

Effects of Preoperative Oral Gabapentin in Reduction of Intraocular Pressure and Cardiovascular Changes Following Laryngoscopy and Tracheal Intubation

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Abstract: Laryngoscopy and tracheal intubation are associated with hypertension, tachycardia and increased circulating catecholamines. They are also associated with increase in intraocular pressure. Various techniques have been studied to prevent increase intraocular pressure. Also there were used various techniques for attenuate the hemodynamic response to laryngoscopy and intubation. Gabapentin is a multimodal perioperative drug. We investigated whether the pre-treatment with gabapentin attenuates the intraocular pressure in addition to a hemodynamic response to tracheal intubation. **Methods:** One hundred patients, 15-50 years of age with ASA class I, II undergoing elective surgery with general anesthesia and endotracheal intubation were divided in two groups. Fifty patients received placebo and fifty patients received 900 mg (capsule) gabapentin two hours before surgery. **Results:** Intraocular pressure and heart rate in 1, 3, 5 and 10 minutes after laryngoscopy and intra-tracheal intubation in the gabapentin group were significantly lower than placebo group. In addition in our study mean arterial pressure in 1, 3, 5 minutes after laryngoscopy and tracheal intubation in the gabapentin group were significantly lower than placebo group. **Conclusion:** preoperative premedication with oral gabapentin is effective in attenuating the hemodynamic response and prevention of increase IOP to laryngoscopy and endotracheal intubation.

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1. Introduction

Laryngoscopy and tracheal intubation are associated with hypertension, tachycardia and increased circulating catecholamines (1, 2, and 3).

Hemodynamic changes are usually transient and without sequel. However, in patients with pre-existing coronary artery disease, hypertension or cerebrovascular disease, these changes may precipitate myocardial ischemia, arrhythmias, myocardial infarction and cerebral hemorrhage (4, 5).

Laryngoscopy and tracheal intubation is associated with increase in intraocular pressure (6).

Brief elevation of IOP is of little consequence in normal or even glaucomatous eyes, as long as the eyeball is intact. However, in a patient with an ocular laceration, perforation, or recent surgical ocular intervention, even a transient increase in IOP may be hazardous (7, 8)

Various techniques have been studied to prevent or attenuate the hemodynamic response to laryngoscopy and intubation, such as omitting cholinergic medications, deepening of anesthesia, pretreatment with nitroglycerine, beta-blockers, calcium channel blockers, gabapentin and opioids like

fentanyl and remifentanyl (9-16). Again various techniques have been studied to prevent increase in the intraocular pressure following laryngoscopy and tracheal intubation (17, 18)

Gabapentin, a structural analogue of γ -aminobutyric acid, is used as an anticonvulsant drug (19). Pretreatment with gabapentin can prevent the development of hyperalgesia (20). Also, gabapentin has a selective effect on the nociceptive process relating central sensitization (21).

Gabapentin is a multimodal perioperative drug. It has a favorable side effect profile and has less interaction with other drugs (22, 23). Gabapentin was shown to be effective in decreasing post-operative analgesic consumption and pain (24).

Memis and colleagues showed that oral administration of gabapentin 800 mg one hour before induction of anesthesia can attenuate the pressor response to the laryngoscopy and tracheal intubation (25). We investigated whether the pre-treatment with gabapentin attenuates the intraocular pressure in addition to a hemodynamic response to tracheal intubation.

2. Methods

After obtaining approval from the institutional ethics committee of our university, and written informed consent, we conducted a prospective, randomized and double-blind study. One hundred patients, 15-50 years of age with ASA class I, II undergoing elective surgery with general anesthesia and endotracheal intubation were divided in two groups. Fifty patients received placebo and fifty patients received 900 mg (capsule) gabapentin two hours before surgery. Exclusion criteria were: anticipated difficulty in intubation (Mallampatti Grade 3 and 4), more than one attempts to intubation, patients on chronic neuroleptic medications and taking tricyclic antidepressants or serotonin and norepinephrine reuptake inhibitors, patients with history of allergy to gabapentin, patients with hypertension, ischemic heart disease, severe renal or hepatic disease. Patients with amblyopia or history of eye surgery and hemodynamically unstable patients (heart rate >120/min, heart rate <50/min, systolic blood pressure <90 mmHg, systolic blood pressure > 140mmHg, diastolic blood pressure <50 mmHg, and diastolic blood pressure >100mmHg) were excluded of our study.

On arriving to the operating room and following insertion of intravenous catheter, all patients were infused with 5 ml/kg normal saline. Routine monitoring comprised, ECG, pulse oximetry, and non-invasive blood pressure. 2µg/kg Fentanyl and 0.05 mg/kg midazolam intravenous was administered before induction of anesthesia. Patients were pre-oxygenated for 3 minutes with oxygen 100% and anesthesia was induced with 5 mg/kg thiopental sodium and 0.5 mg/kg atracurium. Three minutes later, laryngoscopy using Macintosh blade size 3 and intubation using intratracheal tube (size 7.5-8) were performed by an anesthetist or by a two-year trained resident in anesthesiology.

Intraocular pressure (measure by Schiotz Tonometer), heart rate, systolic, diastolic and mean arterial blood pressure were recorded before induction of anesthesia, one minute before laryngoscopy, and 1, 3,5,10 min after intubation.

Data were expressed as mean (SD). Comparison between the groups was performed using the unpaired student's t-tests. Chi-squared test or fisher's exact test, when proper, was utilized for analysis of categorical data. Statistical analyses were done with SPSS 17.0 package program for Windows. A p-value of less than 0.05 was considered statistically significant.

3. Results

In gabapentin group of the 50 patients, 10 patients were excluded from study due to cancellation

of operation (n=5), vertigo (n=2) and decreasing in systolic blood pressure lower than 90 mmHg (n=3).

Demographic variables in term of age and male: female ratio did not differ significantly between the two groups (table 1). The baseline hemodynamic variables (SBP, DBP, MAP and HR) and intraocular pressure were similar between two groups (table 2).

Table 1: distribution of gender and mean of age in the study population

P Value	Placebo n=50	Gaba n=40	Variable
0.28	Mean ±SD 27.6±7.5	Mean ±SD 29.3±6.6	Age(Y/O)
0.39	M:27 F:23	M:18 F:22	Gender

Note: Gaba: Gabapentin, n: number, M: Male, F: Female, Y/O: Years Old, SD: Standard Deviation

Hemodynamic variables (SBP, DBP, MAP and HR) and intraocular pressure one minute after laryngoscopy in the gabapentin group were lower than placebo group. There were significant difference for SBP, MAP and H.R. but there was not significant for DBP (table 2).

Hemodynamic variables (SBP, DBP, MAP and HR) and intraocular pressure three and five minutes after laryngoscopy in the gabapentin group were lower than placebo group. There were significant difference for DBP, MAP and H.R. but there was not significant for SBP (table 2).

Hemodynamic variables (SBP, DBP, MAP and HR) and intraocular pressure ten minutes after laryngoscopy in the gabapentin group were lower than placebo group. But there were only significant for H.R. and intraocular pressure (table 2).

4. Discussion

There are recent evidences that preoperative administration of oral gabapentin is efficacious for attenuation of hemodynamic response to laryngoscopy and intubation. In our study intraocular pressure and heart rate in 1, 3, 5 and 10 minutes after laryngoscopy and intra-tracheal intubation in the gabapentin group were significantly lower than placebo group. Patients with an ocular laceration, perforation, or recent surgical ocular intervention particular with co-existing ischemic heart disease may benefit of oral gabapentin 900mg two hours before operation as a premedication because control of heart rate and IOP are essential in these patients.

In addition in our study mean arterial pressure in 1, 3, 5 minutes after laryngoscopy and tracheal intubation in the gabapentin group were significantly lower than placebo group and patients with cerebrovascular disease and ischemic heart disease that are at risk of cerebral hemorrhage and myocardial

infarction respectively may benefit of preoperative oral gabapentin.

Table 2. Comparison of intraocular and hemodynamic variables after tracheal intubation.

P-Value	Group placebo Mean \pm SD	Group gaba Mean \pm SD	
			H.R.(beats/min)
0.01	94.24 \pm 12.98	86.73 \pm 6.276	1 Min
0.01	88.74 \pm 9.4	83.18 \pm 5.1	3 Min
0.03	85.1 \pm 8.3	80.5 \pm 5.2	5 Min
0.01	82.2 \pm 5.8	77.6 \pm 11.9	10 Min
			SBP (mmHg)
0.03	129.2 \pm 11.7	121.9 \pm 10.1	1 Min
0.09	124.2 \pm 10	118.7 \pm 9.1	3 Min
0.06	120.6 \pm 9.2	115.5 \pm 7.3	5 Min
0.7	114.6 \pm 16.3	113.6 \pm 6.6	10 Min
			DBP (mmHg)
0.06	80.68 \pm 10	76.7 \pm 10	1 Min
0.03	79.9 \pm 9.3	75.5 \pm 10	3 Min
0.04	78.7 \pm 10	74.5 \pm 9	5 Min
0.1	73.5 \pm 8.7	72.2 \pm 8.4	10 Min
			MBP(mmHg)
0.02	95.3 \pm 12.4	90.23 \pm 7.8	1 Min
0.05	93.4 \pm 9.1	88.05 \pm 8.1	3 Min
0.04	92.1 \pm 9.6	86.6 \pm 7.3	5 Min
0.08	87.2 \pm 7.9	84.4 \pm 7.1	10 Min
			IOP(mmHg)
0.001	15 \pm 2.6	11.4 \pm 1.1	1 Min
0.001	14.02 \pm 2.4	10.2 \pm 1.1	3 Min
0.001	13.05 \pm 2.1	9.9 \pm 0.6	5 Min
0.001	12.3 \pm 1.5	9.96 \pm 1.3	10 Min

Note: gaba =gabapentin, Min=minute, IOP=intraocular pressure, SBP=systolic blood pressure, DBP=diastolic blood pressure, MBP=mean blood pressure, HR=heart rate

A.Fassoulaki & colleague (26) found that oral gabapentin used as premedication attenuate the hemodynamic response to laryngoscopy & intubation. In their randomized placebo-controlled trial gabapentin-treated patients (1600 mg in four divided doses, at 6 h intervals starting the day before surgery) had significantly lower systolic ($p<0.004$) and diastolic arterial pressure ($p<0.004$) during the first 10 min after endotracheal intubation when compared with placebo. Nevertheless, gabapentin had no effect on heart rate changes that was differ with our results. In our study heart rate in 1, 3, 5 and 10 minutes after laryngoscopy and intra-tracheal intubation in the gabapentin group were significantly lower than placebo group.

Memis D and colleague (25) found that patients receiving 800 mg of gabapentin 1 h before surgery had significantly decreased mean arterial pressure and heart rate during the first 10 min after endotracheal intubation compared with either 400 mg gabapentin or placebo ($p<0.05$). Serhat Koc and colleague (27) also observed the same response. In

Usha Bafna and colleagues study(28), oral gabapentin 1000 mg given 1 h prior to operation resulted in significant decreases in MAP and HR during study period ($p<0.05$). In our study also MAP and heart rate after laryngoscopy and intra-tracheal intubation in the gabapentin group were significantly lower than placebo group. Results of these recent studies indicate preoperative premedication with oral gabapentin is effective in attenuating the hemodynamic response to laryngoscopy and endotracheal intubation. It acts by decreasing the synthesis of neurotransmitter glutamate and by binding to $\alpha 2\delta$ subunit of voltage dependent calcium channel (29). Action similar to calcium channel blockers may be responsible for blunting hemodynamic response to laryngoscopy and intubation (30).

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