Comparison of Efficacy of Esmolol and Labetalol in Preventing Laryngoscopy and Intubation Related Hemodynamic Response

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ABSTRACT

Introduction: Tracheal intubation is important and frequently performed procedure for anaesthesiologist. This study aimed to compare the effect of esmolol and labetalol in preventing hemodynamic response to laryngoscopy and intubation.

Materials and Methods: This is a prospective, randomized and double blind study. Eighty patients of either sex, aged between 18 to 60 years, American Society of Anesthesiologist (ASA) category I and II, scheduled for elective surgery requiring general anesthesia are included in the study. They were divided into two groups. Pre-oxygenation was done. Then the study drugs were given according to selected group according to lottery method. In esmolol group, esmolol 0.5mg/kg diluted with 10 ml of normal saline was given 2 minutes prior to intubation and in labetalol group, labetalol 0.1mg/kg diluted with 10 ml of normal saline was given 5 min prior to intubation. Anesthesia was induced with injection propofol. Laryngoscopy was done after giving injection vecuronium and intubated with appropriate sized cuffed tube. Heart rate, systolic blood pressure, diastolic blood pressure and mean arterial blood pressure were recorded at post induction, before intubation and immediately after intubation at 1, 3, and 5 minutes of tracheal intubation. Any surgical stimulation was avoided till 5 minutes.

Results: There was no significant difference between two groups regarding the demographic data. Heart Rate, Systolic Blood Pressure (SBP), Diastolic Blood Pressure (DBP) and Mean Arterial Pressure (MAP) at baseline, post induction and at 1 minute, 3 minutes and 5 minutes between two groups were not significant statistically.

Conclusion: This study concluded that the hemodynamic response to laryngoscopy and intubation using esmolol and labetalol are similar.

Keywords: esmolol, labetalol, intubation, hemodynamic response

INTRODUCTION

Laryngoscopy and endotracheal intubation have always been very important aspects in the field of anaesthesia. It has become an integral part in anesthetic management. It is a stressful procedure as tachycardia, bradycardia, hypertension, arrhythmia and increase in intracranial pressure due to symapathoadrenal response.[1] These haemodynamic changes are transient and without any grave consequences to healthy patient. However, in patients with preexisting coronary artery disease, hypertension and cerebrovascular disease, an increase in these parameters may precipitate myocardial ischaemia, arrhythmias, infarction, congestive heart failure, pulmonary edema and cerebral haemorrhage.[2] In susceptible individuals it's consequences may lead to increase in morbidity and mortality.

Laryngoscopy and tracheal intubation is associated with excess catecholamine in the form of increase epinephrine and norepinephrine which results in tachycardia and hypertension.[3] Circulatory responses to laryngeal and tracheal stimulation were known since 1940 (Reid and Brace).[4] The most common response to airway manipulation is hypertension and tachycardia due to widespread release of norepinephrine from adrenergic nerve terminals and secretion of epinephrine from the adrenal medulla.[5]

Different pharmacologic agents like lidocaine, opiods, beta-adrenergic blockers, calcium channel blockers, deep inhalational anaesthesia, magnesium, clonidine and vasodilators such as sodium nitroprusside can be administered prior to tracheal intubation in order to prevent hemodynamic responses to laryngoscopy to intubation. [6-13] Beta blockers have now gained popularity in blocking the pressure response to laryngocopy and intubation. Tachycardia to patient is more detrimental than increase blood pressure as it can lead to myocardial ischemia because of decrease in cardiac output. Among the beta blockers, esmolol, is commonly used in blunting this response as this drug is cardio-selective and its short duration of action. But labetalol has been tried and compared with esmolol in preventing the response as it has both the beta and alpha receptors blocking properties. Tachycardia and hypertension has been postulated more due to increased in cardiac output and less commonly due to increased in systemic vascular resistnace. Labetalol due to its both the beta and alpha receptor blocker properties can decrease cardiac output and systemic vascular resistance.

MATERIALS AND METHODS

This is a randomized, prospective, double blind comparative study done in Pokhara Academy of Health Sciences (PAHS), Western Regional Hospital, Pokhara during the period of 12 months from 1st July 2017 to 30th June 2018. Approval was taken from the Hospital Administration. Patients scheduled for elective surgery were recruited in this study and written informed consent was taken from the patients. The patients were pre-medicated with diazepam 5mg orally. Patients were kept nil per oral after midnight.

Standard monitors such as non-invasive blood pressure (NIBP), pulse-oximeter (SPO2) and electrocardiography were attached. Intravenous line was opened by 18 G canula. A base line value of systolic blood pressure, diastolic blood pressure, mean arterial pressure, heart rate, and SPO2 were recorded. Randomization was done by lottery method. Anaesthesia assistant not involved in the study prepared the drug in a syringe according to the group selected. They labeled the syringes as 2 min. and 5 min. accordingly as follows:

1. Group esmolol (n=40): Patients received esmolol 0.5mg/kg diluted with normal saline to 10ml was given 2 min prior to intubation

2. Group labetalol (n=40): Patients received labetalol 0.1mg/kg diluted with normal saline to 10ml was given 5 min prior to intubation

Primary investigator and the patient were blinded to the study drugs. Assessments of patients were done by primary investigator at all time period of the study.

Patients were premedicated with inj. midazolam 2 mg and inj. pethidine 0.5mg/kg. Pre-oxygenation was done with 100% Oxygen for 3 minutes. Then the study drugs were given. Then anesthesia was induced with inj.propofol in titrating dose sufficient to obtund eyelash reflex. Laryngoscopy was performed 3 min after administration of vecuroniun (0.1mg/kg) and trachea was intubated with proper sized cuffed tube and fixed after confirmation of proper position. Haemodynamic variables i.e. heart rate, systolic blood pressure, diastolic blood

pressure and mean arterial blood pressure were recorded immediately after intubation at 1, 3, and 5 minutes of tracheal intubation. During those five minutes all surgical stimulation were avoided. Maintenance of anesthesia was done with oxygen, isoflurane, intermittent positive pressure ventilation and vecuronium. Isoflurane was discontinued at the end of surgery and the patients were reversed with neostigmine 0.5mg/kg and glycopyrrolate 0.01mg/kg at the end of surgery. Extubation was done when the tidal volume was adequate and protective airway reflexes were intact.

Data entry and statistical analysis were performed using Microsoft Excel 2007 and SPSS 17. Numerical variables such as age, weight, heart rate, systolic blood pressure, diastolic blood pressure, and mean arterial pressure were compared by independent t–test. Categorical variables like gender, weight and ASA were compared by using chi square test. Paired t test was used for comparison of heart rate, systolic blood pressure, diastolic blood pressure and mean arterial pressure within a group at different time intervals. P value less than 0.05 was taken statistically significant.

RESULTS

A total number of 80 patients of ASA I and II were included in the study. Their mean age was 44.54 ± 13.03 years in group esmolol and 42.89 ± 11.67 yrs in group labetalol. In group esmolol, 21 males and 19 females were included and in group labetalol, 22 males and 18 females were included. The average weight was 60.46 ± 9.35 kg in group esmolol and 62.11 ± 7.14 kg in group labetalol. In group esmolol, there were 36 patients of ASA I and 4 patients of ASA II. In group labetalol, there were 38 patients of ASA I and 2 patient of ASA II. These demographic data are shown in Table 1.

Table 1: Demographic Data of the patients

Variable	Group Esmolol (N = 40)	Group Labetalol (N = 40)	Significance (p value)
Age in years	44.54 ± 13.03	42.89 ± 11.67	.428
Gender (Male/ Female)	21/19	22/18	.274
Weight	60.46 ± 9.35	62.11 ± 7.14	.774
ASA I/II	36/4	38/2	.561

In this study, pre-operative heart rate, systolic blood pressure, diastolic blood pressure and mean arterial blood pressure were measured and recorded. Baseline heart rate in group esmolol was 84.54 ± 15.03 bpm and in group labetalol was 84.79 ± 13.92 bpm. In group esmolol, baseline systolic blood pressure was 132.61 ± 27.19 mmHg and in group labetalol, it was 135.75 ± 16.47 mmHg. Baseline diastolic blood pressure in group esmolol was 81.96 ± 10.56 mmHg and 84.25 ± 11.34 mmHg in group labetalol. Baseline mean arterial pressure in group esmolol was 100.18 ± 9.66 mmHg and 99.96 ± 12.69 mmHg in group labetalol. Thus the two groups were comparable in their preoperative hemodynamics as shown in Table 2.

Table 2: Preoperative hemodynamic variables in two groups

Variables	Group Esmolol (n=40)	Group Labetalol (n=40)	Significance (p value)
Heart Rate (bpm)	84.54 ± 15.03	84.79 ± 13.92.	0.949
Systolic BP (mmHg)	132.61 ± 27.19	135.75±16.47	0.603
Diastolic BP (mmHg)	81.96 ± 10.56	84.25 ± 11.34	0.439
Mean arterial pressure (mmHg)	100.18 ± 9.66	99.96 ± 12.69	0.944

In group esmolol, systolic blood pressure at post induction was 112.21 ± 11.70 mmHg and in group labetalol, it was 112.79 ± 11.37 mmHg. Before intubation the systolic blood pressure were 107.71 ± 17.62 mmHg and 109.18 ± 17.13 mmHg in group esmolol and labetalol respectively. They were considered statistically not significant.

After 1 minute of intubation, systolic blood pressure in group esmolol it was 145.71 ± 18.85 mmHg and in group labetalol, it was 139.29 ± 17.62 mmHg. The systolic blood pressure after 3 minute in group esmolol, it was 127.11 ± 16.98 mmHg and in group labetalol, it was 120.46 ± 19.46 mmHg After 5 minutes of intubation, systolic blood pressure in group esmolol, it was 114.36 ± 16.80 mmHg and in group labetalol, it was 114.64 ± 18.37 mmHg. The change was statistically not significant in two groups. Comparison of systolic blood pressure

change between two groups shown in Table 3.

Table 3: Comparison of systolic blood pressure change between two groups

Time of Observation	Group Esmolol (n=40)	Group Labetalol (n=40)	Significance (p value)
Baseline	132.61 ± 27.19	135.75 ± 16.47	.603
Post Induction	112.21 ± 11.70	112.79 ± 11.37	.854
Before Intubation	107.71 ± 17.62	109.18 ± 17.13	.754
After Intubation 1 min	145.71 ± 18.85	139.29 ± 16.47	.193
After Intubation 3 min	127.11 ± 16.98	120.46 ± 19.46	.179
After Intubation 5 min	114.36 ± 16.80	114.69 ± 18.36	.952

Note: Values given as mean ± SD, values given in mmHg

Diastolic blood pressure in group esmolol was 74.29 ± 8.73 mmHg and in group labetalol was 75.29 ± 10.18 mmHg in post induction period. Before intubation the diastolic blood pressure was 70.36 ± 13.48 and 70.04 ± 10.64 mmHg in group esmolol and labetalol respectively. After 1 minute of intubation, diastolic blood pressure in group esmolol, it was 97.57 ± 12.47 mmHg and in group labetalol, it was was 94.07 ± 12.76 mmHg. After 3 minutes, diastolic blood pressure in group esmolol, it was 85.21 ± 12.39 mmHg and in group labetalol, it was 81.29 ± 14.06 mmHg. After 5 minutes, diastolic blood pressure in group esmolol, it was 76.32 ± 11.64 mmHg and in group labetalol, it was 74.79 ± 14.06 mmHg. There was no statistically significant difference in two groups. Comparison of diastolic blood pressure change between two groups shown in table 4.

Table 4: Comparison of diastolic blood pressure change between two groups

Time of Observation	Group Esmolol (n=40)	Group Labetalol (n=40)	Significance (p value)
Baseline	81.96 ± 10.56	84.25 ± 11.34	.439
Post Induction	74.29 ± 8.73	75.29 ± 10.18	.695
Before Intubation	70.36 ± 13.48	70.04 ± 10.64	.922
After Intubation 1 min	97.57 ± 12.47	94.07 ± 12.76	.304
After Intubation 3 min	85.21 ± 12.39	81.29 ± 14.06	.272
After Intubation 5 min	76.32 ± 11.64	74.79 ± 14.06	.658

Note: Values given as mean ± SD, values given in mmHg

In the post induction period mean arterial blood pressure in the group esmolol and labetalol were 87.75 ± 9.49 mmHg and 88.32 ± 10.33 mmHg respectively. Before intubation mean arterial blood pressure was 81.86 ± 12.69 mmHg in group esmolol and in group labetalol, it was 83.14 ± 12.76 mmHg. After 1 minute of intubation, mean arterial blood pressure in group esmolol, it was 114.07 ± 15.68 mmHg and in group labetalol, it was 112.75 ± 12.60 mmHg. After 3 minutes of intubation, mean arterial blood pressure in group esmolol, it was 101.86 ± 14.24 mmHg and in group labetalol, it was 94.68 ± 15.30 mmHg. After 5 minutes, the mean arterial blood pressure inn group esmolol, it was 92.64 ± 12.19 mmHg and in group labetalol, it was 88.39 ± 16.15 mmH. It was not statistically significant difference in two groups. Comparison of mean arterial blood pressure change between two groups as shown in table 5.

Table 5: Comparison of mean arterial blood pressure change between two groups

Time of Observation	Group Esmolol (n=40)	Group Labetalol (n=40)	Significance (p value)
Baseline	100.18 ± 9.66	99.96 ± 12.69	.944
Post Induction	87.75 ± 9.49	88.32 ± 10.33	.830
Before Intubation	81.86 ± 12.69	83.14 ± 12.76	.707
After Intubation 1 min	114.07 ± 15.68	112.75 ± 12.6	.730
After Intubation 3 min	101.86 ± 14.24	94.68 ± 15.30	.075

After Intubation 5 min	92.64 ± 12.19	88.39 ± 16.15	.271

Note: Values given as mean ± SD, values given in mmHg

DISCUSSION

There have been more emerging new airway devices in anesthesiology, still laryngoscopy and intubation remains the gold standard for management of the airway. In this study, comparison was done between esmolol and labetalol in preventing the hemodynamic response to intubation. As esmolol have beta receptors blocking actions and labetalol has both alpha and beta receptors blocking action. Therefore, this study compares the effects of these drugs in blunting of laryngsocopy and intubation reflex.

In this study the general characteristics of the patients in the both groups in relation to age, sex, body weight and ASA were not significantly different. Also, the baseline heart rate, systolic blood pressure, diastolic blood pressure and mean arterial blood pressure were also not significantly different between two groups.

Singh SP et al [14] found that there was no significant effect of esmolol on heart rate compared to control as in esmolol group baseline heart rate was 85.76 bpm and 109.64 bpm at 1 minute, 97.44 bpm at 3 minutes and 93.68 bpm at 5 minutes as this change was significant as p value < 0.05. Also in labetalol group, there was increase in heart rate from baseline (85.24bpm) to 98.16, 90.56, 85.28 bpm at 1, 3, 5 minutes respectively. P value was also < 0.05 within the group comparison versus preinduction value. However as compared to their study, in esmolol group heart rate reached below baseline at 5 min in our study, while it remained increased at that time period in their study. This isolated finding in their study may have been attributed to their patients receiving inj. sodium thiopentone at 5mg/Kg and followed by injection rocorunium for intubation. But we used titrated dose of propofol and vecuronium for muscle relaxation. So, they would have intubated their patients earlier than ours due to rapid onset of action of rocorunium therefore this tachycardia can be due to pharmacodynamics of sodium thiopentone as it has vagolytic properties which might have contributed to this tachycardia being persistent till 5 minutes.

Helfman SM et al[15] esmolol at the dose of 150mg also found that maximum percent increase in heart rate was 19 ± 4 % in esmolol group although it was less compared to placebo, lidocaine, fentanyl groups. As compared to their studies, our studies showed maximum percent increase in heart rate was 12.2 % but our drug dose was also smaller than theirs.

Inada E et al[16] compared between lidocaine, 5 mg and 10 mg of labetalol in attenuation of laryngoscopy and intubation. Their result showed that labetalol, 5mg, and lidocaine did not prevent rise in heart rate after intubation however 10mg of labetalol prevent the rise in heart rate. The result was comparable to ours as most of patients in our study also received labetalol at 4 to 7 mg. Since our drug calculation was based on body weight and none of the patients received 10 mg of labetalol therefore we could not assess its efficacy on our patients.

Singh H et al [17]found that in the esmolol-pretreated patients (1.4 mg/kg), the increase in HR was significantly lower (20% ± 3%) compared with the nitroglycerin (37% ± 8%), lidocaine (52% ± 8%), and control (29% ± 4%) groups after intubation. In our esmolol group study, there was also increase in heart rate after intubation up to 12%.

Bensky KP et al[18] compared the effect of 0.2mg/kg and .4mg/kg of esmolol on 61 patients on blunting the increase in heart rate and blood pressure after intubation. They found that in both groups there was significantly increase in heart rate (p value < .05) although this increase was less compared to placebo group. In our study, there was similar increase in heart rate in esmolol group since we lacked the control group therefore we could not have assessed whether this increase would have been less as compare to control.

Yun JW et al[19] concluded that 1 mg/kg of esmolol is better than 0.2 mg/kg of labetalol in lowering heart rate response to intubation but statistically there was no significance between group. In regard to their study, we used esmolol at 0.5mg/kg and labetalol at 0.1mg/kg so the dose was less compared to them. And also, labetalol was given 4 minutes before

intubation in their study but we gave labetalol 5 minutes of intubation but esmolol was given 2 minutes of intubation in both studies. So, the using of large dose of drug as well as different timing of labetalol administration could have lead to different results.

Singh SP et al[14] compared the esmolol (0.5mg/Kg) and labetalol (0.25 mg/Kg) in attenuation of reflex response to intubation. Comparing with esmolol with control revealed that esmolol had significant less MAP at intubation ($p = 0.044$). When labetalol group was compared with control the MAP was significant less ($p< 0.05$) than control at all times except at 10 minutes of intubation which were comparable. Between esmolol and labetalol group comparison there was no significant findings except at 1 min ($p = 0.042$). Since we lacked control group in our study so esmolol and labetalol could not be compared to control group. But in comparison to them there was no significant difference between esmolol and labetalol at all times of postintubation. They were having significant difference in esmolol and labetalol at 1 minute as compare to ours could have been due to them using labetalol at higher dose than ours.

Ugur B et al[20]also noted the immediate rise in MAP after intubation in 1.5mg/kg esmolol group which was similar to ours though we used smaller dose than them. Keun S et al [21] found that in labetalol group, there was 23% increase in MAP following 1 minute of intubation while in our study it was only 12.7%.

Ebert JP et al [22] concluded that giving esmolol in continuous infusion (500 µg/kg /min for the first 6 minutes followed by 300 µg/kg/min for 9 minutes) prior to intubation in ASA III or IV patients also shown to increase MAP from baseline of 105.7 mmHg to118.4 mmHg after 1 minute of laryngoscopy and intubation which was similar to ours but as compared to them we used one single bolus dose of esmolol in only ASA I or II patients.

CONCLUSION

Our study found that there were no statistically significance difference in comparison between two groups regarding HR, SBP,DBP, MAP at 1, 3 and 5 minutes after larygoscopy and intubation as all the $p > 0.05$. Thus, we concluded that esmolol and labetalol have similar effects in preventing response to laryngoscopy and intubation. Control group should be added to the group so we could have appreciated the magnitude of difference between drugs, which could have provided better analysis.

Invasive arterial blood pressure monitoring should be done to provide better accuracy in changes of blood pressure in response to laryngoscopy and intubation.

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