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OUTCOME OF DIFFERENT DOSES OF LABETALOL FOR CONTROLLING HEMODYNAMIC RESPONSES TO LARYNGOSCOPY AND TRACHEAL INTUBATION IN HYPERTENSIVE PATIENTS

Dr. Sheikh Rukun Uddin Ahmed*[1]

[1]MBBS, MCPS, DA(BSMMU), MD(Anaesthesiology); Senior Consultant (Anaesthesia & Intensive Care Unit), BBMH, USTC, Foy's Lake, Chattogram, Bangladesh.

***Corresponding Author: Dr. Sheikh Rukun Uddin Ahmed**
MBBS, MCPS, DA(BSMMU), MD(Anaesthesiology); Senior Consultant (Anaesthesia & Intensive Care Unit), BBMH, USTC, Foy's Lake, Chattogram, Bangladesh.

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ABSTRACT

Background: Now-a-days, labetalol is used for controlling hemodynamic responses to laryngoscopy and tracheal intubation in hypertensive patients. **Objective:** In this study our main goal is to evaluate the outcome of different doses of labetalol for controlling hemodynamic responses to laryngoscopy and tracheal intubation in hypertensive patients. **Method:** This a prospective, randomized, placebo controlled, double-blinded trial is conducted in tertiary medical college and hospital from January 2019 to December 2020. Where a total of 150 patients, ASA physical status I and II, aged 18–60 years, undergoing elective surgical procedures, requiring general anesthesia and orotracheal intubation were included in the study. Where in Group L1 – Syringe contained Labetalol (0.15 mg/kg diluted with 0.9% saline to 5 ml), Group L2 – Syringe contained Labetalol (0.3 mg/kg diluted with 0.9% saline to 5 ml) and Group C – Syringe contained 5 ml of 0.9% saline. **Results:** During the study, majority were belong to 41-50 years age group, 40% and 61.20% were female. Besides that, there was statistically significant difference in heart rate throughout study time between the L1 and control group ($P < 0.001$), and L2 and control group ($P < 0.001$). in addition, There was no significant difference in DBP between L1 and L2 at intubation and 1 min post-intubation. However, there was statistically significant difference in DBP between L1 and L2 group at 3 min, 5 min and 10 min post intubation ($P < 0.001$). Rate pressure product was significantly less at the time of intubation in the L1 and L2 group ($P < 0.001$) as compared to the control group. **Conclusion:** labetalol at both 0.15 mg/kg and 0.3 mg/kg iv dosages is efficacious in lowering hemodynamic responses to direct laryngoscopy and tracheal intubation in hypertensive patients in a dose-dependent manner. Bradycardia is more prevalent in patients taking labetalol at a dosage of 0.3 mg/kg.

KEYWORDS: Laryngoscopy, tracheal intubation, labetalol.

INTRODUCTION

The main alterations in the cardiovascular system during laryngoscopy and tracheal intubation are increases in heart rate and blood pressure. Stimulation of the laryngeal and tracheal tissues may also stimulate sympathetic and sympatho-adrenal reflex activity. Hemodynamic alterations are often transient and have no long-term consequences. However, in individuals with coronary artery disease, hypertension, or cerebrovascular illness, these alterations can enable and expedite the development of myocardial ischemia, arrhythmia, infarction, and cerebral hemorrhage.[1-4]

Labetalol is an antihypertensive medication that is both a selective and nonselective 1 and 2 adrenergic antagonist. Its maximal action occurs 5–15 minutes after intravenous (IV) infusion and is rapidly redistributed (5.9 min redistribution half-life). It decreases blood pressure by lowering systemic vascular resistance (1-blockade), while concomitant -blockade reduces reflex tachycardia caused by vasodilatation. In this study our main goal is to evaluate the outcome of different doses of labetalol for controlling these hemodynamic responses to laryngoscopy and tracheal intubation under the same anesthetic techniques in hypertensive patients.[5-6]

OBJECTIVE

To evaluate the outcome of different doses of labetalol for controlling these hemodynamic responses to laryngoscopy and tracheal intubation under the same anesthetic techniques in hypertensive patients.

METHODOLOGY

This study was a prospective, randomized, placebo controlled, double-blinded trial is conducted in tertiary medical college and hospital from January 2019 to December 2020.

Therefore, 150 patients, ASA physical status I and II, aged 18–60 years, undergoing elective surgical procedures, requiring general anesthesia and orotracheal intubation were included in the study. Informed consent was obtained from all the patients. The patients were randomly (computer generated randomization schedule) allocated into one of the three groups, of 50 each. Where Group L1 – Syringe contained Labetalol (0.15 mg/kg diluted with 0.9% saline to 5 ml), Group L2 – Syringe contained Labetalol (0.3 mg/kg diluted with 0.9% saline to 5 ml) and Group C – Syringe contained 5 ml of 0.9% saline.

RESULTS

In table-1 shows age distribution where majority were belong to 41-50 years age group, 40% followed by 30% belong to 31-40 years age group, 20% belong to >51 years. The following table is given below in detail:

Table 1: Age distribution.

Age group	Percent
31-40 years	30
41-50 years	40
>51 years	20
Total	100.0

In figure-1 shows gender distribution of the study group where 61.20% were female, and 38.8% were male. The following figure is given below in detail:

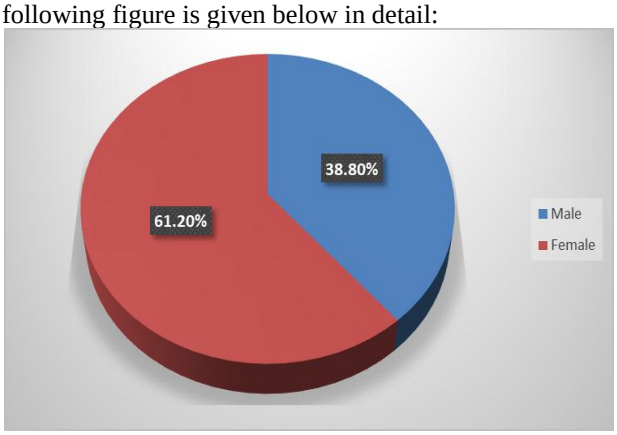

Figure 1: Gender distribution of the study group.

In table-2 shows distribution of the patients according to heart rate where there was statistically significant difference in HR throughout study time between the L1 and control group (P < 0.001), and L2 and control group (P < 0.001). At intubation, 1 min, 3 min and 10th minute post intubation HR was not statistically significantly different in the L1 and L2 group (P > 0.05). At 5 min post intubation, there was significant difference in HR between L1 and L2 groups (P < 0.001). The following table is given below in detail:

Table 2: Distribution of the patients according to heart rate.

Heart rate	Group c	Group L1	Group L2	P value C and L1	P value C and L2	P value L2 and L1
Pre-induction	82.60 ± 5.0	81.42 ± 6.0	82.21 ± 6.1	(*P* > 0.05)	(*P* > 0.05)	(*P* > 0.05)
At intubation	105.30 ± 5.3	91.20 ± 3.0	92.62 ± 5.1	*P* < 0.001	*P* < 0.001	(*P* > 0.05)
I min post-intubation	101.10 ± 5.1	92.20 ± 6.1	93.38 ± 5.0	*P* < 0.001	*P* < 0.001	(*P* > 0.05)
3 min post-intubation	90.64 ± 3.9	85.05 ± 6.0	84.58 ± 5.0	*P* < 0.001	*P* < 0.001	(*P* > 0.05)
5 min post-intubation	83.21 ± 2.4	80.59 ± 6.0	74.04 ± 9.9	*P* < 0.001	*P* < 0.001	*P* < 0.001
10 min post-intubation	72.60 ± 4.8	70.10 ± 6.2	66.04 ± 9.8	*P* < 0.001	*P* < 0.001	(*P* > 0.05)

In table-3 shows distribution of the patients according to systolic blood pressure where compared with the control group values SBP was significantly lower at all time stations in the L1 (P < 0.001) and L2 group (P < 0.001). There were no significant difference in SBP between L1 and L2 at intubation and 1 min post-intubation (P > 0.05). However, there was statistically significant difference in SBP between L1 and L2 group at 3 min, 5 min and 10 min post intubation (P < 0.001). The following table is given below in detail:

Table-3: Distribution of the patients according to systolic blood pressure.

Systolic blood pressure	Group c	Group L1	Group L2	P value C and L1	P value C and L2	P value L2 and L1
Pre-induction	131 ± 5.2	130.44 ± 1.5	132.04 ± 5.0	(*P* > 0.05)	(*P* > 0.05)	(*P* > 0.05)
At intubation	160.15 ± 13.0	146.88 ± 6.7	145.88 ± 6.0	*P* < 0.001	*P* < 0.001	(*P* > 0.05)
I min post-intubation	151.70 ± 12.0	138.96 ± 5.4	135.80 ± 5.8	*P* < 0.001	*P* < 0.001	(*P* > 0.05)
3 min post-intubation	141.90 ± 8.3	132.68 ± 5.2	120.80 ± 9.4	*P* < 0.001	*P* < 0.001	*P* < 0.001
5 min post-intubation	137.28 ± 5.6	124.24 ± 8.6	112.92 ± 11.6	*P* < 0.001	*P* < 0.001	*P* < 0.001
10 min post-intubation	130.64 ± 6.6	112.60 ± 8.2	103.20 ± 7.0	*P* < 0.001	*P* < 0.001	*P* < 0.001

In table-4 shows distribution of the patients according to diastolic blood pressure where compared with the control group values DBP was significantly lower at all time stations in the L1 (P < 0.001) and L2 group (P < 0.001). There was no significant difference in DBP between L1 and L2 at intubation and 1 min post-intubation. However, there was statistically significant difference in DBP between L1 and L2 group at 3 min, 5 min and 10

min post intubation (P < 0.001). The following table is given below in detail:

Table 4: Distribution of the patients according to diastolic blood pressure.

Diastolic blood pressure	Group c	Group L1	Group L2	P value C and L1	P value C and L2	P value L2 and L1
Pre-induction	81.60 ± 5.2	83.40 ± 5.0	80.72 ± 4.9	(*P* > 0.05)	(*P* > 0.05)	(*P* > 0.05)
At intubation	101.56 ± 3.8	92.0 ± 5.1	93.0 ± 5.2	*P* < 0.001	*P* < 0.001	(*P* > 0.05)
I min post-intubation	103.40 ± 7.9	88.48 ± 8.4	85.40 ± 11.4	*P* < 0.001	*P* < 0.001	(*P* > 0.05)
3 min post-intubation	115.01 ± 4.1	101.56 ± 86.8	92.21 ± 7.0	*P* < 0.001	*P* < 0.001	*P* < 0.001
5 min post-intubation	95.28 ± 5.6	82.88 ± 4.4	70.36 ± 9.3	*P* < 0.001	*P* < 0.001	*P* < 0.001
10 min post-intubation	83.20 ± 7.5	73.84 ± 5.2	68.88 ± 7.5	*P* < 0.001	*P* < 0.001	*P* < 0.001

In table-5 shows distribution of the patients according to rate pressure product (RPP) where RPP was significantly less at the time of intubation in the L1 and L2 group (P < 0.001) as compared to the control group. Intubation and 1 min post intubation values were comparable between the L1 and L2 group and not statistically significant (P > 0.05). However, there was statistically significant difference in RPP values between L1 and L2 group at 3 min, 5 min and 10 min post intubation (P < 0.00).

Table-5: Distribution of the patients according to rate pressure product (RPP).

Rate pressure product (RPP)	Group c	Group L1	Group L2	P value C and L1	P value C and L2	P value L2 and L1
Pre-induction	11098.12 ± 993.9	10834.12 ± 921.5	11201.88 ± 878.0	(*P* > 0.05)	(*P* > 0.05)	(*P* > 0.05)
At intubation	17755.48 ± 1948.2	14036.28 ± 1279.0	13570.20 ± 895.4	*P* < 0.001	*P* < 0.001	(*P* > 0.05)
I min post-intubation	15934.16 ± 1766.5	3454.92 ± 861.94	12912.20 ± 875.3	*P* < 0.001	*P* < 0.001	(*P* > 0.05)
3 min post-intubation	13211.44 ± 1179.0	11594.32 ± 927.3	10564.44 ± 1116.9	*P* < 0.001	*P* < 0.001	*P* < 0.001
5 min post-intubation	10184.04 ± 741.1	8055.24 ± 974.4	7218.68 ± 1290.5	*P* < 0.001	*P* < 0.001	*P* < 0.001
10 min post-intubation	83.21 ± 7.5	72.84 ± 5.2	69.88 ± 7.5	*P* < 0.001	*P* < 0.001	*P* < 0.001

DISCUSSION

Levels of RPP > 20,000 are more commonly associated with angina and myocardial ischemia.[9] In the present study, the RPP after tracheal intubation was 17755.48 ± 1948.2 in Group C, but these critical increases in RPP were avoided in Groups L1 and L2. Furthermore, the changes from baseline values in RPP immediately after tracheal intubation in Group L1 and L2 were significantly less than those in Group C. The differences in these changes of RPP following tracheal intubation may be attributed to the differences in those of HR. Tachycardia causes more stress effect on the heart than increases in BP. This effect can be due to the increase in myocardial oxygen requirement, decreased diastolic filling, and reduction in the time needed for effective coronary circulation. Tachycardia accompanied with hypertension increases the existing ischemia risk in patients with coronary artery disease.[10-11]

Values of group L1 and L2 when compared with their pre-operative values show insignificant rise (*P* > 0.05) in heart rate and MAP at the time of intubation as compared to placebo group. Increases in HR and MAP at intubation in the placebo group were 30% and 23%, respectively, in the L1 group, 16% and 12% and L2 group 11% and 11% respectively. Our results corroborate well with the other finding who administered 0.15 mg/kg of labetalol for induction and 0.25–0.3 mg/kg for maintenance of anesthesia in a study investigating its effects on perioperative stress.[12]

Increases in HR and MAP at intubation in the placebo group were 33% and 52%, respectively, and in the labetalol group, 7.3% and 21.3%, respectively.

Another study reported that a single dose of labetalol of dosage 0.25 mg/kg given preoperatively 5 min before intubation decreases HR significantly after intubation up to 10 min. [13] Other study found that labetalol of dosage 1 mg/kg given as an IV bolus 1 min before laryngoscopy was not effective in the attenuation of HR. This failure of the study can be explained by the different time of administration of the study drug because labetalol has peak effect after 5–10 min.[14]

There was statistically significant difference in HR between L1 and L2 group at 5 min post intubation (*P* < 0.00). Similarly, there was statistically significant difference in SBP, DBP, MAP and RPP between L1 and L2 group at 3 min, 5 min and 10 min post intubation (*P* < 0.00). These may because of higher dose of

labetalol used in L2 (0.3 mg/kg) group as compared to L1 (0.15 mg/kg) group.

The only side effect observed was that of group L2 (0.3 mg/kg) in form of bradycardia, intraoperatively. Seven patients (28%) developed bradycardia (pulse rate <50 beats per minute) after the study period of 10 min and atropine in 0.2 mg increments (max. 0.01 mg/kg) was given. All the patients responded to atropine treatment. There were no recurrent episodes of bradycardia. Transient premature ventricular contractions appeared immediately after tracheal intubation in two patients who received placebo saline. These arrhythmias did not need any treatment. Thus, there were no serious complications after laryngoscopy and tracheal intubation in patients who had received labetalol at both the doses.

CONCLUSION

labetalol at both 0.15 mg/kg and 0.3 mg/kg iv dosages is efficacious in lowering hemodynamic responses to direct laryngoscopy and tracheal intubation in hypertensive patients in a dose-dependent manner. Bradycardia is more prevalent in patients taking labetalol at a dosage of 0.3 mg/kg.

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