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Effect of oral gabapentin on haemodynamic variables during microlaryngoscopic surgery

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Abstract

Background: Manipulation of the larynx, such as laryngoscopy and tracheal intubation, is associated with haemodynamic and cardiovascular responses. In microlaryngoscopic procedures, these responses are more severe than laryngoscopy for endotracheal intubation because in microlaryngoscopic surgeries laryngoscope fixes for a longer time (15–20 minutes compared to 15–30 seconds in tracheal intubation).

This study was performed to evaluate the effect of 800 mg oral gabapentin on the haemodynamic variables during microlaryngoscopic surgery.

Methods: 30 patients aged 30–70 years, ASA physical status I or II, who underwent microlaryngeal surgery were included to the study. The night before surgery, 15 patients (group G) received 100 mg gabapentin and 15 patients (group P) received a placebo. Ninety minutes before the operation, they either received 800 mg gabapentin (group G), or received a placebo (group P).

Results: Heart rate, systolic, diastolic and mean arterial blood pressure were measured on the night before the procedure, the morning before the procedure, at arrival to the operating room as baseline, before and after induction, 1, 3 min after tracheal intubation, 1, 5, 15, 25 min after fixing laryngoscope, before laryngoscope removal, and 1 min after that.

Analyses revealed that the systolic blood pressure was lower in group G after induction, 1 and 5 min after fixing laryngoscope and before removing the laryngoscope. Diastolic blood pressure in group G was lower at the time of arriving in the operating room, after induction, 1 min after fixing surgical laryngoscope and before removing the laryngoscope. Mean arterial pressure behaved similarly, and additionally it was lower at 5 min after fixing the laryngoscope. Heart rate was reduced at the time after induction, 1, 3 min after intubation, 5 min after fixing the laryngoscope and before laryngoscope removal in group G. Overall, in the group G, diastolic blood pressure and mean arterial pressure were lower in the first 15 min after microlaryngoscopy compared to group P but there was no difference in mean systolic blood pressure and mean heart rate.

Conclusion: 800 mg oral gabapentin given 90 min before a procedure attenuates the rise of diastolic blood pressure and mean arterial blood pressure in the first 15 min after microlaryngoscopy surgery, but has no effect on systolic blood pressure or heart rate.

Key words: microlaryngoscopy, haemodynamic response, attenuation, gabapentin

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Benign laryngeal tumours include vocal nodules, vocal polyps, vocal fold cysts and papilomas. The most common cause of vocal nodules and vocal polyps is voice abuse. Vocal fold cysts may also be caused by voice abuse and misuse, or they may arise spontaneously. Poor vocal hygiene and smoking are often considered to be risk factors. They may appear in any part of the larynx. Symptoms include hoarseness, dyspnoea, wheezing, cough, pain, otalgia and haemoptysis. Diagnosis is based on direct or indirect visualisation of the larynx and then CT. Voice therapy followed by proper voice use is often effective in reducing or eliminating voice problems from voice nodules, polyps, and occasionally cysts. Vocal nodules, vocal polyps or vocal cysts which do not respond adequately to voice therapy can be removed surgically using laryngeal microsurgery, with highly effective results [1].

Manipulation of the larynx such as laryngoscopy and tracheal intubation is associated with haemodynamic response consisting of an increase in heart rate, arterial blood pressure, myocardial oxygen demand and induction of dysrhythmias. In patients with coronary artery disease, hypertension or cerebrovascular disease, these changes may precipitate myocardial ischaemia, myocardial infarction and cerebral haemorrhage [2].

In microlaryngoscopic surgery, these responses are more intense than in laryngoscopy for endotracheal intubation. In this type of surgery, the laryngoscope is introduced into the upper airways for 15–20 minutes compared to 15–30 seconds in tracheal intubation. Various techniques have been studied to prevent or attenuate the haemodynamic response to laryngoscopy and intubation. They have covered pretreatment with nitroglycerine, beta-blockers, calcium channel blockers and administration with opioids like fentanyl or remifentanyl [3].

Gabapentin, a structural analogue of γ-aminobutyric acid, is used primarily for the treatment of seizures, neuropathic pain, and hot flushes. There are, however, some concerns regarding the quality of the research about its use to treat migraines, bipolar disorders, acquired pendular nystagmus, menopausal symptoms, spasticity in multiple sclerosis and uraemic pruritus [4].

Recently, gabapentin has been found to be effective in reducing the noxious stimuli to laryngoscopy and intubation, thereby attenuating the haemodynamic response [5]. Gabapentin acts by decreasing the synthesis of neurotransmitter glutamate and by binding to α-2δ subunit of voltage dependent calcium channel. Action similar to calcium channel blockers may be responsible for blunting haemodynamic response to laryngoscopy and intubation [4].

This study was performed to evaluate the effect of gabapentin administration on systolic and diastolic blood pressure, mean arterial pressure and heart rate during microlaryngoscopic surgery.

METHODS

After approval by the Ethical Committee and written informed consent, 30 patients were included in this study. The inclusion criteria covered age from 30 to 70 years, physical status according to American Society of Anesthesiologists (ASA) 1 or 2 and qualification for microlaryngeal surgery. Excluded were individuals with an umbilical hernia, gastro-oesophageal reflux, BMI > 30 kg m^{-2}, history of allergy to gabapentin, liver and renal disease, antidepresant and sedative drug use, and difficult intubation in anamnesis. Patients were assigned into one of two groups according to a random–number table. The night before surgery, 100 mg oral gabapentin was prescribed to group G (the gabapentin group) or a placebo to group P (the placebo group). Ninety minutes before the procedure, systolic, diastolic and mean blood pressure as well as heart rate values were recorded and that was followed by oral administration of 800 mg of gabapentin in group G, while patients in group P received a placebo. Monitoring in the operating room included ECG curve, pulse oximetry and non-invasive blood pressure measurements. General anaesthesia was induced with an intravenous injection of fentanyl (1.5 μg kg^{-1}), propofol (2 mg kg^{-1}) and atracurium (0.5 mg kg^{-1}). After tracheal intubation with a cuffed endotracheal tube (size 5.0–5.5), the surgeon fixed the laryngoscope and the procedure started. Anaesthesia was maintained with isoflurane (1 MAC) administered with a mixture of N_2O and O_2 (1:1). Haemodynamic variables were recorded at the 1st, 3rd minute after intubation, 1st, 5th minute after laryngoscope fixation, and every 10 minutes during the procedure and 1 minute after extubation. The presence of nausea, vomiting, headache, vertigo and heartburn was recorded with a questionnaire during the recovery time.

All data was analysed using SPSS software (version 17). A P value < 0.05 was considered significant.

RESULTS

Haemodynamic variables are presented in Tables 1–4. Table 5 presents the frequency of adverse effects in both study groups.

DISCUSSION

Laryngoscopy and tracheal intubation may induce a profound alteration in the haemodynamics of the patient. In the response to these procedures, the plasma concentration of catecholamines is increased and this may provoke myocardial ischaemia and cerebral haemorrhage. Various techniques and agents have been studied to prevent or

Table 1. Changes of systolic blood pressure (mm Hg) during study

	Group G	Group P	*P* value
Night before procedure	131.00 ± 7.36	125.33 ± 8.54	0.06
Morning before procedure	131.00 ± 11.05	132.66 ± 15.17	0.73
Baseline	118.53 ± 11.61	129.93 ± 18.35	0.05
Before induction	118.06 ± 16.42	126.46 ± 20.54	0.22
After induction	87.26 ± 9.38	107.33 ± 17.71	< 0.01
intubation			
1 min	114.00 ± 16.3	111.93 ± 19.60	0.76
3 min	115.07 ± 20.91	109.35 ± 24.18	0.51
laryngoscope fixation			
1 min	116.73 ± 13.85	136.00 ± 29.03	0.02
5 min	122.46 ± 15.67	136.60 ± 20.64	0.04
15 min	121.5813.90	127.84 ± 23.57	0.43
25 min	120.50 ± 7.84	125.00 ± 30.92	0.73
Before laryngoscope removal	119.66 ± 9.26	137.13 ± 22.37	< 0.01
1 min after laryngoscope removal	122.86 ± 18.41	122.53 ± 15.00	0.95

Table 2. Changes of diastolic blood pressure (mm Hg) during study

	Group G	Group P	*P* value
Night before procedure	76.33 ± 6.67	71.67 ± 13.15	0.23
Morning before procedure	73.33 ± 10.11	75.20 ± 14.82	0.69
Baseline	72.46 ± 8.98	84.80 ± 10.95	< 0.01
Before induction	70.66 ± 11.96	79.13 ± 15.23	0.10
After induction	57.73 ± 8.12	71.86 ± 22.47	0.03
intubation			
1 min	74.00 ± 11.80	72.06 ± 12.11	0.66
3 min	75.28 ± 17.61	74.35 ± 21.32	0.90
laryngoscope fixation			
1 min	76.93 ± 11.67	94.20 ± 23.39	0.01
5 min	80.73 ± 13.14	89.40 ± 15.89	0.11
15 min	80.58 ± 8.94	83.61 ± 15.89	0.56
25 min	78.50 ± 5.35	76.83 ± 16.96	0.82
before laryngoscope removal	74.13 ± 11.32	87.86 ± 18.44	0.02
1 min after laryngoscope removal	77.06 ± 12.76	77.73 ± 13.95	0.89

Table 3. Changes of mean blood pressure (mm Hg) during study

	Group G	Group P	*P* value
Night before procedure	94.26 ± 6.05	89.40 ± 9.99	0.11
Morning before procedure	92.00 ± 9.61	94.06 ± 13.36	0.63
Baseline	88.26 ± 10.79	99.33 ± 11.95	0.01
Before induction	86.53 ± 13.49	95.73 ± 16.12	0.10
After induction	69.00 ± 8.10	83.66 ± 20.43	0.01
intubation			
1 min	87.57 ± 13.93	84.66 ± 12.06	0.55
3 min	88.14 ± 17.84	86.21 ± 22.06	0. 80
laryngoscope fixation			
1 min	89.73 ± 11.57	108.26 ± 24.91	0.01
5 min	94.66 ± 13.17	106.66 ± 16.96	0.03
15 min	94.16 ± 9.99	99.84 ± 18.85	0.36
25 min	89.83 ± 7.52	95.16 ± 22.76	0.60
Before laryngoscope removal	89.06 ± 8.81	105.93 ± 20.09	< 0.01
1 min after laryngoscope removal	91.06 ± 15.82	93.00 ± 13.66	0.72

Table 4. Changes of heart rate (min^{-1}) during study

	Group G	Group P	*P* value
Night before procedure	73.13 ± 5.55	84.73 ± 9.22	0.05
Morning before procedure	76.33 ± 6.58	93.60 ± 12.70	< 0.01
Baseline	81.53 ± 20.05	90.26 ± 16.85	0.20
Before induction	83.40 ± 16.70	93.26 ± 16.21	0.11
After induction	75.26 ± 19.47	93.86 ± 15.24	< 0.01
intubation			
1 min	79.35 ± 6.78	93.06 ± 16.42	< 0.01
3 min	79.92 ± 10.85	96.07 ± 10.63	< 0.01
laryngoscope fixation			
1 min	80.80 ± 12.22	92.60 ± 20.96	0.07
5 min	79.40 ± 12.39	91.33 ± 18.24	0.04
15 min	76.83 ± 11.95	88.30 ± 16.73	0.06
25 min	65.66 ± 12.73	84.50 ± 24.63	0.13
Before laryngoscope removal	74.60 ± 13.04	89.93 ± 20.50	0.02
1 min after laryngoscope removal	78.20 ± 11.77	87.80 ± 18.78	0.10

Table5. Adverse effects between the two groups (numbers and %)

Variable	Group P	Group G	*P* value
Headache	0 0%	2 13.3%	0.48
Vertigo	4 26.7%	2 13.3%	0.65
Nausea	2 13.3%	0 0%	0.48
Vomiting	1 6.7%	1 6.7%	1.0
Heartburn	1 6.7%	0 0%	1.0

attenuate the haemodynamic response to laryngoscopy and intubation. Recently, gabapentin has been found to be effective in reducing the noxious stimuli to laryngoscopy and intubation, thereby attenuating the haemodynamic response. The effect of pain attenuation of gabapentin is due to its binding to calcium channels of presynaptic terminals of dorsal root ganglion neurons and dorsal horn neurons. Furthermore, gabapentin's effect on NMDA receptors, protein kinase C and inflammatory cytokines is responsible for its anti-hypersensitivity action in neuropathic pain [6]. It has been shown that gabapentin induces an inhibition of the sodium channels in excitable dorsal root ganglion neurons. Also, gabapentin has an antinociceptive action in the painful diabetic neuropathy in rats because of its effect on the specific proteins [7].

In the present study, we evaluated the effect of oral gabapentin on the haemodynamic variables during microlaryngoscopic surgery. Analysis revealed that administration of 800 mg of oral gabapentin 90 minutes before laryngoscopy which follows the administration of 100 mg of oral gabapentin in the night before surgery reduced mean diastolic blood pressure and mean arterial blood pressure during the first 15 minutes after microlaryngoscopy when compared to a placebo. But mean systolic blood pressure and mean heart rate did not fall.

Despite an extensive search, we could find no study to exactly evaluate the effect of oral gabapentin on haemodynamic changes during microlaryngoscopic surgery. In one study from Sweden, the efficacy of propofol and methohexital on haemodynamic changes during microlaryngeal surgery was compared. The authors showed that the increase in heart rate was more extensive in the methohexital group compared to propofol [8]. Bharti et al. [9] compared the haemodynamic changes and emergence characteristics of sevoflurane versus propofol anaesthesia for microlaryngeal surgery**.** They found that sevoflurane showed an advantage over propofol in respect of intraoperative cardiovascular stability without increasing recovery time in microlaryngeal surgery. Boussofara et al. [10] evaluated the effect of esmolol on cardiovascular changes during microlaryngeal surgery. They showed that infusion of esmolol can prevent cardiovascular changes after microlaryngeal surgery.

Some studies have evaluated the effects of different doses of gabapentin on haemodynamic responses to laryngoscopy and intubation in different types of surgery. In one of them, investigators assessed the effect of 800 mg gabapentin administered orally. Similarly to our study, they showed that 800 mg gabapentin given 1 hour before surgery can decrease mean arterial pressure after laryngoscopy and tracheal intubation. But according to our study, gabapentin has no effect on systolic blood pressure and heart rate [11]. Memis et al. [12] evaluated the efficacy of oral gabapentin on cardiovascular responses to laryngoscopy and tracheal

intubation. They showed that 800 mg gabapentin given 1 h before operation blunted the mean arterial blood pressure and heart rate increase in the first 10 min due to endotracheal intubation. In another study, researchers evaluated the efficacy and safety of oral 1,200 mg gabapentin two hours before induction on haemodynamic response to laryngoscopy and tracheal intubation. They showed that preoperative oral gabapentin suppressed the haemodynamic response (MAP, HR) to laryngoscopy and tracheal intubation [5]. In another study, the effect of clonidine and 900 mg gabapentin premedication in modifying the hyperdynamic response following laryngoscopy and tracheal intubation was compared. The authors suggested that both clonidine and gabapentin were effective in blunting hyperdynamic responses due to laryngoscopy [2]. Koc et al. [13] evaluated the effects of 800 mg gabapentin and dexamethasone given together or separately one hour before the start of surgery on laryngoscopy, tracheal intubation, intraoperative haemodynamics, opioid consumption, and postoperative pain in patients undergoing varicocele operations.

They showed that gabapentin and dexamethasone administered together one hour before varicocele surgery results in less laryngeal and tracheal intubation response, improves postoperative analgesia, and prevents postoperative nausea and vomiting better than individual administration of each drug. Other authors have investigated the effect and safety of 600 mg of gabapentin given two hours before induction, esmolol or their combination on the haemodynamic response to laryngoscopy and intubation. They revealed that a combination of gabapentin and esmolol is safe and better attenuates both the pressure and tachycardic response to laryngoscopy and intubation, than either agent alone [14]. Kong et al. [15] evaluated the efficacy and safety of gabapentin in the setting of perioperative anaesthetic management. They showed that gabapentin, as a potential multimodal perioperative drug, could be given in the dose of 900 mg 1–2 h before surgery to prevent increasing systolic blood pressure and heart rate after surgery. Turkish investigators determined the effects of pre-treatment with 800 mg gabapentin two hours before surgery on intraocular pressure in addition to a haemodynamic response to tracheal intubation. They suggested that gabapentin is a useful adjuvant in order to prevent an increase in the IOP in response to laryngoscopy and tracheal intubation [16]. Bhandari et al. [3] evaluated the effects of gabapentin on arterial blood pressure and heart rate after induction of tracheal intubation in a prospective, randomised, double-blind study. They suggested that premedication with 900 mg gabapentin two hours before induction of anaesthesia attenuates increasing heart rate associated with laryngoscopy and intubation, but not the pressor response completely. Montazeri et al. [17] compared the efficacy of oral gabapentin and clonidine premedication for controlling the haemodynamic responses to laryngoscopy and tracheal intubation. They demonstrated that premedication with oral gabapentin 800 mg or clonidine 0.3 mg blunted the hyperdynamic response after laryngoscopy and intubation. Also SBP, DBP, MAP and HR at one, three, five, ten, and 15 minutes after intubation were significantly lower in the gabapentin group compared to the placebo group [17].

According to our study, 800 mg gabapentin 90 minutes before the microlaryngoscopy can attenuate increasing diastolic blood pressure and mean arterial blood pressure in the first 15 min after this procedure, but has no effect on systolic blood pressure or heart rate. As managing heart rate changes following laryngoscopy and tracheal intubation, especially after microlaryngoscopy, is more difficult than managing other haemodynamic changes, so higher doses of gabapentin could be recommended for this reason.

More studies focusing on the effective dose to attenuate haemodynamic and cardiovascular responses during microlaryngoscopy are needed.

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