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Original Article

Effect of gabapentin pretreatment on the hemodynamic response to laryngoscopy and tracheal intubation in treated hypertensive patients †

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ABSTRACT

Objective: This randomized, double-blind study was conducted to evaluate the effect of gabapentin pretreatment on the hemodynamic response to laryngoscopy and endotracheal intubation (LETI) in treated hypertensive patients undergoing surgery.

Methods: A total of 100 controlled hypertensive patients aged 35–60 years, undergoing elective surgery under general anesthesia with endotracheal intubation, were randomly allocated into three groups. Group 1 patients received placebo at night and 2 hours prior to induction of anesthesia. Group 2 patients received placebo at night and 800 mg gabapentin 2 hours prior to induction of anesthesia. Group 3 patients received 800 mg gabapentin at night and 2 hours prior to induction of anesthesia. Anesthesia was induced with thiopentone, fentanyl, and vecuronium and maintained with isoflurane in oxygen and nitrous oxide. Patients' heart rate (HR), blood pressure (BP), and electrocardiography (ECG) changes were recorded prior to induction, after induction, and at 0 minutes, 1 minute, 3 minutes, 5 minutes, and 10 minutes after intubation. Any episodes of hypotension, bradycardia, tachycardia, hypertension, arrhythmia, and ST-T wave changes were recorded and treated accordingly.

Results: The HR was comparable among groups, with a transient rise just after intubation, followed by a gradual fall thereafter at 3 minutes, 5 minutes, and 10 minutes compared with baseline. A significant increase in BP after intubation was reported in Group 1 but not in Group 2 and Group 3. The mean arterial pressure (MAP) was significantly higher in Group 1 at 0 minute, 1 minute and 3 minutes post-intubation as compared with Group 2 and Group 3 ($p = 0.014$). Three patients in Group 1, four patients in Group 2, and 10 patients in Group 3 developed hypotension and were treated with ephedrine, whereas five patients in Group 1 and one patient in Group 2 had hypertension after tracheal intubation. There was no significant difference between the groups with respect to the number of patients who received ephedrine boluses and in whom isoflurane had to be increased due to hypertension. No episode of bradycardia, tachycardia, dysrhythmia, or ST-T wave changes was reported.

Conclusion: Gabapentin 800 mg in a single or double dose was equally effective in attenuating the hypertensive response to laryngoscopy and tracheal intubation in treated hypertensive patients.

1. Introduction

Laryngoscopy and endotracheal intubation (LETI) is accompanied by reflex hemodynamic changes in the form of hypertension, tachycardia, and dysrhythmias. Patients with hypertension, both treated and untreated, are more prone to exaggerated pressor response to LETI than are normotensive patients.[1,2] Hypertensive patients also have a greater incidence of coexisting coronary artery and cerebrovascular disease. The exaggerated pressor response to LETI in these patients can evoke life-threatening conditions which include myocardial ischemia, pulmonary edema, cardiac failure and cerebral hemorrhage.[2–4] Various drugs have been used to attenuate the hemodynamic response to LETI in this group of patients like nitroglycerine,[5] verapamil,[6] diltiazem,[7] esmolol,[8] alfentanil, and remifentanil[9] with variable success rates.

Gabapentin, a third-generation antiepileptic drug, has been found to be effective for the prevention of LETI response in

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normotensive patients.[10–14] In a study comparing gabapentin with clonidine, Marashi et al[15] reported that gabapentin was better than clonidine in attenuating the hemodynamic response to LETI. However, there are no reports on the efficacy of gabapentin in attenuating the hemodynamic response to LETI in hypertensive patients. Therefore, this double-blind, randomized study was planned to evaluate the effect of pretreatment with gabapentin on the hemodynamic response to LETI in treated hypertensive patients undergoing elective surgery.

2. Methods

After institutional ethical committee approval and written informed consent, 100 controlled hypertensive patients [blood pressure (BP) ≤ 140/90 mmHg], aged 35–60 years undergoing elective surgery requiring general anesthesia with endotracheal intubation were included in the study. Patients with anticipated difficult intubation, having risk of aspiration (hiatus hernia, gastroesophageal reflux disease), obesity (body mass index > 30 kg/m^2) or previous history of myocardial infarction, angina pectoris, congestive heart failure, second and third degree heart blocks, cerebrovascular accident, impaired renal functions, and those receiving sedatives, hypnotics, antidepressants, or antacids were excluded.

Patients were randomly allocated into three groups using a computer generated random number table. Group 1 patients received placebo at night before surgery and 2 hours prior to induction of anesthesia. Group 2 patients received placebo at night before surgery and 800 mg gabapentin 2 hours prior to induction of anesthesia. Group 3 patients received 800 mg gabapentin at night before surgery and 2 hours prior to induction of anesthesia. The allocation sequence was concealed in sealed opaque envelopes which were opened just before administration of the drug. Placebo capsules were of the same color, shape, and size as that of study drug and contained finely ground sugar. Personnel involved in the patient management and data collection were not aware of the group assignment. Patients received their regular antihypertensive medications 2 hours prior to induction of anesthesia. No other premedication was given. Before shifting to the operating room, the patients were assessed for any side effects of gabapentin such as headache, nausea, somnolence, dizziness, asthenia, and ataxia in the preanesthesia room.

Anesthesia was induced with thiopentone 5 mg/kg and fentanyl 2 μg/kg followed by vecuronium 0.1 mg/kg to facilitate endotracheal intubation and maintained with isoflurane in 60% nitrous oxide and oxygen. Intraoperative monitoring included electrocardiography (ECG), noninvasive BP, pulse oximetry (SpO_2), end-tidal concentration of carbon dioxide, and neuromuscular transmission on a Datex-Ohmeda S/5 Avance work station (Datex-Ohmeda, USA). Laryngoscopy was performed when train of four count reached zero and the trachea was intubated with an appropriate size cuffed endotracheal tube. All intubations were performed by an experienced anesthesiologist and the time taken from the start of laryngoscopy until cuff inflation was considered as the duration of intubation. If the duration of intubation exceeded 30 seconds or multiple attempts were required for intubation, the patient was excluded from the study.

The patients' heart rate (HR), BP, and ECG were recorded before induction (baseline), after induction (before intubation), immediately after intubation (time 0), and at 1 minute, 3 minutes, 5 minutes, and 10 minutes after intubation. Any episodes of hypotension, bradycardia, tachycardia, hypertension, arrhythmia, and ST-T wave changes were recorded. ST segment elevation of 1 mm or depression of 0.5 mm at 80 ms after the J point was considered significant. Hypotension [systolic BP (SBP) < 90 mmHg or > 30% decrease from baseline lasting for > 60 seconds] was managed with administration of intravenous fluid or incremental doses of ephedrine 3 mg and bradycardia (HR < 40/minute) was treated with atropine. In cases of tachycardia (HR > 130/minute or > 30% increase from baseline lasting for > 60 seconds) or hypertension (SBP > 200 mmHg or > 30% increase from baseline lasting for > 60 seconds) the inspired concentration of isoflurane was increased. The patients were followed up for 24 hours postoperatively for any side effects of gabapentin, such as headache, dizziness, and ataxia.

This study was approved by the Hospital Ethics Review Committee PGIMER, Chandigarh, India.

2.1. Statistical analysis

The results of parametric variables were expressed as mean and standard deviation. Nonparametric data were presented as median and interquartile range. One way analysis of variance (ANOVA) was used to analyze the demographic data and hemodynamic variables among groups. The changes in intraoperative HR and BP were compared with the baseline by repeated measures ANOVA followed by the paired t test. The incidence of side effects was compared among groups by using the Pearson's Chi-square test and Fisher exact test.

3. Results

All patients were intubated successfully. There were a total of 34 patients in Group 1 and Group 3 each, and 32 patients in Group 2. The groups were similar with respect to demographic variables (Table 1). There was no significant difference among groups with respect to the duration of hypertension prior to surgery ($p = 0.344$). Beta blockers, calcium channel blockers, angiotensin receptor blockers, angiotensin converting enzyme inhibitors, and diuretics or their combination were the drugs used for the treatment of hypertension. There was no significant difference between the groups with respect to the distribution of patients consuming different antihypertensive drugs or their combination ($p = 0.654$) (Table 2).

The baseline HR and mean arterial pressure (MAP) were comparable among groups. There was a significant rise in HR after intubation in all the groups. It returned to normal after 5 minutes with no significant difference between the groups (Figure 1). A significant increase in MAP after intubation was reported in Group 1 but not in Group 2 and Group 3. The MAP values at 3 minutes, 5 minutes, and 10 minutes were significantly lower than baseline in Group 2 and Group 3 with no difference between the two groups (Figure 2). At 0 minutes, 1 minute, and 3 minutes postintubation, the MAP was significantly higher in Group 1 as compared with Group 2 and Group 3 ($p = 0.014$). After that, there was no difference in MAP among the three groups. Three patients in Group 1, four patients in Group 2, and 10 patients in Group 3 developed

Table 1
Demographic data.

Variables	Group 1 ($n = 34$)	Group 2 ($n = 32$)	Group 3 ($n = 34$)
Age (y)	53 ± 3	55 ± 2	56 ± 2
Sex (M:F)	14:20	7:25	11:23
Height (cm)	165.3 ± 1.9	163.9 ± 1.7	162.9 ± 4.3
Weight (kg)	62.2 ± 2.3	62.9 ± 2.9	62.9 ± 1.8
Duration of HTN (month)	44 ± 14.9	51.8 ± 15.7	38 ± 15

Values are expressed as mean ± standard deviation or number of patients. Group 1 = placebo group, Group 2 = patients receiving gabapentin 800 mg before induction, and Group 3 = patients receiving gabapentin 800 mg at night and before induction.
F = female; HTN = hypertension; M = male.