



## Attenuation of Haemodynamic Responses to Laryngoscopy and Endotracheal Intubation after Rapid Sequence Induction in Patients Undergoing Cesarean Delivery: Labetalol vs Lignocaine

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### Abstract

**Objectives:** Laryngoscopy and tracheal intubation are associated with exaggerated pressor responses in obstetric patients during rapid sequence induction of anesthesia for cesarean delivery. It is associated with increased morbidity and mortality especially in high-risk patients with comorbidities. The aim of this study was to compare the efficacies of intravenous (i.v) labetalol and lignocaine in attenuating these responses.

**Materials and methods:** In this prospective randomized controlled study, 60 women undergoing cesarean delivery were randomly assigned to two groups to receive either labetalol 0.25 mg/kg or lignocaine 1.5 mg/kg before the induction of anesthesia. Heart rate (HR), systolic blood pressure (SBP) and mean arterial pressure (MAP) were measured before induction, after injection of study drug, at the time of laryngoscopy and intubation followed by 1, 3, 5 and 10 minutes post intubation. Any adverse effects like hypotension, bradycardia, desaturation, arrhythmias were noted.

**Results:** Both labetalol and lignocaine attenuated the pressor response to laryngoscopy and intubation. Labetalol causes significant decrease in heart rate and blood pressure than lignocaine group. In labetalol group two patients developed bradycardia (HR<50) after administration of study drug. No adverse effect noted in lignocaine group.

**Conclusion:** Labetalol when compared to lignocaine causes greater attenuation of stress response to laryngoscopy and endotracheal intubation resulting in greater reduction of HR, SBP and MAP thus causing better hemodynamic stability.

**Keywords:** Laryngoscopy, Intubation, Lignocaine, Labetalol

### Introduction

The dilemma of obstetric anaesthesia is conflicting situation arising from the goals of general anaesthesia and management for cesarean delivery. On one hand it is to ensure an appropriate level of anaesthesia that optimises surgical conditions, perfusion and oxygenation for mother and fetus and on other it is to

minimise the risk of awareness and to limit fetal drug transmission and neonatal respiratory depression<sup>1,2</sup>.

Induction to anaesthesia-delivery (I-D) time and uterine incision-delivery (U-D) time are important prognostic factors for the neonatal outcome<sup>2,3</sup>. Rapid sequence induction using succinylcholine or rocuronium is preferred for pregnant patients.

Anaesthesia is maintained using inhalation agents; opioids are traditionally withheld until delivery<sup>4,5,6</sup>.

Cesarean delivery under general anaesthesia involves several major risk factors, such as rapid sequence induction, difficult airway management, omission of opioids, urgency, insufficient time between intravenous induction and start of inhalational anaesthesia<sup>7</sup>. Intraoperative awareness is one of the major problems with incidence of 0.2-0.9%. The other serious problem is exaggerated stress response to laryngoscopy, endotracheal intubation, and surgical incision during the I-D period under light anaesthesia which presents as tachycardia, hypertension, and arrhythmias.

Reid and Brace (1940) were the first to report the circulatory response to laryngeal and tracheal stimulation in anaesthetised individuals; those circulatory responses were tachycardia and rise in arterial blood pressure<sup>8</sup>. Increase in blood pressure and heart rate occurs most commonly from reflex sympathetic discharge in response to laryngotracheal stimulation, which in turn leads to increased plasma norepinephrine concentration<sup>9</sup>.

The elevation in arterial pressure typically starts within 5 s and peaks in 1-2 min and returns to baseline within 5 min<sup>10</sup>. This increase in blood pressure and heart rate is usually transient and of no consequence in healthy individuals. However, it may lead to increased morbidity and mortality in high-risk patients having comorbid conditions like preeclampsia/eclampsia or HELLP syndrome, coronary artery disease, cerebrovascular disease, myocardial infarction and thyrotoxicosis<sup>11</sup>.

Due to increase in heart rate and blood pressure myocardial oxygen demand increases and there is risk of myocardial ischemia, arrhythmias, or cardiac failure with pulmonary edema. There is also increased risk of intracranial haemorrhage. Systemic vasoconstriction can decrease the utero-placental blood flow and adversely affects neonates<sup>1</sup>.

Several drugs and techniques have been used to attenuate the stress response to laryngoscopy and intubation, all of which depend on blockade of adrenergic responses. Drugs such as hydralazine<sup>12</sup>, magnesium sulfate<sup>13</sup>, labetalol<sup>14</sup>, fentanyl<sup>15</sup>, sodium nitroprusside<sup>16</sup>, lidocaine<sup>17</sup>, nitroglycerin<sup>19</sup> and nifedipine<sup>20</sup> have been used with varying degrees of

success. However, no modality was devoid of drawbacks and limitations.

Labetalol is  $\alpha$  and  $\beta$  blocker, is often used for control of raised BP perioperatively and has good safety profile. It does not cross placenta and does not cause rebound hypertension. Although it may cause hypotension and bradycardia when given in higher doses. Lignocaine when given i.v before induction decreases sympathetic response associated with intubation, which appears to result from an increased threshold for airway stimulation, central inhibition of sympathetic transmission and direct depression of cardiovascular response.

Studies comparing labetalol with lignocaine given before induction for decreasing haemodynamic response are limited. Hence, this prospective randomised controlled trial was designed to compare the efficacy of i.v labetalol 0.25 mg/kg against i.v lignocaine 1.5 mg/kg in blunting haemodynamic response to rapid sequence induction using thiopentone and succinylcholine in normotensive patients. The incidence of bradycardia and hypotension was also assessed.

## Materials And Methods

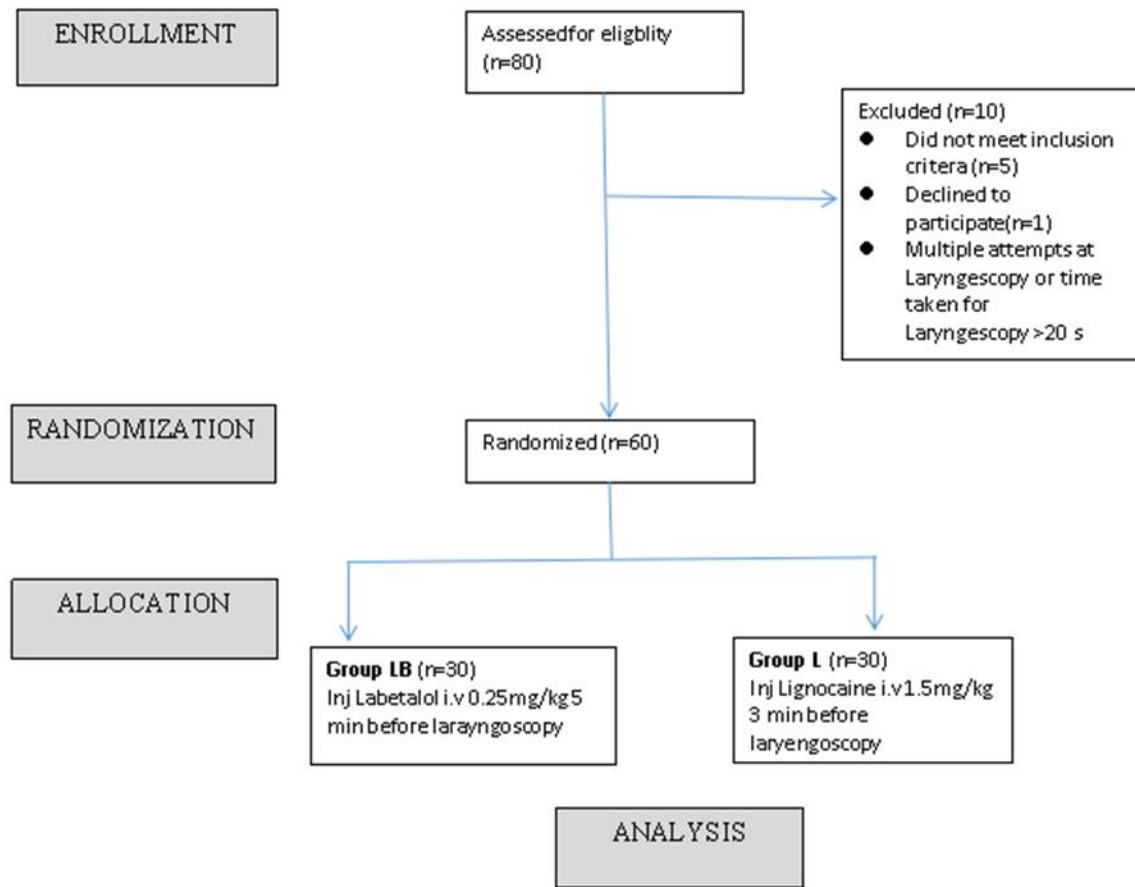
After obtaining approval from institutional ethics committee, this prospective, randomized controlled study was carried out in the Department of Anaesthesia and Critical Care, Government Medical College Srinagar, a tertiary care hospital for a period of eight months from February 2021 to September 2021.

Patients were enrolled in the study after a thorough preanesthetic check up, routine investigations and obtaining a written informed consent. The study population included those with American society of Anesthesiologists (ASA) physical status I-II and Mallampalli classification grade I-II, aged 20-45 years and scheduled for elective cesarean delivery under General Anaesthesia with endotracheal intubation. No patient had contraindications for use of labetalol or intravenous lignocaine. Patients with anticipated difficult intubation, multiple attempts, or laryngoscopy time more than 20 s, history of hypertension, coronary artery disease, diabetes, hepatic or renal disease, preoperative use of beta blockers and cerebrovascular disease were excluded from the study.

80 patients were initially assessed for eligibility and 60 patients among them could fulfil inclusion criteria

and were enrolled in this study. Participants flow diagram is shown in figure 1.

**Figure 1: Enrollment and progression of patients in the study**



Patients were randomly assigned using computer generated random numbers to one of the two groups (30 in each group) **Group LB** (to receive i.v Labetalol 0.25 mg/kg 5 mins prior to laryngoscopy) or **Group L** (to receive i.v preservative free lignocaine 1.5 mg/kg 3 mins prior to laryngoscopy).

A resident anaesthesiologist who was not part of study made the study drug for a total volume of 10 ml by diluting it with 0.9% normal saline.

Routine protocol for anaesthesia induction was applied similarly for both the groups. Patients were kept fasting for 8 hrs prior to surgery. All patients received ranitidine 30 mg i.v about 30 minutes before induction. Upon arrival in operating room patient was placed supine with left uterine displacement, an i.v line was secured and crystalloids started. Monitors for pulse oximetry, electrocardiogram and non-invasive blood pressure were attached. Fetal heart

rate was confirmed. The mean of two BP and HR readings taken 2 mins apart in operating room was taken as baseline value.

Patients were preoxygenated with 100% oxygen using a tight fitted mask for about 3 min. The study drug was given prior to laryngoscopy and intubation. Rapid sequence induction was initiated with gentle cricoid pressure while patient was awake and increasing it to 40N once patient lost consciousness.

Patient was induced with 4-5 mg/kg of Inj. Thiopentone Sodium i.v till the loss of eyelash reflex. It was followed by Inj Succinylcholine 1.5 mg/kg. Direct laryngoscopy and endotracheal intubation was done after 30-40 sec. After endotracheal intubation, cuff was inflated and position checked and after proper confirmation it was secured. All the intubations were done by an experienced anaesthetist

and the same doctor did all the cases to minimise bias.

HR, SBP and MAP were recorded after injection of study drug, at the time of laryngoscopy and intubation followed by 1, 3, 5 and 10 minutes post intubation. Any adverse effects like hypotension, bradycardia, desaturation, arrhythmias were noted. Fall in mean blood pressure below 60 was treated with inj. Ephedrine IV and heart rate of less than 50 was treated with inj. atropine i.v. Neonatal outcome was also noted.

**Statistical Analysis**

Data was compiled and continuous data are presented as Mean & SD and categorized data as percentages.

Demographic characteristics, perioperative vitals were compared using student ‘t’ test and nominal data were compared with Chi Square test. Repeated measures of analysis of variance (RMANOVA) were used to compare continuous variables. Statistical analysis was performed using graph pad instat software package. A ‘p’ value of <0.05 was considered statistically significant.

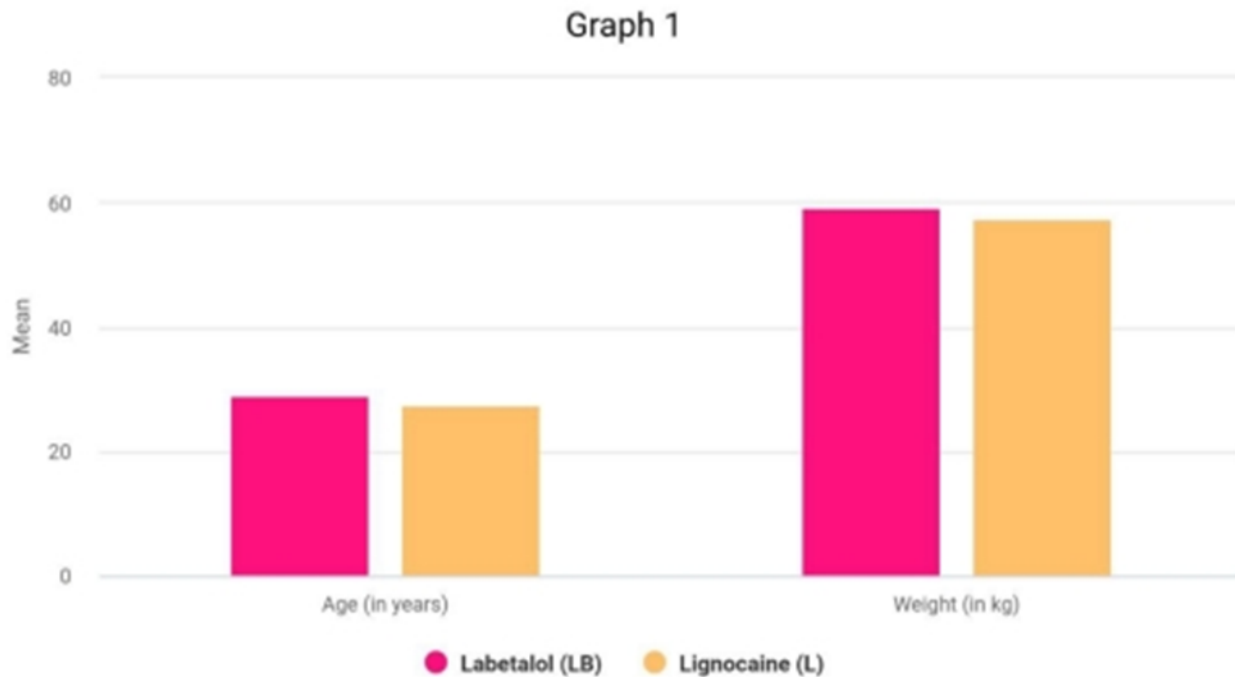
**Results**

60 patients posted for cesarean delivery and requiring general anaesthesia were included in the study to compare the effects of intravenous Labetalol and intravenous lignocaine on hemodynamic response to laryngoscopy and endotracheal intubation.

**Table 1: Comparison of mean of age and weight of two groups.**

	Labetalol (LB) Mean ± SD	Lignocaine (L) Mean ± SD	P- value (Two sample t test)
Age (in years)	29 ± 11.2	27.4 ± 12.2	0.529 (NS)
Weight (in kg)	59.3 ± 10.1	57.3 ± 9.7	0.479 (NS)

**Graph 1: Comparison of mean of age and weight of two groups**

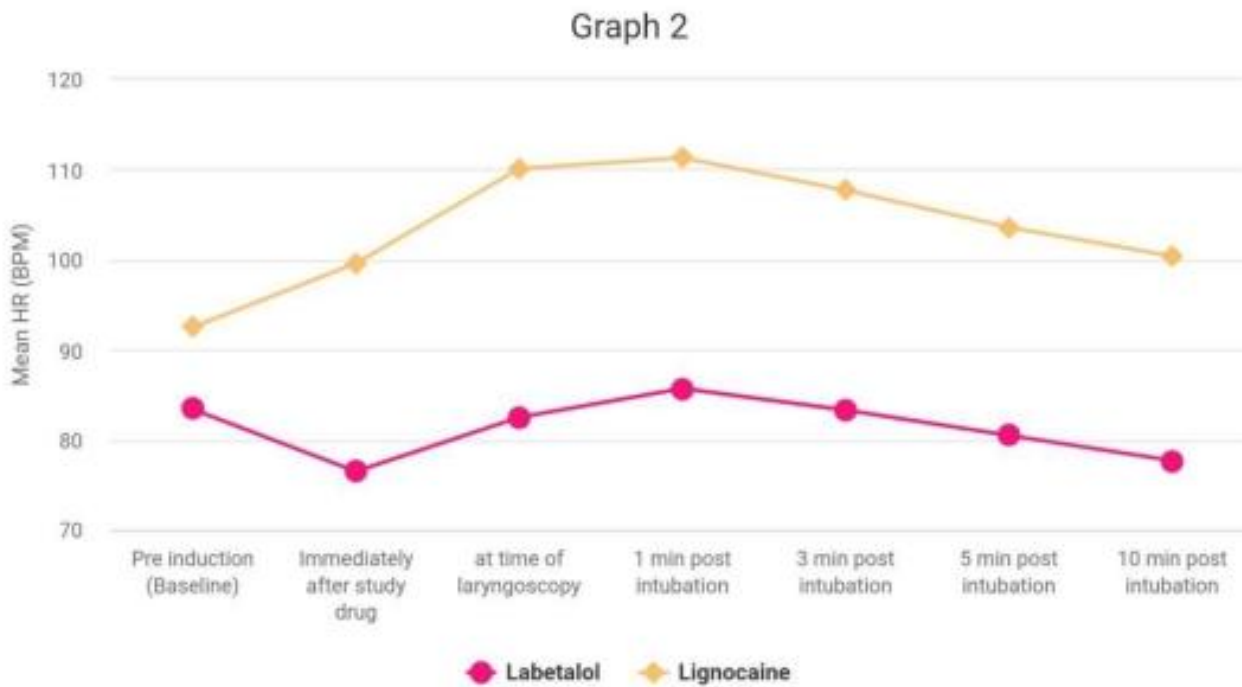


The above table1 and graph 1 showed that there is no significant difference between age and weight of patients of both the groups (LB & L) since p value > 0.05.

**Table 2: Comparison of heart rate (BPM) in two groups of patients studied.**

Time (T)	Labetalol (LB) Mean ± S.D.	Lignocaine Mean ± S.D.	P-Value(Two sample t-test)
Pre induction (Baseline) - T1	83.4 ± 14.0	92.5 ± 15.1	0.449 (NS)
Immediately after Study drug - T2	76.5 ± 9.4 (8.3%)	99.6 ± 15.3 (7.8%)	0.004 (S)
at the time of laryngoscopy -T3	82.5 ± 12.1 (1.1%)	110.1 ± 15.9(19.1%)	0.049 (S)
1 minute post intubation -T4	85.7 ± 12.5 (2.7%)	111.3 ± 15.5(20.4%)	0.012 (S)
3 min post intubation -T5	83.3 ± 12.9 (0.2%)	107.7 ± 15.2(16.4%)	0.044 (S)
5 min post intubation - T6	80.5± 12.4 (3.5%)	103.6 ± 15.0(12.0%)	0.045 (S)
10 min post intubation -T7	77.7 ± 12.1 (6.9%)	100.4 ± 14.3 (8.6%)	0.376 (NS)

**Graph 2: Changes in HR (BPM) at various time interval.**



The above table 2 and graph 2 showed that there was no statistically significant difference (p=0.449) in baseline mean heart rate between both the groups. The mean baseline heart rate (T1) in Group LB was 83.4 beats/min, whereas that in group L was 92.5 beats/min.

Immediately after giving drug (T2), heart rate decreased by 8.3% from baseline in group LB, in group L there was increase by 7.8%.

When heart rates in Group L & Group LB were compared the following observations were made. At the time of laryngoscopy (T3), heart rate increased by 19.1% above the baseline in Group L but In Group

LB heart rate decreased by 1.1% from baseline. Difference is statistically significant (p=0.049).

At 1 minute post intubation, there was 20.4% rise in heart rate from baseline in Group L. In group LB heart rate increased by 2.7% from baseline. Which is statistically significant (P=0.012).

At 3 minutes post intubation (T5), heart rate became near normal (baseline) in group LB. In Group L, the

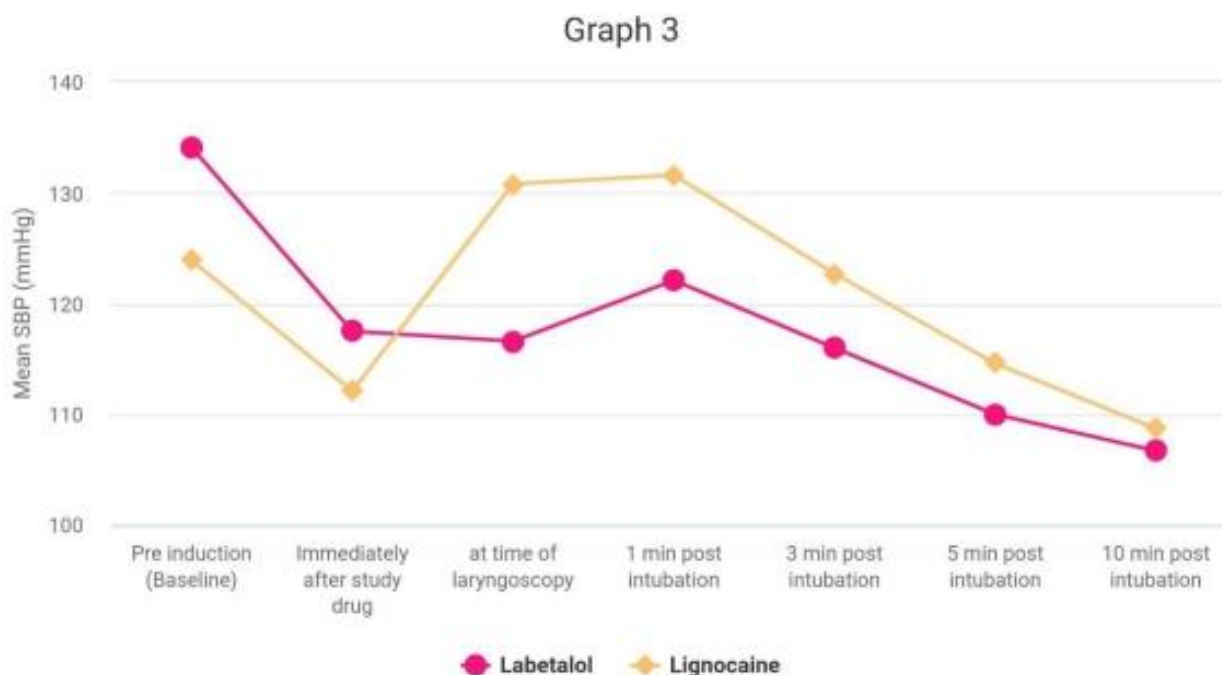
heart rate increased during laryngoscopy (T3) and remained high even 10 minutes after intubation.

There was statistically significant difference between group LB and group L immediately after giving drug, at the time of laryngoscopy and at 1, 3, 5 minutes after intubation. No significant difference was noted at 10 minutes after intubation.

**Table 3: Comparison of SBP (mmHg) in two groups of patients studied.**

Time	Labetalol Mean ± S.D.	Lignocaine Mean ± S.D.	P-Value (Two sample t-test)
Pre induction (Baseline)	134.1 ± 16.1	123.9 ± 13.6	0.187 (NS)
Immediately after Study drug at the time of laryngoscopy	117.5 ± 6.2(12.4%)	112.1 ± 16.7(9.5%)	0.028 (S)
1 minute post intubation	116.6 ± 19.5(13%)	130.8 ± 19.1(5.5%)	0.031 (S)
3 min post intubation	122.1 ± 21.0(8.9%)	131.9 ± 18.7(6.4%)	0.013 (S)
5 min post intubation	116.0± 14.7(13.4%)	122.7 ± 15.2(0.9%)	0.014 (S)
10 min post intubation	110.0± 13.8(17.9%)	114.6 ± 10.7(7.5%)	0.036 (S)
	106.7± 11.8(20.4%)	108.7 ± 9.6(12.26%)	0.441 (NS)

**Graph 3: Changes in SBP at Various Time Intervals.**



The above table 3 and graph 3 showed that the mean baseline systolic B.P. was 134.10 mmHg in Group LB and that in Group L was 123.90 mmHg. Both the values are comparable but not statistically significant ( $p > 0.05$ ).

Immediately after giving drug (T2), SBP decreased by 12.4% and 9.5% below baseline in group LB and group L respectively which is statistically significant ( $p = 0.028$ ).

At the time of laryngoscopy (T3), SBP increased by 5.5% above the baseline in Group L & decreased by 13% in group LB which is statistically significant ( $p = 0.031$ ).

At one minute post intubation(T4), group L showed rise in SBP by 6.4% and group LB showed reduction in SBP by 8.9% from baseline which is statistically significant ( $p = 0.013$ ).

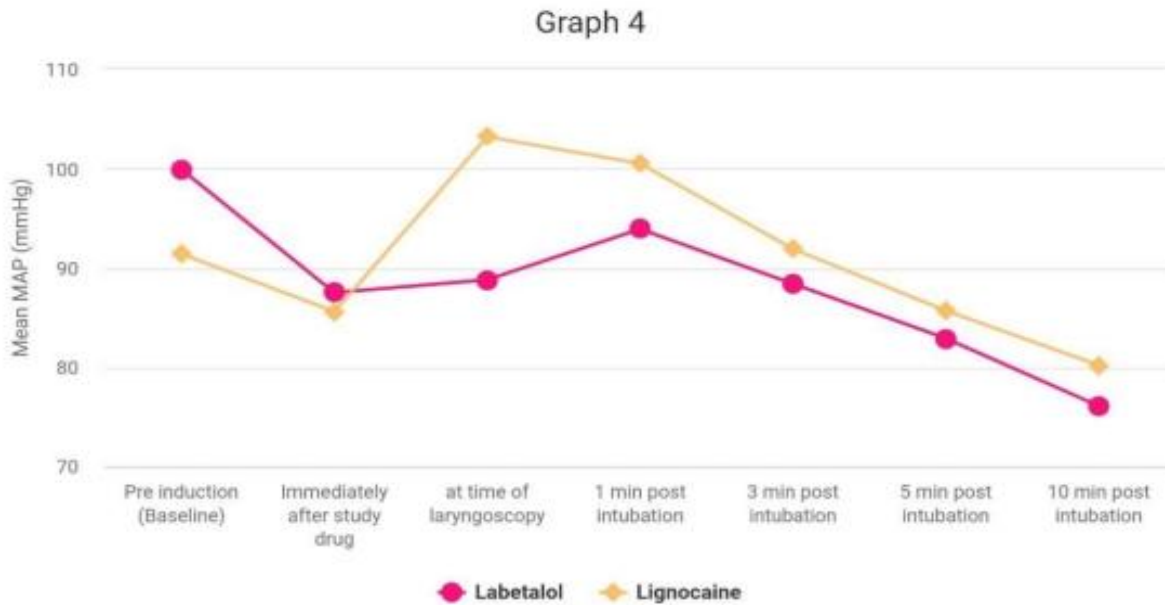
SBP became near normal at 3-minute post intubation (T5) in group L and no rise in SBP was noted in group LB.

At 10-minute post intubation (T7), SBP dropped by 20.4% and 12.26% in group LB and group L respectively. This is not statistically significant (p value = 0.441).

**Table 4: Comparison of MAP (mmHg) in two groups of patients studied.**

Time	Labetalol Mean ± S.D.	Lignocaine Mean ± S.D.	P-Value (Two sample t-test)
Pre induction (Baseline)	99.9 ± 13.6	91.4 ± 11.8	0.807(NS)
Immediately after Study drug	87.5 ± 13.9(12.4%)	85.6 ± 15.3(6.3%)	0.029 (S)
at the time of laryngoscopy	88.8 ± 15.5(11.1%)	103.2 ± 16.3(12.9%)	0.035 (S)
1 minute post intubation	93.9 ± 15.9(6%)	100.5 ± 15.0(9.9%)	0.025(S)
3 min post intubation	88.4 ± 12.5(11.5%)	91.9 ± 12.1(0.5%)	0.027 (S)
5 min post intubation	82.9 ± 11.3(17%)	85.7 ± 9.2(6.2%)	0.041 (S)
10 min post intubation	76.1 ± 9.6(23.8%)	80.2 ± 7.9(12.2%)	0.047 (S)

**Graph 4: Changes in MAP at Various Time Intervals.**



The above table 4 and graph 4 showed that the mean baseline MAP in Group LB was 99.9 mmHg and that in Group L was 91.4 mmHg, which were comparable and the difference was not statistically significant ( $p=0.807$ ).

When MAP of both the groups was compared the following observations were made:

Immediately after study drug (T2), MAP reduced by 12.4% and 6.3% below baseline in group LB and group L respectively which is statistically significant ( $p=0.029$ )

At the time of laryngoscopy (T3), Group L showed rise of MAP of 12.9% from baseline and group LB showed reduction in MAP by 11.1% which is significant ( $p$  value=0.035).

1 minute post intubation (T4), MAP increased by 9.9% in Group L & decreased by 6% in Group LB from baseline which is significant ( $p=0.025$ ).

The MAP became near normal i.e., 91.9 mmHg in Group L by 3-minute post intubation (T5).

The difference between the two groups was significant at time points (T5, T6, T7) with  $p$  value  $<0.05$ .

### Comparison of adverse effects

In Group LB two patients (6.6%) developed bradycardia ( $HR<50$ ) after administration of study drug whereas none developed in Group L. Patients in Group LB who had heart rate  $<50$  were given Inj.atropine.

No other adverse effects were noted in either of the group.

### Discussion

Laryngoscopy and intubation result in a significant hemodynamic response in patients undergoing general anaesthesia and more so in obstetric patients for cesarean delivery. It is a cause of concern and a reason of increased morbidity and mortality in patients with risk factors like hypertensive disorders of pregnancy or other systemic disease. Several drugs belonging to different classes have been tried for obliteration of this pressor response.

Lignocaine given i.v, intratracheal or as nebulization has been well studied for attenuation of cardiovascular responses and has been found to be quite effective. Hamil et al<sup>20</sup> studied effect of intravenous lignocaine on intubation response and concluded that intravenous route was ideal and preferred for lignocaine before laryngoscopy and intubation. In our study we used lignocaine in a dose of 1.5mg/kg, 3 minutes prior to laryngoscopy and endotracheal intubation. Similar dose was used by



Robert K Stoelting *et al*<sup>21</sup> who suggested that, Intravenous Lignocaine given in the doses of 1.5 mg/kg 3 minutes before laryngoscopy and intubation, sufficiently attenuate the laryngoscopy responses.

Labetalol is a combined  $\alpha_1$  and non-selective  $\beta$ -adrenergic blocking drug, it has a better safety profile and haemodynamic stability. Onset time after i.v administration is 5 minutes and peak effect is seen at 5-15 min. Its low placental transfer is due to its high degree of ionization at physiological pH. Its effect on pressor responses has not been studied well.

The present study was done to compare effect of labetalol and lignocaine in attenuation of haemodynamic responses after laryngoscopy and intubation after rapid sequence induction for cesarean delivery. Limited studies have been done to study effect of these two drugs in this group of patients.

In our study the demographic data showed that Group LB (Labetalol) and Group L (Lignocaine) were comparable in terms of number of patients, age, and weight.

**Heart rate changes:** In our study mean baseline heart rate in both the groups was comparable. Immediately after giving study drug, there was a significant decrease in heart rate of group LB (Labetalol). Heart rate increased at the time of laryngoscopy but the rise was more pronounced in the group L (Lignocaine) and statistically significant. It can be noted that heart rate did not settle to baseline in group L even after 10 min post intubation.

CD Miller *et al*<sup>22</sup> employed a dose of 1.5 mg lignocaine intravenously and noticed a rise in the heart rate (HR) of 25 bpm and Splinter *et al*<sup>23</sup> noticed it to be 19 bpm. Hence our findings are in accordance with that of above-mentioned authors.

Though there was a rise in heart rate in the Labetalol group, the rise was not significant when compared with the same in the Lignocaine group and basal values of heart rate were reached within 1 min after intubation in case of labetalol group.

**Blood Pressure changes:** The baseline mean SBP and MAP was comparable between the two groups. In group L (Lignocaine), at the time of laryngoscopy and intubation, rise in mean Systolic blood pressure (SBP) was found to be 6.9 mm Hg (5.6%) and that of Mean arterial pressure (MAP) was 11.8 mm Hg

(12.9%). These elevated pressure readings started coming down by 3 minutes and reached baseline by 5 minutes. In group LB (Labetalol), after laryngoscopy and intubation, there was no rise in Systolic blood pressure (SBP) or mean arterial pressure (MAP). One minute after intubation, fall in Systolic blood pressure (SBP) was found to be 12 mm Hg and that of Mean arterial pressure (MAP) was 6 mm Hg.

At three-minute post intubation (T5), SBP reached around the baseline in group L where as in group LB SBP remained below baseline even after laryngoscopy and intubation.

Inada E, Cullen DJ, Nemeskal AR, Teplick R<sup>24</sup> compared Labetalol with lignocaine and saline to minimize the haemodynamic response to intubation in patients undergoing surgical procedures under general anesthesia. They found that, Labetalol 10 mg prevented a rise in heart rate after intubation compared to patients who received placebo, lignocaine 100 mg, or labetalol 5 mg. Thus, they concluded that, Labetalol 10 mg IV just prior to induction of anesthesia is a safe and cost-effective in attenuating haemodynamic response to laryngoscopy and intubation.

In our study, labetalol at the dose of 0.25mg/kg five minutes before intubation, attenuated both heart rate and blood pressure in response to laryngoscopy and intubation. There was statistically significant decrease in haemodynamic response in the labetalol group as compared to Lignocaine group at all times till 10 min.

So, both Labetalol and Lignocaine attenuated the pressor response to laryngoscopy and intubation. Labetalol causes significant decrease in heart rate and blood pressure than Lignocaine group.

### Limitations of the study

Only 60 patients were studied, number was limited due to presence of only one investigator for this study. Also, measurement of serum catecholamine levels could have provided more specific effect of the study drugs. Patients having pre-eclampsia will be major beneficiaries from this study but they were not included in the study.

### Conclusion

Thus, to conclude Labetalol (in dose of 0.25/kg iv 5 minutes prior to laryngoscopy) when compared to

Lignocaine (in dose of 1.5mg/kg IV bolus 3 minutes prior laryngoscopy) causes greater attenuation of stress response to laryngoscopy and endotracheal intubation resulting in greater reduction of HR, SBP and MAP thus causing better hemodynamic stability.

In patients with PIH or eclampsia and history of coronary artery disease or cerebrovascular disease keeping HR and MAP low is beneficial.

Labetalol in dose of 0.25mg/kg iv may be recommended to blunt the hemodynamic response to laryngoscopy and intubation in normotensive pregnant patients and in patients with hypertensive disorders pregnancy but enough studies must be done on this topic.

### Contributions

1. Nasir Jeelani Wani: This author helped in the conception and design of the study, literature search, performing the procedures, acquisition of data and revising the article.

2. Asma Hassan Mufti: This author helped in acquisition of data, analysis and interpretation of data and Manuscript editing

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