Efficacy of Oral Gabapentin on Intraocular Pressure and Cardiovascular Responses Induced by Laryngoscopy and Endotracheal Intubation in Thyroidectomy Surgery- A Randomized Controlled Trial

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ABSTRACT

BACKGROUND

Laryngoscopy and intubation during surgery are often associated with an increase in cardiovascular stress and intraocular pressure. This may result in increased complications in patients with hypertension or glaucoma conditions. In the study, we looked into the oral efficacy of gabapentin on the cardiovascular responses and intraocular pressure induced by endotracheal intubation.

METHODS

142 patients undergoing thyroidectomy were randomly assigned to gabapentin treated group and control group. The Gabapentin treated group was given 800mg Gabapentin orally two hours before endotracheal intubation. The heart rate, blood pressure, and intraocular pressure were recorded before intubation and at different time intervals (1 min, 3 min, 5 min, and 10 min) after post-intubation. Mean arterial pressure (MAP) was also calculated.

RESULTS

Gabapentin treated group showed a significant decrease in heart rate compared to the control group during the post-intubation intervals. In gabapentin treated group, no significant increase in diastolic blood pressure, systolic blood pressure, and arterial pressure were observed compared to the control group. Moreover, the MAP and intraocular pressure were also found to be reduced in the gabapentin-treated group.

CONCLUSIONS

The study provides an insight into the efficacy of gabapentin in reducing the cardiovascular response and intraocular pressure in connection with laryngoscopy and intubation. Gabapentin can thus act as a life-saving drug during surgical procedures in patients with severe hypertension and patients with impending perforation in ocular injury.

KEYWORDS

Laryngoscopy, Endotracheal Intubation, Gabapentin, Intraocular Pressure, Cardiovascular Responses

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BACKGROUND

Laryngoscopy and intubation are often associated with a transient cardiovascular stress response characterized by hypertension, tachycardia, arrhythmias, and dysrhythmias. An increased intraocular pressure (IOP) and intracranial pressure is another physiological complication related to laryngoscopy. In normal patients, laryngoscopy and intubation are reported to show no major health issues. However, in patients with coronary arterial disease, systemic hypertension, hyperglycaemia, pre-eclampsia, and other cerebrovascular pathologies, these techniques can lead to serious adverse outcome. Similarly, an acute increase in IOP during laryngoscopy and intubation is a major risk factor in patients with impending perforation ocular injury and glaucoma.

Techniques like deepening of anaesthesia, exclusion of cholinergic premedication and inclusion of pre-treatment strategies using vasodilators, beta-blockers, calcium channel blockers, and opioids are reported to be beneficial in controlling haemodynamic response. However, more initiatives have to be taken to develop new promising treatment regime for preventing the hemodynamic response and other complications associated with laryngoscopy and intubation.

Gabapentin, a structural analogue of Gamma-amino-butyric acid, is a relatively new drug used for the prophylaxis of epilepsy. The drug is well tolerated with limited side-effects and is proven to be effective in controlling neuropathic pain. Recent observation emphasizes the use of gabapentin in reducing acute postoperative pain and minimizes the requirement of analgesics like an opioid. In the present study, we determined the efficacy of gabapentin in preventing the changes in IOP and haemodynamics in response to endotracheal intubation.

METHODS

The experiment was conducted with the prior approval of institutional human ethical committee (IEC NO: 16/12/2009). A prospective, randomized double-blind study was conducted on 142 American Society of Anesthesiologists (ASA) I & II patients undergoing thyroidectomy after obtaining informed consent. Patients between the age group of 19-41 yrs. were divided into two groups of 71 each, gabapentin treated group (group G) and control group (group C). Group G received oral gabapentin before intubation and group C received no drug other than those for standard general anaesthesia.

Exclusion criteria included patients with anticipated difficult intubation, ASA physical status III or greater, hiatus hernia and gastro-oesophageal reflux, renal insufficiency, asthma and cardiac disease. Patients with body weight more than 20% of the ideal body weight, and patients consuming antihypertensive drugs, sedatives, hypnotics, antidepressants or drugs with an effect on the nervous system, except those determined by the study protocol, hypovolemia, known allergy or contraindication to anaesthetics or any drug used were also excluded. Pregnant women were also excluded from the study.

Metoclopramide 10 mg, Ranitidine 150 mg and Diazepam 5 mg tablets were given orally to the patient as premedication on the night and next morning before surgery. Baseline parameters such as of heart rate, non-invasive blood pressure and intraocular pressure were recorded in the premedication room. Gabapentin 800 mg was given orally to group G patient. Intravenous (I.V.) line was started using 18G cannula with normal saline solution. The patient was shifted to the operation theatre and baseline parameters were recorded with the aid of electrocardiogram, pulse oximeter and non-invasive cuff BP apparatus. The patient was pre-oxygenated with 100% oxygen for 3 min before anaesthesia. Patient was given I.V. Midazolam 1 mg, I.V. Metoclopramide 10 mg, I.V. Glycopyrrolate 0.2 mg and I.V. Fentanyl 1 µg/Kg. Anaesthesia was induced using Propofol (2 mg/Kg). For facilitation of laryngoscopy and intubation, Inj. Vecuronium (1 mg/Kg) was given. One minute after induction, heart rate, blood pressure, and intraocular pressure of the patients was recorded. Intermittent positive pressure ventilation was maintained using Nitrous oxide and Oxygen in a 4:2 ratio. No other drug was given during the study period for the first 10 minutes post-intubation. Rescue doses of ephedrine (0.3 mg increments) and atropine (0.6 mg) were kept for hypotension (mean arterial pressure 30% less than the original value) and bradycardia (heart rate falling >20% from the baseline value) respectively. Heart rate, blood pressure, MAP and intraocular pressure were recorded for 1 minute, 3 min, 5 min and 10 min after intubation. At the end of surgery, patients were reversed using I.V. Neostigmine 0.05 mg/Kg body weight and I.V. Glycopyrrolate 0.01 mg/Kg body. Patients were also observed postoperatively (24 hrs) for any somnolence, respiratory depression (respiratory rate less than 6 breaths per minute), dizziness, nausea, vomiting or peripheral oedema.

RESULTS

Demographic profile (concerning age and weight) of the patients showed no significant differences and were comparable between the two groups (Table 1).

Observation	Group C (n=71)	Group G (n=71)
Age (Years)	40.8 ± 5.5	40.2 ± 5.1
Weight (Kg)	51.2 ± 4.8	50.6 ± 5.3

Table 1. Demographic Profile of Patients in the Two Groups; Values are Mean ± SD

The heart rate in group C showed a significant increase from the baseline (82.5 ± 3.9 bpm) for 1 min (112.3 ± 3.5 bpm) and 3 min (112.2 ± 3.5 bpm) of intubation, after which it started to decrease. However, this decrease in heart rate at 5 min (99.3 ± 3.7 bpm) and 10 min (89.3 ± 2.5 bpm)

remained significantly higher than that of the baseline value. But in group G patients, the heart rate remained almost to the baseline (83.4 ± 3.3 bpm) at 1 min (84.4 ± 3.4 bpm), 3 min (84.4 ± 3.0 bpm) and 5 min (82.4 ± 3.3 bpm) followed by a significant decrease at 10 min (80.5 ± 3.1 bpm) of intubation. Furthermore, the heart rate showed a significant decrease in group G at all the time periods after intubation compared to group C patients.

The systolic blood pressure (SBP) also showed a significant increase from the baseline value (130.8 ± 7.3 mmHg) at 1 min (141.5 ± 7.8 mmHg) of intubation in group C patients. However, at 3 min (128 ± 8.8 mmHg) SBP reached almost to the baseline followed by a significant decrease in 5 min (120.2 ± 7.9 mmHg) and 10 min (118 ± 7.7 mmHg). However, in Group G patients SBP decreased significant with an increase in intubation time of 1 min (120.9 ± 9.9 mmHg), 3 min (114.0 ± 9.8 mmHg), 5 min (110 ± 9.8 mmHg) and 10 min (106 ± 8.9 mmHg) from its respective baseline value (132.2 ± 8.8 mmHg) and also from its control group. Similarly, the diastolic blood pressure (DBP) in group C patients showed a significant increase from the baseline value (79.0 ± 6.1 mmHg) at 1 min (85.4 ± 6.8 mmHg) of intubation and then reached the baseline value at 3 min (78.1 ± 7.1 mmHg) followed by a steady decrease at 5 min (71.2 ± 7.2 mmHg) and 10 min (71.2 ± 7.5 mmHg) of intubation. Group G patients showed a significant decreased in DBP during 1 min (74.7 ± 5.8 mmHg), 3 min (68.8 ± 5.5 mmHg), 5 min (66.8 ± 5.5 mmHg) and 10 min (65.3 ± 5.0 mmHg) from its respective baseline value (80.6 ± 6.2 mmHg) and also from its control group.

The MAP in the control group showed a significant increase in 1 min (104 ± 5.0) followed by a significant decrease in 3 min (94.4 ± 5.7 mmHg), 5 min (87.3 ± 5.0 mmHg) and 10 min (86 ± 5.2 mmHg) respectively. However, Group G showed a significant decrease in MAP at 1 min (90.1 ± 3.2 mmHg), 3 min (83.9 ± 3.3 mmHg), 5 min (81.9 ± 5.1 mmHg) and 10 min (79.9 ± 4.6 mmHg) from its baseline value (97.9 ± 3.4 mmHg). Besides, the MPA of group G was significantly reduced compared to its respective control.

Group C showed a significant increase in IOP at 1 min, 3 min, 5 min and 10 min of intubation. But, when compared to 1 min (25.1 ± 1.8 mmHg), IOP value showed a significant reduction at 3 min (23.2 ± 1.9 mmHg), 5 min (21.2 ± 1.5 mmHg) and 10 min (18.6 ± 2.6 mmHg) of intubation. However, these values were significantly more compared to the baseline value (15.4 ± 2.2 mmHg). In group G, the IOP showed a significant decrease in 1 min (15.0 ± 1.8 mmHg), 3 min (14.0 ± 1.5 mmHg), 5 min (12.8 ± 1.6 mmHg) and 10 min (12.5 ± 1.3 mmHg) from its baseline value and its respective control group.

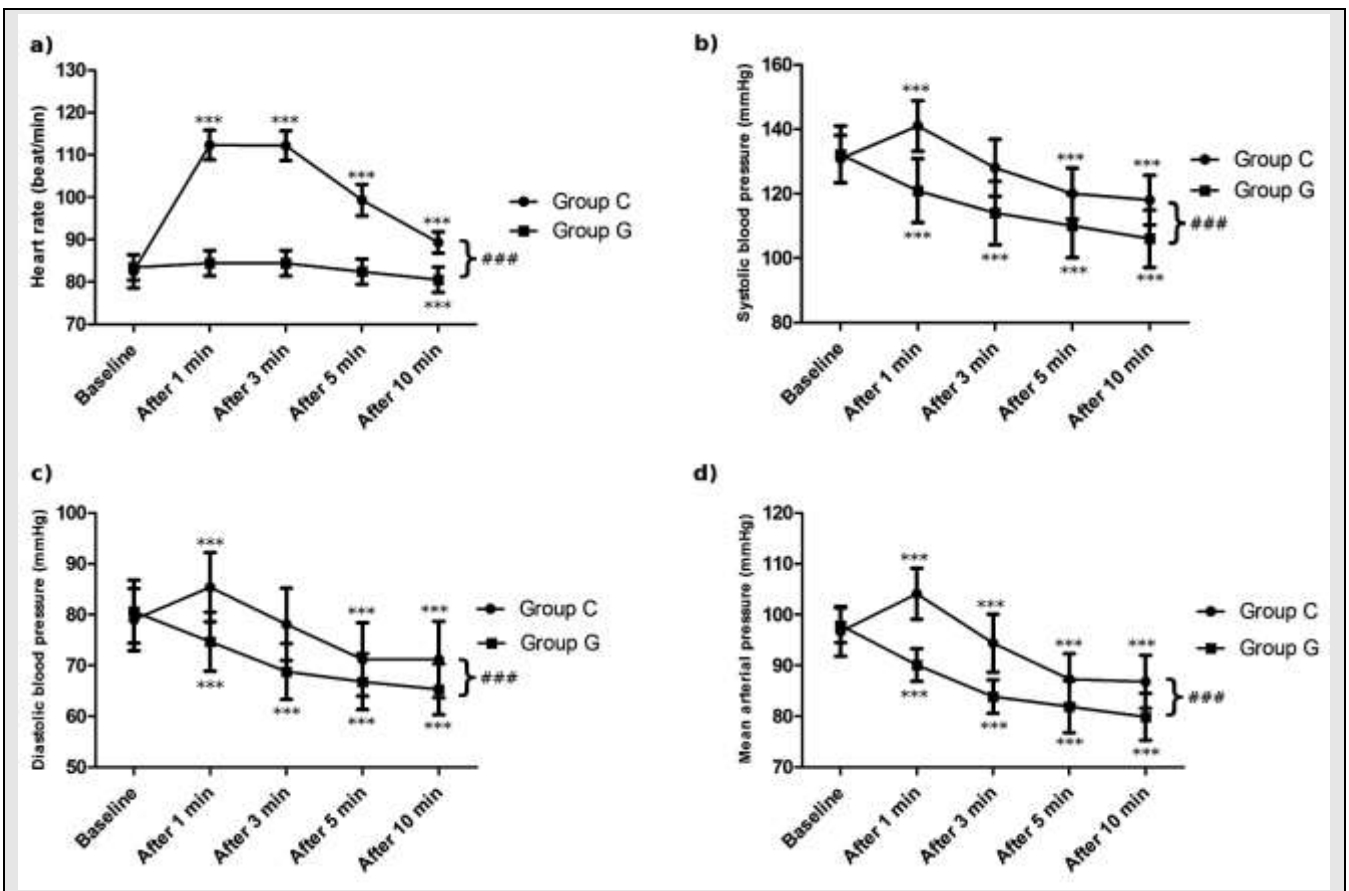

Figure 1

The effect of gabapentin on heart rate (a), systolic blood pressure (b), diastolic blood pressure (c) and mean arterial blood pressure (d) at different time intervals of intubation. The values are represented as Mean ± SD. ### p<0.001 group G vs group C and *** p<0.001 baseline value vs respective time intervals within groups.

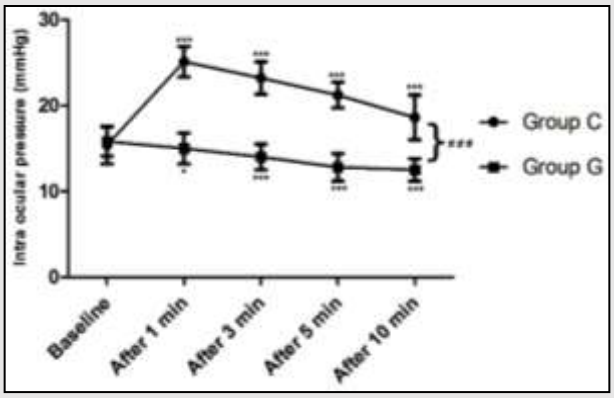

Figure 2. Effect of Gabapentin on Intraocular Pressure at Different Time Intervals of Intubation

The values are represented as Mean ± SD. ### p<0.001 group G vs group C and *p<0.05, ***p<0.001 baseline value vs respective time intervals within groups.

During the study, none of the patients in both groups developed hypotension and respiratory depression. Among the 71 patients, one patient developed transient bradycardia but required no atropine. Patients in the gabapentin group induced better sedated than the control group. Though five patients showed postoperative sedation, they were not deeply sedated.

DISCUSSION

Laryngoscopy and intubation procedure during surgery can often result in an unstable hemodynamic response. The transient sympathetic response that is evoked during the intubation procedure is responsible for this inconsistent stress responses. The response gets initiated within 5 seconds reaches a peak by about 2 minutes and then slowly reaches the baseline value between 5 to 10 minutes after intubation. The level of catecholamine in plasma during intubation has been attributed to the occurrence of cardiovascular responses like increase in HR.[1] Furthermore, an increase in IOP has been reported during the intubation procedures which can lead to loss of intraocular contents, haemorrhage, and permanent loss of vision in patients with impending perforation ocular injury. The type of intubation devices used for the procedure also demonstrated varying responses towards the hemodynamic stress response associated with surgery.[2] Use of direct laryngoscopy or fibreoptic bronchoscope has shown to produce a comparable level of the stress response.[3] Likewise, the use of direct Macintosh laryngoscope and indirect Macintosh C-MAC laryngoscope showed a similar and stable hemodynamic stress response.[4] However, the use of Glidescope™ video laryngoscope was reported to induced less thermodynamic response compared to direct Macintosh laryngoscope.[5] In yet another study, laryngeal mask airway Proseal™ was shown to induce less circulatory response than tracheal intubation in non-obese patients.[6] In this study, we used Macintosh laryngoscope for intubation and the procedure showed an increase in hemodynamic stress responses. This response may have resulted from the sympathetic response initiated during the laryngoscope being pressed at the base of the tongue as reported by others. However, stress mediators such as endogenous plasma catecholamines or cortisone were not measured in this study. This can be considered as limitations of the study since measurements of endogenous catecholamines would have given useful information.

Variation in hemodynamic responses can lead to a serious outcome in patients suffering from coronary artery heart disease, cerebrovascular diseases and other related disease conditions. Hence, pre-medication has always been attempted to reduce complications during surgical procedures. The combination of Fentanyl and Pancuronium has shown to stabilize the hemodynamic stress response.[7] Similarly, esmolol and diltiazem in combination showed an attenuation in the stress response during intubation.[8] Another study[9] compared the effect of clonidine and lidocaine in the attenuation of hemodynamic responses to laryngoscopy and tracheal intubation in controlled hypertensive patients. Tachycardia and rhythm disturbances resulted from intubation were reduced by omitting atropine as premedication.[10] Though, nitroglycerin administered intranasally reduced hypertensive response towards laryngoscopy and intubation, events of tachycardia have been reported.[11] Intravenous administration lidocaine was shown to prevent the increase in mean arterial blood pressure without any effect on the heart rate.[12] Use of gabapentin before varicocele surgery had shown to reduce hemodynamic stress response.[13] Gabapentin was also reported to reduce postoperative pain,[14] along with reducing the dose of morphine consumption.[15]

In the present study, an attempt has been made to determine the efficacy of oral gabapentin, 800 mg two hours before intubation, in attenuating the hemodynamic stress responses in patients undergoing thyroidectomy. Gabapentin was shown to attenuated the stress response to tracheal intubation. Systolic blood pressure, diastolic blood pressure, heart rate and intraocular pressure associated with laryngoscopy and endotracheal intubation was found to be reduced. Our observations were in line with the reports of a previous study published.[16] The mechanism by which Gabapentin attenuates the pressor response to laryngoscopy and intubation is yet to be identified. However, the drug is reported to inhibit membrane voltage-gated calcium channels. Hence, it may act similar to calcium channel blockers. It was demonstrated that the hypotensive effect of gabapentin in animal model was due to its ability to reduce the peripheral sympathetic nerve transmission.[17]

In conclusion, pretreatment with gabapentin under the dose given in the present study design attenuates the cardiovascular stress response to laryngoscopy and intubation of the trachea. As the use of gabapentin in the peri-operative setting is becoming more frequent more studies have to be focused on its cardiovascular effects, intraocular pressure and other stress mediators.

CONCLUSIONS

Laryngoscopy and tracheal intubation are often associated with a stress response. Though these responses remain harmless in most of the patients, it can be deadly in patients with coronary artery heart disease, cerebrovascular pathology, hypertension and preeclampsia. Hence studies are aiming at controlling or attenuating the haemodynamic response to intubation and laryngoscopy with a major focus on the effect of remifentanil at different dosing regimens. The present study showed that pre-treatment with gabapentin, a drug commonly used to prevent epilepsy and neuropathic pain can also attenuate the cardiovascular and intraocular pressure stress in response to laryngoscopy and intubation of the trachea. Thus, gabapentin could be suggested as a promising drug that can be used with lesser side effect during surgical procedures in patients suffering from severe hypertension or with impending perforation ocular injury. However, further studies have to be carried out to study the effect of gabapentin on other features of stress during a surgical procedure, its mode of action and also to optimize the drug dosage in the different study population to make it more relevant in clinical settings.

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