolic BP, mean BP and Diastolic BP significantly below the baseline while these pressures where either retained at or slightly elevated above the control in Esmolol group [16].

In our study rise in heart rate was minimal in Esmolol group compared to Fentanyl group, but it was not below the baseline. Rise in Mean MAP was also lower in Esmolol group compared to Fentanyl group. No significant differences in Systolic BP and Diastolic BP were found between 2 groups. There was significant difference in Rate Pressure Product between 2 groups with mean RPP being lower in Esmolol group.

Helfman et al in their study to compare the effects of Fentanyl, Esmolol and Lidocaine found that only Esmolol provided consistent and reliable protection against increase in both heart rate and systolic BP accompanying laryngoscopy and intubation. [17]

Goubatz et al in their study found that Esmolol has a tissue distribution time of 2 minutes and an elimination half life of 9 minutes. The window of its availability to tissues is narrow and timing of bolus administration is more critical than its administration by infusion [18]. In our study we administered Esmolol as bolus dose 3 minutes prior to laryngoscopy and intubation.

In 2005, Hussain AM studied the effectiveness of single bolus dose of Esmolol or Fentanyl in attenuating the hemodynamic responses during laryngoscopy and endotracheal intubation. He found that bolus injection of Fentanyl 2 microgram/kg given 2 minutes prior to laryngoscopy and intubation failed to protect against elevation of both the heart rate and systolic blood pressure, whereas Esmolol at 2 mg/kg provided consistent and reliable protection against the increase of heart rate but not arterial blood pressure [19].

In 2012, H Boston and Ahmet Eroglu showed that when administered before induction of anaesthesia 1mg/kg of Esmolol, lidocaine 1mg/kg and 1 µ g/kg of Fentanyl, Esmolol was more effective to prevent the rise in mean SBP as compared to the other two [20].

In 2001, Figueredo-E, Garcia – Fuentes EM in Acta Anaesthesiologica Scandinavica stated that esmolol is effective in a dose-dependent manner, in the attenuation of the adrenergic response to laryngotracheal intubation [21]

## Conclusion

We conclude that in patients with ASA-PS grade I and II, intravenous bolus dose of Fentanyl (2microgram/kg) and Esmolol (1mg/kg) given 3 minute prior to laryngoscopy and intubation is safe and effective prophylactic method for attenuating hemodynamic response to laryngoscopy and intubation. Esmolol provides reliable and consistent protection against rise in heart rate. Esmolol provides better cardioprotection in patients against hyperadrenergic responses to laryngoscopy and endotracheal intubation.

## References


1. Gupta S, Tank P. A comparative study of efficacy of Esmolol and Fentanyl for pressure attenuation during laryngoscopy and endotracheal intubation. Saudi J Anaesth. 2011 Jan;5(1):2–8.
2. Gupta C et al. Clinical efficacy of Esmolol, Lignocaine and Diltiazem as premedicant for attenuation of hemodynamic responses of laryngoscopy and endotracheal intubation- a comparative evaluation. Int J Res Med Sci. 2017 oct;5(10):4443-4449
3. Bruder N, Ortega D, Granthil C. Consequences and prevention methods of hemodynamic changes during laryngoscopy and intratracheal intubation. In: Annalesfrancaisesd' anesthesie et de reanimation. 1992. page 57–71
4. Savio KH, Tait G, Karkouti K, Wijeysundera D, McCluskey S, Beattie WS. The safety of perioperative esmolol: a systematic review and meta-analysis of randomized controlled trials. Anesth Analg 2011;112(2):267–281.
5. Rovenstine E, Papper E: Glossopharyngeal nerve block. Am J Surg 75:713-715,1948
6. Miller DR, Martineau RJ, Wynands JE, et al: Bolus administration of esmolol for controlling the hemodynamic response to tracheal intubation: The Canadian multicentre Trial. Can J Anaesth 38:849-858,1991.
7. Landesberg G, Luria MH, Cotev S, et al: Importance of long duration ST-segment depression in cardiac morbidity after vascular surgery. Lancet 341:715-719,1993
8. Jain P, Vats A. Comparison of esmolol and lidocaine for blunting of stress response during laryngoscopy and endotracheal intubation. Int J Sci Study 2017; 5:12–17.
9. Russell WJ, DREW S, MORRIS R, FREWIN D. Changes in plasma catecholamine concentrations during endotracheal intubation. BJA Br J Anaesth 1981;53(8):837–839.
10. Derbyshire DR, Chmielewski A, Fell D, Vater M, Achola K, Smith G. Plasma catecholamine responses to tracheal intubation. BJA Br J Anaesth 1983;55(9):855–860.
11. Thomson IR. The haemodynamic response to intubation: a perspective. Can J Anesth Can Anesth 1989;36(4):367–369.
12. Yukioka H, Yoshimoto N, Nishimura K, Fujimori M. Intravenous lidocaine as a suppressant of coughing during tracheal intubation. Anesth Analg 1985;64(12):1189–1192
13. Vucevic M, Purdy GM, Ellis FR. Esmolol hydrochloride for management of the cardiovascular stress responses to laryngoscopy and tracheal intubation. BJA Br J Anaesth 1992;68(5):529–530.
14. Louizos AA, Hadzilia SJ, Davilis DI, Samanta EG, Georgiou LG. Administration of esmolol in microlaryngeal surgery for blunting the hemodynamic response during laryngoscopy and tracheal intubation in cigarette smokers. Ann Otol Rhinol Laryngol 2007;116(2):107–111.
15. Chung KS, Sinatra RS, Halevy JD, Paige D, Silverman DG. A comparison

of Fentanyl, Esmolol, and their combination for blunting the haemodynamic responses during rapid-sequence induction. Can J Anaesth J Can Anesth. 1992 Oct;39(8):774–9.
16. Ebert JP, Pearson JD, Gelman S, Harris C, Bradley EL. Circulatory responses to Laryngoscopy: the comparitive effects of placebo, Fentanyl and Esmolol. Can J Anesth 1989 May;36(3 Pt 1);301-6
17. Helfman SM, Gold MI, DeLisser E A, Herrington CA. Which drug prevents tachycardia and hypertension associated with tracheal intubation: lidocaine, Fentanyl or Esmolol? Anaesth Analg. 1991 Apr 72(4); 482-6
18. Goubatz CL, Wehner RJ. Evaluation of esmolol and Fentanyl in controlling increase in heart rate and BP during endotracheal intubation. AANA J. 1991 Feb; 59 (1);91-6
19. Hussain AM, Sultan ST. Efficacy of fentanyl and esmolol in the prevention of haemodynamic response to laryngoscopy and endotracheal intubation. J Coll Physicians Surg JCPSP 2005;15(8):454–457.
20. Bostan H, Eroglu A. Comparison of the clinical efficacies of fentanyl, esmolol and lidocaine in preventing the hemodynamic responses to endotracheal intubation and extubation. J Curr Surg 2012;2(1):24–28.
21. Figueredo E, Garcia-Fuentes EM. Assessment of the efficacy of esmolol on the haemodynamic changes induced by laryngoscopy and tracheal intubation: a metaanalysis. Acta Anaesthesiol Scand 2001;45(8):1011–1022.