

# To Study The Efficacy Of Intravenous Esmolol, Lidocaine And Diltiazem In Attenuating Haemodynamic Response To Laryngoscopy And Intubation

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## Abstract

Hypertension and tachycardia have been reported since 1950 during intubation under light anesthesia. Increase in blood pressure and heart rate occurs most commonly from reflex sympathetic discharge in response to laryngotracheal stimulation. Hypertensive response of normal subjects to laryngoscopy and intubation might be enhanced and prove dangerous to hypertensive subjects. Various agents have been used to attenuate hypertensive response. Seventy five patients fulfilling eligibility criteria were included in study. The patients were randomly assigned to one of three groups of twenty five each through a computer generated number. Group A = received 1mg/ kg of esmolol intravenously (n=25), Group B = received 1.5mg/ kg of lidocaine intravenously (n=25), Group C = received 0.2mg/ kg of diltiazem intravenously (n=25). These agents were administered three minutes prior laryngoscopy. Patients were premedicated with fixed dose of injection fortwin and phenegan according to body weight and anesthesia was induced with thiopentone, intubation facilitated by use of succinylcholine. No surgical stimulation, analgesics or inhalational anesthetics were allowed till five minutes after intubation and haemodynamic parameter noted. The results were statistically analyzed. We concluded that esmolol in dose of 1 mg/kg intravenously 3 min prior to laryngoscopy and intubation prevented the rise in heart rate effectively. Esmolol was also effective in attenuating systolic blood pressure increase, diastolic blood pressure increase and increase in mean blood pressure except at 1 min after intubation whereas in comparison lidocaine and diltiazem were not that effective.

## OBJECTIVES OF STUDY

1. To study the efficacy of intravenous esmolol, lidocaine, and diltiazem in attenuating haemodynamic response to laryngoscopy and intubation.
2. To study safety of intravenous esmolol, lidocaine, and diltiazem in attenuating haemodynamic response to laryngoscopy and intubation.

## INTRODUCTION

Hypertension and tachycardia have been reported since 1950 during intubation under light anesthesia (Burstein 1950, Forbes and Dally 1970)<sup>1</sup>. Tachycardia is the most common rhythm disturbance during anesthesia and surgery. Increase in blood pressure and heart rate occurs most commonly from reflex sympathetic discharge in response to laryngotracheal stimulation, which in turn leads to increase plasma

norepinephrine concentration. Hill (1932)<sup>2</sup> also concluded from ECG studies that arrhythmias were a feature of induction of anesthesia. Dingle (1966)<sup>3</sup> and Forbes and Dally (1970)<sup>1</sup> suggested that the hypertensive response of normal subjects to laryngoscopy and intubation might be enhanced and prove dangerous to hypertensive subjects.

This sympathoadrenal response to laryngoscopy results in an increased cardiac work load which in turn may culminate in perioperative myocardial ischaemia and acute heart failure in susceptible individuals. This response is undesirable in any patient with heart disease undergoing surgery, irrespective of the nature of surgery. Various agents have been used to attenuate hypertensive response including :topical lignocaine – sprays, deeper plane of anesthesia – by inhalational agents, narcotics like fentanyl, alfentanil, sufentanil, remifentanyl, magnesium sulphate, ca-channel blockers, vasodilators like SNP and NTG. The topic of study was chosen because it has been noted previously by many workers that increase in blood pressure and heart rate that results from sympathetic

discharge in response to laryngotracheal stimulation may get further enhanced and prove dangerous to hypertensive and ischemic heart disease patients.

Esmolol, (methyl 3-[4- [2 – hydroxyl – 3) isopropylamino] propoxyl] phenyl ] proprionate HCl) is a cardio selective water soluble ultrashort acting  $\beta_1$  adrenergic receptor antagonist that can be administered only intravenously. Esmolol is rapidly hydrolysed by cytoplasmic esterases in red blood cells, therefore has short elimination of approximately 9 min., distribution half-life with 2 min and peak haemodynamic effect with 6 to 10 min. of administration. Its metabolism is not influenced by renal or hepatic function and less than 1% excreted in urine as unchanged drug.

Diltiazem is one of the drugs belonging to the benzothiazepine class of calcium channel blockers. Injectable diltiazem is a clear, colourless, sterile, non-pyrogenic solution with a pH range of 3.7 – 4.1. Diltiazem is 70% to 80% bound to plasma proteins. Albumin appears to bind 30% Of the drug. The drug should be used with caution in patients with impaired renal or hepatic function.

Lidocaine is [2-(Diethylamino)-N-2,6-Dimethyl phenyl acetamide)] an amide group of local anaesthetic agent . It is metabolized by oxidases and amidases from microsomes of liver and the metabolites are excreted in the urine, hastened when the urine is acidic. Lidocaine blood concentration peak within the first minute after an I/V bolus, but blood levels do not correlate with clinical effects.

## **MATERIAL & METHOD**

The study was conducted in the Department of Anesthesiology of Jaipur Golden Hospital, Delhi. This is a 265-bedded multi specialty hospital.

## **INCLUSION CRITERIA**

Patients between age < 70 years and > 18 years, weighing < 90 kg and < 40 kg of either sex; urban/ rural, posted for elective Surgical Procedure belonging to ASA physical status – Grade I, requiring general Anesthesia and Endotracheal Intubation were included in the study.

## **EXCLUSION CRITERIA**

Patients between age  $\geq 70$  years and Age  $\leq 18$  years, weighing  $\geq 90$  kg and  $\leq 40$  kg; hypertensive patients – systolic blood pressure  $\geq 160$ mm Hg and or diastolic blood pressure  $\geq 95$ mm Hg were excluded from the study. Patients

with significant renal, hepatic or gastrointestinal disease were not excluded in the study. Patients suspected to have difficult tracheal intubation and patients with chronic obstructive lung disease especially bronchial asthma were excluded from the study. Patients with significant heart disease: past history or angina or myocardial infarction, heart blocks, and congestive cardiac failure were also excluded from the study.

## **SAMPLE SIZE & SAMPLE TECHNIQUE**

Patients were randomly assigned to one of three groups of twenty five each through a computer generated number. Group A = received 1mg/ kg of esmolol intravenously (n=25); group B = received 1.5mg/ kg of lidocaine intravenously (n=25), group C = received 0.2mg/ kg of diltiazem intravenously (n=25). Details pertaining to the patients clinical history, general, physical and systemic examination and basic routine investigations like hemoglobin, blood sugar, blood urea, serum creatinine, bleeding time, clotting time, electrograph (ECG) and chest X-ray were checked. Proper consent was taken. Patients received injection fortwin (0.5mg/kg) and injection phenargan (25mg) intramuscular 45 minutes prior to shifting to the operation theatre. Upon arrival in operation theatre, non-invasive blood pressure and standard lead II and V ECG monitoring was established by Datex Ohmeda S/5. Appropriate intravenous line was started with Ringer Lactate. The base line blood pressure and heart rate were recorded after a resting period of 5 minutes. Preoxygenation was done for three minutes. Group A (n = 25) received 1 mg/kg of esmolol bolus iv, group B (n = 25) received 1.5 mg/kg of lidocaine iv, group C (n = 25) received 0.2 mg/kg of diltiazem iv. After 1 minute, anesthesia was induced by intravenous thiopentone sodium 5mg/kg and followed by succinylcholine 2 mg/kg. Patients were ventilated by mask with 100% oxygen. After 2 minutes of administration of thiopentone direct laryngoscopy was performed with Macintosh laryngoscope and trachea intubated with proper sized tube-poly vinyl chloride/ red rubber/ flexometallic. Following intubation the lungs were ventilated with 66% nitrous oxide in oxygen. Non-depolarizing muscle relaxant, vecuronium 0.06–0.12mg/kg given at appropriate time. For the next 5 minutes after laryngoscopy and intubation, all surgical stimuli/analgesic supplements and inhalational anaesthetics were avoided. After observations were finished, anaesthesia was continued according to the requirements of surgery and the discretion of the attendant anaesthesiologist. Data was collected using a multiparameter monitor – Datex

Ohmeda-S/5. Parameters assessed and recorded were  $T_b$  – base line heart rate [HR], systolic blood pressure [SBP], diastolic blood pressure [DBP], mean blood pressure [MBP].  $T_s$  – time at which study drug was given.  $T_1$  – at induction,  $T_a = 1$  min after thiopentone  $T$  – at laryngoscopy and intubation, i.e. 2 min after administration of thiopentone.  $T_1$ ,  $T_2$ ,  $T_3$ ,  $T_4$ ,  $T_5$  – at 1<sup>st</sup>, 2<sup>nd</sup>, 3<sup>rd</sup>, 4<sup>th</sup>, and 5<sup>th</sup> min after intubation respectively. The data were analyzed using paired-‘t’-test and student-‘t’-test.

## RESULTS

Mean age was comparable in all groups, when statistically analyzed. [Table 1]. Distribution of patients according to sex in each group was statistically comparable. [Table 2]. Mean weight was also comparable in all groups. [Table 3]. In group A, there was significant fall in HR after 1 min of study drug, HR was comparable to basal value after 4 min of intubation. In group B and C –there was rise in HR, which was statistically significant after 1 min of study drug administration. In group A [esmolol] – SBP decreased after 2 min of study drug that was statistically significant but not significantly affected at other time intervals. In group B [lidocaine] – SBP increased after intubation that was statistically significant up to 2 min after intubation, thereafter not significantly raised. In group C [diltiazem] – SBP increased significantly at 1 min and 2 min after intubation. In group A [esmolol] – DBP was not much affected throughout study period, except for a rise only 1 min after intubation. In group B [lidocaine] – DBP increased significantly 2 min after study drug up to 2 min after intubation. Group C [diltiazem] – DBP decreased significantly up to 2 min after study, but later increased at 1 min and 2 min after intubation. In group A [esmolol] – MBP was not much affected, except for a rise at 1 min after intubation. In group B [lidocaine] – MBP increased significantly at 2 min after study drug up to 3 min after intubation. In group C [diltiazem] – MBP was not much affected, except for a significant fall 1 min and 2 min after study drug and a significant rise 1 min after intubation. One patient in each group A [esmolol] and B [lidocaine] and two patients in group C [diltiazem] had hypotension. One patient in group A had bradycardia. None of the patients had arrhythmias/ bronchospasm. Base Line heart rate is comparable in all groups. Heart Rate at timing of study drug is also comparable, but Heart Rate at all other intervals vary significantly among different groups. SBP at all time intervals is comparable in all the three groups except at time of intubation where it varies significantly. The diastolic

blood pressure varies significantly among three groups upto 2 min. after study, there after mean DBP is comparable at other time intervals among the three groups. Mean blood pressure comparison among groups: MBP varies significant upto intubation ( $T_0$ ) among three groups, there after MBP is statistically comparable in all three groups.

**Figure 1**

Table-1 shows distribution of cases according to age in each group. Majority of patients were in 2 or 3 decade of life. Mean age is comparable in all groups

AGE GROUP	GROUP			TOTAL
	A	B	C	
≤ 20 Count	4	3	3	10
% within GR	16.0%	12.0%	12.0%	13.3%
21-30 Count	8	6	1	15
% within GR	32.0%	24.0%	4.0%	20.0%
31-40 Count	2	4	14	20
% within GR	8.0%	16.0%	56.0%	26.7%
41-50% Count	6	6	5	17
% within GR	24.0%	24.0%	20.0%	22.7%
51-60% Count	5	4		9
% within GR	20.0%	16.0%		12.0%
61-70% Count		2	2	4
% within GR		8.0%	8.0%	5.3%
Count	25	25	25	75
Total % within GR	100%	100%	100%	100.0%
Mean Age	35.32 ±13.08	39.72 ±14.53	37.48 ±11.15	

P= 0.492 (N.S.)

\*N.S. = Not significant

H.S = Highly significant

V.H.S = Very Highly significant.

**Figure 2**

Table-2 This table shows distribution of patients according to sex in each group is statistically comparable.

SEX	GROUP			Total
	A Esmolol	B Lidocaine	C Diltiazem	
<b>Male</b> Count % within Group	12 48.0%	13 52.0%	11 44.0%	36 48.0%
<b>Female</b> Count % within Group	13 52.0%	12 48.0%	14 56.0%	39 52.0%
<b>Total</b>	25 100.0%	25 100.0%	25 100.0%	75 100.0%

P= 0.852 (N.S.)

**Figure 3**

Table- 3 shows distribution of patients according to weight in each group. Majority of patients are between 50-69 kg weight group. Mean age (Mean  $\pm$  S.D.) kg is comparable in all groups.

WEIGHT GROUP	GROUP			Total
	A	B	C	
<b>41-49</b> Count % Within Group	2 8.0%		5 20.0%	7 9.33%
<b>50-59</b> Count % Within Group	10 40.0%	10 40.0%	8 32.0%	28 37.33%
<b>60-69</b> Count % Within Group	4 16.0%	10 40.0%	8 32.0%	22 29.33%
<b>70-79</b> Count % Within Group	7 28.0%	3 12.0%	4 16.0%	4 18.7%
<b>80-89</b> Count % Within Group	2 8.0%	2 8.0%		4 5.3%
<b>Total</b> Count % Within Group	25 100%	25 100.0%	25 100.0%	75 100.0%
<b>Mean Weight</b>	62.56% $\pm 11.56$	61.88% $\pm 10.08$	56.72% $\pm 8.77$	

P= .094 (N.S.)

## DISCUSSION

Pre-operative mean heart rate was comparable in all three groups. Findings in esmolol group (group-A) when compared with their pre-operative values showed significant rise in heart rate only 1 minute and 2 minute after intubation. At 4 minutes after intubation, it comes to less than preoperative value, although fall was not statistically significant ( $P > .05$ ). Korenaga et al (1985)<sup>4</sup> also agreed with the fact that mean  $\pm$  sd of heart rate in esmolol group were at statistically different from the basal value. Miller (1991)<sup>5</sup>

also agreed with the same fact that there was a significant difference ( $P < .05$ ) in the heart rate between the placebo group and both 100 mg and 200 mg groups upto 1 min after endotracheal intubation. But our findings differ from the findings of Korpinen R. et al (1995)<sup>6</sup> who said that esmolol did not prevent increase in heart rate in response to laryngoscopy and intubation.

Findings in the diltiazem group when compared with their pre-operative values show significant increase in heart rate after study drug upto 4 minute after intubation. At 5 minutes after intubation, no significant difference with the basal value has been observed. These findings are consistent with that of Mikawa et al (1990)<sup>7</sup> who said I.V. diltiazem (0.2 and 0.3 mg/kg) failed to protect against the increase in heart rate after laryngoscopy and intubation, despite the negative chronotropic effect of drug.

Findings in the lidocaine group when compared to basal values show significant increase in heart rate from study drug upto 4 minutes after intubation. At 5 minutes after intubation there is no significant difference with basal value. Helfman et al (1991)<sup>8</sup> found that dose of 1.5 mg/kg lidocaine administered 1.5 min, 2 min and 4 min. before intubation failed to protect against increase in heart rate. Stoelting (1977)<sup>9</sup> said that arterial pressure begin to increase 15 seconds after laryngoscopy with a peak increase after 30-40 second. In hypertensive patients SBP may rise to more than 100 mm Hg during endotracheal intubation. This rise of BP can cause LVF (Masson 1964)<sup>10</sup> and cerebral haemorrhage. Menkhaus et al (1985)<sup>11</sup> and Vucevic et al (1992)<sup>12</sup> found that SBP was lower in esmolol group after intubation. Korenaga et al (1985)<sup>4</sup> also stated that esmolol moderated the increase in SBP after intubation. The findings of systolic and diastolic blood pressure in the diltiazem group when compared with basal values at different time intervals show that there is significant fall in the SBP at 1 min and 2 min. after study drug, but significant increase in SBP at 1 min and 2 min after intubation. Thereafter significant fall was observed at 5 min after intubation. As regards DBP, there is significant fall in DBP upto 2 min after study drug. The DBP increased significantly at 1 min. and 2 min. after intubation and thereafter DBP values were comparable to basal values. Our findings are similar to the result of Mikawa et al (1996)<sup>13</sup> who found that increase in systolic and diastolic blood pressure was significantly less in the diltiazem group (.2mg/kg) 1 min before laryngoscopy and intubation. The findings in the lidocaine group show that there is significant

rise in SBP after lidocaine upto 2 min. after intubation. There after SBP values were comparable to basal values. As regards DBP, there was insignificant increase up 2 min after study drug, but DBP increased significantly thereafter upto 2 min. after intubation. Thereafter DBP values were comparable to basal values. Hamill et al (1981)<sup>14</sup> found that I.V. lidocaine 1.5 mg/kg did not entirely prevent cardiovascular stimulation in response to endotracheal stimulation. Values of mean arterial pressure in esmolol group when compared to basal value show that there was significant increase in MBP only at 1 minute after intubation. There was significant fall in MBP 5 min. after intubation and at rest of time intervals; the MBP value was comparable to basal value in esmolol group. Korpinen R et al (1995)<sup>6</sup> studied the effect of esmolol and found that esmolol did not prevent increase in arterial pressure in response to laryngoscopy and intubation. These findings differ from our results. In the diltiazem group, comparison of MAP at different time intervals with its pre operative value shows significant fall in MAP at 1 min and 2 min after drug administration; but there was a significant increase in MAP at 1 min after intubation, there after the MAP was comparable to the basal value. Hasegawa et al (1992)<sup>15</sup> reported that MAP decreased significantly after diltiazem. Fuji et al (1995)<sup>16</sup> found that increase in MAP following tracheal intubation in the diltiazem group was lower. Findings in the lidocaine group as regards MAP when compared at different time intervals with basal value show that MAP increased significantly 2 min after drug administration upto 3 min after intubation. There after MAP values at 4<sup>th</sup> & 5<sup>th</sup> minute after intubation were comparable to basal value. Robert K. Stoelting (1978)<sup>17</sup> found that maximal increase in MAP above awake level occurred 5-15 second after tracheal intubation in patients receiving lidocaine. Helfman (1991)<sup>8</sup> found that usual dose of lidocaine (100mg) does not reliably blunt the increase in MAP. All the above studies are comparable to our result in which significant increase in MAP occurred upto 3 minute after intubation.

## CONCLUSIONS

Esmolol in dose of 1 mg/kg intravenously 3 min prior to laryngoscopy and intubation prevented the rise in heart rate effectively. Esmolol was also effective in attenuating systolic blood pressure increase, diastolic blood pressure increase and increase in mean blood pressure except at 1 min after intubation whereas in comparison lidocaine and diltiazem were not that effective. Esmolol may be used in

ischemic heart disease patients and in hypertensive patients where increase in blood pressure and heart rate can be detrimental to the patient or surgical procedure itself, like ophthalmic surgeries and neurosurgical procedures. We need to have more RCTs to make it a recommendation as our sample size was small.

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