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Research Article

Attenuation of hemodynamic response to laryngoscopy and endotracheal intubation with two different doses of labetalol in hypertensive patients

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KEYWORDS

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Abstract *Purpose:* The present study compared the efficacy of two different doses of labetalol, for attenuation of hemodynamic response to laryngoscopy and intubation in hypertensive patients.
Patients and methods: 75 hypertensive patients, aged 18–60 years undergoing elective surgical procedures, require general anesthesia and orotracheal intubation. Patients were allocated to any of the three groups (25 each), Group C (control) 5 ml 0.9% saline. Group L1 (labetalol) 0.15 mg/kg diluted with 0.9% saline to 5 ml. Group L2 (labetalol) 0.3 mg/kg diluted with 0.9% saline to 5 ml. In the control group 5 ml of 0.9% saline was given i.v. 5 min prior to intubation. In the L1 group 0.15 mg/kg of labetalol was given i.v. 5 min prior to intubation. In the L2 group 0.3 mg/kg of labetalol was given i.v. 5 min prior to intubation. All the patients were subjected to the same standard anesthetic technique. Heart rate (HR), systolic blood pressure (SBP) and diastolic blood pressure (DBP) were recorded prior to induction, at time of intubation and 1, 3, 5, and 10 min after intubation. Mean arterial pressure (MAP) and rate pressure product (RPP) were calculated.
Results: Compared to placebo both the doses of labetalol (0.15 mg/kg) and (0.3 mg/kg) significantly attenuated the rise in heart rate, systolic blood pressure, and RPP during laryngoscopy and intubation. However, the difference was not statistically significant between both doses of labetalol at intubation, 1 min, 3 min and 10 min post-intubation.
Conclusion: Both doses of labetalol (0.15 mg/kg and 0.3 mg/kg) attenuate hemodynamic response to laryngoscopy and intubation in dose dependent manner.

1. Introduction

Increases in heart rate and blood pressure are the principal changes in the cardiovascular system during laryngoscopy and tracheal intubation. Stimulus of the laryngeal and tracheal

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tissues may also cause increases in both sympathetic and sympatho-adrenal reflex activities [1,2]. Hemodynamic changes are generally temporary without any sequelae. However, these changes can facilitate and accelerate the development of myocardial ischemia, arrhythmia, infarction and cerebral hemorrhage in patients with coronary artery disease, hypertension or cerebrovascular disease [3,4]. Different pharmacologic agents such as lidocaine, vasodilator agents inhibiting sympatho-adrenal response, α- and ß-adrenergic blockers, opioids and calcium channel blockers can be administered prior to tracheal intubation in order to prevent hemodynamic responses [5–10].

Labetalol is an unique oral and parenteral antihypertensive drug that is α1- and nonselective β1- and β2-adrenergic antagonist. It reaches its peak effect at 5–15 min after intravenous (IV) injection and rapidly redistributes (5.9 min redistribution half-life). It lowers BP by decreasing systemic vascular resistance (α1-blockade), whereas reflex tachycardia triggered by vasodilatation is attenuated by simultaneous β-blockade. Cardiac output remains unchanged [11–19]. The aim of the present study was to compare the efficacy of two different doses of labetalol for controlling these hemodynamic responses to laryngoscopy and tracheal intubation under the same anesthetic techniques in hypertensive patients.

2. Patients and methods

This study was a prospective, randomized, placebo controlled, double-blinded trial comparing two different doses of labetalol in decreasing the hemodynamic response during rigid laryngoscopy and intubation. The protocol was approved by the Institutional Review Board and was in accordance with International Conference on Harmonization; Good Clinical Practice (ICH-GCP) standards.

Sample size was calculated by power analysis, using a two-sample *t* test, with a two-sided type I error of 5% ($\alpha = 0.05$) and power at 80.37 ($\alpha = 0.19$). Therefore, 75 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. According to the diagnostic criteria of the Joint National Committee on Hypertension (JNC-8), hypertension was defined if systolic blood pressure was >140 mmHg and/or diastolic blood pressures were >90 mmHg. During pre-anesthetic evaluation patients were identified who are hypertensive but their hypertension was controlled by antihypertensive drugs such as calcium channel antagonists (e.g., nifedipine, nicardipine, diltiazem) and renin-angiotensin inhibitors (e.g., captopril) for varying periods of time. None had a history of myocardial ischemia or infarction, nor had an abnormal ECG on admission to the hospital. Patients with cardiovascular, pulmonary, hepatic, and renal disease; those on B blockers; patients with difficult airway; laryngoscopy and intubation time more than 20 s, or requiring more than two attempts were excluded from the study.

The patients were randomly (computer generated randomization schedule) allocated into one of the three groups, of 25 each. Blinding was done using the sequentially numbered opaque sealed envelope (SNOSE) technique. Patients were kept nil orally for 8 h prior to surgery and morning dose of antihypertensive drugs was given at 6 am with sips of water on the day of the surgery. All patients were premedicated intravenously 10 min prior to induction with inj. ondansetron 0.1 mg/kg, and inj. midazolam 0.05 mg/kg. In a double blind manner, one 5 ml syringe was prepared for each patient.

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).
Group C – Syringe contained 5 ml of 0.9% saline.

After recording the baseline parameters, patients were pre-oxygenated with 100% O_2 by a face mask for 3 min and then study drug was administered *iv* five minutes before intubation. Anesthesia was induced with 5 mg kg^{-1} thiopentone *iv*, and loss of the eyelash reflex was confirmed followed by 0.1 mg kg^{-1} vecuronium *iv*. Direct laryngoscopy with a standard Macintosh laryngoscope blade for tracheal intubation was initiated five minute after administration of study drug. None received topical lidocaine and opioids before laryngoscopy for tracheal intubation. All intubations were performed by the first author, and were accomplished within 20 s. Tracheal tubes of ID 7.0 mm and 8.0 mm were used for female and male patients, respectively. After tracheal intubation, anesthesia was maintained with 4 L min^{-1} nitrous oxide, 2 L min^{-1} oxygen and isoflurane 1.0% and intermittent boluses of I mg vecuronium bromide. Manual ventilation of the lungs was adjusted to maintain an end-tidal CO_2 tensions between 35 mmHg and 40 mmHg as measured by an anesthetic/respiratory gas analyzer (AS/3™, Datex, Helsinki, Finland). At the end of surgery, neuromuscular blockade was reversed with inj. neostigmine (40 μg/kg) and inj. glycopyrrolate (10 μg/kg). Heart rate, systolic blood pressure (SBP), and diastolic blood pressure (DBP) were recorded prior to induction, at time of intubation and 1, 3, 5, and 10 min after intubation. Mean arterial pressure (MAP) and rate pressure product (RPP) were calculated for the same time stations. Abnormal ECG changes were also recorded.

2.1. Statistical analysis

Statistical analysis was performed using the SPSS software version 20 (Chicago, IL, USA). Patient demographics were compared with analysis of variance (ANOVA). The study data were analyzed using statistical methods of mean, standard deviation, paired students "*t*" test (for values within the group at different time stations) and independent samples "*t*" test (for comparison of intergroup values). All values were expressed as mean ± SD. $P < 0.05$ was considered as significant (*S*) and $P > 0.05$ as statistically non-significant (NS).

3. Results

The patients in the three groups were comparable with respect to age, weight, sex, and duration of surgery or anesthesia (Table 1).

The pre-induction values of heart rate (HR) were comparable between groups with no significant difference (Table 2). 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