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Original Article

Comparison of Lignocaine and Esmolol in attenuating cardiovascular response to laryngoscopy and endotracheal intubation.

Anil Shrestha,* Subhash Prasad Acharya,** Roshna Amatya**

****Patan Academy of Health Sciences, Lalitpur, Nepal.***

*****Tribhuvan University Teaching Hospital, Institute of Medicine, Maharajgunj, Kathmandu, Nepal.***

ABSTRACT

Background: Laryngoscopy and tracheal intubation induces cardiovascular stress response characterized by tachycardia and hypertension, which are well tolerated in normotensive individuals but are of greater significance in patients with cardiovascular and cerebrovascular disorders. The quest for an effective suppression of these responses continues.

Materials and Methods: A randomized, prospective, double blind, placebo controlled study was conducted in which the efficacy of Lignocaine 1.5 mg/kg and Esmolol 1.5 mg/kg were compared in attenuating the cardiovascular response to laryngoscopy and tracheal intubation in sixty patients undergoing elective surgery under general endotracheal anaesthesia. Patients were divided into three groups receiving Lignocaine, Esmolol or Normal saline (control). Anaesthesia was induced with intravenous Thiopental Sodium 5 mg/kg and intubation was facilitated with Vecuronium 0.12 mg/kg after administering the study drug. Blood pressure and heart rate were compared among the three groups.

Results: The increase in Systolic blood pressure was not significant, but Diastolic and Mean Arterial Pressures increased significantly in control group whereas it was attenuated more effectively in Esmolol group ($p<0.05$) compared to lignocaine group. The increase in HR was significantly lower ($p<0.05$) in Esmolol group compared with lignocaine and control group.

Conclusion: Esmolol is more effective than lignocaine in attenuating cardiovascular response to laryngoscopy and tracheal intubation.

Keywords Cardiovascular physiology, Endotracheal intubation, Esmolol, Hemodynamics, Lignocaine.

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Introduction

It has been established reasonably well that laryngoscopy and tracheal intubation manoeuvres induce marked increases in heart rate and blood pressure, which in combination, results in an increase in myocardial oxygen demand.[1] These circulatory changes may be especially harmful in patients with cardiovascular or cerebrovascular

Corresponding Author
Anil Shrestha, MD
Lecturer, Patan Academy of Health Sciences, Lalitpur, Nepal.
Email: shresanil@gmail.com
Phone: +977-9841259420

disease because of the associated risk of myocardial ischemia, arrhythmias and, even, infarction and cerebral hemorrhage.[2] Lignocaine is commonly used for attenuation of haemodynamic response to laryngoscopy and intubation as it is devoid of cardiovascular effects except when used in larger doses. Among the β-adrenergic antagonists, Esmolol has shown to be an attractive option because of its β_1 (cardio-selective) adrenergic receptor blocking properties and its ultra-short duration of action.[3] Therefore, this study was done to compare the efficacy of intravenous lignocaine and Esmolol in attenuating the acute haemodynamic response to laryngoscopy and tracheal intubation.

Materials and methods

After approval from Department of Anaesthesiology, and Research Department, the study was conducted over a period of four months. Patients scheduled for elective surgery requiring general anaesthesia with endotracheal intubation were admitted to hospital a day or two before the operation date. Preanaesthetic assessment and investigations were done. Patients between 18 and 65 years of age, with ASA physical status I & II were included in the study. Patients were then randomly divided into three groups by sealed envelope method. Each group contained 20 patients. Patients with ASA physical status III or more, with preexisting cardiopulmonary diseases like hypertension, asthma, Chronic obstructive pulmonary disease (COPD); with sinus bradycardia, heart block greater than first degree, overt heart failure, cardiogenic shock; on anti hypertensive drugs; pregnant patients; patient with anticipated difficult intubation, encountered difficult ventilation and/ or difficult intubation after induction, and those patients who refused to consent were excluded. Also, patient weighing 70kgs or more, with contraindication to study drugs, with known hypersensitivity to the study drugs, and those patients undergoing nasopharyngeal, oropharyngeal & laryngeal surgeries were excluded from the study.

All the patients received premedication with Diazepam 0.1mg/kg per orally at 10 pm the night before and repeated two hours before the predicted time of surgery. On arrival to the preanaesthesia preparation room, vein was cannulated with 18G cannula and Ringer lactate started at 15 ml/hr. The patients were then shifted to operating room and monitors were attached which included automated noninvasive BP, pulse oximeter, ECG and capnography. Baseline heart rate, systolic blood pressure, diastolic blood pressure and mean arterial pressure were noted. Intravenous (IV) Pethidine 0.75mg/kg was given for analgesia and anaesthesia was induced with 5 mg/kg Thiopental sodium IV given over 30 seconds, effects confirmed by loss of eyelash reflexes. Then manual ventilation was checked and if adequate, Vecuronium 0.12 mg/kg IV was given for muscle relaxation. The patients were then ventilated by mask with 100% oxygen and anaesthesia was maintained with Halothane 1% & Oxygen. Blood pressure and heart rate were measured again. After injecting Vecuronium, the study drug was administered. Group L received lignocaine 1.5mg/kg as an IV bolus diluted to total volume of 10 ml with normal saline; Group E received Esmolol 1.5mg/kg as an IV bolus diluted to total volume of 10 ml with normal saline and Group N received normal saline 10ml IV bolus as placebo. The study drugs were prepared and administered by the anaesthesia assistants who were not involved in the study. The observer was unaware of the drugs administered. Exactly three minutes after the administration of the study drug, direct laryngoscopy using a standard Macintosh laryngoscope was attempted. Trachea was then intubated with cuffed endotracheal tube. The duration of laryngoscopy was noted. The same anesthesiologist performed all the intubations. Following confirmation of endotracheal intubation, by auscultation and capnography, the tube was connected to the breathing circuit and ventilation maintained with mechanical ventilator. The immediate time after intubation was considered as 0min. Systolic blood pressure (SBP), diastolic blood pressure (DBP), mean arterial pressure (MAP) and heart rate (HR) were noted at 0min, 1min, 2min, and 5min after which only the surgical incision was allowed. The rise in blood pressure or heart rate by more than 20% of baseline value was considered significant. The heart rate below 50 beats per min was treated with IV atropine 0.3mg and fall in systolic blood pressure 20% below the baseline was treated with IV Mephentermine 6mg bolus. If the blood pressure and heart rate was >20% of the baseline, halothane was increased to 2% or 2.5% till the blood pressure was controlled. Any ventricular ectopic beats were treated with IV lignocaine 1mg/kg. At the end of the surgery, muscle relaxation was reversed with IV Neostigmine 0.05 mg/kg and IV Atropine 0.02 mg/kg and trachea was extubated. Patients were observed for few minutes in the operating room and then shifted to post anesthesia care unit where they were observed till patient met the recovery room discharge criteria. They were then shifted to post operative room. All the data were recorded in and were presented in the form of mean +/- standard deviation. p-value less than 0.05 were taken as significant.

Results

The three groups were comparable in age, weight and sex and also in baseline SBP, DBP, MAP and HR. (P>0.05) (Table 1).

Table1: Baseline characteristics of the patients shown as mean (SD)

	Lignocaine (n=20)	**Esmolol (n=20)**	**Normal Saline (n=20)**	**Total (n=60)**	**p-value**
Female	14(70.0)	10(50.0)	18(90.0)	42(70.0)	0.22
Male	6(30.0)	10(50.0)	2(10.0)	18(30.0)	
Age (yrs)	36.45(11.26)	37.7(10.73)	36.10(11.92)	36.75(11.14)	0.896
Weight (kgs)	56.00(6.13)	55.35(7.88)	54.60(7.58)	55.31(7.14)	0.830
Baseline SBP (mmHg)	124.9(11.04)	125.70(8.27)	123.20(9.11)	124.60(9.44)	0.701
Baseline DBP (mmHg)	80.05(9.98)	81.95(8.05)	76.55(9.14)	79.52(9.22)	0.172
Baseline MAP (mmHg)	94.50(9.15)	97.35(9.05)	92.45(9.32)	94.77(9.24)	0.246
Baseline HR (bpm)	84.20(17.47)	77.10(14.77)	82.65(11.23)	82.32(14.79)	0.284

In response to laryngoscopy and endotracheal intubation, SBP, DBP and MAP significantly increased in the control group (Group N) by more than 20%. But in the lignocaine group (Group L), these responses were attenuated. All the parameters were increased but by less than 20%. Also, in the Esmolol group (Group E), these responses were attenuated. All the parameters were increased but by less than 20%.

While comparing the change in Group L and Group E, it was seen that there were significant difference between the two groups in DBP and MAP but there was no significant change in SBP (Table 2).

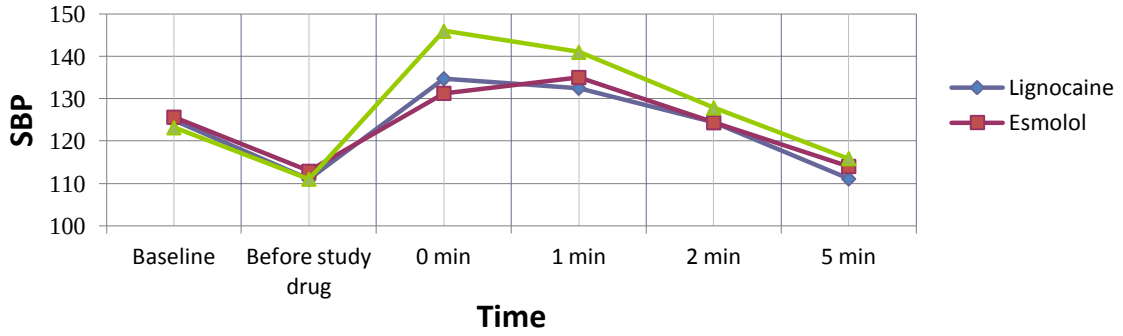
Table 2: Change of SBP, DBP and MAP before and after tracheal intubation: mean (SD)

	Lignocaine				**Esmolol**				**p-value**
	Before	**After**	**Change**	**p-value**	**Before**	**After**	**Change**	**p-value**	
SBP (mmHg)	124.90 (11.04)	134.80 (21.12)	9.90	0.797	125.70 (8.27)	131.35 (17.19)	5.65	0.574	0.464
DBP (mmHg)	80.05 (9.98)	95.00 (16.55)	14.95	0.512	81.95 (8.05)	96.20 (15.58)	14.25	0.815	**0.028**
MAP (mmHg)	94.50 (9.15)	111.60 (18.36)	17.1	0.328	97.35 (9.05)	111.65 (16.56)	14.30	0.993	**0.013**

During the study, it was also observed that the SBP decreased from baseline values before study drug but it increased to the highest degree just after intubation in Group L & Group N while in Group E it was highest 1 minute

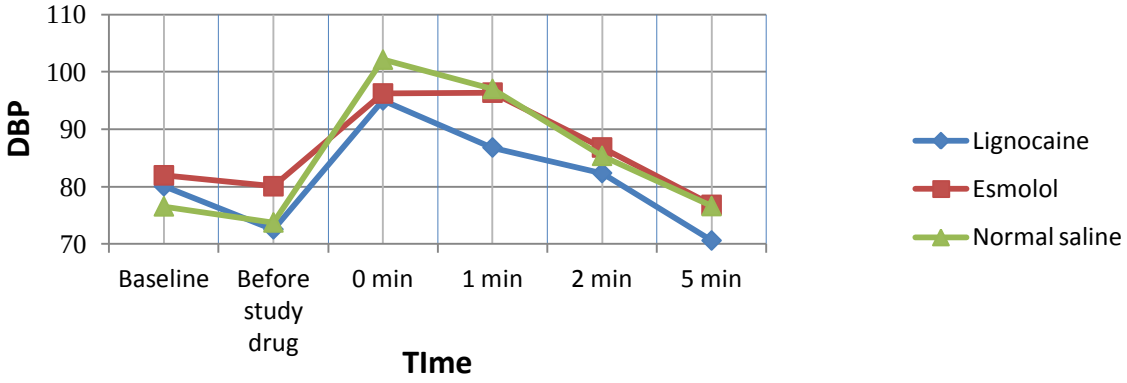
after intubation. The SBP remained above the baseline till 1min in Group L & Group N (Figure 1). These observations of SBP were near about baseline after 2 min and below the baseline after 5 min. This was similar for all the three groups.

Figure 1: Change of Systolic Blood Pressure



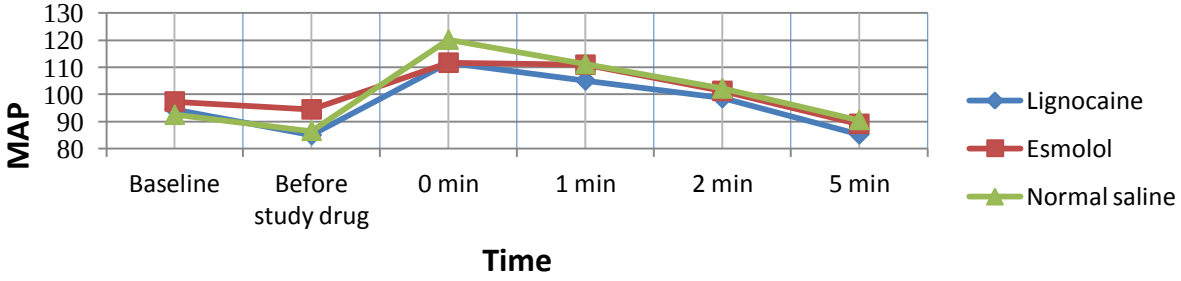
Similarly, the DBP also decreased from baseline values before study drug but it increased to the highest degree just after endotracheal intubation in all the three groups. It remained above the baseline till 1minute in all the three groups (Figure 2). The DBP then further decreased to near about baseline at 2 min and below baseline values 5 min after intubation. This was similar for all three groups.

Figure 2: Change of Diastolic Blood Pressure



Similarly, the comparison of MAP shows that it decreased below baseline values before study drug but increased to the highest degree just after intubation in all the three groups. It declined at 1& 2 min and was below baseline values after 5 min. (Figure 3)

Figure 3: Change of Mean Arterial Pressure



Considering change in HR in response to laryngoscopy, HR increase was not significant only in Group E. (Table 3). In fact, there was decrease in HR by 0.97%. Esmolol attenuated the tachycardic response to laryngoscopy and

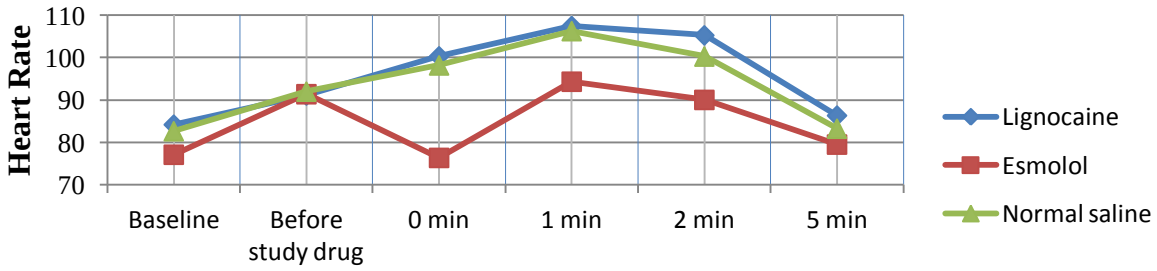
intubation. This change in HR was significantly different from the control group (P<0.05) When Group L and E were compared for the change in heart rate, there was significant difference (P<0.05). Thus, Esmolol was found to be efficient in attenuation of heart rate response to laryngoscopy and intubation compared to lignocaine.

Table 3: Change in mean (SD) of Heart Rate (beats/minute) before and after intubation.

	Lignocaine	Esmolol	Normal Saline
Before	84.20(17.47)	77.10(14.77)	82.65(11.23)
After	100.35(23.04)	76.35(9.72)	98.20(13.85)
Change	16.15(23.03)	- 0.75(18.94)	15.55(19.54)
Percentage change	19.18%	- 0.97%	18.81%
p value	0.284	<0.001	> 0.5

It was also observed that heart rate increased just after intubation in Group L & Group N while it was near baseline in Group E. It increased to the maximum at 1 minute and returned to the baseline at 5 minutes (Fig 4).

Figure 4: Change of heart rate



During the study period, hypotension was observed in 2 patients 10 minutes after laryngoscopy in one patient and after 14 minutes in another patient. Retrospectively, both patients were in Group E and had received Esmolol. They were treated with IV Mephentermine 6mg single bolus and BP became normal. In one patient, bradycardia occurred 20 minutes after the intubation and retrospectively belonged to Group N who received normal saline. The patient was treated with IV Atropine 0.6 mg. There were no other complications noted during the entire study period.

Discussion

Laryngoscopy and tracheal intubation are stressful stimuli resulting in increased blood catecholamine levels; attenuating sympathetically mediated hyperdynamic responses to stimulation. The degree of reflex response to laryngeal stimulation appears to vary with depth of anaesthesia, duration of laryngoscopy, difficulties encountered during laryngoscopy and tracheal intubation as well as patient dependent variables including age, cardiovascular or endocrine disease. The devices used for airway management can also affect the response. Hypertensive patients whether treated or not are prone to much greater changes in arterial pressure than normotensive patients of the same age.[4] Thus the quest for an effective blockade of these responses continues and different drugs has been used that includes opioids, local anesthetics administered either topically or intravenously, α or β-adrenergic blocking drugs, angiotensin converting enzyme inhibitors, clonidine, vasodilating drugs such as sodium nitroprusside, prostaglandin E_1, calcium channel blocking drugs, nitroglycerine and magnesium sulphate. Short acting opioids appear to have a reliable and constant effect but they may contribute to truncal rigidity and prolong recovery time from general anaesthesia in addition to respiratory depression. Clonidine has also been tried for the

purpose. It blunts the increase in heart rate, but does not have any effect on the blood pressure response to laryngoscopy and tracheal intubation.[5] Since tachycardia appears to be associated more frequently with myocardial ischemia than does hypertension[6], one approach towards is the use of β- adrenergic antagonists. However, excessive negative chronotopic and inotropic action of the β-receptor blockers may reduce coronary perfusion and precipitate heart failure in susceptible patients.[7] Calcium channel blockers have also been used but it has revealed to reduce afterload and may, therefore, be expected to influence hypertensive response rather than tachycardia after laryngoscopy and intubation. Myocardial depression and peripheral vasodilatation produced by volatile anaesthetics could be exaggerated by similar action of calcium channel blockers. Vasodilators oppose increased BP, but do not control HR or arrhythmias. Volatile anesthetics are useful for attenuating the activity of the sympathetic nervous system, which is responsible for pressure responses. Isoflurane, Sevoflurane and Desflurane produce dose dependent decrease in systemic blood pressure, reflecting decrease in systemic vascular resistance and to a lesser extent direct myocardial depression and decrease in cardiac output, however, when used as a sole agent; even at high concentration, isoflurane is unable to suppress the hemodynamic response to noxious stimuli. Glossopharyngeal and superior laryngeal nerve blocks may also be effective method to blunt adverse hemodynamic response. Similarly the evaluation of skin vasomotor reflex (SVmR) provided useful information for determining the optimal anaesthetic depth for laryngoscopy and intubation in the individual patients during which the stress to intubation was minimal.[8]

Because of all these above-mentioned disadvantages, lignocaine and Esmolol are the commonest drugs used to blunt haemodynamic response to laryngoscopy and intubation. The mechanism of action of lignocaine in attenuation of reflex haemodynamic response is due to direct cardiac depression and peripheral vasodilatation. Esmolol has a β_1 (cardioselective) adrenoceptor blocking property. Both these drugs have been studied in attenuating the response to intubation and have been compared among themselves with different doses and with other drugs.

Intravenous lignocaine has been studied repeatedly in terms of attenuating the rise in HR and BP in different doses ranging from 0.5mg/kg to 2 mg/kg and in different routes. Many of these results have revealed that lignocaine was not effective in attenuating the cardiovascular response to laryngoscopy[9], while other studies support the fact that this drug is effective for the same.[10] Abou-Madi et al found only borderline protection against hypertension and tachycardia following tracheal intubation when IV lignocaine 1.5 mg/kg was given 2 to 3 minutes before laryngoscopy.[11] Tam et al concluded that IV lignocaine 1.5 mg/kg had to be administered exactly 3 minutes before laryngoscopy to have significant attenuating effects on HR and SBP increases following intubation.[12] Wilson et al suggested that the time interval between administration of IV lignocaine 1.5mg/kg and laryngoscopy should be at least 4 minutes to achieve a complete attenuation of the pressure response, although in this study lignocaine failed to show any effect on HR increase.[13] Using the same dose of lignocaine, Stoelting also observed that in patients with no known heart disease only the SBP response was attenuated.[14] Esmolol is considered to have a significant effect in both tachycardiac and hypertensive reactions following intubation.[15]

In our study, all the three groups were comparable regarding their demographic data and baseline haemodynamic parameters. It was seen that SBP, DBP & MAP all decreased from baseline values before administration of study drug, this might have been contributed due to combined effect of sodium thiopentone & halothane. Just after the intubation SBP, DBP & MAP all increased in the placebo group, among which increase in DBP & MAP was significant as the values were >20% greater than the baseline values. This increase was attenuated in both Esmolol and lignocaine groups. However compared to control group the change was significant only in Esmolol group ($P<0.05$). Esmolol was found to be better than lignocaine in attenuating the pressure response to laryngoscopy and intubation but the difference in increase in SBP, DBP & MAP between the two groups was not significant. Harbhej Singh et al reported similar finding in their study.[16] Similarly, Esmolol significantly blunted the increase in heart rate after laryngoscopy and intubation whereas lignocaine was not effective. It is known that tachycardia may impose more stress in the heart than do increase in BP[17], perhaps due to the dual effect of tachycardia in increasing myocardial oxygen consumption while decreasing the diastolic filling and diminishing the time for effective coronary flow.[15] In this study, we focused only on haemodynamic changes before and after intubation. For details of the changes in haemodynamic variables, the influence of patient's characteristics, the effect of other drugs on the results, and the effects of different types of surgery further investigations are also required.

Conclusion

Both lignocaine and Esmolol attenuated the pressor response to laryngoscopy and intubation. However, Esmolol 1.5 mg/kg was found to be more effective than lignocaine 1.5 mg/kg in minimizing the increase in DBP & MAP. Lignocaine did not prevent the increase in heart rate associated with laryngoscopy and intubation. In contrast, Esmolol prevented increase in heart rate without any deleterious side effects.

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