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## SCIENTIFIC ARTICLE

# Effect of gabapentin pretreatment on myoclonus after etomidate: a randomized, double-blind, placebo-controlled study



Mensure Yılmaz Çakirgöz<sup>a,\*</sup>, İsmail Demirel<sup>b</sup>, Esra Duran<sup>c</sup>, Ayşe Belin Özer<sup>b</sup>, Volkan Hancı<sup>d</sup>, Ülkü Aygen Türkmen<sup>a</sup>, Ahmet Aydın<sup>b</sup>, Ayşın Ersoy<sup>a</sup>, Aslıhan Büyükyıldırım<sup>a</sup>

<sup>a</sup> Okmeydanı Training and Research Hospital, Department of Anesthesiology and Reanimation, Şişli, İstanbul, Turkey

<sup>b</sup> Fırat University, School of Medicine, Department of Anesthesiology and Reanimation, Elazığ, Turkey

<sup>c</sup> Şehit Kamil State Hospital, Gaziantep, Turkey

<sup>d</sup> Dokuz Eylül University, School of Medicine, Department of Anesthesiology and Reanimation, İzmir, Turkey

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### KEYWORDS

Etomidate;  
Injection pain;  
Myoclonus;  
Gabapentin

### Abstract

**Aim:** To evaluate the effects of three different doses of gabapentin pretreatment on the incidence and severity of myoclonic movements linked to etomidate injection.

**Method:** One hundred patients, between 18 and 60 years of age and risk category American Society of Anesthesiologists I–II, with planned elective surgery under general anesthetic were included in the study. The patients were randomly divided into four groups and 2 h before the operation were given oral capsules of placebo (Group P,  $n = 25$ ), 400 mg gabapentin (Group G400,  $n = 25$ ), 800 mg gabapentin (Group G800,  $n = 25$ ) or 1200 mg gabapentin (Group G1200,  $n = 25$ ). Side effects before the operation were recorded. After preoxygenation for anesthesia induction  $0.3 \text{ mg kg}^{-1}$  etomidate was administered for 10 s. A single anesthetist with no knowledge of the study medication evaluated sedation and myoclonic movements on a scale between 0 and 3. Two minutes after induction,  $2 \mu\text{g kg}^{-1}$  fentanyl and  $0.8 \text{ mg kg}^{-1}$  rocuronium were administered for tracheal intubation.

**Results:** Demographic data were similar. Incidence and severity of myoclonus in Group G1200 and Group G800 were significantly lower than in Group P; sedation incidence and level were appreciably higher compared to Group P and Group G400. While there was no difference in the

\* Corresponding author.

E-mail: [drmeasure@gmail.com](mailto:drmeasure@gmail.com) (M. Yılmaz Çakirgöz).

incidence of myoclonus between Group P and Group G400, the severity of myoclonus in Group G400 was lower than in the placebo group. In the two-hour period before induction other than sedation none of the side effects related to gabapentin were observed in any patient.

**Conclusion:** Pretreatment with 800 mg and 1200 mg gabapentin 2 h before the operation increased the level of sedation and reduced the incidence and severity of myoclonic movements due to etomidate.

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## PALAVRAS-CHAVE

Etomidato;  
Dor à injeção;  
Mioclonia;  
Gabapentina

## Efeito do pré-tratamento com gabapentina sobre a mioclonia após etomidato: um estudo randômico, duplo-cego e controlado por placebo

### Resumo

**Objetivo:** Avaliar os efeitos de três doses diferentes de gabapentina como pré-tratamento sobre a incidência e gravidade dos movimentos mioclônicos associados à injeção de etomidato.

**Método:** Cem pacientes, com idades entre 18-60 anos, estado físico ASA I-II, programados para cirurgia eletiva sob anestesia geral foram incluídos no estudo. Os pacientes foram randomicamente divididos em quatro grupos e, 2 horas antes da operação, receberam cápsulas orais de placebo (Grupo P,  $n = 25$ ), 400 mg de gabapentina (Grupo G400,  $n = 25$ ), 800 mg de gabapentina (Grupo G800,  $n = 25$ ) ou 1200 mg de gabapentina (Grupo G1200,  $n = 25$ ). Os efeitos colaterais antes da cirurgia foram registrados. Após pré-oxigenação para a indução da anestesia, etomidate ( $0,3 \text{ mg.kg}^{-1}$ ) foi administrado por 10 segundos. Um único anestesista, cego para a medicação do estudo, avaliou a sedação e os movimentos mioclônicos usando uma escala de 0 a 3. Dois minutos após a indução, fentanil ( $2 \mu\text{g.kg}^{-1}$ ) e rocurônio ( $0,8 \text{ mg.kg}^{-1}$ ) foram administrados para a intubação traqueal.

**Resultados:** Os dados demográficos foram semelhantes. A incidência e gravidade da mioclonia nos grupos G1200 e G800 foram significativamente menores que no Grupo P; a incidência e o nível de sedação foram consideravelmente maiores comparados ao Grupo P e Grupo G400. Enquanto não houve diferença na incidência de mioclonia entre os grupos P e G400, a gravidade da mioclonia no Grupo G400 foi menor que no grupo placebo. No período de 2 horas antes da indução, nenhum dos efeitos colaterais relacionados à gabapentina, exceto sedação, foi observado em qualquer paciente.

**Conclusão:** O pré-tratamento com 800 mg e 1200 mg de gabapentina 2 horas antes da operação aumentou o nível de sedação e reduziu a incidência e gravidade dos movimentos mioclônicos associados ao etomidato.

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## Introduction

Etomidate, a derivative of imidazole, is a popular hypnotic agent chosen for patients with cardiovascular instability due to minimal cardiovascular side effects and extremely stable hemodynamic profile. Myoclonus and injection pain are two disagreeable side effects of anesthesia induction with etomidate. As many side effects due to etomidate are thought to be linked to the solvent propylene glycol, a lipid formulation was developed. While this new formulation prevented injection pain, venous irritation and hemolysis, myoclonus incidence was not affected by the solvent.<sup>1</sup>

The formation of myoclonus during anesthesia induction with etomidate has clinical importance in select groups of patients. Myoclonus can increase the risk of regurgitation and aspiration in patients with full stomach, as it

increases intraocular pressure it may cause vitreous prolapse in patients with open eye injuries, and as myocardial oxygen consumption increases during myoclonus it may cause problems in patients with limited cardiovascular reserves.<sup>2</sup> Finally myoclonus has been observed to be responsible for hypoxemia attacks during spontaneous respiration when etomidate is administered for sedation.<sup>2,3</sup> Despite the variety of medications that reduce the incidence and severity of myoclonic movements after etomidate administration, the mechanism is not clear. Doenicke et al. reported that myoclonus after treatment with etomidate was a phenomenon of subcortical disinhibition, like the phenomenon of restless legs during normal human sleep, and is not generated by an epileptic focus.<sup>1,4</sup>

Gabapentin, produced in 1993 as a treatment for chronic partial convulsions, is a new generation of anti-epileptic

with antinociceptive, analgesic and antihyperalgesic properties. The most widespread use of gabapentin, outside of epilepsy, is for neuropathic pain.<sup>5</sup> Also gabapentin and its analogs have been effective in the treatment of motion disorders such as periodic leg movements in sleep, restless leg syndrome, essential tremor and acquired nystagmus.<sup>6</sup> Recently many clinical studies evaluating the potential role of gabapentin in the preoperative period for a variety of aims have been published.<sup>5</sup> However though myoclonus linked to etomidate has similar pathophysiology and EEG results as restless leg syndrome which has been successfully treated by gabapentin, no studies were found on gabapentin's effect on myoclonus linked to etomidate. The hypothesis of this study is that pretreatment with three different doses of oral gabapentin will reduce the incidence and severity of myoclonic movements linked to etomidate in a dose-dependent fashion.

To test this hypothesis the aim was to complete a prospective, randomized, double-blind and placebo-controlled study to research the effects of three different doses of oral gabapentin pretreatment on the incidence and severity of myoclonic movements linked to etomidate.

## Methods

This study was completed with permission of Firat University Medical Faculty Pharmaceutical Research Ethics Committee (Head: Prof. Mehmet Tokdemir, dated 12.07.2012, decision n° 07) between July 2012 and December 2012 in the operating theaters of Firat University Medical Faculty and Okmeydani Educational and Research Hospital after patients signed an informed consent form. One-hundred patients in I-II risk group, according to the American Society of Anesthesiologists (ASA) classification of physical condition, who were to undergo elective surgical intervention under general anesthesia between the ages of 18–60 were included in the study.

Patients considered have airway management difficulties, cardiac disease, diabetes mellitus, history of neuromuscular disease, impaired renal status, liver failure, COPD and asthma, hiatal hernia and symptomatic gastroesophageal reflux, gastrointestinal dysfunction affecting absorption of oral treatments, history of allergic reaction to the study drugs, pregnancy, lactating female patients, drug or alcohol addiction, and patients with a history of chronic opioid, tricyclic antidepressant, benzodiazepine anticonvulsant, clonidine, beta blocker, systemic and/or topical steroid use were not included in the study.

No patient received any premedication. The patients were randomly assigned using a computer-generated random numbers table to one of the following four treatment groups: 1 – Group P received an oral placebo; 2 – Group G400 received gabapentin 400 mg, po; 3 – Group G800 received gabapentin 800 mg, po; and 4 – Group G1200 received gabapentin 1200 mg, po. The study medication capsules were put in numbered envelopes containing two placebo capsules (Group P), one gabapentin 400 mg with one placebo capsule (Group G400), two gabapentin 400 mg capsules (Group G800), or two gabapentin 600 mg capsules (Group G1200). Two hours before the operation study medications were administered with a small amount of water

by an anesthetist not included in the study. The study drugs were prepared by the pharmacy in order to maintain double-blind conditions, and an appropriate code number was assigned. Patients and the anesthetist in charge of patient management and data collection were unaware of the groups. Before being taken to the operating room side effects developing in the patients, such as nausea, vomiting, dizziness, headache, confusion, weakness, fatigue, nystagmus, skin rash, drowsiness, peripheral edema, vision disorders etc., were evaluated and recorded by an anesthetist blind to the contents of the study drugs and not included in the study.

After patients were transferred to the operating table preoxygenation was begun with 6 L min<sup>-1</sup> oxygen administered through a mask and non-invasive blood pressure, electrocardiogram, and pulse oxymetry monitoring was applied. A vein was opened in the back of the left hand with a 20G cannula and infusion of 0.9% NaCl solution was started. After preoxygenation for anesthesia induction 0.3 mg kg<sup>-1</sup> etomidate was administered for 10 s. After the eyelash reflex was lost after induction the patient was manually administered 100% O<sub>2</sub> through a mask until end tidal CO<sub>2</sub> (ET<sub>CO2</sub>) was 35–40 mmHg. Two minutes after induction 2 µg kg<sup>-1</sup> fentanyl and 0.8 mg kg<sup>-1</sup> rocuronium were given for tracheal intubation. After endotracheal intubation anesthesia was maintained with 30% oxygen, 70% nitrous oxide with 2% sevoflourane.

Sedation and myoclonic movements were evaluated and recorded on a 0–3 scale by an anesthetist blind to the studied medication. Evaluation of sedation was completed before induction with etomidate was begun; sedation level was evaluated as 0 = none/awake (alert), 1 = slight (drowsy but responds to name said in normal voice), 2 = moderate (responds to loud voice and/or repeated calls) and 3 = deep (responds when prodded lightly or shaken).<sup>2</sup> Myoclonic movements were evaluated in the 2 min period after induction; myoclonic severity was evaluated according to 0 = no myoclonus, 1 = slight myoclonus (slight fasciculation of face and/or distal upper and/or lower extremities), 2 = moderate myoclonus (definite movements of face and/or extremities) and 3 = severe myoclonus (movements of extremities and trunk).<sup>7</sup>

Heart rate (HR), mean arterial pressure (MAP) and peripheral oxygen saturation were recorded before induction (base value), immediately before intubation and in the 1st, 3rd and 5th minutes after tracheal intubation. At the end of the study period, anesthesia management was transferred to the anesthesia team responsible for the operating theater and aware of the medications administered to the patient.

## Statistical method

SPSS 16.0 program was used for statistical evaluation. Continuous data were evaluated by using descriptive statistics (mean, median, standard deviation, min–max). For evaluation of normally distributed data between groups (age, BMI, HR, MAP) one-way ANOVA and Tukey HSD tests (for Post Hoc evaluation). For categorical data Pearson Chi-square and Fisher Exact test (where at least one expected value of a cell is less than 5) were used. Mann Whitney U test and Kruskal Wallis tests were used for comparing non-normally

**Table 1** Demographic characteristics of patients.

	Group P (n = 25)	Group G400 (n = 25)	Group G800 (n = 25)	Group G1200 (n = 25)
Age (years)	35.5 ± 12.4	34.9 ± 6.2	36.1 ± 9.4	35.8 ± 12.4
BMI (kg/m <sup>2</sup> )	24.0 ± 3.6	23.8 ± 3.0	23.9 ± 4.8	23.6 ± 3.3
Gender (male/female)	13/12	12/13	14/11	12/13
ASA physical status (I/II)	11/14	12/13	13/12	14/11

Data are given as number of patients or mean ± standard deviation. ASA – American Society of Anesthesiologists.

distributed data. Significance was accepted as  $p < 0.05$ . In the placebo group the incidence of myoclonus was about 70%, assuming  $\alpha = 0.05$ , and  $1 - \beta = 0.80$ , and with a predicted average reduction of myoclonus incidence of 40%<sup>8</sup>; for the study at least 22 patients were required in each group. Working from this data, in the study 25 patients was included in each group.

## Results

In terms of demographic data there was no significant statistical difference between the groups ( $p > 0.05$ ) (Table 1). In the two hour period before induction other than sedation none of the side effects related to gabapentin were observed in any patient.

There was a significant difference in the incidence, severity and median values of myoclonus linked to etomidate between the groups ( $p = 0.002$  Chi-square,  $p = 0.006$  Fisher Exact test, Kruskal Wallis  $p = 0.002$  respectively). The myoclonus severity levels in the G1200 and G800 groups were significantly lower than in Group P ( $p = 0.006$ ,  $p = 0.003$  Fisher Exact test). The myoclonus incidence in G1200 and G800 was significantly lower than in Group P ( $p = 0.001$ ,  $p = 0.002$  Chi-square), and in Group G800 the incidence was significantly lower than in Group G400 ( $p = 0.045$  Chi-square). Compared to the placebo group, in G800 there was

2.71 times and in G1200 there was 2.38 times less myoclonus observed (Table 2).

The frequency, intensities and median values of sedation between the groups were statistically significantly different ( $p < 0.01$ ). The frequency and intensities of perioperative sedation in Group G1200 and G800 were significantly higher than in Group P and G400 ( $p = 0.001$ ,  $p = 0.001$ ,  $p = 0.04$ ,  $p = 0.021$  respectively) (Table 3). Compared to the placebo group, in G800 there was 4.76 times and in G1200 there was 5.26 times more sedation observed (Table 2).

The mean arterial blood pressure and the heart rate were similar among the groups at all measurement times. No bradycardia or hypotension was observed in any patient. Peripheral oxygen saturation in the four groups during the study period was above  $\geq 97\%$  and there was no significant difference observed between the groups.

## Discussion

In this study, while 800 mg and 1200 mg of gabapentin 2 h before the operation reduced the frequency and severity of myoclonic movements linked to anesthesia induction with etomidate, it was determined that it also increased the preoperative sedation level.

Preventing myoclonus related to etomidate is clinically important. Etomidate is frequently used as it allows early

**Table 2** Number of patients (%) and severity of myoclonus after injection of etomidate.

	Group P (n = 25)	Group G400 (n = 25)	Group G800 (n = 25)	Group G1200 (n = 25)	p
Severity of myoclonus					0.006 <sup>a</sup>
None (0)	6 (24)	11 (44)	18 (72) <sup>f</sup>	17 (68) <sup>f</sup>	
Mild (1)	7 (28)	8 (32)	2 (8) <sup>f</sup>	3 (12) <sup>f</sup>	
Moderate (2)	8 (32)	6 (24)	5 (20)	5 (20)	
Severe (3)	4 (16)	0 (0)	0 (0)	0 (0)	
Myoclonus (%)	19 (76)	14 (56)	7 (28) <sup>d,e</sup>	8 (32) <sup>d</sup>	0.002 <sup>b</sup>
Severity of myoclonus Median (min–max) (0–3)	1 (0–3)	1 (0–2) <sup>g</sup>	0 (0–2) <sup>g</sup>	0 (0–2) <sup>g</sup>	0.002 <sup>c</sup>
Relative risk (95% CI)		1.36 (0.9–2.0)	2.7 (1.39–5.28)	2.38 (1.29–4.38)	

Group P, placebo group; Group G400, Gabapentin 400 mg; Group G800, Gabapentin 800 mg; Group G1200, Gabapentin 1200 mg.

<sup>a</sup> Fisher exact test.

<sup>b</sup> Chi-square test.

<sup>c</sup> Kruskal Wallis test. Comparisons for incidence of myoclonus.

<sup>d</sup>  $p < 0.01$  compared with group P.

<sup>e</sup>  $p < 0.05$  compared with group G400. Comparisons for severity levels of myoclonus.

<sup>f</sup>  $p < 0.02$  compared with group P. Comparisons for severity of myoclonus median.

<sup>g</sup>  $p < 0.05$  compared with group P.

**Table 3** Comparison of frequency and intensities of sedation between in four groups.

	Group P (n = 25)	Group G400 (n = 25)	Group G800 (n = 25)	Group G1200 (n = 25)	p
Sedation n (%)	3 (12)	6 (24)	14 (56) <sup>c,d</sup>	16 (64) <sup>c,d</sup>	<0.001 <sup>a</sup>
Sedation score median (0–3)	0 (0–1)	0 (0–1)	1 (0–1) <sup>c,d</sup>	1 (0–1) <sup>c,d</sup>	<0.001 <sup>b</sup>
Relative risk of sedation (95% CI) compared with Group P		0.5 (0.14–1.78)	0.21 (0.7–0.66)	0.19 (0.06–0.56)	

Group P, placebo group; Group G400, Gabapentin 400 mg; Group G800, Gabapentin 800 mg; Group G1200, Gabapentin 1200 mg. Frequency of sedation.

<sup>a</sup> Chi-square test  $p < 0.001$ .

Intensities of sedation with four groups

<sup>b</sup> Fisher-exact test/Kruskal Wallis test  $p < 0.001$ .

<sup>c</sup>  $p < 0.002$  compared with group P.

<sup>d</sup>  $p < 0.05$  compared with group 400.

recovery and stable hemodynamics in interventions requiring short-term anesthesia like elective cardioversion.<sup>7</sup> In the absence of neuromuscular blocker agents when used for induction myoclonus is observed in 50–80% of patients without premedication, while the incidence is reported as 20–45% when used for sedation of patients.<sup>1,9</sup> Reported cases are generally mostly minor myoclonic events of short/brief duration or tremor. However a few patients have myoclonic events characterized as serious, described as generalized rigidity and stiffness and lasting several minutes. In addition during myoclonus ECG electrodes were displaced and oxygen saturation falls are frequently reported on pulse oxymetry. In this situation it should be noted that myoclonic events may be large enough to delay evaluation of monitoring and success of intervention in patients.<sup>3</sup> However especially for short duration interventions the medication given to prevent myoclonus due to etomidate should not disrupt the positive hemodynamic and early recovery properties of etomidate.<sup>2</sup> In our study at the doses of gabapentin used no effect on respiration or consciousness after the intervention was expected, so in this study there was no postoperative record kept.

In our study, similar to previous studies, observed myoclonic activity at 76% in the placebo group. It is known that in more than half of cases myoclonus due to etomidate starts after the 1st minute<sup>1</sup> so the observation period in this study was fixed at 2 min. To denote the difference between hand-arm pull movements due to pain of the etomidate injection and myoclonus, movement during intravenous etomidate administration was accepted as injection pain, while movement in the 2 min after the injection was fully finished were accepted as myoclonus. It is known from previous studies that slow injection speed, with a effect similar to priming dose of etomidate, reduced myoclonus incidence.<sup>1</sup> In this study etomidate was injected over 10s. It is thought that this allowed us to capture the true rate of myoclonus.

The neurologic mechanism of myoclonic activity after etomidate is not clear and one possibility is that it may be a form of seizure activity. Another theory is that its initial cause may be due to differences in local brain blood flow or in receptor affinities in the CNS asynchronous to the effect of etomidate, together with a possible subcortical

disinhibition developing due to quick suppression of cortical inhibition linked to earlier and lower doses depressing the excitatory circuits of inhibitor pathways.<sup>1,10</sup> Disruption of GABA neurons makes pathways related to skeletal muscle control more sensitive to spontaneous nerve transmissions, which causes myoclonic muscle movements.<sup>7</sup> Choi et al.<sup>11</sup> showed that rocuronium premedication blocked the neuromuscular junction transmission and definitively reduced myoclonus due to etomidate.

Structurally an anticonvulsant GABA analog, after use for neuropathic pain syndromes, in the 1990s gabapentin began to be used successfully to treat restless leg syndrome.<sup>12</sup> The experimental evidence from studies to date indicate a disinhibition role in RLS pathogenesis at supraspinal levels.<sup>6</sup> In an electroencephalogram (EEG) study by Doenicke et al.<sup>1</sup> on EEG epileptic activity was not encountered, as myoclonus linked to etomidate, similar to restless leg syndrome, is linked to subcortical disinhibition they reported that low doses with etomidate administration reduced myoclonus, supporting the subcortical disinhibition theory. In addition, after premedication with benzodiazepans and opioids, with known limiting effects on subcortical structures, the reduction in myoclonus linked to etomidate supports the theory of disinhibition of subcortical structures.<sup>1,4</sup> While the effective mechanism of gabapentin is not definitely known, it increases non-synaptic GABA release and synthesis from glial structures in the whole brain in dose-linked fashion. Linkage with high affinity for  $\alpha 2\delta$  subunits of voltage sensitive calcium channels, reduction in the release of monoamine neurotransmitters, inhibition of voltage active sodium channels and increase in serotonin concentration are among the other effects proven for gabapentin.<sup>13</sup> In this study while the incidence of myoclonus in Group P was 76%, it dropped to 28% and 32% in Group G800 and Group G 1200 respectively. In the groups the total moderate and severe myoclonus incidence was 48% in Group P, 24% in Group G400, and 20% in Group G800 and Group G1200. After gabapentin premedication, the reduction in severity and frequency of myoclonus due to etomidate clearly supports reduction in subcortical disinhibition as gabapentin, similar to opioids and benzodiazepines, increases GABA inhibition in the whole brain including the subcortical structures.



Gabapentin is a medication with low incidence of side effects and little interaction with other medications which is well tolerated. Non-epileptic focal and multi-focal myoclonus is among the side effects of long-term treatment with gabapentin and pregabalin, such as for epilepsy, neuropathic pain and restless leg syndrome, though the incidence is less than for other anticonvulsants.<sup>13</sup> Recently reports of myoclonus related to gabapentin (GBP) use been case studies or been formed of small patient series. In available case studies, frequently a clinical tableau of myoclonus a few days after gabapentin dose increase from stable dose in cases with a history of serious neurologic and/or systemic disease and polytherapy administration, which quickly resolves within days after stopping. In pre-marketing studies of 1486 patients using gabapentin for epilepsy a myoclonus rate of 0.1% was reported.<sup>14</sup> Contrary to this Asconap et al. when inquiring about myoclonus in patients receiving gabapentin treatment found 12.5% of 104 patients had observed myoclonus. This high incidence may be partly explained by questioning specifically for myoclonic situations. In the patient population late period renal failure which interferes with the medications renal excretion, chronic static encephalopathy, mental retardation or diffuse brain damage may be risk factors for myoclonus due to gabapentin. This relationship is known from the development of choreoathetosis and other movement disorders during use of gabapentin and other antiepileptic medications. The role of other possible risk factors, such as polytherapy and refractory seizures is not clear.<sup>14</sup> The anti-epileptic effective mechanism of gabapentin, similar to its induction mechanism for myoclonus, is not fully understood. Myoclonus linked to gabapentin is thought to form in the serotonergic neurotransmitter system linked to myoclonus.<sup>15</sup> In addition, in posthypoxic animal models a dose-linked antimyoclonic effect of gabapentin was found.<sup>16</sup> In order to more clearly understand the relationship between gabapentin and myoclonus more advanced studies on the pathophysiology of myoclonus and the effective mechanism of gabapentin are needed.

In the peroperative period the most frequently reported side effects of single-dose or short-term gabapentin administration are dizziness (16%), sedation (23%), nausea/retching/vomiting (19–25%), somnolence, urinary retention, and lightheadedness.<sup>6</sup> After preoperative gabapentin administration studies on the presence of a sedation effect in the preoperative period has a mixed structure. In the literature for a variety of surgery types, 600 or 1200 mg gabapentin in the preoperative period 1–2 h after administration in the limited number of studies evaluating the sedation level,<sup>17–20</sup> while some report no statistical difference in sedation level between placebo group and gabapentin group, Clarke et al.<sup>21</sup> in a study evaluating the effect of 1200 mg gabapentin 2 h before operation on high-anxiety levels reported observing a significant level of sedation in the gabapentin group compared to the placebo group. Together with this, gabapentin's structural analog pregabalin is reported to increase sedation in a dose-linked fashion in the preoperative period.<sup>22,23</sup> In this study in the 2 hour period before the operation similar to previous studies,<sup>17–21</sup> no side effects linked to gabapentin such as nausea and vomiting, dizziness, lightheadedness, somnolence, peripheral edema, and visual disturbances or

headache were observed. Comparing the frequency and intensities of sedation in the groups in the preoperative period, a definite frequency and intensities of sedation was identified in Group G800 and Group G1200 compared to the placebo and G400 group ( $p=0.001$ ,  $p=0.001$ ,  $p=0.04$ ,  $p=0.021$  respectively). The results of this study are similar to that of Clarke et al.<sup>21</sup> in that increasing dose increased sedation levels.

In our study the primary limitation is that the patient group was younger and more healthy than the patient group to whom etomidate is most frequently administered in clinical practice. Generalizations should not be made from this study for high-risk and/or geriatric patients who use antidepressants, hypnotic or antihypertensive medications, including gabapentin, who may show increased sensitivity to medication. For similar future research more advanced studies are needed to firstly identify the optimal dose for these types of patients and possible side effects. In the period before surgery, concerns related to anesthesia and surgery are known to cause anxiety in 60–80% of patients.<sup>24,25</sup> Stress and anxiety are widely accepted to delay gastric emptying.<sup>26</sup> As it is thought that absorption of orally administered medication and peak plasma concentration values are affected by anxiety,<sup>27</sup> another limitation of our study is that to standardize patients basal anxiety levels and gabapentin serum levels were not examined.

In conclusion in this study, 800 mg and 1200 mg gabapentin oral administration 2 h before operation reduced the frequency and severity of myoclonic movements during anesthesia induction with etomidate and increased the sedation level before the operation. It is concluded that the lowest effective dose of 800 mg gabapentin should be considered to prevent myoclonus linked to etomidate. However the sedative properties of gabapentin and possibility of delaying postoperative recovery in cases of elective ambulatory surgery should be noted.

## Conflicts of interest

The authors declare no conflicts of interest.

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