Attenuation of Pressor Response during Laryngoscopy and Tracheal Intubation by Placebo, Lignocaine and Esmolol – A Comparative Clinical Study

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Abstract
Background and Aims: Laryngoscopy and tracheal intubation causes sympathoadrenal stimulation and cause transient rise in pulse rate and blood pressure. We evaluated the efficacy of Esmolol and Lignocaine in attenuating the pressor response during laryngoscopy and intubation as compared to placebo.

Methods: 60 patients of ASA I & II between the age group of 20-60 were randomized to receive either Esmolol 1.5 mg/Kg, Lignocaine 1.5mg/Kg or 5ml normal saline just prior to induction of anaesthesia. Heart rate (HR), systolic blood pressure (SBP) and diastolic blood pressure (DBP) were recorded before induction (baseline) and at regular intervals of 1, 3, 5, 7 and 10 minutes after induction. Statistical analysis was done using Student’s t test and chi-square test and p values obtained.

Results: There is an increase in HR, SBP and DBP in the control group which is maximum at 3 mins after induction (i.e. during laryngoscopy and tracheal intubation). Whereas in the study groups there was no significant variation in these parameters from baseline which is found to be more effective with Esmolol (p-value < 0.001) than Lignocaine.

Conclusion: Esmolol 1.5mg/Kg was found to be more effective in attenuating pressor response to laryngoscopy and intubation compared to Lignocaine.

Keywords: Esmolol, lignocaine, attenuation of pressor response, laryngoscopy, tracheal intubation, pressor response, blood pressure, heart rate.

Introduction
General anaesthesia with controlled ventilation is the most popular anaesthetic technique worldwide. Direct Laryngoscopy and endotracheal intubation produced reflex cardiovascular responses characterised by tachycardia and hypertension¹,². Rise in pulse rate and blood pressure are usually transitory and are of no consequences in healthy individuals, but can be harmful to patients with hypertension, coronary artery and cerebrovascular diseases³,⁴.
Increase in heart rate and blood pressure produces imbalance in myocardial oxygen supply and demand. Tachycardia can both decrease myocardial oxygen supply (by shortening the duration of diastole) and increase myocardial oxygen demand (due to the positive ionotropic state) thus acting as a double edged sword. Hypertension increases myocardial oxygen demand by increasing the afterload against which the left ventricle has to pump. Both in combination can increase myocardial oxygen consumption and can cause myocardial ischemia, infarction, various arrhythmias, cerebrovascular events. Various drugs and techniques have been used to attenuate this pressor response\textsuperscript{[5],[6],[7]}. Light plane of anaesthesia and prolonged time for laryngoscopy are some factors precipitating this pressor response. Opioids especially short acting ones like Fentanyl, Lignocaine (intravenous, nebulized, gargle, spray etc). Clonidine, Dexmedetomine, Esmolol, Labetolol, Magnesium sulphate, Nitroglycerin etc are some of the drugs used\textsuperscript{[8],[9],[10]-[15]}. Superior laryngeal nerve block is a regional technique to suppress laryngo-tracheal stimulation.

The present study is designed to compare the efficacy of intravenous bolus of Esmolol, an ultra short acting cardio selective beta blocker with that of intravenous Lignocaine in attenuating the hemodynamic response to laryngoscopy and intubation.

Materials and Methods
The study was undertaken after getting approval from institutional ethics committee during the period from Sept 2000 to Feb 2001. Informed consent was obtained from all patients in the study. This was a randomised control trial, single blinded study (the patients were blinded against the drugs they were getting). 60 patients of ASA grade-I and II aged 20-60yrs involving both sexes coming for major elective procedures like thyroidectomy, radical mastectomy, laparotomies, orthopaedic procedures were studied with 20 patients at random in each group.

1-Control Group – where 5 ml normal saline was given during induction
2-Study group with Lignocaine– where preservative free Lignocaine 1.5 mg/Kg was given during induction
3-Study group with Esmolol– where Esmolol 1.5mg/Kg was given during induction

Exclusion criteria included uncontrolled hypertension, diabetes, other systemic illnesses, difficult airway, ASA-III and IV patients.

All the 60 patients underwent a preanesthetic evaluation on the day before surgery. They were investigated to rule out any systemic illnesses. Baseline pulse rate and blood pressure were recorded. Informed consent was obtained, advised overnight fasting and all were pre-medicated with Diazepam 10mg HS and early morning for overnight sedation and anxiolysis. On the day of surgery, all of them received inj. Pethidine 1mg/Kg + inj. Phenergan 0.5mg/Kg 45-50 mins prior to induction in the pre-medication room.

On the operating table, ECG and NIBP were attached and baseline HR and blood pressure (SBP & DBP) were recorded before induction. After securing IV access, an infusion of isotonic saline was started. All the patients were pre-oxygenated for three minutes with 100% oxygen. This was followed by the study drug i.e. either Lignocaine 1.5mg/Kg or Esmolol 1.5mg/Kg or normal saline (for control group) as a slow IV bolus. This was followed by induction with Thiopentone sodium in a dose of 5-6mg/Kg over 30 seconds followed by Succinyl choline in a dose of 2mg/Kg IV bolus after confirming successful mask ventilation. Ventilation was assisted with Bag and mask with 100% oxygen during the period of choline apnoea (1min). After 1 min following choline and 3 mins following the study drug a gentle laryngoscopy was performed and trachea was intubated with appropriate size cuffed oroendotraheal tube. HR, SBP and DBP were recorded before induction (baseline) and at regular intervals of 1, 3, 5, 7 and 10 mins.
Anaesthesia was maintained with 66% Nitrous Oxide in Oxygen and Isoflurane. Vecuronium was used as the muscle relaxant as it is cardiostable. At the end of surgery, residual neuromuscular blockade was reversed with inj. Neostigmine 0.05mg/Kg and Atropine 0.02mg/Kg followed by extubation.

All values were expressed as mean ± std deviation. Statistical comparisons were performed by Student’s t-test and chi-square test and p-values were calculated. P < 0.05 was considered statistically significant and P < 0.001 was considered highly significant.

Results
The data were analysed by comparing demographic profiles such as age, weight and type of surgery to see whether the three groups were identical. The effects of drugs were compared with control group by considering variables such as heart rate, SBP and DBP.

The demographic profiles and type of surgery were comparable in all the three groups. Baseline hemodynamic parameters were comparable in the three groups (p > 0.05). Changes in hemodynamic parameters – HR, SBP and DBP at 1, 3, 5, 7 and 10 mins after induction is shown in Table 1. There is an increase in these variables in the control group which is maximum at 3 mins after induction (i.e. during laryngoscopy and intubation). Whereas in the study groups there was no significant variation from baseline which is more effective with Esmolol than Lignocaine. In Table 2, statistical comparisons are shown as p-values.

Table 1 Changes in HR, SBP and DBP in control and study groups

| PARAMETER | BASELINE (Mean ± SD) | 1 MIN | 3 MIN | 5MIN | 7MIN | 10MIN |
|-----------|----------------------|-------|-------|------|------|-------|
| CONTROL   |                      |       |       |      |      |       |
| HR        | 86.6 ± 5.9           | 84.2 ± 5.2 | 112.1 ± 9.7 | 108 ± 9.3 | 104 ± 9.1 | 99.9 ± 7.9 |
| SBP       | 131.6 ± 11.1         | 127.8 ± 9.3 | 154.8 ± 9.3 | 149.2 ± 8.6 | 144.3 ± 8.8 | 139.8 ± 8.6 |
| DBP       | 85.1 ± 5.2           | 83.3 ± 4.9  | 92.1 ± 3.5  | 88.5 ± 3.4  | 85.3 ± 3.5  | 85 ± 3.7   |
| LIGNOCAINE|                      |       |       |      |      |       |
| HR        | 87.6 ± 9.3           | 89.4 ± 12  | 104 ± 8.3  | 101 ± 8.3  | 96.4 ± 6.9  | 93.9 ± 6.7 |
| SBP       | 125.7 ± 16.5         | 125.9 ± 12.3 | 145.2 ± 10.7 | 139.5 ± 10.4 | 136.6 ± 8.6 | 132.2 ± 6.6 |
| DBP       | 84.2 ± 8.2           | 81.1 ± 6.7  | 89.9 ± 3.7  | 87 ± 3.9   | 85 ± 4.1    | 84 ± 3.9   |
| ESMOLOL   |                      |       |       |      |      |       |
| HR        | 90.7 ± 17.3          | 83.5 ± 14.8 | 85.5 ± 12.7 | 86.4 ± 10.8 | 87.5 ± 10.5 | 87 ± 11.06 |
| SBP       | 125.6 ± 14.1         | 111 ± 13.9  | 120.3 ± 30.6 | 124.4 ± 13.7 | 122 ± 13.9  | 121 ± 14.5 |
| DBP       | 84.6 ± 5.73          | 77.3 ± 7.4  | 84.3 ± 5.6  | 83.3 ± 3.3  | 82.4 ± 3.22 | 83 ± 4.3   |

Table 2 Comparison of study groups with control group (p-value)

|        | BASELINE | 1 MIN | 3 MIN | 5MIN | 7MIN | 10MIN |
|--------|----------|-------|-------|------|------|-------|
| CONTROL VS LIGNOCAINE |          |       |       |      |      |       |
| HR     | P > 0.05 | P < 0.05 | P < 0.01 | P < 0.05 | P < 0.05 | P < 0.01 |
| SBP    | P > 0.05 | P > 0.05 | P < 0.05 | P < 0.01 | P < 0.01 | P < 0.01 |
| DBP    | P > 0.05 | P > 0.05 | P > 0.05 | P > 0.05 | P > 0.05 | P > 0.05 |
| CONTROL VS ESMOLOL |          |       |       |      |      |       |
| HR     | P > 0.05 | P > 0.05 | P < 0.001 | P < 0.001 | P < 0.001 | P < 0.001 |
| SBP    | P > 0.05 | P < 0.001 | P < 0.001 | P < 0.001 | P < 0.001 | P < 0.001 |
| DBP    | P > 0.05 | P < 0.01  | P < 0.01  | P < 0.01  | P < 0.01  | P < 0.01  |
| LIGNOCAINE VS ESMOLOL |          |       |       |      |      |       |
| HR     | P > 0.05 | P > 0.05 | P < 0.001 | P < 0.001 | P < 0.001 | P < 0.001 |
| SBP    | P > 0.05 | P < 0.01  | P < 0.01  | P < 0.01  | P < 0.01  | P < 0.01  |
| DBP    | P > 0.05 | P > 0.05 | P > 0.05 | P > 0.05 | P > 0.05 | P > 0.05 |

Discussion
Considering HR, the baseline values were comparable in all the three groups – p > 0.05 (Table 1). At the time of laryngoscopy and intubation the HR rose to a mean level of 112.1 in the control group from a mean level of 86.6 whereas in the
Lignocaine group the rise in HR was less (mean level of 104) compared to control. The difference in HR was statistically significant (p < 0.05) which is suggestive of effectiveness of Lignocaine in attenuating pressor response to a certain extent. In case of Esmolol, the mean HR at the time of laryngoscopy and intubation was only 85.5 and continued to be almost in the same level till the end of 10\textsuperscript{th} min. P value was less than 0.001 (highly significant). The findings were matching with Canadian multicentre trial in 1991\textsuperscript{[14]}. The SBP was also almost similar in all the three groups before induction and at 1 min (Table 1). From 3\textsuperscript{rd} min onwards i.e. from the time of intubation, the SBP started to increase. At the 3\textsuperscript{rd} min, the mean SBP was 154.8 in the control group, 145.2 in the Lignocaine group and 120.3 in the Esmolol group. This was found to be highly significant statistically (p < 0.001) and continued in the same way till the end of 10 mins. So it is proved beyond doubt that Esmolol is definitely a superior pressor response attenuating agent over Lignocaine as supported by the study of Helfman S M, Gold MI et al in 1991\textsuperscript{[5]}. When considering the attenuation of DBP it is quite evident from the tables that response with Lignocaine was not at all significant statistically (p > 0.05) as the DBP values were remaining more or less identical compared to the control group. Thus the attenuation produced by Lignocaine was better for SBP than DBP (R K Stoelting in 1977\textsuperscript{[7]}) But when Esmolol was compared with control and Lignocaine, the values were statistically significant. This proves the efficacy of Esmolol over Lignocaine. (Singh H, Vichitvejpaisal P, Gaines G Y, White P F 1995\textsuperscript{[9]}).

Conclusions
The study has confirmed that there is significant rise in HR and blood pressure during laryngoscopy and intubation when no drug was given to attenuate the pressor response. Intravenous Lignocaine 1.5mg/Kg did attenuate the rise in HR and SBP but did not attenuate the rise in DBP. Whereas in the Esmolol group a stable HR with modestly reduced SBP and DBP were attained. Thus Esmolol 1.5mg/Kg was found to be more effective in attenuating pressor response to Laryngoscopy and intubation when compared to Lignocaine.

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