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Original Article

Comparison of Esmolol and Lignocaine in Attenuation of Stress Response to Laryngoscopy and Intubation – A Study in Kerala, South India

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ABSTRACT

Context: Hypertension and tachycardia occurring during laryngoscopy and intubation could be deleterious to certain patients. Esmolol at doses of 100mg and 200mg have been studied extensively to attenuate the stress response to laryngoscopy and intubation. But this may produce undue bradycardia and hypotension. Using Esmolol at a lower dose of 1 mg/kg to attenuate the stress response will decrease its side effects.

Aims: To compare Esmolol at a low dose of 1 mg/kg and Lignocaine 1.5 mg/kg in attenuation of the stress response to laryngoscopy and intubation

Settings and Design: The study was a randomized, parallel group, active controlled trial conducted at SGMCRF.

Methods and Material: 60 healthy patients requiring general anesthesia were randomly allocated to two groups of 30 each. Group L received intravenous Lignocaine without preservative 1.5 mg/kg and Group E received intravenous Esmolol 1.0 mg/kg 3 minutes prior to laryngoscopy and intubation. Patients were premedicated with intravenous Midazolam 1 mg , induced with 2 mg/kg of intravenous Propofol and intubation facilitated by intravenous Vecuronium 0.1 mg/kg . No surgical stimulation, analgesics or inhalational agents were allowed till 5 minutes after intubation and haemodynamic parameters were noted. There were no arrhythmias. The results were statistically analyzed.

Statistical analysis used: Statistical analysis was done by Student's t test for quantitative data and Chi Square test and Fischer's exact test for qualitative data.

Results: Compared with the Lignocaine group, the attenuation of the stress response variables was better in the Esmolol group. The difference in the mean Heart Rate ,Systolic Blood Pressure, Diastolic Blood Pressure and Mean Arterial Pressure between the two groups was significant statistically ($P<0.05$) at all time points from the time of laryngoscopy and intubation till 5 min after laryngoscopy.

Conclusions: Esmolol at a low dose of 1 mg/kg was found to be more effective than Lignocaine 1.5 mg/kg in controlling the stress response to laryngoscopy and intubation. Esmolol 1 mg/kg was found to be safe and effective in controlling the pressor response to laryngoscopy and intubation.

Keywords*: Esmolol; Lignocaine; Stress Response; Laryngoscopy; Intubation.*

INTRODUCTION:

The procedure of endotracheal intubation produces tachycardia and hypertension[1]. These reflex responses are mediated by increased sympathetic nervous system activity. This could be life threatening to certain patients, especially hypertensive patients with ischaemic heart disease or raised intracranial pressures.[2]In view of these complications and in an attempt to maintain normal physiology during anesthesia and surgery , various attempts were made to attenuate these hemodynamic responses to intubation , like minimizing stimulation of airway proprioceptors using topical and regional anesthesia , inhalational anesthetics ,intravenous anesthetic agents , intravenous nonanesthetic adjuvants. IV lidocaine blunts hemodynamic and cerebrovascular responses to intubation. When given in an IV bolus of 1.5 mg/kg, it adds

approximately 0.3 MAC of anesthetic potency. The general anesthetic properties of lidocaine tend to reduce the cerebral metabolic rate for oxygen and CBF, thus lowering ICP in patients with compromised intracranial compliance.[3] Furthermore, lidocaine effectively prevents increases in ICP when used as an adjunct prior to endotracheal intubation in patients susceptible to intracranial hypertension. [4]Abou- Madi et al [5] found intravenous Lignocaine (1.5 mg/kg) 3 minutes before laryngoscopy as optimal dose for attenuating the response. Out of the various beta blockers Esmolol is an attractive option because of its cardioselectivity and ultra short duration of action (9 minutes). Esmolol at a dose of 100 or 200 mg suppressed the hemodynamic response to endotracheal intubation, particularly when combined with a moderate-dose opiate [6-11]. But such doses of Esmolol may produce undue bradycardia and hypotension. So we have chosen to compare the effectiveness of intravenous Esmololat a lower dose of 1 mg/kg and Lignocaine 1.5 mg/kg in attenuating the stress response to laryngoscopy and intubation and thereby decrease the side effects of Esmolol by using a lower dose.

SUBJECTS AND METHODS:

The study was a randomized, parallel group, active controlled trial conducted after obtaining Institutional Research and Ethical Committee clearance . The sample size (n) had been calculated using a formula to find out the significance of difference in proportion of two drugs . The percentage increase in heart rate after intubation, after using Lignocaine and Esmolol was taken from a previous study[12] . At 95% confidence limit and 95% power, a sample size of 23.6 was obtained which was rounded to 30 in each group.60 patients belonging to ASA Grade I and II , of either sex , in the age group of 18-60 years , Mallampatti Class I or II, weighing 40 – 90 kg, coming for elective non-cardiac surgery requiring general anesthesia were included in the study.Patients with heart rate <70/mt, basal systolic blood pressure<100mm Hg, history of asthma, cardiac disease & presence of heart block, ASA PS > II, anticipated difficult intubation, anxious or apprehensive patients, intubation time more than 15 seconds were excluded from the study. All patients were provided with patient information sheet and written informed consent was obtained. All patients were evaluated a day before surgery. The patients were kept fasting overnight after 10:00 pm and received Tablet Pantoprazole 40mg an hour before procedure.60 patients were randomly divided into 2 groups of 30 patients each, based on simple randomisation by lottery method. There was no method employed for concealment. The Participant and Outcome Assessor were Blinded.Group L was given intravenous Lignocaine without preservative 1.5 mg/kg (2% solution) just after induction for attenuation of pressor response to laryngoscopy and intubation. Group E was given intravenous Esmolol 1.0 mg/kg (diluted to 0.5% solution) as slow bolus injection just after induction for attenuation of pressor response to laryngoscopy and intubation.Patient was taken to the operating room. Pre-induction monitors were attached- ECG, NonInvasive Blood Pressure, Pulse Oximetry. Heart Rate, Systolic and Diastolic Blood pressure, Mean Arterial Pressure was recorded from the monitor .These variables were noted at certain time points by my colleague who is equally qualified. Heart rate and Blood Pressure was noted (time T0.) . Intravenous line was established on the forearm with an 18G cannula after local anesthesia with 1ml of 2% Lignocaine (without adrenaline) using intradermal needle. Ringer's Lactate solution was started at 80- 100 ml/hr. Midazolam 1 mg and priming dose of Vecuronium 0.01 mg/kg were given intravenously . Heart rate and Blood Pressure was noted(time T1 just before induction).Patient was induced with 2 mg/kg of Intravenous Propofol . As soon as the patient lost verbal response, mask ventilation was checked and 0.1 mg/kg of IntravenousVecuronium bromide was given. Then the patient was given intravenous Lignocaine without preservative 1.5 mg/kg (2% solution) or intravenous Esmolol 1.0 mg/kg (diluted to 0.5% solution) as slow bolus injection according to the random group allocation. Meanwhile the patient was ventilated with 100% oxygen for 3 minutes after induction. Then laryngoscopy was performed with a Macintosh curved blade laryngoscope. Heart rate and Blood Pressure was noted during laryngoscopy(time T2). The patients were intubated with appropriate sized endotracheal tubes within 15 seconds of laryngoscopy. All the intubations were be done by the same person. Patients were then ventilated with 60% nitrous oxide in oxygen. Heart rate and Blood Pressure were noted at 1 minute, 3 minutes and 5 minutes after laryngoscopy(time points T3 ,T4 ,T5). During these 8 minutes of monitoring, patients were not manipulated or subjected to any surgical stimulation, analgesics or inhalational agents. IPPV was continued throughout the surgery. Anesthesia was maintained with maintainence doses of Vecuronium bromide, Sevoflurane and analgesics as needed. Heart rate and blood pressure were recorded every 10 minutes. At the end of surgery patients were reversed with 0.05 mg/kg of Neostigmine and 10mcg/kg of Glycopyrrolate. Patient were extubated , adequate recovery ensured and patients transferred to the recovery room. The primary objective of the study was to find out the effectiveness of esmolol and lignocaine in prevention of rise in Blood Pressure and Heart Rate due to laryngoscopy and intubation . The data collected was transformed into a master sheet one for each group. In order to compare the data and to draw conclusions the mean and standard deviation of heart rate, systolic BP, diastolic BP and MAP were calculated. The effect of the drugs were compared by considering the above pressor response variables. Statistical analysis was done by Student's t test for quantitative data and Chi Square test and Fischer's exact test for qualitative data. Results on continuous measurements are presented as mean ± SD and results on categorical measurements are presented in number (%). Significance was assessed at 5 % level of significance.

RESULTS:

The groups were comparable based on their age. gender. weight ASA grading MP grading .

The heart rate , systolic blood pressure ,diastolic blood pressure and mean arterial pressure of patients in both groups were recorded on entering the operating room(Baseline), just before induction,during laryngoscopy and intubation and at 1 min ,3 min and 5 min after laryngoscopy and compared between the two groups.

At base line and just before induction the mean heart rate , systolic blood pressure ,diastolic blood pressure and mean arterial pressure does not differ between groups ($p>0.05$).

At all the other stages the HR is significantly less ($p<0.01$) among patients in the Esmolol group as compared to Lignocaine group.

The mean heart rate in the Esmolol group showed a decline from the baseline value at all time points from the time of laryngoscopy and intubation till 5 min after laryngoscopy while in the Lignocaine group, it had increased above the baseline value, at all time points from the time of laryngoscopy and intubation, except at 5 min after laryngoscopy.
At the time of laryngoscopy and intubation, the heart rate had increased considerably in the Lignocaine group and attained a mean level of 93.3/ min. At the same time , in the Esmolol group the heart rate was lower, with a mean level of 78.3/ min.

At the time of laryngoscopy and intubation, the difference in the heart rate was extremely significant statistically ($P<0.001$) which suggests that Esmolol is better than Lignocaine in controlling the heart rate response to laryngoscopy and intubation.

At the time of laryngoscopy and intubation, the mean systolic blood pressure in the Lignocaine group was 124.3 mm Hg. At the same time , in the Esmolol group the systolic blood pressure was lower, with a mean level of 120.5 mm Hg. The difference in the systolic blood pressure was significant statistically ($P<0.05$) which suggests that Esmolol is better than Lignocaine in controlling the systolic blood pressure response to laryngoscopy and intubation.

A constant reduction in systolic blood pressure was noted during 1 min, 3 min, and 5 min after laryngoscopy in the Esmolol group as well as in the Lignocaine group. The mean systolic blood pressure was only 119.1,117.6 and 116.1 mm Hg in the Esmolol group where as it was 122.8, 121.1 and 119.6 mm Hg in the Lignocaine group at 1 min, 3 min, and 5 min after laryngoscopy respectively. The difference in the mean systolic blood pressure was significant statistically ($P<0.05$) at all these time points.

At the time of laryngoscopy and intubation, the mean diastolic blood pressure in the Lignocaine group was 84.9 mm Hg. At the same time , in the Esmolol group the mean diastolic blood pressure was lower, with a mean level of 82.3 mm Hg. The difference in the diastolic blood pressure was significant statistically ($P<0.05$) which suggests that Esmolol is better than Lignocaine in controlling the systolic blood pressure response to laryngoscopy and intubation.

A constant reduction in diastolic blood pressure was noted during 1 min, 3 min, and 5 min after laryngoscopy in the Esmolol group as well as in the Lignocaine group. The mean diastolic blood pressure was only 80.9,79.9 and 78.9 mm Hg in the Esmolol group where as it was 83.5,82.4 and 81.5 mm Hg in the Lignocaine group at 1 min, 3 min, and 5 min after laryngoscopy respectively. The difference in the mean diastolic blood pressure was significant statistically ($P<0.05$) at all these time points.

At the time of laryngoscopy and intubation, the mean MAP (mean arterial pressure) in the Lignocaine group was 98.0 mm Hg. At the same time , in the Esmolol group the mean MAP (mean arterial pressure) was lower, with a mean level of 95.0 mm Hg. The difference in the mean MAP (mean arterial pressure) was significant statistically ($P<0.05$) which suggests that Esmolol is better than Lignocaine in controlling the MAP (mean arterial pressure) response to laryngoscopy and intubation.

A constant reduction in MAP (mean arterial pressure) was noted during 1 min, 3 min, and 5 min after laryngoscopy in the Esmolol group as well as in the Lignocaine group. The mean MAP (mean arterial pressure) was only 93.7,92.5 and 91.3 mm Hg in the Esmolol group where as it was 96.6,95.3 and 94.2 mm Hg in the Lignocaine group at 1 min, 3 min, and 5 min after laryngoscopy respectively. The difference in the mean MAP (mean arterial pressure) was significant statistically ($P<0.05$) at all these time points.

The systolic blood pressure ,diastolic blood pressure and mean arterial pressure are also significantly less ($p<0.05$) among patients in the Esmolol group as compared to Lignocaine group during laryngoscopy and intubation and at 1 min, 3 min and 5 min after laryngoscopy.

HEART RATE

Mean, standard deviation and level of significance of heart rate in Lignocaine and Esmolol group according to time of assessment.

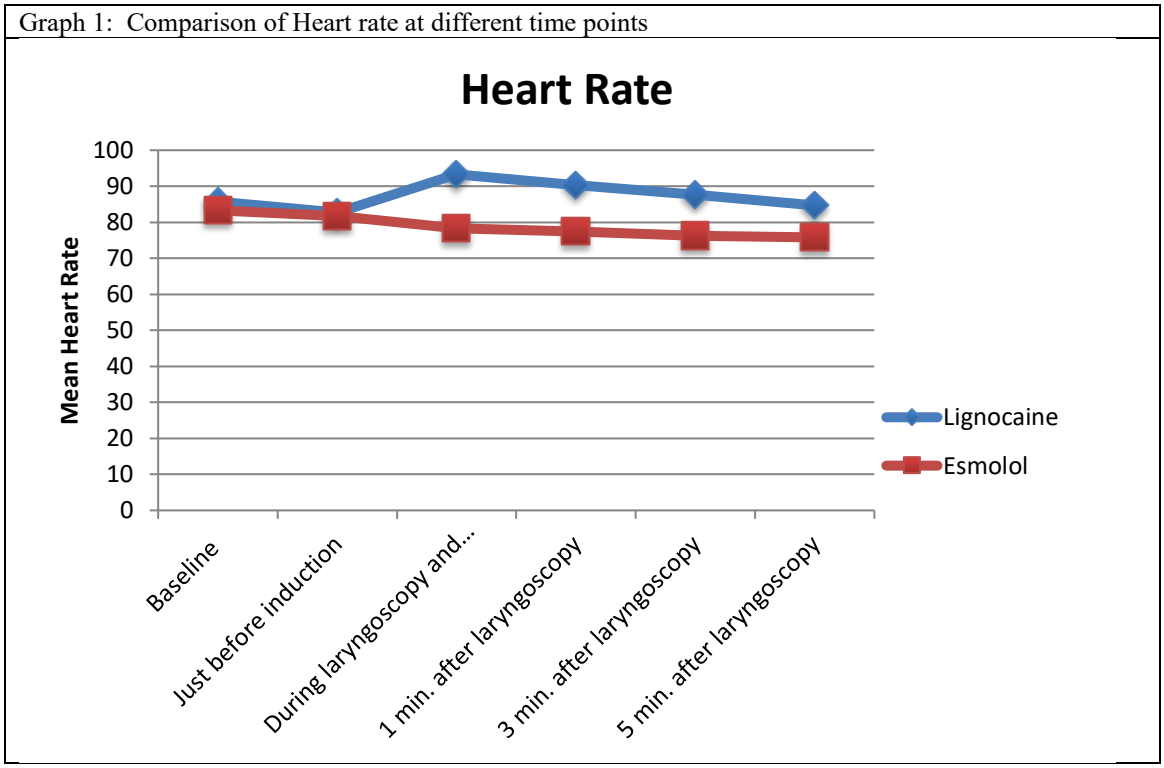
Table 1: Comparison of Heart rate at different time points

	Lignocaine			Esmolol			t	p
	Mean	SD	N	Mean	SD	N		
Baseline	85.7	5.8	30	83.3	5.8	30	1.56	0.124

Just before induction	82.7	5.9	30	81.7	5.9	30	0.63	0.532
During laryngoscopy and intubation	93.3	4.8	30	78.3	4.8	30	13.22***	0.000
1 min. after laryngoscopy	90.3	4.8	30	77.4	4.8	30	11.37***	0.000
3 min. after laryngoscopy	87.7	4.1	30	76.2	4.1	30	10.30***	0.000
5 min. after laryngoscopy	84.7	4.6	30	75.8	4.6	30	7.50***	0.000

***: - Significant at 0.001 level

Graph 1: Comparison of Heart rate at different time points



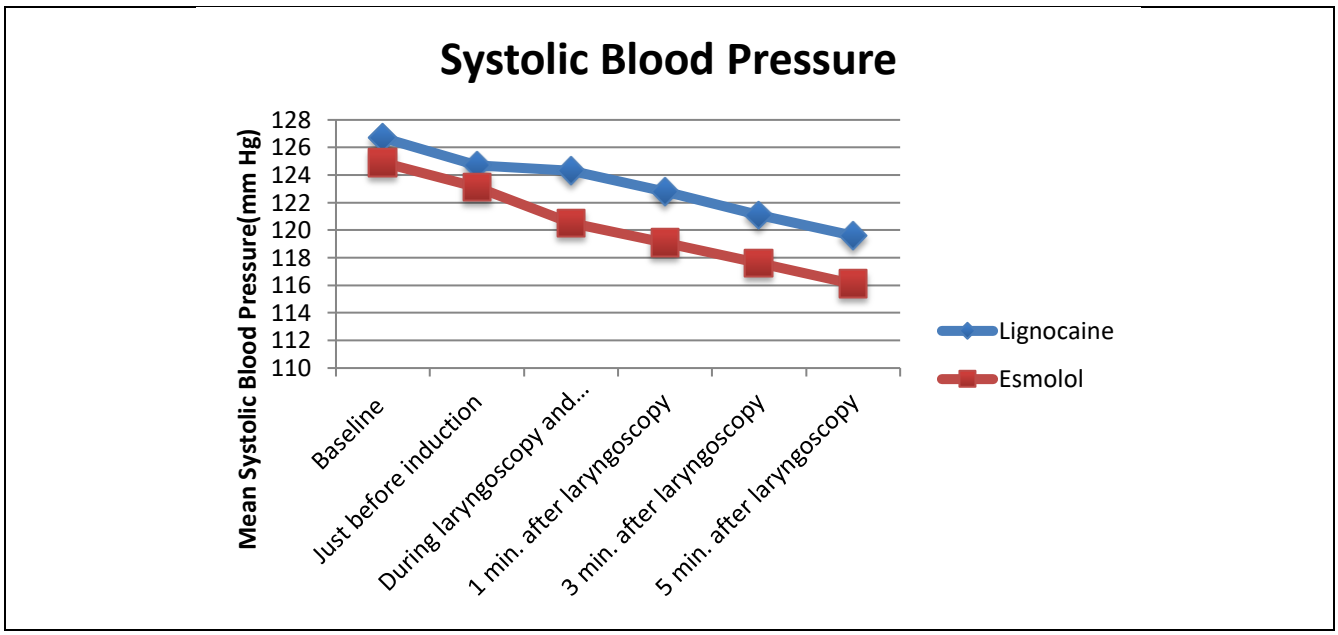
SYSTOLIC BLOOD PRESSURE

Mean, standard deviation and level of significance of systolic blood pressurein Lignocaine and Esmolol group according to time of assessment.

Table 2: Comparison of Systolic Blood Pressure at different time points

	Lignocaine			Esmolol			t	p
	Mean	SD	N	Mean	SD	N		
Baseline	126.7	7.8	30	124.9	10.1	30	0.77	0.442
Just before induction	124.7	8.0	30	123.1	10.6	30	0.68	0.496
During laryngoscopy and intubation	124.3	7.0	30	120.5	6.3	30	2.2*	0.031
1 min. after laryngoscopy	122.8	7.2	30	119.1	6.1	30	2.13*	0.037
3 min. after laryngoscopy	121.1	7.2	30	117.6	4.7	30	2.25*	0.028
5 min. after laryngoscopy	119.6	6.8	30	116.1	5.5	30	2.17*	0.034

*: - Significant at 0.05 level



Graph 2: Comparison of Systolic Blood Pressure at different time points

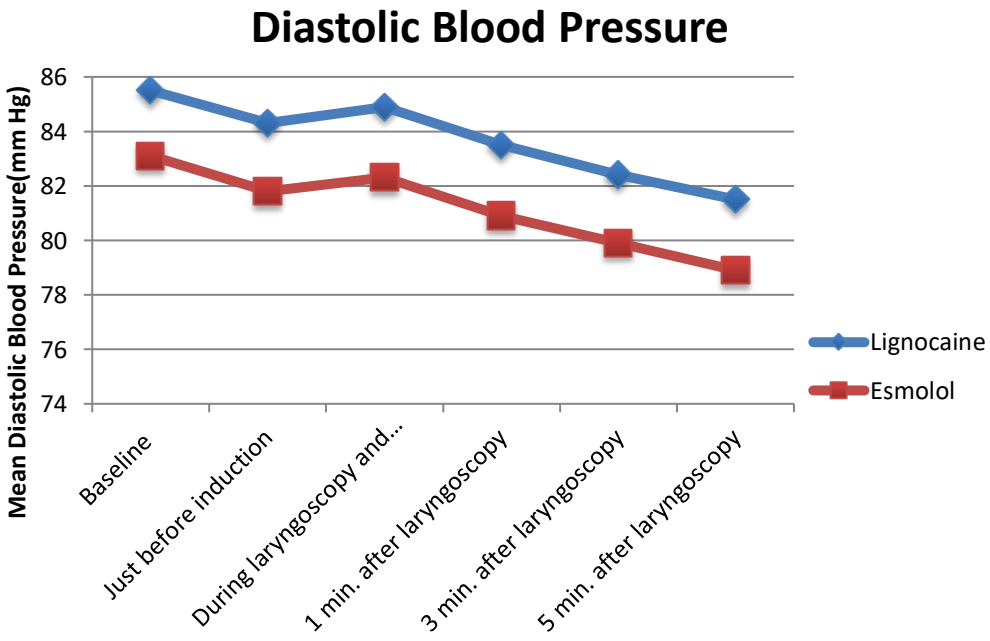
DIASTOLIC BLOOD PRESSURE

Mean, standard deviation and level of significance of diastolic blood pressurein Lignocaine and Esmolol group according to time of assessment.

Table 3: Comparison of Diastolic Blood Pressure at different time points

	Lignocaine			Esmolol			t	p
	Mean	SD	N	Mean	SD	N		
Baseline	85.5	4.5	30	83.1	6.3	30	1.7	0.094
Just before induction	84.3	4.3	30	81.8	6.1	30	1.86	0.068
During laryngoscopy and intubation	84.9	4.9	30	82.3	4.5	30	2.08*	0.042
1 min. after laryngoscopy	83.5	4.4	30	80.9	4.6	30	2.19*	0.033
3 min. after laryngoscopy	82.4	4.4	30	79.9	4.5	30	2.14*	0.037
5 min. after laryngoscopy	81.5	4.3	30	78.9	4.9	30	2.13*	0.037

*: - Significant at 0.05 level



Graph 3: Comparison of Diastolic Blood Pressure at different time points

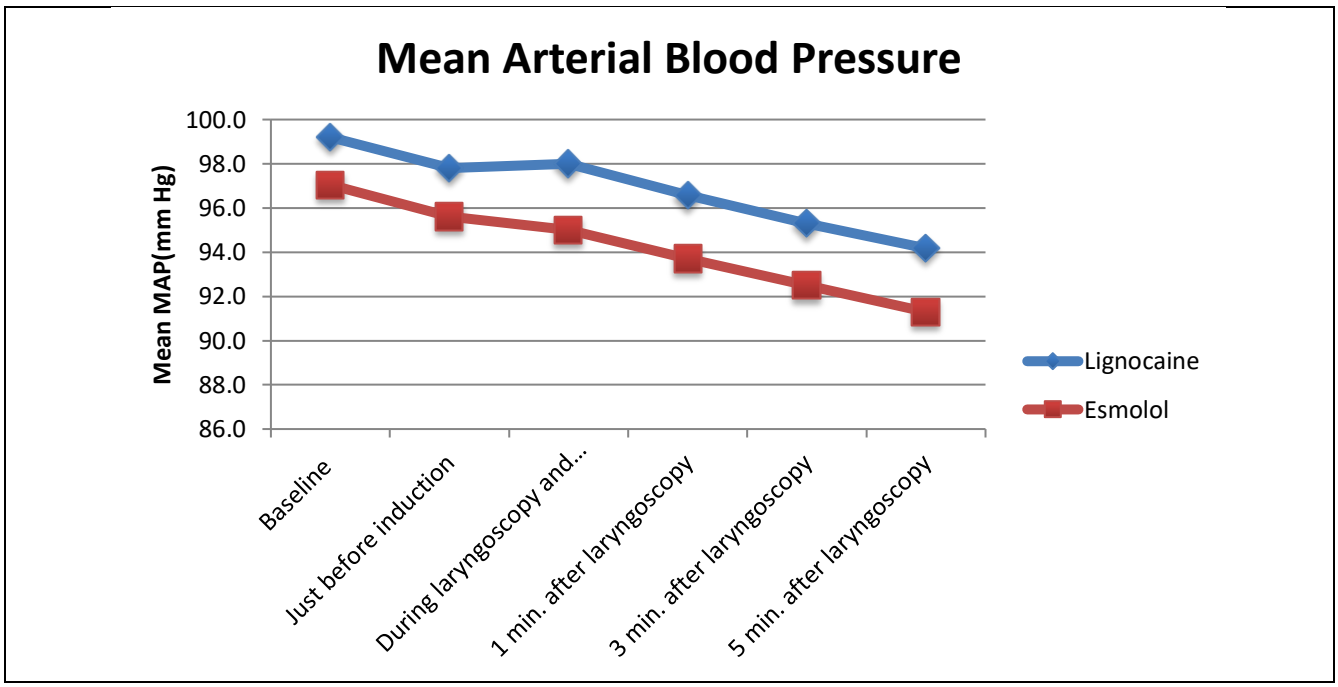
MEAN ARTERIAL PRESSURE

Mean, standard deviation and level of significance of mean arterial pressurein Lignocaine and Esmolol group according to time of assessment.

Table 4: Comparison of Mean Arterial Blood Pressure at different time points

	Lignocaine			Esmolol			t	p
	Mean	SD	N	Mean	SD	N		
Baseline	99.2	5.3	30	97.0	7.3	30	1.34	0.185
Just before induction	97.8	5.3	30	95.6	7.4	30	1.36	0.180
During laryngoscopy and intubation	98.0	5.3	30	95.0	4.2	30	2.38*	0.021
1 min. after laryngoscopy	96.6	4.9	30	93.7	4.6	30	2.37*	0.021
3 min. after laryngoscopy	95.3	5.1	30	92.5	4.0	30	2.4*	0.020
5 min. after laryngoscopy	94.2	4.7	30	91.3	4.4	30	2.42*	0.019

*: - Significant at 0.05 level



Graph 4: Comparison of Mean Arterial Blood Pressure at different time points

DISCUSSION:

The present study was designed to compare the effectiveness of Esmolol at a low dose of 1 mg/kg with Lignocaine 1.5 mg/kg in attenuating the stress response to laryngoscopy and intubation in normal healthy patients of ASA grade I and II,of either sex in the age group of 18-60 years for elective non-cardiac surgery requiring general anesthesia.

This was done by noting the pressor response variables namely Heart Rate, Systolic Blood pressure , Diastolic Blood pressure and Mean Arterial Pressure. The trends of these parameters were noted at frequent intervals in the first 8 minutes after induction of anesthesia.

60 patients were included in the study and all of them were pre medicated with intravenous Midazolam 1 mg before induction for anxiolysis. Priming dose of Vecuronium 0.01 mg/kg was given intravenously . All patients were induced with 2 mg/kg of Intravenous Propofol . The non depolarizingmuscle relaxant used to facilitate laryngoscopy and intubation was 0.1 mg/kg of Intravenous Vecuronium bromide as it is cardio-stable. Patients in the Lignocaine group received intravenous Lignocaine without preservative 1.5 mg/kg (2% solution) and patients in the Esmolol group received intravenous Esmolol 1.0 mg/kg (diluted to 0.5% solution) as slow bolus injection . The patients were ventilated with 100% oxygen for 3 minutes after induction.

The anesthetic technique was the same in all the cases, and the laryngoscopy and intubation was done by the same person. In all the cases, the recording of Heart Rate, Systolic Blood Pressure and Diastolic Blood Pressure was done on entering the operating room, just before induction, during laryngoscopy and intubation ,1 min after laryngoscopy, 3 min after laryngoscopy and 5 min after laryngoscopy.

The mean values of Heart Rate, Systolic Blood Pressure, Diastolic Blood Pressure and Mean Arterial Pressure recorded on entering the operating room(Baseline) and just before induction showed no statistical difference between the two groups. So, before the intervention (intravenous Lignocaine without preservative 1.5 mg/kg or intravenous Esmolol 1.0 mg/kg according to random group allocation), there was no statistical difference between the pressor response variables of the two groups.

There were no occurrences of arrhythmias during the 8 minutes of monitoring and the intraoperative period and recovery were uneventful for all the patients included in the study.

The mean heart rate in the Esmolol group showed a decline from the baseline value at all time points from the time of laryngoscopy and intubation till 5 min after laryngoscopy while in the Lignocaine group, it had increased above the baseline value, at all time points from the time of laryngoscopy and intubation, except at 5 min after laryngoscopy. Maximum rise in heart rate was observed during laryngoscopy and intubation in the Lignocaine group.

Compared with the Lignocaine group the attenuation of the heart rate response to the stress of intubation was better in the Esmolol group. The difference in the mean heart rate between the two groups was significant statistically ($P<0.001$) at all time points from the time of laryngoscopy and intubation till 5 min after laryngoscopy ,which suggests that Esmolol is better than Lignocaine in controlling the heart rate response to laryngoscopy and intubation.

This inference proved to be consistent with the studies of Helfman SM et al[13] , Feng CK et al [14] , Singh H, Vichitvejpaisal P et al [12] , Ugur et al [15] , Agrawal et al [16], Gupta A et al [17] and Saravanan D et al [18.] The mean systolic blood pressure in the Esmolol group and the Lignocaine group showed a decline from the baseline value at all time points from the time of laryngoscopy and intubation till 5 min after laryngoscopy.

Compared with the Lignocaine group the attenuation of the systolic blood pressure response to the stress of intubation was better in the Esmolol group. The difference in the mean systolic blood pressure between the two groups was significant statistically ($P<0.05$) at all time points from the time of laryngoscopy and intubation till 5 min after laryngoscopy ,which suggests that Esmolol is better than Lignocaine in controlling the systolic blood pressure response to laryngoscopy and intubation.

This inference proved to be consistent with the studies of Feng CK et al [14] , Ugur et al [15] , Agrawal et al [16], Gupta A et al [17] and Saravanan D et al [18].

The mean diastolic blood pressure in the Esmolol group and the Lignocaine group showed a decline from the baseline value at all time points from the time of laryngoscopy and intubation till 5 min after laryngoscopy.

Compared with the Lignocaine group the attenuation of the diastolic blood pressure response to the stress of intubation was better in the Esmolol group. The difference in the mean diastolic blood pressure between the two groups was significant statistically ($P<0.05$) at all time points from the time of laryngoscopy and intubation till 5 min after laryngoscopy ,which suggests that Esmolol is better than Lignocaine in controlling the diastolic blood pressure response to laryngoscopy and intubation.

This inference proved to be consistent with the studies of Agrawal et al [16], Gupta A et al [17] and Saravanan D et al [18]. The mean MAP (mean arterial pressure) in the Esmolol group and the Lignocaine group showed a decline from the baseline value at all time points from the time of laryngoscopy and intubation till 5 min after laryngoscopy.

Compared with the Lignocaine group the attenuation of the MAP (mean arterial pressure) response to the stress of intubation was better in the Esmolol group. The difference in the mean MAP (mean arterial pressure) between the two groups was significant statistically ($P<0.05$) at all time points from the time of laryngoscopy and intubation till 5 min after laryngoscopy , which suggests that Esmolol is better than Lignocaine in controlling the MAP (mean arterial pressure) response to laryngoscopy and intubation.

This inference proved to be consistent with the studies of Agrawal et al [16,] Gupta A et al 17 and Saravanan D et al 18.
Various drugs have been evaluated in the past for their effect on attenuation of pressor response. Larger doses of narcotics lead to post operative respiratory depression. Vasodilators may produce hypotension, and conventional beta blockers have their own intrinsic disadvantages.Esmolol at a dose of 200 mgtends to produce undue bradycardia and hypotension. In our study , we have used 1 mg/kg of Esmolol, the ultra short acting β-blocker and observed better stress response attenuation than Lignocaine 1.5 mg/kg. There was no hemodynamic instability or arrhythmias seen with this dose of Esmolol.

CONCLUSIONS

- Esmolol at a lower dose of 1 mg/kg is found to be more effective than Lignocaine 1.5 mg/kg in controlling the increase in heart rate in response to laryngoscopy and intubation. This difference was found to be significant statistically($P < 0.001$).
- Esmolol at a lower dose of 1 mg/kg is found to be more effective than Lignocaine 1.5 mg/kgin controlling the increase in systolic blood pressure, diastolic blood pressure and mean arterial pressure in response to laryngoscopy and intubation. This difference was found to be significant statistically($P<0.05$).
- Esmolol 1 mg/kg is found to be safe and effective in controlling the pressor response to laryngoscopy and intubation.

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