ORİJİNAL ARAŞTIRMA ORIGINAL RESEARCH

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Evaluation of Preoperative Anxiolytic and Postoperative Analgesic Effects of Pregabalin Premedication

Pregabalin Premedikasyonunun Preoperatif Anksiyolitik ve Postoperatif Analjezik Etkilerinin Değerlendirilmesi

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ABSTRACT Objective: The studies about use of pregabalin for premedication have been recently carried out due to pregabalin has analgesic and anxiolytic effects together. We aimed to evaluate the effects of preoperative pregabalin on anxiety score, hemodynamic parameters, postoperative pain and analgesic consumption in patients undergoing elective abdominal hysterectomy. **Material and Methods:** The patients were randomly separated into 34 patients of two groups. This prospective randomized, double-blind and placebo-controlled study was performed in patients undergoing elective abdominal hysterectomy. Pregabalin 150 mg (Pregabalin Group) or placebo 150 mg empty capsule (Control Group) was given to the patients 12 hours and 1 hour before operation. STAI-I (State-Trait Anxiety Inventory-I) anxiety scale were performed to the patients during preoperative examination and 1 hour before operation. In both groups, intraoperative hemodynamic parameters, postoperative pain levels with VAS (Visual Analogue Scale), morphine consumption and developing side effects were recorded and analyzed. **Results:** When all patients were compared from the point of demographic data, no difference was found between groups. STAI-I points were found significantly different between Pregabalin and Control groups both premedication and postmedication phases. MAP (Mean Arterial Pressure) data were found lower in pregabalin group at intraoperative 30th, 40th and 75th minutes and postoperative 1st minute ($p<0.05$). Postoperative VAS values were found lower in Pregabalin Group. Additional analgesic use and morphine consumption, were lower in Pregabalin group except 1st and 30th minutes. When both groups, examined with regard to side effects, side effect rates of Control Group were 29% and rates of Pregabalin Group were 10%. **Conclusion:** In this study, it was concluded that pregabalin use at 12 and 1 hour before operation decreased preoperative anxiety score, provided postoperative analgesia and found superior to placebo due to decreasing side effects via decreasing the consumption of analgesics, however for the routine use of pregabalin in premedication it was needed further studies with different doses and large sample sizes.

Keywords: Premedication; postoperative pain; pregabalin; preoperative anxiety

ÖZET Amaç: Pregabalinin analjezik ve anksiyolitik etkinliği birarada taşıması nedeniyle son dönemde premedikasyonda kullanımı ile ilgili çalışmalar yapılmaktadır. Elektif abdominal histerektomi geçirecek hastalarda preoperatif pregabalin kullanımının anksiyete skoru, hemodinamik parametreler, postoperatif ağrı ve analjezik tüketimi üzerine etkilerini değerlendirmeyi amaçladık. **Gereç ve Yöntemler:** Hastalar rastgele 34 kişilik 2 gruba ayrıldı. Bu prospektif randomize, çift kör ve plasebo kontrollü çalışma elektif abdominal histerektomi geçirecek hastalarda gerçekleştirildi. Hastalara operasyondan 12 saat ve 1 saat önce pregabalin 150 mg (Pregabalin grubu) veya plasebo 150 mg boş kapsül (Kontrol grubu) verildi. Hastalara preoperatif muayene sırasında ve operasyondan 1 saat önce State-Trait Anxiety Inventory-I (STAI-I) anksiyete ölçeği uygulandı. Her iki grupta, peroperatif hemodinamik parametreler, VAS ile postoperatif ağrı düzeyleri, morfin tüketimleri ve gelişen yan etkiler kaydedilerek analiz edildi. **Bulgular:** Tüm hastalar demografik veriler yönünden karşılaştırıldığında gruplararası anlamlı bir fark görülmedi. Pregabalin ve Kontrol grubunda, premedikasyonda ilaç verilmeden önceki ve sonraki STAI-I puanları yönünden gruplararası farklılık anlamlı bulundu. İntraoperatif 30., 45., 75. ve postoperatif 1. dakikadaki OAB (Ortalama Arteryal Basınç) Pregabalin grubunda daha düşük seyretti. Postoperatif VAS (Vizüel Analog Skala) değerleri Pregabalin grubunda daha düşük bulundu. Ek analjezik kullanımı ve morfin tüketimleri 30 dakikadan sonra Pregabalin grubunda daha düşüktü. Her iki grup, yan etki yönünden incelendiğinde Kontrol grubunda %29 yan etki izlenirken, Pregabalin grubunda %10 olarak izlendi. **Sonuç:** Genel anestezi altında abdominal histerektomi geçirecek hastalarda, operasyondan 12 saat ve 1 saat önce uygulanan 150 mg pregabalinin preoperatif anksiyete skorlarını azalttığı, postoperatif analjezi sağladığı ve analjezik tüketimini azaltarak buna bağlı yan etkileri de azaltması nedeniyle plaseboya üstün olduğu, ancak pregabalinin rutin premedikasyona kazandırılabilmesi için farklı dozlar ve geniş örneklem grupları ile çalışmaların yapılması gerektiği sonucuna varıldı.

Anahtar Kelimeler: Premedikasyon; postoperatif ağrı; pregabalin; preoperatif anksiyete

Preoperative anxiety is seen in 60-80% of patients who are planned for surgery and adversely affects anesthesia, surgery and postoperative healing.[1,2] This may lead to pathophysiological responses such as hypertension and dysrhythmia, or even to the patient's rejection of planned surgery.[3,4] It may also increase the anesthetic need and the risk of "awareness" during the operation.[3,5] Anxiety in the preoperative period can have many causes. Patients may have concerns such as distancing from their home and relatives, interruption of daily work, as well as worries about complications and awakening after the operation, insufficient knowledge about anesthesia and the surgery.[6]

Postoperative pain cannot be avoided after any operation. The severity of the pain depends on the size and location of the operation being performed. Whatever the source may be, pain causes physiopathological changes in the human body. Postoperative pain slows down the healing process and prolongs the length of stay in the hospital. Therefore, appropriate and adequate postoperative pain management is an important factor in accelerating postoperative healing, shortening the duration of hospitalisation, and reducing treatment costs.[7]

Anesthesia management begins with the application of selected drugs to psychologically prepare the patient and to reveal specific pharmacological responses in the preoperative period. Reducing anxiety, sympathetic nervous system responses and the need for anesthetic drugs and providing sedation, analgesia and amnesia are among the primary objectives of premedication.[8-10] Many drugs can be used to achieve the goals of premedication. Benzodiazepines, opioids, antihistamines, α2-adrenergic agonists, anticholinergics, H2 antagonists, antacids can be used in premedication.[8-10] The best medication or best combination to achieve the desired goals in premedication is unknown.[8] Pregabalin is a GABA structural analogue, has no direct effect on GABA-like mechanisms, and has anticonvulsant, analgesic and anxiolytic effects.[11,12] The coexistence of anxiolytic and analgesic activity has recently led to its evaluation in premedication as a different alternative.

In this prospective, randomized, double blind and placebo-controlled study, we aimed to evaluate the effects of pregabalin on peroperative hemodynamic parameters, preoperative anxiety, postoperative pain and analgesic consumption.

MATERIAL AND METHODS

Ethics committee approval and consent of the patients were taken for the study with the decision dated 21/05/2013 and numbered 2013-05/24. This study is designed on principles of Helsinki Declaration properly. This randomized placebo-controlled double-blind study was conducted with 68 patients aged 18-60 years in ASA I-II groups, who prospectively underwent abdominal hysterectomy after their informed consent was obtained. When α= 0.05, β=0.20, and (1-β)=0.80 were taken, it was decided to include 34 patients in each study group and the power of the test was found to be p=0.80642. Patients who have renal, cardiac, or liver disease, who use antidepressants or antipsychotics, who have drug dependence, who have a history of epilepsy, who use gabapentine or pregabalin, those with diabetes mellitus and diabetic neuropathy, drug allergy or contraindication, and patients with peroperative complications were excluded from the study.

Information was provided on the use of Visual Analogue Scale (VAS) and Patient Controlled Analgesia (PCA) to all patients. An anxiety questionnaire was performed with State-Trait Anxiety Inventory-I (STAI-I) anxiety scale during preoperative medical examination.[13] The STAI anxiety scale was developed by Spielberger, and there are two subscales consisting of 20 multiple-choice questions for state and continuity anxiety. Each item is rated as 1, 2 or 3 according to the severity of the symptom, the lowest possible score on scales is 20, and the highest total score is 80. State anxiety describes the anxiety that an individual feels within certain circumstances at a particular time, and can vary with external factors. Continuous anxiety describes how the individual feels in general and reflects the individual's general anxiety predi sposition. Randomization was based on a computer-generated code. The drugs were prepared by an anesthetist, who was not one of the observers.

They were marked only with a coded label to maintain the double-blind nature of study. All patients were fasted 8 hours before surgery and Isolyte M was given at 2 ml/kg. Patients were randomly divided to two groups. 12 hours prior to the operation, pregabalin 150 mg capsule (Regapen, İlko İlaç) and placebo 150 mg capsule were orally given to patients in the pregabalin group (n=34) and the control group (n=34), respectively. Anxiety questionnaires were performed 1 hour before the operation again using the STAI-I anxiety scale, followed by a second oral application of pregabalin 150 mg capsule (Regapen, İlko İlaç) in the pregabalin group (n=34) and placebo 150 mg capsule in the control group. Patients were then taken to the operating room and their heart rate (HR), DII lead electrocardiogram (ECG), peripheral oxygen saturation (SpO_2) and mean arterial blood pressure (MAP) were monitored using anesthesia monitor (Drager Infinity Vista XL) in the preoperative and perioperative period. Anesthesia induction of all patients was applied with 2 mg/kg propofol (Propofol 2%, Fresenius-Kabi Pharma) and 1 μg/kg fentanyl (Fentanyl, Janssen-Cilag) and 0.6 mg/kg rocuronium vial (Esmeron vial, Schering- Plough). Following endotracheal intubation, 4-6% Desfluran (Suprane Volatile Solution, Eczacıbaşı-Baxter) and 50% N_2O in oxygen were used in anesthesia maintenance. During the operation, $ETCO_2$ value was kept in the range of 35-45 mmHg in all patients. Patients were given the necessary fluid replacement. During the operation, basal pre-intubation values and post-intubation values at the 1^{st}, 5^{th}, 15^{th}, 30^{th}, 45^{th}, 60^{th}, 75^{th}, 90^{th}, 105^{th}, 120^{th} minutes of HR, MAP and SpO_2 were recorded. The depth of anesthesia was monitored according to the physiological parameters. Desflurane was titrated so as to keep the mean arterial pressure at 65-75 mmHg. An additional dose of iv 0.5 μg/kg fentanyl was administered to patients with a greater than 20% increase in mean arterial pressure.

After the surgery, patients were awakened by decurarizing with atropine ampoule (Atropine sulphate ampoule, Biofarma) and neostigmine ampoule (Neostigmine ampoule, Adeka İlaç) and extubation time was recorded. After extubation, patients with a Modified Aldrete Recovery Score of 9 or more were taken to the postoperative recovery unit. In the postoperative recovery unit, Patient-Controlled Analgesia Device (PCA, Meditera) was used, which was prepared with morphine (Morphine HCL, Galen Drug) applied as intravenous at a concentration of 0.3 mg/mL, a bolus dose of 1 mg, lock-in time of 7/min and a 4 hour limit of 10 mg . Postoperative HR, MAP and VAS values at 1 and 30 minutes and at 1, 2, 4, 6, 12, 24 hours along with patients' initial morphine use times, total morphine needs, additional non-morphine analgesic use and side effects were recorded. An additional 50 mg of dexketoprofen trometamol iv was administered to patients with VAS≥3 after PCA use.

STATISTICAL METHOD

The data acquired from our study were uploaded to SPSS (Ver: 14.0) program. After the Kolmogorov Smirnov test and the normality test, Difference between Two Means Significance Test was used when the parametric test assumptions were fulfilled; the Mann Whitney U test was used when the parametric test assumptions were not fulfilled. Chi-square test was used to compare qualitative data. Variance Analysis and Tukey Tests were used for parametric repetitive measurements, Friedman and Wilcoxon tests were used for non-parametric repetitive measurements. Our data was indicated as arithmetic mean±standard deviation, number of individuals and percentages in tables. The level of error was taken as 0.05.

RESULTS

The difference between pregabalin and control groups was not significant ($p>0.05$) when the age, height, weight, BMI (Body Mass Index) and duration of operation of patients were compared (Table 1).

There was a significant difference between the two groups in terms of STAI-I anxiety score before premedication and STAI-I anxiety score after drug administration ($p<0.05$). In the pregabalin group, STAI-I anxiety scores assessed before the drug administration were higher than the control group, whereas STAI-I anxiety scores after the drug ad-

ministration were lower in the Pregabalin group. The control group had no significant difference ($p>0.05$) in itself, when the STAI-I anxiety score before the drug administration and the STAI-I anxiety score after the drug administration were compared, whereas the difference in the Pregabalin group was significant ($p<0.05$) (Table 2).

When the groups were compared in terms of HR values measured at different times, difference between groups at the postoperative 6th hour was found to be significant ($p<0.05$), while group differences were not significant at other times ($p>0.05$) (Figure 1). The difference in HR at the 6th hour was not considered clinically significant.

TABLE 1: Demographic data.

	Pregabaline Group (n=34)	Control Group (n=34)	Result
Age (year)	49.02±6.00	49.29±7.20	t=0.16 p=0.870
Height (cm.)	161.20±4.19	161.41±3.93	t=0.20 p=0.835
Weight (kg.)	77.64±12.85	77.02±11.87	t=0.21 p=0.838
BMI (kg/m^2)	29.64±4.71	29.67±5.06	t=0.02 p=0.980
Duration of Operation (min.)	99.26±21.21	102.35±18.63	t=0.38 p=0.536

TABLE 2: Comparison of STAI-I Anxiety scores.

	STAI-I Anxiety Score		
	Pregabaline Group (n=34)	Control Group (n=34)	Result
Before Drug	53.85±11.44*,#	45.41±8.99	t=3.38 p=0.001
After Drug	40.50±7.39*	47.41±10.20	t=3.19 p=0.002
Result	p=0.000	p=0.195	

*p<0.05; When it is compared with control group

#p<0.05; When it is compared with STAI-I anxiety score after drug administration

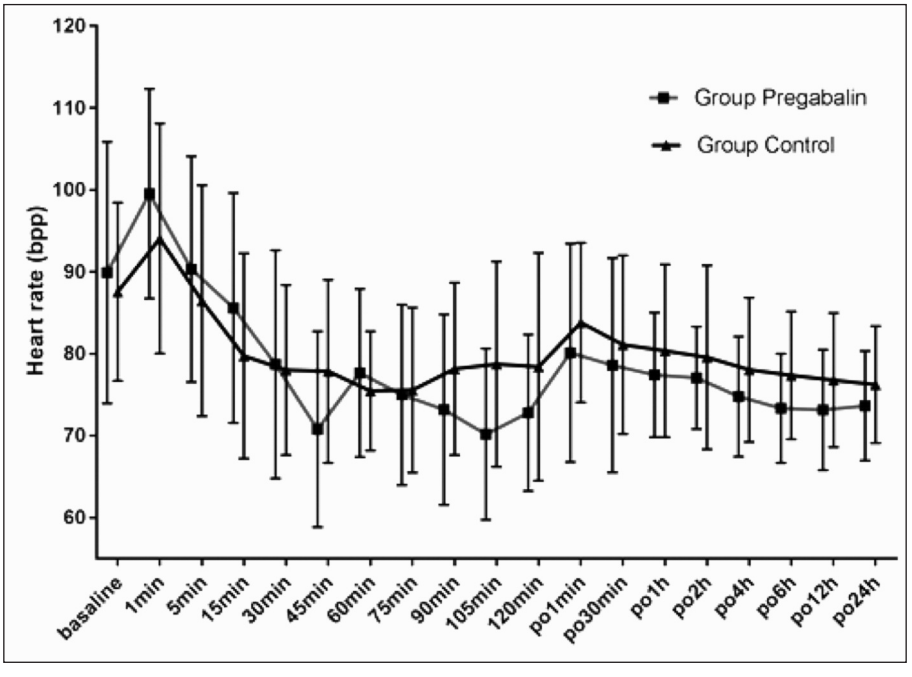

FIGURE 1: Comparison of Changes in Heart Rate (HR).

When the two groups were compared in terms of SpO_2 values measured at different times, the difference between the groups was not significant ($p>0.05$).

When the two groups were compared in terms of MAP measured at different times, there was a significant difference between the groups in terms of 30th, 45th, 75th and postoperative 1st minute MAP ($p<0.05$), while the difference at other times were insignificant ($p>0.05$). 30th, 45th, 75th and postoperative 1st minute MAP were found to be higher in the control group compared to the Pregabalin group (Figure 2).

When the groups were compared in terms of recovery and the time of first analgesic treatment, the difference between the groups was not significant ($p>0.05$).

When both groups were compared in terms of VAS values at different times in the postoperative period, the difference between the groups was significant ($p<0.05$). Postoperative VAS values at 1, 30 min and 1, 2, 4, 6, 12, 24 hours were significantly lower in the Pregabalin group compared to the control group (Figure 3). The relationship between VAS values and MAP at different times in the postoperative period was investigated in both groups; the correlation coefficients were statistically insignificant ($p>0.05$).

When both groups were compared in terms of morphine consumption from PCA in the postoperative term, the differences between the groups were not significant at 1 and 30 min ($p>0.05$), while the difference between the groups was significant at other times ($p<0.05$). Morphine consumption at postoperative 1st, 2nd, 4th, 6th, 12th and 24th hours was found to be higher in the Control group (Table 3).

When the two groups were compared with regard to morphine demand in the postoperative period, the difference between the groups at the 1st minute was not significant ($p>0.05$), while the difference between the groups was significant at other times ($p<0.05$). It was observed that morphine demand at postoperative 30 min and at 1st, 2nd, 4th, 6th, 12th and 24th hours was more in the Control group.

When the two groups were compared in terms of successful morphine demand in the postopera-

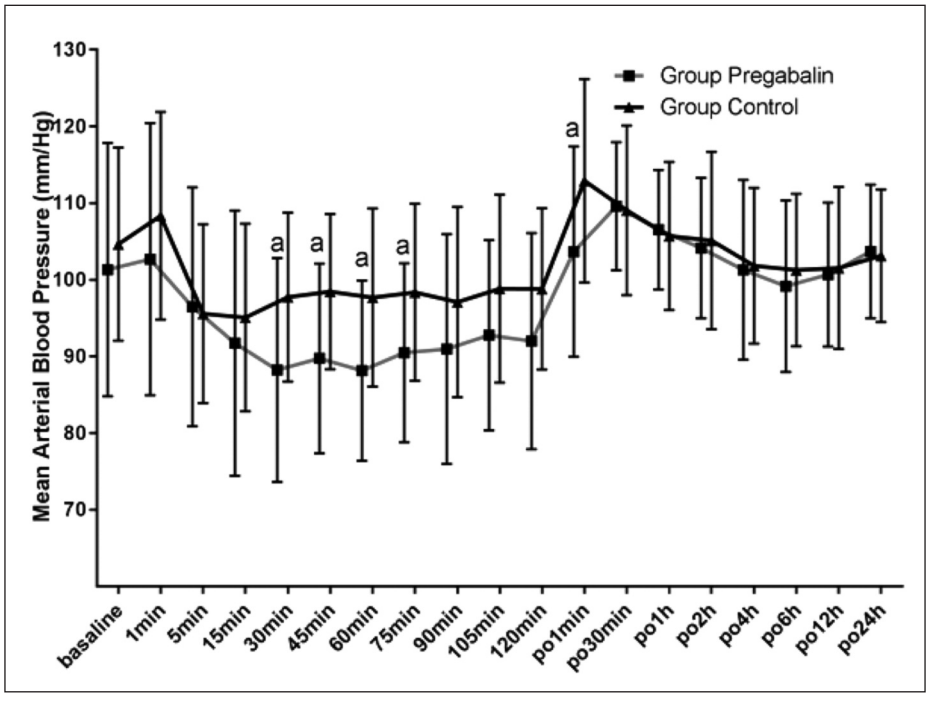

FIGURE 2: Comparison of Changes in Mean Arterial Blood Pressure (MABP). [a]$p<0.05$; When pregabalin group is compared with control group.

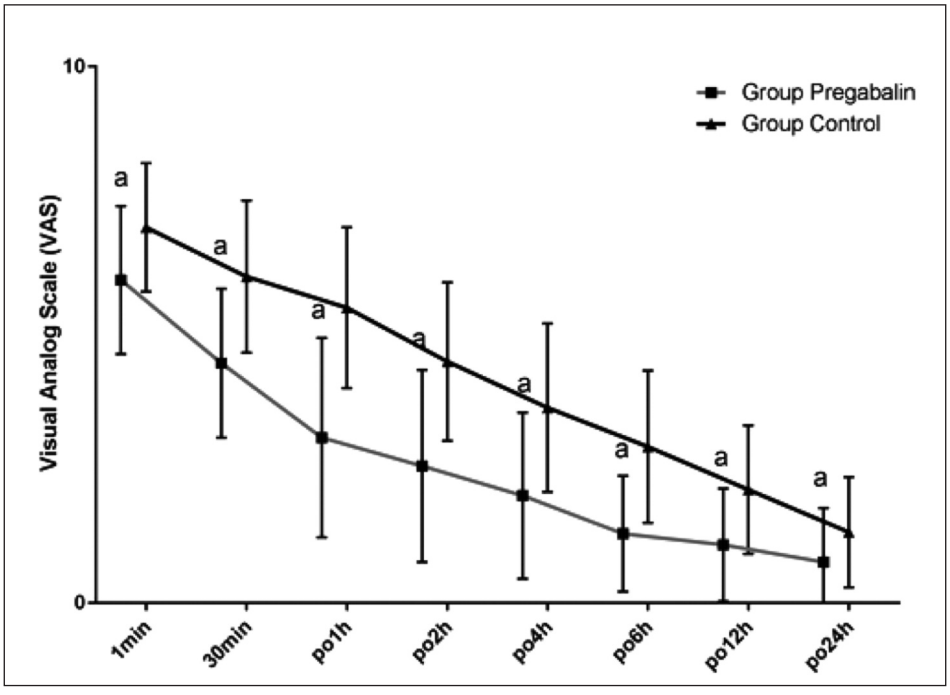

FIGURE 3: Comparison of Postoperative Visual Analog Scale (VAS) Values[a]p<0.05; When pregabalin group is compared with control group.

TABLE 3: Comparison of postoperative morphine consumption.

	Morphine Consumption		
	Pregabaline Group (n=34)	**Control Group (n=34)**	**Result**
1st min.	1.00±0.00	1.08±0.51	t=1.00 p=0.321
30th min.	2.97±1.11	3.32±1.14	t=1.28 p=0.203
1st hour	5.44±1.86*	6.50±2.04	t=2.23 p=0.029
2nd hour	8.05±3.12*	10.67±3.30	t=3.35 p=0.001
4th hour	10.41±4.59*	15.35±6.30	t=3.69 p=0.001
6th hour	12.32±5.65*	18.67±7.53	t=3.93 p=0.001
12th hour	14.35±5.75*	21.97±8.79	t=4.22 p=0.001
24th hour	17.08±6.73*	25.35±10.54	t=3.85 p=0.001

*p<0.05; When it is compared with control group.

tive stage, the difference between the groups was not significant at 1 and 30 min (p>0.05), while the difference between the groups was significant at other times (p<0.05). It was also found that successful morphine demand at the postoperative 1st, 2nd, 4th, 6th, 12th and 24th hours was higher in the Control group.

When the pregabalin group and the control group were compared in terms of additional analgesic use, the difference between the groups was significant (p<0.05). It was seen that the control group had higher additional analgesic requirement in the postoperative period (Table 4).

When patients in both groups were examined for adverse effects, side effects were seen in 39% of patients in the study: 29% being in the control group and 10% being in the pregabalin group. The remaining 61% of patients showed no signs of adverse effects. The prevalence rate of side effects in the pregabalin group was 21%, while it was 59% in the control group. No side effects were observed in 79.4% of the patients in the pregabalin group and 41.2% of the patients in the control group. Nausea was observed in 17.6% of the patients in the pregabalin group and in 35.3% of the patients in the

TABLE 4: Comparison of postoperative additional analgesia demand.

	Additional Analgesia Demand	
	Pregabalin Group (n=34)	Control Group (n=34)
	Number -%	Number -%
No	27-%79.4	15-%44.1
Yes	7-%20.6	19-%55.9
Total	**34 - %100**	**34 - %100**

X^2=8.9 p=0.003 p<0.05 significant

control group. 2.9% of the Pregabalin group had dizziness, compared to 5.9% in the Control group. In the pregabalin group, headache/dizziness and nausea were not seen at the same time, but these symptoms were seen together in 2.9% of patients in the control group. While the patients in the pregabalin group had no headache and dizziness together, this rate was 8.8% in the Control group. In addition, other side effects such as hypotension and desaturation were not observed in the patients participating in the study. As a result, more side effects were seen in the control group compared to the Pregabalin group.

DISCUSSION

Pregabalin is an anticonvulsant agent that has been increasingly prevalent in pain treatment, especially with its anxiolytic efficacy in the recent period. There is a limited number of studies showing the efficacy of pregabalin on preoperative anxiety.[14] In addition, the analgesic activity of pregabalin is known, but the results of postoperative analgesic activity is controversial.[15-17] We investigated the efficacy of pregabalin on preoperative anxiety and postoperative pain in patients that have abdominal hysterectomy. The main results of our study showed that pregabalin premedication reduced preoperative anxiety scores, mean arterial pressure, pain score, morphine consumption and additional analgesic requirement. In addition, pregabalin use reduced opioid-related side effects such as nausea, dizziness, and headache. The incidence of side effects was 29% in the control group and 10% in the Pregabalin group.

Premedication is an important step to relieve both the anxiety and pain of the patient. Despite the availability of a large number of new drugs, techniques, and studies, it is reported that 80% of postoperative patients have moderate to high severity of pain, indicating postoperative pain management is still not effective.[18] Therefore, anesthesiologists have a great duty to evaluate and apply appropriate methods and drug combinations to reduce preoperative anxiety and postoperative pain.

In a prospective study by Güz et al. 92 patients who had undergone lomber disc hernia operation were evaluated by STAI scale and Visual Analog Scale (VAS) to research preoperative anxiety and existing anxiety related variables by recording pain, anxiety and demographic information in preoperative 1-3 days, and observed that STAI anxiety scores and VAS scores were higher in women.[19] In their systematic review of postoperative pain prediction, Ip et al. stated that preoperative pain, anxiety, age and type of surgery are important for postoperative pain, and that age, type of surgery and psychological distress are important for analgesic consumption.[20] Our study was conducted in cases of abdominal hysterectomy performed on female patients. Thus, it was aimed to be objective in evaluating pain and anxiety levels which are dependent on both gender and operation region.

The STAI-I anxiety scale used for preoperative anxiety measurement is indicated as the gold standard in the literature, so STAI-I scale was used to evaluate the preoperative anxiety of the patients in our study. Gonano and colleagues assessed the anxiolytic effect using pregabalin 300 mg preoperatively in 40 patients who underwent a randomized, placebo-controlled study and 40 patients who had minor orthopedic surgery and pregabalin reduced preoperative anxiety.[14] Gonano et al. assessed the anxiolytic effect using pregabalin 300 mg preoperatively in 40 patients who underwent minor orthopedic surgery in their randomized, placebo-controlled study and found that pregabalin reduced preoperative anxiety.[14] In our study, pregabalin 150 mg premedication given 12 hours before the operation reduced preoperative anxiety scores compared to placebo.

The main use of drugs in premedication is their anxiolytic effects in the preoperative period. One of the reasons for the use of pregabalin in premedication is the anxiolytic activity. Oral bioavailability of pregabalin is over 90%. It peaks at the plasma level within 0.7 to 1.3 hours after usage.[21] In the light of this information, it was thought to be enough for pregabalin to start being effective when used one hour before surgery.

To evaluate the effect of pregabalin on hemodynamic parameters, Salman et al. observed that 150 mg of pregabalin premedication attenuated the hemodynamic response associated with laryngoscopy and intubation in a prospective, placebo-controlled study including 60 patients who underwent elective surgery for 1-3 hours.[22] Similarly, in their prospective placebo-controlled study, Eren et al. found that mean arterial pressure and heart rate values during and after intubation were lower in the Pregabalin group and concluded that the use of preoperative 150 mg pregabalin suppressed laryngoscopy and intubation related tachycardia and hypertension.[23] In our study, mean arterial pressure, heart rate, and hemodynamic responses to anesthesia induction and subsequent laryngoscopy and tracheal intubation were also assessed. Oral use of pregabalin 150 mg premedication did not alter hemodynamic response to laryngoscopy and intubation.

In response to these studies on the suppressive effect of preoperative pregabalin on hemodynamic parameters, Upendra et al. concluded that hemodynamic parameters did not change after preoperative pregabalin 150 mg in their study including 80 patients who underwent cholecystectom.[24] Again, as a result of a prospective, placebo-controlled study including 60 patients with axillary block, Pürcü et al. reached the conclusion that pregabalin did not affect hemodynamic parameters after a single dose of preoperative pregabalin 150 mg.[25]

In their placebo-controlled studies on the effects of pregabalin 75 mg and 150 mg premedication on hemodynamic responses, Rastogi et al. have concluded that the premedication did not result in a clinically significant respiratory depression and reduction in oxygen saturation.[26] In our study, no changes in favor of desaturation in intraoperative peripheral oxygen saturation values were observed in both groups.

Duration of surgery and quality of the postoperative period are among the factors affecting the severity of postoperative pain.[27] Akarsu et al. reported delayed recovery times with pregabalin, as a result of their study comparing 300 mg pregabalin with placebo-diclofenac combination in 60 patients.[28] In their study where the effects of different doses of pregabalin premedication on hemodynamic responses were evaluated, Rastogi et al. found that there was no difference between groups in terms of recovery.[26] In our study, the distribution of the groups was similar in terms of operation time, recovery time and first analgesic initiation time. Regarding the duration of recovery, preoperative pregabalin use of 150 mg 12 hours and 1 hour priorly did not cause late recovery. In our study, it was thought that the reason for non-prolonged recovery time was due to the use of 150 mg pregabalin.

To assess the effects of pregabalin on postoperative pain and opioid need, Ho et al. have shown that gabapentine and pregabalin reduced opioid need and opioid-related side effects by increasing analgesic activity in their systemic review of 16 randomized controlled trials involving the use of gabapentine or pregabalin in postoperative pain.[15]

In several studies evaluating postoperative pain and analgesic consumption by administering pregabalin 150 mg premedication in different types of surgery under general anesthesia, different researchers have observed that reported that pregabalin reduced postoperative pain and analgesic consumption.[24] In addition to general anesthesia, effects of pregabalin premedication on postoperative pain and opioid consumption has been studied in regional anesthesia applications and it was concluded that pregabalin reduced postoperative pain and analgesic consumption.[25] In their study including 40 patients who underwent prospective placebo-controlled elective thoracotomy, Tunç et al. assessed pain scores and epidural opioid use by

administering thoracic epidural patient-controlled analgesia to all patients after the use of preoperative 150 mg pregabalin and reached the conclusion that pain scores and epidural opioid consumption decreased.[29] Yücel et al. have concluded that pregabalin at a total dose of 600 mg, administered before operation and at 12 hours postoperatively after abdominal hysterectomy, reduced morphine consumption and pain intensity and increased patient satisfaction.[30] Eman et al. have concluded that a 150 mg pregabalin administered preoperatively is an efficient and safe agent for preemptive analgesia. Premedication with pregabalin reduces postoperative pain scores and total analgesic consumption without increasing sedation or other side effects in the postoperative period.[31] Canihuante et al. concluded the use of perioperative pregabalin in major surgeries probably does not produce a clinically important decrease in acute postoperative pain. Although it could decrease nausea, postoperative vomiting and opioid requirements, it also produces an increase in sedation.[32]

In response to these studies, in their placebo-controlled study including 40 patients who underwent minor orthopedic surgery, where postoperative pain was evaluated after preoperative 300 mg of pregabalin application, Gonano et al. observed that there was no difference between the groups in terms of pain scores but they observed a decrease in postoperative analgesic requirement by half and reported a decrease in analgesic consumption in the pregabalin group.[14] As a result of our study, using pregabalin 150 mg preoperatively twice, both 12 hours and 1 hour priorly reduced postoperative pain, morphine consumption and additional analgesic use, supporting studies reporting increased postoperative analgesic activity and decreased opioid consumption with the use of pregabalin in premedication.

As a result of their study, which included patients undergoing minor orthopedic surgery who were given preoperative 300 mg of pregabalin, Gonano et al. concluded that pregabalin did not have any side effects that resulted in dizziness or in long-term stay in postoperative care unit.[14] Alimian et al. observed fewer side effects in the Pregabalin group in their placebo-compared study with 300 mg pregabalin in patients undergoing laparoscopic gastric bypass surgery.[33] Many studies assessing preoperative 150 mg pregabalin efficacy on postoperative pain after operations performed with different anesthesia and surgical methods have also shown fewer side effects due to reduced opioid consumption.[17,24]

As a result of all this information; we reached the conclusion that the preoperative use of Pregabalin 150 mg 12 hours and 1 hour prior to surgery reduced preoperative anxiety, provided postoperative analgesia, reduced analgesic consumption and associated side effects, thus proving to be superior to placebo. However, in order for pregabalin to be used as routine premedication, larger sample groups and studies with different doses are required.

Source of Finance

During this study, no financial or spiritual support was received neither from any pharmaceutical company that has a direct connection with the research subject, nor from a company that provides or produces medical instruments and materials which may negatively affect the evaluation process of this study.

Conflict of Interest

No conflicts of interest between the authors and / or family members of the scientific and medical committee members or members of the potential conflicts of interest, counseling, expertise, working conditions, share holding and similar situations in any firm.

Authorship Contributions

Idea/Concept: *Selma Bora Polat, İclal Özdemir Kol, Onur Avcı;* ***Design:*** *Ahmet Cemil İşbir, Kenan Kaygusuz, Sinan Gürsoy;* ***Control/Supervision:*** *Selma Bora Polat, İclal Özdemir Kol;* ***Data Collection and/or Processing:*** *Onur Avcı, Ahmet Cemil İşbir;* ***Analysis and/or Interpretation:*** *İclal Özdemir Kol, Kenan Kaygusuz, Sinan Gürsoy;* ***Literature Review:*** *Selma Bora Polat, İclal Özdemir Kol, Onur Avcı;* ***Writing the Article:*** *Selma Bora Polat, İclal Özdemir Kol, Onur Avcı;* ***Critical Review:*** *hmet Cemil İşbir, Kenan Kaygusuz, Sinan Gürsoy;* ***References and Fundings:*** *Selma Bora Polat, Onur Avcı.*

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