



Original Research Article

Attenuation of sympathoadrenal response to direct laryngoscopy and intubation using 0.25mg/kg injection labetalol

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ABSTRACT

Introduction and Objective: Direct laryngoscopy and endotracheal intubation evokes autonomic disturbances in the form of tachycardia, raise in blood pressure, intracranial, and intraocular pressure.

Thus the present study was undertaken to evaluate the efficacy of injection Labetalol 0.25mg/kg body weight in the attenuation of sympathoadrenal response to direct laryngoscopy and endotracheal intubation.

Materials and Methods: The study was conducted on 60 participants belonging to ASA grade 1 or 2 aged between 18 – 55 yrs undergoing elective surgeries under general anaesthesia. The study population was randomly divided into 2 groups with 30 subjects in each group.

Group LAB (Labetalol group) – received 0.25mg/kg body weight diluted upto 10ml with normal saline intravenously, over 10minutes using a syringe pump, given 10minutes before induction.

Group CR (Control) received 10ml of normal saline intravenously.

The study drug was administered over 10 minutes using syringe pump followed by induction with inj Thiopentone 5mg/kg body weight and inj vecuronium 0.1mg/kg body weight three minutes prior to laryngoscopy and intubation. HR(Heart rate), Systolic arterial pressure, diastolic arterial pressure, MAP(mean arterial pressure) were recorded at basal, 2 minutes, 5 minutes, 8 minutes after study drug infusion, before induction, after induction, 1st, 2nd, 3rd, 5th, 10th, 15th minute after laryngoscopy and intubation.

Results: The result showed statistically significant ($p < 0.05$) decrease in Heart rate, Systolic arterial Pressure, Diastolic arterial pressure and Mean arterial pressure in Group LAB compared to Group CR at all the time intervals.

Interpretation and Conclusion: In the present study, it was found that inj Labetalol 0.25mg/kg body weight had effectively attenuated the sympathoadrenal response to laryngoscopy and intubation.

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1. Introduction

Direct laryngoscopy and endotracheal intubation evokes autonomic nervous response in the form of tachycardia, hypertension, cardiac arrhythmia, and increased myocardial oxygen demand, laryngospasm, bronchospasm, increased intracranial pressure and intraocular pressure. These haemodynamic changes begin within 5 seconds of laryngoscopy, reaches a peak in 1–2 min and comes back to baseline levels by 5 minutes.^{1–3}

Various pharmacological agents such as lignocaine,⁴ opioids^{5,6} sodium nitroprusside,⁷ nitroglycerine,⁸ calcium channel blockers.^{9,10} have been tried but results are not effective.

Labetalol is a unique oral and parenteral antihypertensive drug that is alpha-1 and nonselective beta-1 and beta-2 adrenergic antagonist. Its overall effect on cardiac output remains unchanged.^{11,12} Thus the present study is undertaken to know the effectiveness of 0.25mg/kg body weight of labetalol in attenuating the sympathoadrenal response to laryngoscopy and endotracheal intubation.

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2. Materials and Methods

The study was conducted in a tertiary care hospital, Mysore after obtaining clearance from ethical committee and informed consent was taken from all the subjects involved in the study. The sixty participants of study population belonging to [ASA grade 1 or 2, aged between 18- 55 yrs posted for elective surgeries under general anaesthesia with endotracheal intubation techniques. Subjects with cardiac, renal, hepatic, cerebral diseases and peripheral vascular diseases, Hypertension, Heart rate < 60bpm, systolic BP <100 mmHg, Presence of 1st, 2nd, 3rd degree heart block, difficult airway and obese patients (BMI>30), Subjects with Hyperthyroidism, Hypothyroidism and Diabetes Mellitus were excluded from the study.

Each patient involved in the study was asked to pick the envelope from the shuffled opaque sealed envelopes containing the name of the group and thereby the 60 participants involved in the study were randomly allocated into 2 groups with 30 subjects in each group. The envelope was opened by the senior anaesthesiologist who was assigned to prepare the test drugs but not involved in the study.

Group CR – Control group – received 10ml of normal saline intravenously over 10minutes using a syringe pump 10minutes before induction.

Group LAB – Labetalol group – received 0.25mg/kg body weight diluted upto 10ml with normal saline intravenously over 10minutes using a syringe pump given 10minutes before induction.

All subjects were connected and monitored through non-invasive monitoring pulse oximetry, Non-Invasive Blood Pressure and electro cardiogram (ECG) using multiparameter monitor (EDAN iM80). The baseline HR, SBP and DBP, MAP was recorded. The heart rate and rhythm were also monitored from a continuous display of ECG. After recording the baseline parameters such as HR, SBP and DBP, MAP, subjects in group CR was received 10ml of normal saline intravenously over 10minutes using a syringe pump. Subjects in group LAB was received Inj Labetalol 0.25mg/kg body weight diluted up to 10ml with normal saline intravenously over 10minutes using a syringe pump. The study drugs were prepared by senior anaesthesiologist who was not involved with the study and observer as well as subject was blinded for the study.

All the subjects were premedicated with injection Midazolam 0.05mg/kg body weight and injection ondansetron 0.1mg/kg body weight after test drug administration. The subjects were preoxygenated for 3min with 100% oxygen. Anaesthesia was induced with injection Thiopentone 5mg/kg body weight and injection vecuronium 0.1mg/kg body weight three minutes prior to laryngoscopy and intubation. All the subjects received 1.5mg/kg body weight of Lidocaine ninety seconds before intubation. After ventilation with 50% oxygen and 50% nitrous

oxide and 0.6% isoflurane for three minutes, laryngoscopy and endotracheal intubation was performed and after confirmation of bilateral equal air entry with ETCO₂ the endotracheal tube was fixed and connected to ventilator.

Anaesthesia was maintained using 50% nitrous oxide and 50% oxygen with 0.6% isoflurane. At the end of the procedure, neuromuscular blockade was reversed with Inj neostigmine 0.05mg/kg body weight and Inj glycopyrrolate 0.01mg/kg body weight.

The haemodynamic parameters such as HR, SBP and DBP, MAP were recorded at 2,5,8 minutes after study drug infusion, before and after induction, 1,2,3, 5,8,10 and 15 minutes after laryngoscopy and intubation were recorded.

2.1. Statistical methods

The calculation of sample size was done after discussion with the statistician, on the basis of pilot study observations. The observation conducted showed approximately each group should have 23 patients for ensuring a power of study 0.80 for detecting clinically meaningful difference by 15% in heart rate and mean arterial blood pressure. With assumption of 5% patients would drop out, the final study sample size was fixed at 30 patients in each group, allowing a type 1 alpha error =0.05 and a type 2 error of beta=0.2 and power of 0.8. All the statistical methods were carried out through Microsoft excel SPSS for Windows (version 20.0)

In the present study the data in the three groups was compared using descriptive statistics and inferential statistics i.e crosstabs and repeated measure Analysis of Variance (ANOVA) test. A 'p' Value of < 0.05 was considered statistically significant and less <0.01 was considered as highly significant. All data was tabulated and presented depicting the mean ± standard deviation.

3. Results

Both the groups were comparable and there was no statistically significant difference with regard to mean age, sex, weight, duration of laryngoscopy and intubation.

3.1. Heart rate

The basal mean Heart rate between Group LAB and Group CR was found to be statistically insignificant. The group LAB showed a lowered heart rate response at 2nd, 5th, 8th minute after study drug infusion, before induction, after induction, 1st, 2nd, 3rd, 5th, 8th, 10th, 15th minute after laryngoscopy and intubation compared to Group CR which was statistically significant.

There was a maximum rise in mean Heart rate in Group CR by 40bpm compared to basal value at 1st minute after laryngoscopy and intubation and the mean heart rate had not approached the basal value even 15 minutes after laryngoscopy and intubation.

The mean heart rate had showed an increased value by 3bpm at 1st minute after laryngoscopy and intubation compared to basal mean heart rate in Group LAB and thereafter the mean heart rate remained below the baseline value even at 15 minutes after laryngoscopy and intubation which was statistically highly significant (p=0.00).

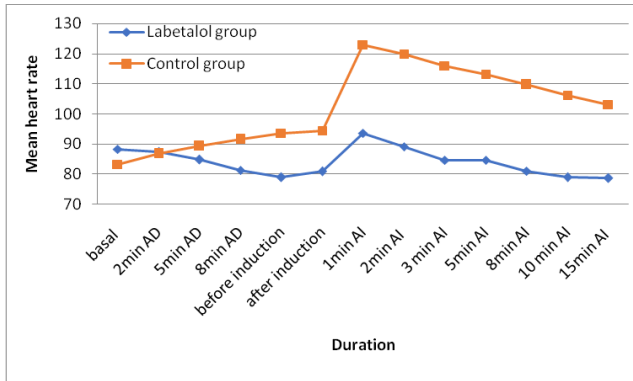


Fig. 1: Showing variation in mean heart rate between Labetalol and Control group.

3.2. Systolic blood pressure

Group LAB and Group CR showed a comparable basal mean Systolic blood pressure and it was statistically insignificant (P = 0.17). The Group LAB showed a better decrease in mean systolic blood pressure at 2nd, 5th, 8th minute after drug infusion, before induction, after induction, 1st, 2nd, 3rd, 5th, 8th, 10th, 15th minute after laryngoscopy and intubation compared to Group CR which was statistically significant.

Group CR showed a maximum rise of mean systolic blood pressure of about 25mmHg compared to basal value at 1st minute after laryngoscopy and intubation and it almost reached the basal value at 15th minute after laryngoscopy and intubation whereas in Group LAB the mean systolic blood pressure was lowered by 6mmHg at 1minute after laryngoscopy and intubation compared to the basal value and it remained below the basal value even at 15minutes after laryngoscopy and intubation which was statistically highly significant(p=0.00).

3.3. Diastolic blood pressure

The mean basal Diastolic Blood Pressure between the Group LAB and Group CR was comparable and was not statistically significant (P= 0.34). The Group LAB showed a statistically significant decrease in mean Diastolic Blood Pressure response at 2nd, 5th, 8th minutes after drug infusion, before induction, after induction, 1st, 2nd, 3rd, 5th, 8th, 10th and 15th minute after laryngoscopy and intubation compared to Group CR. There was a maximum increase of 18mmHg of mean diastolic blood pressure in Group CR at 1st minute

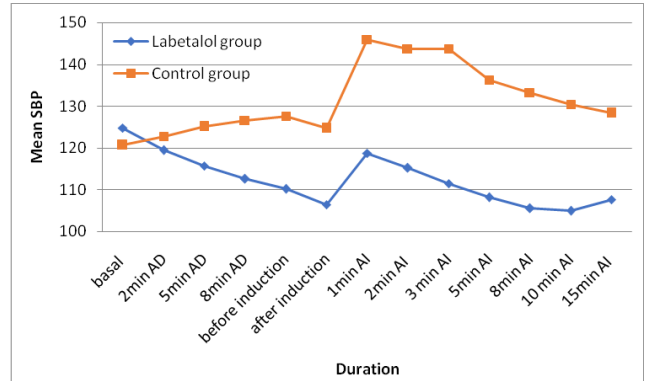


Fig. 2: Showing variation in mean systolic blood pressure between Labetalol and Control group.

after laryngoscopy and intubation compared to basal value and it had almost reached the basal value at 15th minute after laryngoscopy and intubation.

In Group LAB, there was a decrease of 6mmHg of mean diastolic blood pressure at 1st minute after laryngoscopy and intubation compared to the basal value and remained below the basal value even at 15th minutes after laryngoscopy and intubation which was statistically highly significant(p=0.00).

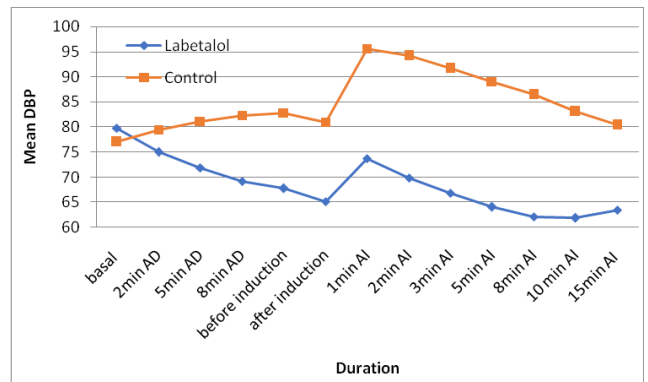


Fig. 3: Showing variations in mean diastolic blood pressure between Labetalol and Control group.

3.4. Mean arterial pressure

The basal mean arterial pressure between the Group LAB and Group CR was comparable and was not statistically significant (p=0.15). The decrease in mean arterial pressure was statistically highly significant at 2nd, 5th, 8th minute after drug infusion, before induction, after induction, 1st, 2nd, 3rd, 5th, 8th, 10th and 15th minute after laryngoscopy and intubation in Group LAB compared to Group CR.

There was a maximum increase of about 20mmHg in mean arterial pressure at 1st minute after laryngoscopy and

intubation compared to basal value in Group CR and it had almost reached the basal value at 15th minute after laryngoscopy and intubation whereas in Group LAB, there was a decrease in mean arterial pressure by 6mmHg at 1st minute after laryngoscopy and intubation compared to basal value and it remained below the basal value at all the time intervals during the study which was statistically highly significant($p=0.00$).

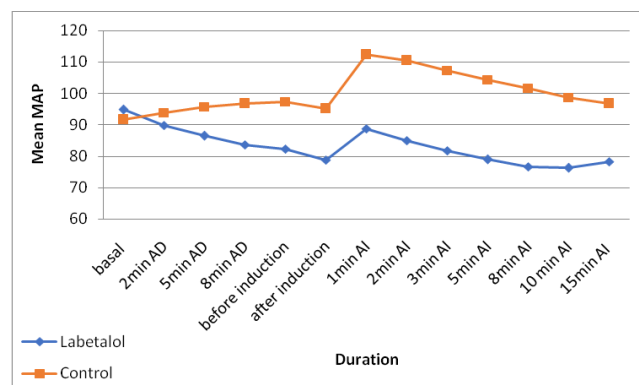


Fig. 4: Showing variations in mean arterial pressure between Labetalol and Control group

4. Discussion

The noxious effect of direct laryngoscopy and endotracheal intubation can evoke marked sympathoadrenal response in the form tachycardia and hypertension. These can produce hazardous consequences such as left heart failure, pulmonary edema, ischemic heart disease, dysrhythmias and cerebral haemorrhage in patients with raised blood pressure, coronary artery disease and cerebrovascular disease.^{2,13,14}

The limitations associated with the use of inhalational anaesthetic agents, lidocaine 4 opioids^{5,6} direct acting vasodilator^{7,8} calcium channel blockers^{9,10} has evoked the need and opportunity to discover a new agents to attenuate the sympathoadrenal response associated with direct laryngoscopy and endotracheal intubation.

Labetalol is an antihypertensive drug which is selective alpha-1 and nonselective beta-1 and beta-2 adrenergic antagonist.¹⁵ It decreases the systemic vascular resistance by alpha-1 blockade and thereby lowers the blood pressure. It also causes simultaneous beta blockade which attenuates the reflex tachycardia occurring as a result of vasodilatation.^{12,15}

Labetalol is an oral and parenteral antihypertensive drug with alpha: beta blockade ratio of 1:7 for iv and 1:3 for PO administration.^{11,16} It has two optical centres with four isomers.¹⁷

Thus Labetalol has been tried to attenuate the sympathoadrenal response to direct laryngoscopy and endotracheal intubation and found to have better results.

4.1. Heart rate

In our study basal mean heart rate between Labetalol and Control group was comparable and was not statistically significant.

In our study after infusion of Labetalol at a dose of 0.25mg/kg, there was a statistically significant decrease in mean heart rate response at 2nd, 5th, 8th minute after Labetalol infusion, before and after induction when compared to Control group. These findings were at par with the studies done by Kim et al¹⁸ and Kumar A et al.¹⁹

In our study at 1st minute after laryngoscopy and intubation there was a maximum increase in mean heart rate response by 40 bpm in Control group whereas in Labetalol group, the mean Heart Rate was increased by only 3 bpm which was statistically highly significant ($p=0.00$). This correlates with the studies done by Singh SP et al,¹⁶ Babita et al,¹¹ Kunakeri SB et al,¹² Kewalramani et al²⁰ and Kumar A et al.¹⁹

In our study Labetalol effectively attenuated the mean Heart rate response at 2nd, 3rd, 5th, 8th, 10th and 15th minute after laryngoscopy and intubation and the mean heart rate remained below the basal value even at 15th minute after laryngoscopy and intubation which was statistically highly significant($p=0.00$) compared to control group where there was an increase in mean heart rate till 15th minute after laryngoscopy and intubation compared to basal value. This correlates with the studies done by Singh SP et al¹⁶ Kewalramani et al,²⁰ El-Shmaa et al²¹ and Kumar A et al.¹⁹

4.2. Systolic blood pressure

In our study, the basal mean Systolic Blood Pressure between Labetalol and Control group was comparable and was not statistically significant.

In the present study, there was a statistically highly significant decrease in mean Systolic Blood pressure in Labetalol group compared to Control group at 2nd, 5th, 8th minute after study drug, before induction and after induction. These findings were similar to the studies of Kewalramani et al,²⁰ El-Shmaa et al²¹ and Kumar A et al.¹⁹

At 1st minute after laryngoscopy and intubation, in Labetalol group there was a decrease in mean Systolic arterial Pressure response by 6mmHg compared to basal value whereas in Control group there was an increase in mean Systolic Blood Pressure response by 25mmHg compared to basal value which was statistically highly significant($p=0.00$) in our study. Thus, Labetalol was better in attenuating the Systolic Blood Pressure response at 1st minute after laryngoscopy and intubation compared to Control group in our study. This correlates with the studies done by Singh SP et al,¹⁶ Lakshmi BS et al,²² Kewalramani et al,²⁰ El-Shmaa et al²¹ and Kumar A et al.¹⁹

The decrease in mean Systolic Blood Pressure in Labetalol group at 2nd, 3rd, 5th, 8th, 10th and 15th minute

after laryngoscopy and intubation was statistically highly significant ($p=0.00$) compared to Control group. The mean Systolic Blood Pressure remained below the basal value even at 15th minute after laryngoscopy and intubation in Labetalol group whereas in Control group the mean Systolic Blood Pressure had almost reached the basal value at 15th minute after laryngoscopy and intubation. Our study results were similar with the findings of Singh SP et al,¹⁶ Lakshmi BS et al,²² Kewalramani et al,²⁰ El- Shmaa et al²¹ and Kumar A et al¹⁹ studies. Thus Labetalol, a combined alpha 1 and nonselective beta blocker²² at a dose of 0.25mg/kg body was preferentially better in attenuating the Systolic Blood pressure response to laryngoscopy and intubation compared to Control group.

4.3. Diastolic blood pressure

The basal mean Diastolic blood Pressure was comparable between Control and Labetalol group and was not statistically significant.

In the present study, there was a statistically significant ($p<0.05$) decrease in mean Diastolic Blood Pressure in Labetalol group compared to Control group at 2nd, 5th, 8th minute after study drug, before induction and after induction. This was similar to the findings of Kewalramani et al²⁰ and El-Shmaa et al.²¹

At 1st minute after laryngoscopy and intubation, there was a decrease in mean Diastolic Blood Pressure response by 6mmHg compared to basal value in Labetalol group whereas in Control group there was an increase in mean Diastolic Blood Pressure response by 16mmHg compared to basal value which was statistically highly significant ($p=0.00$). Thus, Labetalol was better in attenuation of Diastolic Blood Pressure response at 1st minute after laryngoscopy and intubation compared to control group in our study. This was similar to the findings found in the studies such as Kumar A et al,¹⁹ Kewalramani et al²⁰ and El-Shmaa et al.²¹

The decrease in mean Diastolic arterial pressure in Labetalol group at 2nd, 3rd, 5th, 8th, 10th and 15th minute after laryngoscopy and intubation was statistically highly significant ($p=0.00$) compared to Control group. The mean Diastolic arterial pressure remained below the basal value even at 15th minute after laryngoscopy and intubation whereas in Control group, the mean Diastolic arterial Pressure had almost reached the basal value at 15th minute after laryngoscopy and intubation. This correlates with the studies of Kewalramani et al,²⁰ El-Shmaa et al,²¹ Kunakeri SB et al¹² and Kumar A et al.¹⁹

4.4. Mean arterial pressure

The basal Mean arterial pressure was comparable in between Labetalol and Control group and was not statistically significant.

In our study the decrease in mean arterial pressure at 2nd, 5th, 8th minute after study drug, before induction, after induction was statistically highly significant ($p=0.00$) in Labetalol group compared to Control group. This was similar to the findings of Kewalramani et al²⁰ and El- Shmaa et al.²¹

In our study, the mean arterial pressure decreased by 6mmHg in Labetalol group whereas it had increased by 20mmHg in control group compared to basal value at 1st minute after laryngoscopy and intubation. Thus, Labetalol was better in attenuating the mean arterial pressure effectively compared to Control group at 1st minute after laryngoscopy and intubation which was statistically highly significant ($p=0.00$) in our study. This was similar to the findings of Kewalramani et al,²⁰ El-Shmaa et al,²¹ Kumar A et al,¹⁹ Kunakeri SB et al¹² and Singh SP et al¹⁶ studies.

In our study, the decrease in mean arterial pressure at 2nd, 3rd, 5th, 8th, 10th and 15th minute after laryngoscopy and intubation was statistically highly significant in Labetalol group compared to Control group. The mean arterial pressure remained below the basal value even at 15th minute after laryngoscopy and intubation in Labetalol group whereas it had almost reached the basal value at 15th minute after laryngoscopy and intubation in Control group. This was similar to the findings of Kunakeri SB et al,¹² Kewalramani et al,²⁰ El-Shmaa et al,²¹ Kumar A et al¹⁹ and Kunakeri SB et al.¹²

5. Conclusion

Our study demonstrates that a single dose of Injection Labetalol 0.25mg/kg body weight given iv over 10 minutes just 10 minutes before induction effectively attenuated the haemodynamic response to laryngoscopy and endotracheal intubation without any significant side effects.

6. Source of funding

None.

7. Conflict of interest

None.

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