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Effect of Low Doses of Intravenous Labetalol and Lignocaine for Attenuation of Sympathomimetic Responses to Laryngoscopy and Endotracheal Intubation

[1]Mona Bhalavi , [2]Meena Singh , [3]Ritesh Upadhyay , [4]Sonali Tripathi , [5]Ekta Ratnani
[1,4,3]Assistant Professor, [2]Associate Professor, [5]Consultant Anaesthesiologist,
[1,2,4]Department of Anaesthesiology, [3]Department of Community Medicine,
[1,3,4]Chhindwara Institute of Medical Sciences, Chhindwara, Madhya Pradesh, India
[2]Super Speciality Hospital, NSCB Medical College, Jabalpur, Madhya Pradesh, India.
[5]Chandan Hospital Limited, Lucknow, Uttar Pradesh, India

***Corresponding Author:**
Dr. Sonali Tripathi
Assistant Professor, Department of Anaesthesiology, Chhindwara Institute of Medical Sciences, Chhindwara, Madhya Pradesh, India

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Abstract

Introduction:

Direct laryngoscopy and endotracheal intubation are noxious stimulus and induces sympathomimetic responses. Although well tolerated in healthy subjects, it may impose life threatening arrhythmias, left ventricular failure or rupture of cerebral aneurysm in susceptible patients. Labetalol and Lignocaine attenuate these responses but are associated with side effects of bradycardia, hypotension etc. In lower doses, chances of these side effects are comparatively low. So we designed this prospective clinical trial to assess the efficacy of intravenous labetalol and lignocaine in low doses for attenuation of sympathomimetic responses to endotracheal intubation.

Materials and Methods:

Fifty consenting patients of ASA physical status I or II of age range 20 to 60 years, scheduled for different general surgical procedures were randomly assigned to two groups; group LB and group LG. Participants of group LB and group LG were given inj. labetalol HCL 0.25 mg/kg and inj. lignocaine HCL 1 mg/Kg body weight respectively. Outcome variables were HR, SBP, DBP and MAP. These variables were recorded just after intubation and thereafter at 1, 3, 5, 7 and 10 minutes of intubation.

Results:

There was no statistically significant difference regarding the demographic characteristics of the groups. Heart rate and systolic blood pressure was lower throughout the study period in labetalol group. But the values of study parameters were always higher than the baseline in lignocaine group. Values of mean arterial pressure were slightly higher in labetalol group but it was much higher in the other group throughout the study period. Diastolic blood pressure was higher in both the groups.

Conclusion:

Labetalol 0.25 mg/Kg is an effective and safe drug to be used for attenuation of sympathomimetic responses to endotracheal intubation. Lignocaine 1 mg/Kg is also safe and effective to some extent.

Keywords: Labetalol, laryngoscopy and endotracheal intubation, lignocaine, sympathomimetic reflexes.

Introduction

Direct laryngoscopy and endotracheal intubation frequently induces a cardiovascular stress response manifesting as hypertension, tachycardia, and increase in serum catecholamine.[1]

This reflex hemodynamic changes are better tolerated in healthy individuals, but they are greatly exaggerated and detrimental in patients with co-morbidities.[2-4]

In susceptible individuals, these hemodynamic stress responses can evoke life-threatening conditions such as left ventricular failure, myocardial ischemia, cerebral hemorrhage, and ruptured cerebral aneurysm etc.[5] Intravenous (IV) lignocaine[6-8] has showed a promising result. The mechanism of IV local anesthetics appears to result from an increased threshold for airway stimulation and central inhibition of sympathetic transmission. Although increasing dose of lignocaine may lead to hypotension, bradycardia, and hypoxia. Labetalol, an α and β blocker, has also been found to be useful in preventing perioperative undesirable cardiovascular events,[9-12] but in higher doses, it may cause hypotension and bradycardia.

Here, originates in the rationale to continue the quest for an ideal anesthetic technique which is effective as well as safe to attenuate undesirable cardiovascular effects. Numerous efforts have been made to obtund these untoward reflexes by the use of various measures and drugs. Selection of a pharmacological adjunct is tricky because efficacy has to be weighed against its safety. Both the study drugs have shown their efficacy but in higher doses and only limited studies are available with low doses. Hence, this clinical study was carried out to evaluate the effects of IV lignocaine HCl and labetalol HCl in low doses for attenuation of hemodynamic response to laryngoscopy and intubation.

Aim and objectives:

The primary objectives of this study are:

1. To assess the hemodynamic changes during laryngoscopy (DL) and endotracheal intubation.
2. To evaluate the efficacy of labetalol HCl and lignocaine HCl in attenuating sympathomimetic response to laryngoscopy and endotracheal intubation.
3. To compare and select best among the drugs in prevention of sympathomimetic response to laryngoscopy and endotracheal intubation.
4. To observe any untoward, adverse and beneficial effects.

Materials and Methods:

After approval from the institutional ethical committee, this study was conducted on 50 consenting patients of age group 20–60 years of either sex and American Society of Anesthesiologists (ASA) Grade I or II scheduled for various general surgical procedures under endotracheal anesthesia were included in this study.

Patients of ASA Grade III or more, pregnant and lactating women, morbid obesity, hypertension, and anticipated difficult intubation were excluded from the study.

Intervention plan and group allocation:

Patients were blinded by sealed envelope technique and observer anesthesiologist was kept unaware of which drug was injected to which patient thus avoiding observer bias. The anesthesiologist who injected the study drugs took no further part in the study. Selected 50 patients were randomly divided into two groups depending on the study drug to be given:

• Group LB: Injection labetalol HCl 0.25 mg/kg body weight diluted to 10ml with 0.9% saline was given IV 5min before intubation over 60 s

• Group LG: Injection lignocaine HCl 1 mg/kg body weight diluted to 10ml with 0.9% saline was given IV 5min before intubation over 60 s.

Preanesthetic assessment:

All the selected patients were carried out with complete history, general examination, airway assessment, systemic examination along with routine blood investigations, chest X-ray, and

electrocardiogram (ECG).

Premedication

All the patients were kept nil orally for at least 8hours before procedure. Tablet Lorazepam 1mg and tablet ranitidine 150mg were given night before surgery. All the patients were uniformly premedicated with injection Glycopyrrolate 0.2mg intramuscular, 30min before shifting to Operation Theater.

Anesthesia management

On arrival of patient in the operation theater, IV access with 18 gauge cannula was established and

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ringer lactate (RL) infusion was started. All patients were preloaded with 500 ml RL before starting induction. Noninvasive monitoring such as non-invasive blood pressure, pulse oximeter, 5 leads ECG were connected and basal pulse rate, systolic blood Pressure (SBP), diastolic blood pressure (DBP) and mean blood pressure (MBP) were measured and recorded. Study drug was given 5min before intubation over 60 sec.

Thereafter, preoxygenation with 100% oxygen was started and general anesthesia was induced with injection fentanyl 2 µg/kg, injection Thiopentone sodium up to 5 mg/kg body weight. After securing mask ventilation injection vecuronium bromide 0.1 mg/kg body weight administered IV to facilitate endotracheal intubation. Mask ventilation with 100% oxygen was continued for 3 or more min in order to time endotracheal intubation after 5min of administration of study drugs. Laryngoscopy was done with Macintosh laryngoscope blade and trachea was intubated with appropriate sized endotracheal tube. Tube was secured after confirming bilateral equal air entry on auscultation. Intermittent positive pressure ventilation was started with tidal volume 8 ml/kg body weight and frequency suitable to maintain end-tidal carbon-di-oxide within normal range. Anesthesia was maintained with 50% oxygen in air and Isoflurane up to 1 minimum alveolar concentration with intermittent doses of fentanyl and vecuronium. After intubation (AI) till conclusion of surgery and reversal of anesthesia, both continual and continuous monitoring of vital parameters was done. Any bradycardia, that is, heart rate (HR) below 50 beats/min was treated with small aliquots of 0.3mg of IV atropine. Fall in MBP below 60mm of Hg was treated with small boluses of Mephentermine 6mg. The incidence of bradycardia and hypotension was noted. At the conclusion of surgery, residual effect of muscle relaxant was reversed with combination of Glycopyrrolate 0.01 mg/kg body weight and Neostigmine 0.05 mg/kg body weight. Any complications occurred perioperatively were noted.

Total duration of laryngoscopy was noted. Those cases where duration of laryngoscopy and endotracheal intubation was more than 20 sec were excluded from the study and equal number of new cases was added to complete the study.

Outcome variables

HR, SBP, DBP and MAP.

Frequency of data recordings

Readings of hemodynamic parameters were taken before starting study drug and was taken as basal value (BV) and then during laryngoscopy & endotracheal intubation (DL). Five more readings were recorded at 1(AI 1), 3(AI 3), 5(AI 5), 7(AI 7) and 10 (AI 10) minute after endotracheal intubation.

Statistical analysis

Sample size was calculated on assumption of 30% reduction in HR with study drugs and with power of 80% and 95% confidence level. The sample size came to be 22 in each group.

Although there was no chance of the loss of follow up of cases, however 10% more subjects were added in each group. Hence, finally, there were 25 cases in each group. Statistical analysis was carried out using SPSS version 19 (SPSS, IBM, Chicago, IL, USA). The study data were presented as mean±standard deviation. Demographic data were analyzed with Chi-square test and independent t-test. For comparison of means between groups ANOVA statistical tool was used.

Results:

In the present study, both the study groups were comparable on demographic pattern such as age, weight and sex. [Table 1]

Basal hemodynamic variables such as mean HR, SBP, DBP and MAP [Tables 2-5] were also comparable between the groups (P>0.05 insignificant).

The increase in mean HR was observed in both the groups but lower in labetalol group [Table 2]. There was increase in SBP in group lignocaine but not in labetalol group [Table 3]. DBP increased in both the groups almost similarly [Table 4]. Increase in MBP was higher in group LB than that of group LG [Table 5].

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Table 1: Demographic pattern of the study population

Parameters	Group LB	Group LG	P-value
Age (years)	42.32±10.63	39.40±8.27	0.283
Weight (kg)	61.48±9.35	61.76±6.71	0.904
Sex(male/female)	14/11	13/12	0.951

Table 2: Comparison of mean heart rate among different groups

Recording Time	Group LB Mean±SD	Group LG Mean±SD	Group LB versus Group LG P-value
BV	98.52±8.53	98.84±11.95	0.91
DL	103.4±8.73	111.6±9.40	0.00
AI 1	101.08±8.65	111.04±10.74	0.00
AI 3	96.68±8.43	108.4±10.70	0.00
AI 5	97.4±6.91	105.6±11.06	0.00
AI 7	96.48±7.10	103.16±8.85	0.00
AI 10	97.6±6.91	100.24±8.70	0.24

BV=Basal value, DL=During laryngoscopy, AI=After intubation, SD=Standard deviation.

Table 3: Comparison of mean systolic blood pressure among different groups

Recording Time	Group LB Mean±SD	Group LG Mean±SD	Group LB versus Group LG P-value
BV	122.76±7.76	122.16±7.06	0.77
DL	127.72±9.41	138.92±12.26	0.00
AI 1	123.12±6.10	139.08±10.91	0.00
AI 3	121.72±6.52	136.04±11.76	0.00
AI 5	120.28±7.71	135±12.23	0.00
AI 7	121.08±8.23	134.6±13.19	0.00
AI 10	120.08±9.78	133.72±10.86	0.00

BV=Basal value, DL=During laryngoscopy, AI=After intubation, SD=Standard deviation.

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Table 4: Comparison of mean diastolic blood pressure among different groups

Recording Time	Group LB Mean±SD	Group LG Mean±SD	Group LB versus Group LG P-value
BV	78.88±2.94	79.6±5.53	0.57
DL	87.16±8.28	94.32±12.13	0.01
AI 1	85.16±5.94	91.76±13.09	0.02
AI 3	84.32±7.15	89.65±11.75	0.05
AI 5	85.04±8.83	89.36±12.29	0.16
AI 7	86.00±7.76	88.56±12.87	0.40
AI 10	83.6±10.22	87.36±11.65	0.23

BV=Basal value, DL=During laryngoscopy, AI=After intubation, SD=Standard deviation.

Table 5: Comparison of mean arterial pressure among different groups

Recording Time	Group LB Mean±SD	Group LG Mean±SD	Group LB versus Group LG P-value
BV	93.507±3.67	93.786±5.27	0.82
DL	100.68±7.95	109.186±10.21	0.00
AI 1	97.813±5.57	107.533±11.01	0.00
AI 3	96.786±6.37	105.133±10.46	0.00
AI 5	96.786±7.74	104.573±11.38	0.00
AI 7	97.693±6.96	103.906±12.05	0.03
AI 10	95.76±9.33	102.833±10.31	0.01

BV=Basal value, DL=During laryngoscopy, AI=After intubation, SD=Standard deviation.

Discussion:

Our study showed a sudden increase in all the hemodynamic parameters up to variable extent after direct laryngoscopy and endotracheal intubation in both the groups. Thereafter all hemodynamic variables started to fall throughout the study. These hemodynamic changes were reduced to varying degrees by both the study drugs used but most effectively attenuated by labetalol. The hemodynamic changes stemming from airway instrumentation are due to sympathoadrenal discharges caused by epipharyngeal and par pharyngeal stimulation.[13] This stimulation elicit physiological response in the form of sympathoadrenal response seen in adults and vasovagal reflex predominantly seen in children. Reid and Brace were the first to report the circulatory response to laryngeal and tracheal stimulation in anaesthetized man as tachycardia and increase in arterial blood pressure.[14] Takeshima et al found rise in mean arterial pressure of 20mmHg at the time of laryngoscopy and tracheal intubation and they concluded that laryngoscopy was a more potent stimulus to hypertension than intubation.[15]

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In our study, lignocaine attenuated the HR but showed significantly less effective attenuation as compared to labetalol group. There was only slight and statistically insignificant increase in SBP in labetalol group at 1min AI [Table 3]. Thereafter up to 10th min of intubation SBP was significantly lower than baseline values. Contrary to labetalol group, in lignocaine group SBP was significantly higher at laryngoscopy and intubation, and remained higher till 10th min of study period. Hence, on comparison of labetalol and lignocaine, Labetolol was found to be more efficacious than lignocaine in attenuating the SBP response to laryngoscopy and intubation. Labetalol is selective α1 and nonselective β1 and β2 adrenergic receptor blocking agent, it lowers the systolic blood pressure by decreasing systemic vascular resistance (α1 action) and also controls reflex tachycardia triggered by vasodilatation by β blockade. It also has weak β2 agonistic activity therefore may cause vasodilatation. Cardiac output remains unchanged.[16] Lignocaine practically has minimal hypertensive and no vasodilating properties. Thus, the change in mean SBP was more effectively attenuated by labetalol, whereas lignocaine showed lower attenuation effect among both the study drugs.

In our study, the rise in DBP was not significantly attenuated ($P<0.05$) by lignocaine, whereas labetalol showed statistically significant attenuation at least up to 3min [Table 4]. The reason might be that our study drugs labetalol and lignocaine are not very effective in controlling DBP rise. It is stated in the pharmacology of labetalol that "Increase in SBP rise during exercise are reduced by labetalol but corresponding changes in DBP are essentially normal.[17] Labetalol found to be more efficacious in attenuating the mean arterial pressure response to laryngoscopy and intubation. However, this effect was not observed at laryngoscopy and immediately thereafter. However, grossly the change in mean arterial pressure was more effectively attenuated by labetalol, while lignocaine showed very less attenuation effect among both the study drugs.

In a recent study by Kewalramani et al on comparison of Labetalol with dexmedetomidine, dexmedetomidine better attenuated the sympathomimetic responses to endotracheal intubation. Although labetalol had maintained the stability of the blood pressure, HR response was not attenuated better DL and intubation.[18] Two patients of labetalol group had hypotension. Bradycardia was treated with injection atropine 0.3mg and for treatment of hypotension injection Mephentermine 6mg IV was given. These three cases were excluded from the study. Moreover, three other patients were recruited to complete the study. With both intra and inter-group comparison, labetalol found to be better for the attenuation of HR, SBP, DBP and mean arterial pressure during and after laryngoscopy and endotracheal intubation. The hemodynamic parameters were relatively more stable in labetalol group intraoperatively as compared to lignocaine.

Conclusion:

Laryngoscopy and endotracheal intubation is invariably associated with increase in hemodynamic variables. Labetalol 0.25 mg/kg is an effective and safe drug to be used for attenuation of sympathomimetic responses to endotracheal intubation. Lignocaine 1 mg/kg is also safe and effective to some extent.

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