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Original Article

A Comparative Study of Intravenous Esmolol and Labetalol in Low Doses for Attenuation of Sympathomimetic Responses to Laryngoscopy and Endotracheal Intubation

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Abstract

Introduction: Direct laryngoscopy and endotracheal intubation are a noxious stimulus and induce sympathomimetic responses. Although properly tolerated in normal and healthy subjects, it is able to impose serious arrhythmias, left ventricular failure, or rupture of cerebral aneurysm in vulnerable patients. Esmolol and labetalol attenuate those responses however are related to some untoward outcomes such as bradycardia and hypotension. In low doses, chances of those expected untoward outcomes are relatively low.

Purpose: We designed this prospective observational clinical study to assess the efficacy of intravenous esmolol and labetalol in low doses for attenuation of sympathomimetic responses to endotracheal intubation.

Materials and Methods: Fifty consenting patients of American Society of Anesthesiologists physical repute I or II of age between 20 and 60 years, scheduled for surgeries requiring general anesthesia, were randomly allocated to two groups; group ES and group LB, given esmolol hydrochloride (HCL) 0.5 mg/kg and labetalol HCL 0.25 mg/kg body weight, respectively. Final result variables were heart rate (HR), systolic blood pressure (SBP), diastolic blood pressure (DBP), and mean arterial pressure (MAP). These variables had been recorded immediately after intubation (AI) and then at 1, 3, 5, 7, and 10 min AI.

Results: There was no statistically considerable distinction regarding the demographic traits of both the groups. HR and SBP were significantly lower throughout the study period in labetalol group. Values of MAP were slightly higher in labetalol group but it was much higher in esmolol group throughout the study period. DBP 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. Esmolol 0.5 mg/kg is also safe and effective to some extent.

Key words: Endotracheal intubation, Esmolol, Labetalol, Laryngoscopy, Sympathomimetic reflexes

INTRODUCTION

Cardiovascular stress response is frequently induced by laryngoscopy and endotracheal intubation results in tachycardia and hypertension due to increase in serum catecholamine.[1]

These hemodynamic changes are well tolerated in healthy individuals, but are life threatening in susceptible patients having multiple coexisting diseases.[2-4] In susceptible individuals, these hemodynamic stress responses can evoke life-threatening conditions such as myocardial ischemia, left ventricular failure, and cerebral hemorrhage.[5] Esmolol is a cardio selective b1-blocker having quicker onset and ultra-short duration of action. It causes depressor action on myocardium; hence, its place still remains to be defined

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especially in cardiac risk patients. Labetalol, a combined α and β blocker, has also been found to be effective for prevention of perioperative detrimental cardiovascular events,[6-9] but it can cause hypotension and bradycardia, when used in the higher doses.

Various efforts have been made to attenuate these untoward reflexes by the use of a variety of drugs. Selection of a pharmacological adjunct is tricky because efficacy has to be weighed against its safety. Hence, this clinical study was carried out to evaluate the effects of IV esmolol hydrochloride (HCl) and labetalol HCl in low doses for attenuation of hemodynamic response to laryngoscopy and intubation.

Aim and Objectives

The objectives of the study are as follows:

1. To assess and compare the efficacy of esmolol and labetalol for attenuation of sympathomimetic response to laryngoscopy and endotracheal intubation
2. To observe any adverse or beneficial effects.

MATERIALS AND METHODS

After approval of the institute ethical committee and informed consent, this study was conducted on 50 patients between the age of 20 and 60 years of either sex of American Society of Anesthesiologists (ASA) Grade I or II scheduled for different surgeries requiring general anesthesia was 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 kept blinded by sealed envelope method and observer anesthesiologist was also uninformed of which drug was injected to which patient to avoid observer bias. The anesthesiologist who injected the study drugs took no further part in the study. Selected 50 patients were randomly allocated into two groups based on the study drug to be given:

1. Group ES: Inj. Esmolol 0.5 mg/kg body weight diluted to 10 ml with normal saline was given intravenously 5 min before intubation over 60 s
2. Group LB: Inj. Labetalol 0.25 mg/kg body weight diluted to 10 ml with normal saline was given intravenously 5 min before intubation over 60 s.

Pre-anesthetic Assessment

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

Premedication

All the patients were kept nil orally for at least 8 h before procedure. Tablet Lorazepam 1 mg and tablet ranitidine 150 mg were given night before surgery. Inj. Glycopyrrolate 0.2 mg intramuscularly had given to all the patients as premedication, 30 min before shifting the patient to operation theater.

Anesthesia Management

After taking the patient in the operation theater, intravenous cannulation was done and ringer lactate infusion was started. Basal parameters such as heart rate (HR), mean blood pressure (MBP), systolic blood pressure (SBP), and diastolic blood pressure (DBP) had been recorded. Study drug was given 5 min before intubation over 60 s.

Thereafter, preoxygenation with 100% oxygen was started and general anesthesia was induced with inj. fentanyl 2 μg/kg and inj. Thiopentone up to 5 mg/kg body weight. After securing mask ventilation, inj. vecuronium 0.1 mg/kg body weight administered intravenously for endotracheal intubation. Mask ventilation with 100% oxygen was continued for three or more min to time endotracheal intubation after 5 min of administration of study drugs, followed by endotracheal intubation. Anesthesia was maintained with 50% oxygen in air and isoflurane with intermittent doses of fentanyl and vecuronium, along with intermittent positive pressure ventilation. After intubation (AI) till conclusion of surgery and reversal of anesthesia, continuous monitoring of vital parameters was done. The incidence of bradycardia and hypotension was noted. After surgery, reversal done with combination of inj. Glycopyrrolate 0.01 mg/kg body weight and Neostigmine 0.05 mg/kg body weight. Any complications occurred perioperatively were noted.

Frequency of Data Recordings

Readings of hemodynamic parameters were taken before starting study drug and were taken as basal value (BV) and then during laryngoscopy (DL) and 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) min after endotracheal intubation.

Statistical Analysis

Statistical analysis was carried out using Statistical Package for the Social Sciences (SPSS) version 19 (SPSS, IBM, Chicago, IL, USA). The study data were presented as mean ± standard deviation. Student's "*t*"-test was used for inter-group comparison. $P > 0.05$ and <0.05 were considered statistically insignificant and significant, respectively.

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 mean arterial pressure (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 esmolol but not in labetalol group [Table 3]. DBP increased in both the groups almost similarly [Table 4]. Increase in MBP was higher in group ES than that in group LB [Table 5].

DISCUSSION

Our study showed a sudden increase in all the hemodynamic parameters up to variable extent DL and endotracheal intubation in different 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 the most effectively attenuated by labetalol. Esmolol was not as effective as labetalol to attenuate the hemodynamic response. The hemodynamic changes resulted from laryngoscopy and intubation are due to sympathoadrenal discharges caused by epipharyngeal stimulation.[10] Reid and Brace had reported the circulatory responses to laryngeal and tracheal stimulation in anesthetized man as tachycardia and increase in arterial blood pressure.[11] Takeshima *et al.* found rise in MAP of 20 mmHg at the time of laryngoscopy and tracheal intubation and they concluded that laryngoscopy was a more potent stimulus to hypertension than intubation.[12]

In our study, we used 0.5 mg/kg of esmolol, given 5 min before intubation, which though attenuated the HR but showed significantly less effective attenuation as compared to labetalol group. The reason might be that both the drugs showed their maximum effect in 5 min and peak hemodynamic effects occurred within 6–10 min of administration[13] but esmolol had a shorter duration of action (elimination half-life of 9 min) as compared to labetalol (elimination half-life of 5–8 h). Even in study with bolus dose of esmolol 2 mg/kg was found to be successful for attenuation of rise in HR due to laryngoscopy and endotracheal intubation and the augmentation of blood pressure was not completely and effectively abolished.[14]

Table 1: Demographic pattern of the study population

Parameters	Group ES	Group LB	*P*-value
Age (years)	41.12±10.23	42.32±10.63	0.686
Weight (kg)	58.08±6.62	61.48±9.35	0.144
Sex (male/female)	15/10	14/11	–

Table 2: Comparison of mean HR among different groups

Recording time	Group ES (Mean±SD)	Group LB (Mean±SD)	*P*-value
BV	97.64±11.98	98.52±8.53	0.76
DL	109.16±9.84	103.4±8.73	0.03
AI 1	106.44±8.84	101.08±8.65	0.03
AI 3	104.28±5.01	96.68±8.43	0.00
AI 5	102.28±3.63	97.4±6.91	0.00
AI 7	100.76±6.93	96.48±7.10	0.03
AI 10	100.08±6.12	97.6±6.91	0.18

BV: Basal value, DL: During laryngoscopy, AI: After intubation, SD: Standard deviation, HR: Heart rate

Table 3: Comparison of mean SBP among different groups

Recording time	Group ES (Mean±SD)	Group LB (Mean±SD)	*P*-value
BV	121.32±6.56	122.76±7.76	0.48
DL	133.88±9.40	127.72±9.41	0.01
AI 1	130.36±11.63	123.12±6.10	0.00
AI 3	130.04±6.95	121.72±6.52	0.00
AI 5	128.56±5.51	120.28±7.71	0.00
AI 7	128.92±7.26	121.08±8.23	0.00
AI 10	127.44±7.42	120.08±9.78	0.00

BV: Basal value, DL: During laryngoscopy, AI: After intubation, SD: Standard deviation, SBP: Systolic blood pressure

Table 4: Comparison of mean DBP among different groups

Recording time	Group ES	Group LB	*P*-value
BV	77.76±6.90	78.88±2.94	0.46
DL	89.12±11.79	87.16±8.28	0.50
AI 1	88.40±8.45	85.16±5.94	0.12
AI 3	87.16±8.48	84.32±7.15	0.20
AI 5	87.08±4.99	85.04±8.83	0.32
AI 7	89.68±5.58	86.00±7.76	0.06
AI 10	86.47±7.8	83.6±10.22	0.26

BV: Basal value, DL: During laryngoscopy, AI: After intubation, SD: Standard deviation, DBP: Diastolic blood pressure

Table 5: Comparison of MAP among different groups

Recording time	Group ES	Group LB	*P*-value
BV	92.280±5.69	93.507±3.67	0.37
DL	104.040±9.74	100.68±7.95	0.18
AI 1	102.386±8.19	97.813±5.57	0.02
AI 3	101.453±6.35	96.786±6.37	0.01
AI 5	100.906±4.05	96.786±7.74	0.02
AI 7	102.760±5.64	97.693±6.96	0.00
AI 10	100.133±6.89	95.76±9.33	0.06

BV: Basal value, DL: During laryngoscopy, AI: After intubation, SD: Standard deviation, MAP: Mean arterial pressure

There was only slight and statistically insignificant increase in SBP in labetalol group at 1 min AI [Table 3]. Thereafter, up to 10th min of intubation, SBP was significantly lower than baseline values. Contrary to labetalol group, SBP was significantly higher in esmolol group at DL and intubation, and remained higher till 10th min of study period. We found that, labetolol was more effective than esmolol for attenuation of rise in SBP due to laryngoscopy and intubation. Esmolol is a β1 (cardio selective) adrenergic receptor blocking agent with no action on peripheral vasculature whereas labetalol is selective α1 and non-selective β1 and β2 adrenergic receptor blocking agent, it decreases blood pressure by lowering peripheral vascular resistance (α1 action) and also attenuates reflex tachycardia. It also has weak β2 agonistic activity therefore may cause vasodilatation. Cardiac output remains unchanged.[13]

In our study, the increase in DBP was not significantly decreased ($P < 0.05$) by esmolol, whereas labetalol showed statistically significant attenuation at least up to 3 min [Table 4]. It is stated in the pharmacology of labetalol that "Increase in SBP rise during exercise is reduced by labetalol but corresponding changes in DBP are essentially normal." Esmolol also has more effect on SBP than on DBP.[15,16] Labetalol was found to be more effective than esmolol for attenuation of MAP in response to endotracheal intubation. However, this effect was not observed at DL and immediately thereafter. However, grossly the change in MAP was most effectively attenuated by labetalol, followed by esmolol. Our results concurred with the study of Bensky *et al.*[17] They found that esmolol at dose of 0.2–0.4 mg/kg resulted in 21.7–11.1% increase in MAP just after endotracheal intubation. Whereas, the increase in MAP was 27% in control group.

Bradycardia was noted in one patient in group esmolol. Hypotension was seen in two patients of group labetalol. Bradycardia was treated with injection atropine 0.3 mg and for the treatment of hypotension injection Mephentermine 6 mg 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 MAP during and after laryngoscopy and endotracheal intubation. The hemodynamic parameters were relatively more stable in labetalol group intraoperatively as compared to esmolol.

CONCLUSION

Laryngoscopy and endotracheal intubation is consistently associated with increase in hemodynamic variables. Labetalol 0.25 mg/kg is a safe and effective drug which can be used for attenuation of sympathomimetic responses to laryngoscopy and endotracheal intubation. Esmolol 0.5 mg/kg is also safe and effective to some extent.

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