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Does Pregabalin Affect Renal Functions and Plasma Electrolytes?

Pregabalin Böbrek Fonksiyonlarını ve Plazma Elektrolitlerini Etkiler mi?

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ÖZET

Amaç: Pregabalin, nöropatik ağrı tedavisinde, parsiyel başlangıçlı epilepsisi olan yetişkinlerde antiepileptik olarak kullanılmaktadır. Pregabalinin yarı ömrünün yaşla ilişkili olarak uzadığı, bu durumun yaşla birlikte böbrek fonksiyonlarındaki zayıflık ile ilgili olabileceği düşünülmektedir. Bu çalışmada pregabalinin neden olabileceği renal toksisitenin araştırılması amaçlanmıştır.
Gereç ve Yöntemler: 2019-2020 yılları arasında Nöroloji Anabilim Dalı'nda izlenen 100 hasta çalışmaya dahil edildi. Pregabalin kullanan erişkin hasta grubunun retrospektif olarak hastane dosyalarının taranması planlandı. Hastaların periferik kan üre, ürik asit, kreatinin, serum elektrolit düzeyleri belirlendi ve böbrek fonksiyonlarındaki olası değişiklikler için altı ayda bir, iki kez glomerüler filtrasyon oranı değerlendirildi.
Bulgular: Altı aylık dilimde iki kez ölçüm yapılan hastalarda aritmetik ortalama değerleri ve değişimleri incelendi. Pregabalin kullanımının, renal fonksiyon belirteçleri olan üre ve ürik asit değerleri üzerine etkisi istatistiksel olarak anlamlı bulundu ($p<0.05$). GFR, kreatinin, Na^{+}, Cl^{-}, K^{+}, Ca^{+2}, Mg^{+2} ve P^{+3} parametreleri üzerinde ise istatistiksel olarak anlamlı bir etkisi görülmedi ($p>0.05$).
Sonuç: Pregabalinin GFR, kreatinin ve kan elektrolitlerini anlamlı düzeyde değiştirecek bir etkisinin olmadığı gözlenmedi. Üre ve ürik asit değerlerinde oluşan anlamlı farkın verinin normal dağılım göstermemesinden kaynaklandığı düşünüldü. Bu çalışma pregabalinin diğer organlar üzerindeki etkilerinin retrospektif olarak değerlendirilerek araştırılması için ışık tutacak niteliktedir. Böylece disiplinler arası yaklaşımlarla birlikte ilaç güvenilirliğinin artırılmasına katkı sağlanabilir.

Anahtar Kelimeler: Pregabalin, kreatinin, renal toksisite, böbrek fonksiyonu

ABSTRACT

Aim: It is known that the half-life of pregabalin increases with age. This may be related to the decline in kidney function with age. In this study, it was aimed to investigate the neurotoxicity and renal toxicity that pregabalin may cause.
Materials and Methods: 100 patients followed up in the Department of Neurology between 2019-2020 were included for the study.It was planned to scan the hospital files of the adult patient group using pregabalin. The data obtained as a result of possible changes in serum electrolyte levels and kidney functions of patients with pregabalin indication were evaluated. Peripheral blood urea, uric acid, creatinine, serum electrolyte levels of the patients were determined and glomerular filtration rate (GFR) was analyzed twice, in six months for possible changes in kidney functions.
Results: Arithmetic mean values and changes were examined in patients who were measured twice in a six-month period. The effect of pregabalin use on urea and uric acid values, which are markers of renal function, was found to be statistically significant ($p<0.05$). There was no statistically significant effect on GFR, creatinine, Na^{+}, Cl^{-}, K^{+}, Ca^{+2}, Mg^{+2} and P^{+3} parameters ($p>0.05$).
Conclusion: This study may be useful to investigate the effects of pregabalin on other organs. The data obtained may contribute to the provision of information that may be useful to drug research and development institutions and to increase drug safety.

Key words: Pregabalin, creatinine, renal toxicity, renal function

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INTRODUCTION

Pregabalin was discovered by Richard B. Silverman in the 1980s. It is a compound synthesized as a lipophilic analogue by adding an aliphatic side chain to the γ-aminobutyric acid (GABA) structure so that it can cross the blood-brain barrier (1).

Pregabalin is from the gabapentinoid class and is pharmacodynamically similar to gabapentin. It is designed as a lipophilic GABA analogue to replace GABA at position 3 to facilitate diffusion across blood-brain barrier. Pregabalin exists as one of the isomeric forms of 3-isobutyl-GABA. It is the pharmacologically active enantiomer. Although pregabalin is structurally related to GABA, it is inactive at GABA receptors. It appears to physiologically mimic GABA. Also, pregabalin shows no affinity for the receptor sites. Pregabalin does not alter the responses associated with the action of many common drugs used to treat seizure and pain. Like gabapentin, the pharmacological effects of pregabalin are thought to be due to its ability to act as a ligand at alpha-2-delta binding site associated with calcium channels in central nervous system. In many animal experiments, it was observed that pregabalin exhibited strong anticonvulsant, anxiolytic and analgesic activity (2).

Pregabalin is used in treatment of pain caused by nerve damage caused by various pathologies. Pregabalin is also an antiepileptic. Although it is one of the drugs used in the treatment of epilepsy, due to the new generation antiepileptic drugs produced in recent years, it is preferred more in neuropathic pain treatment than antiepileptic treatment today. The type of pain that responds best to pregabalin treatment is neuropathic pain caused by nerve damage. These pains are regional pains that previously occurred due to shingles; includes post-herpetic neuralgia, trigeminal neuralgia, diabetes-related painful neuropathy, and fibromyalgia. According to studies conducted in the literature, while most of the patients with this type of pain benefited moderately from the treatment, it was observed that the symptoms were almost completely regressed in a small group of patients (3). Pregabalin is primarily approved for treatment of peripheral neuropathic pain and as adjunctive therapy for partial seizures in epilepsy patients. Later, it was approved by the Food and Drug Administration (FDA) and started to be used for treatment of neuropathic pain associated with post-herpetic neuralgia and diabetic peripheral neuropathy (4). The pregabalin binds strongly and selectively to alpha-2-delta subunit of stimulated voltage-gated calcium channels. Binding of pregabalin to calcium channels reduces the flow of calcium in the boundary terminals by changing the three- dimensional comfort of the channels. Pregabalin modulates the release of excitatory neurotransmitters in overexcited neurons, allowing them to return to the normal physiological state. In addition to the neuropathic pain treatment of the pregabalin with this action mechanism, anxiolytic, analgesic and anticonvulsant effects were thought to have occurred (5). In case of peripheral neuropathic pain, in addition to treatment for adults with parsiyel onset epilepsy, it is also used in the case of central neuropathic pain and widespread anxiety disorder. Although it is a relatively new drug, it is common to prescribe. It is in the group of antiepileptics, in pharmacotherapeutic. Daily dose received through mouth at specified indications is 150-600 mg in adults. The absorption is mainly performed in the proximal colon and the dose is dependent. The blood-brain barrier and cell membrane are passed by the special L-amino acid transport system. It reaches maximum concentration in about an hour and a half. The average half-life is between 2.5 and 7 hours. It has been reported that 98% of pregabalin is excreted unchanged, 0.9% as an N-methylated derivative in the urine, and less than 0.1% in the faeces in humans (6). Pregabalin is rapidly-extensively absorbed after oral administration in the fasting state, reaching maximum plasma concentration approximately 1 hour after single/multiple doses. After repeated applications, it reaches a stable concentration in plasma within 24-48 hours (7). Pregabalin does not enter hepatic metabolism and does not connect to plasma proteins. It is excreted renally and almost all of the absorbed dose is excreted unchanged in urine. Pregabalin elimination is proportional to creatinine clearance, so pregabalin clearance decreases for patients with kidney dysfunction. In addition, no pharmacokinetic drug-drug interaction has been defined in the drug interaction studies (8). Many therapeutic agents can produce nephrotoxic effects, especially when their half-life is prolonged in serum or when their blood level is elevated due to reduced renal excretion. The nephrotoxicity that occurs as the GFR decreases continues to increase. In this process, even though creatinine levels are initially within the normal range, the current creatinine concentrations can pose serious problems for elderly patients (9). Researchers stated that since pregabalin is excreted from the kidneys with almost no metabolism, dose adjustment should be made when using it in patients with renal failure or low creatinine clearance. They argued that after hemodialysis, an additional dose of 25-100 mg should be administered because approximately 50-60% of the drug is removed from the blood circulation (10).

Early detection of renal failure is very important as it facilitates the use of methods that can prevent and delay the progression of the disease and reduce the risk of adverse outcomes (11). GFR is considered the best indicator of renal function in healthy or diseased individuals (12). In this study, it was planned to scan the hospital files and patient epicrisis of the adult patient group using pregabalin. It was aimed to evaluate the data obtained as a result of possible changes in serum electrolyte levels and renal functions (GFR) of patients

with pregabalin indication.

MATERIALS AND METHODS

Approval for the study was granted by the Ethics Committee for Pharmaceutical and Non-Medical Device Research, under decision number 2019/1747, and all procedures in the study were conducted in accordance with the ethics committee protocol.

In the study, the data of 100 patients followed in the Neurology Department between 2019-2020 were analyzed retrospectively. Patients who applied to the clinic due to long-term pain caused by damage to peripheral nerves such as neuropathic pain, fibromyalgia, postherpetic pain and trigeminal neuralgia, which are known as diffuse pain mainly affecting the muscles and the areas where the muscles attach to the bone, were evaluated. Various doses of pregabalin were prescribed to these patients. The criteria for inclusion in the study were to have an indication to use pregabalin and to be at an adult age. Exclusion criteria from the study were defined as having chronic renal failure, having a serious condition that may affect kidney functions, and not being at an adult age. Past hospital epicrisis and patient cards of these patients with pregabalin indications were scanned. The mean values of serum electrolytes, urea, uric acid, creatinine and GFR measured twice in a six-month period, on the first day of pregabalin use and at the 6th month after treatment, were compared. GFR, which is a marker of renal function values; was measured twice a month to detect possible changes in kidney functions. Arithmetic mean GFR values and changes in patients measured twice within a six-month period were examined. The average of each parameter was evaluated quantitatively, taking into account the error rate and standard deviation.

In this study, the SGLT-2 method was used for drug use that may affect kidney function tests. In this study, epicrisis and patient cards of adult patients using pregabalin were scanned and questioned and included in the research. During the study, patients did not use any medication that would affect electrolyte levels. In addition, conditions such as diet were not observed and the patients were not standardized. As a result of the data obtained from adult patients (30-70 age group) during the study; It was observed that the patients did not have any additional disease that could affect their kidney functions.

Statistical analyzes

Serum electrolyte, urea, uric acid, creatinine and GFR values measured twice in a six-month period, on the first day of pregabalin use and in the 6th month after treatment. These values were first evaluated quantitatively by comparing their average values. The average of each parameter was evaluated quantitatively, taking into account the error rate and standard deviation. Statistical analyzes were performed for each parameter by selecting analyzes appropriate to the distribution of the data in the SPSS 21 program. In addition, comparative analyzes were made.

RESULTS

The average changes in serum GFR, urea, uric acid, creatinine values and serum electrolyte levels, determined from peripheral blood of the cases with the use of pregabalin, are shown in graphs.

GFR Values

The GFR values and changes which have been measured twice in a six-month period have been examined. The average GFR value was 99.01 mL/min/1.73 m^2 in the first measurement, and this value was averaged 97.59 mL/min/1.73 m^2 in the sixth month. The minimum values between patients during the six-month period were measured between 41,00 mL/min/1.73 m^2 and 47.00 mL/min/1.73 m^2 respectively. The maximum values for GFR over the six-month period were measured 187.00 mL/min/1.73 m^2 and 134.00 mL/min/ respectively. The standard error rate was calculated separately for both measurements and was observed very low (Figure 1, Table 1).

Urea Values

In patients the urea values and changes which have been measured twice in a six-month period have been examined. The average urea value was 31.64 mg/dL in the first measurement, and this value was averaged to 34.00 mg/dL in the sixth month. In the six-month period, the minimum values were 14.00 mg/dL - 14.00 mg/dL, and the maximum urea values were 67.80 mg/dL - 60.6 mg/dL respectively in the first and sixth month. The standard error rate was also

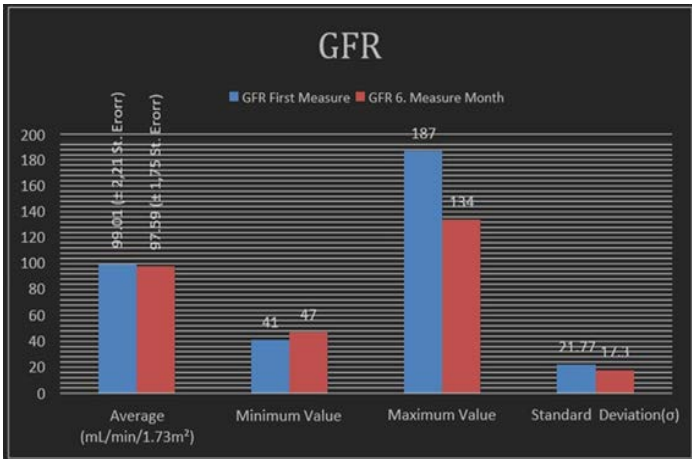

Figure 1. GFR changes based on two measurements in the six month period

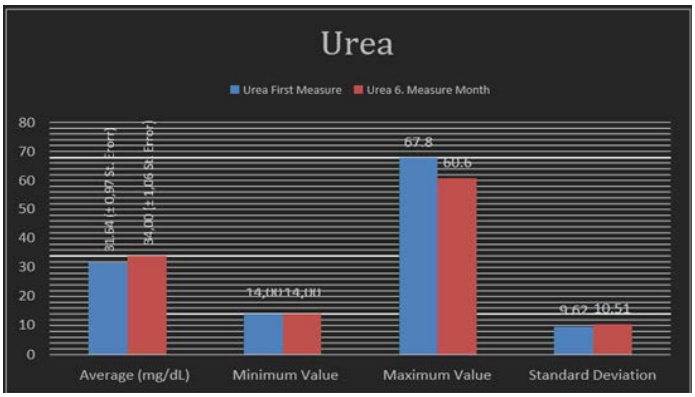

Figure 2. Urging changes based on two measurements in the six month period

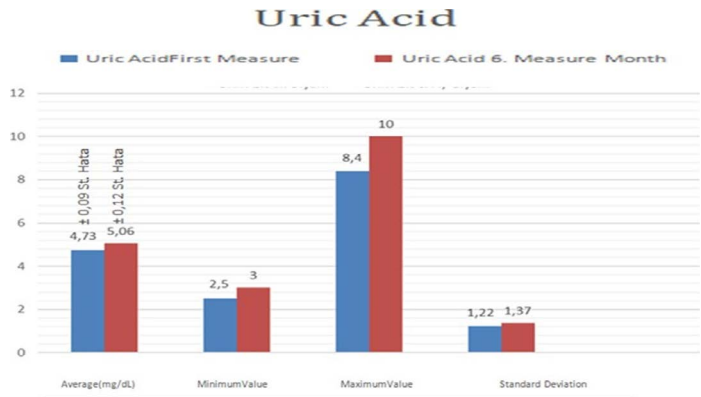

Figure 3. Uric acid changes based on two measurements in the six month period

calculated and observed very low for measurements at both different times (Figure 2, Table 1).

Uric Acid Values

The uric acid values and variations which have been measured twice in the six-month period were examined. The average uric acid value was 4.73 mg/dL in the first measurement taken when patients started using pregabalin, and this value was averaged to 5.06 mg/dL in the sixth month. The minimum values measured in the six-month period were 2.50 mg/dL - 3.00 mg/dL respectively and the maximum values measured for uric acid were 8.40 mg/dL - 10.00 mg/dL respectively. The standard error rate was also calculated and observed very low for measurements at both different times (Figure 3, Table 1).

Creatinine Values

The creatinine values and changes which were measured twice and averaged, were analyzed. The average creatinine value was 0.75 mg/dL at the first measurement when patients started using pregabalin, and this value was averaged to 0.76 mg/dL by the sixth month. During the six-month period, the minimum values between patients were 0.44 mg/dL - 0.43 mg/dL respectively, and the maximum creatinine values were 1.69 mg/dL - 1.50 mg/dL respectively. The standard error rate was calculated and observed very low for measurements at both different times (Figure 4, Table 1).

Na^+ and Cl^- Values

The mean values of Na^+ and Cl^- measured twice in a six-month period have been analyzed. The average Na^+ and Cl^- values were calculated at 139.71 mEq/L and 103.08 mEq/L in the first measurement, when patients started using pregabalin, for average Na^+ and Cl^- in the sixth month, respectively at 140.08 mEq/L - 102.72 mEq/L. In the six-month period, the minimum values between patients were 126.00 mEq/L - 95.00 mEq/L respectively for Na^+ and Cl^- in the first measurement, and the first maximum values were 148.00 mEq/L - 112.00 mEq/L respectively for the two electrolytes. For the sixth month measurement, the minimum values for Na+ and Cl– were 132.00 mEq/L - 97.00 mEq/L respectively, while the maximum values were 148.00 mEq/L - 108.00 mEq/L respectively. The standard error rate was calculated and

Table 1. Standard deviation and P values

	Standard Deviation 1th Month	Standard Deviation 6th Month	P values	p<0.05	p>0.05
GFR	21.77	17.30	0.322	-	+
Urea	9.62	10.51	0.006	+	-
Uric acid	1.22	1.37	0.002	+	-
Creatinine	0.22	0.20	0.435	-	+
Na^+	2.82	2.70	0.258	-	+
Cl^-	3.08	2.64	0.311	-	+
K^+	0.42	0.37	0.866	-	+
Ca^{+2}	0.47	0.58	0.989	-	+
Mg^{+2}	0.23	0.33	0.627	-	+
P^{+3}	0.66	0.62	0.099	-	+

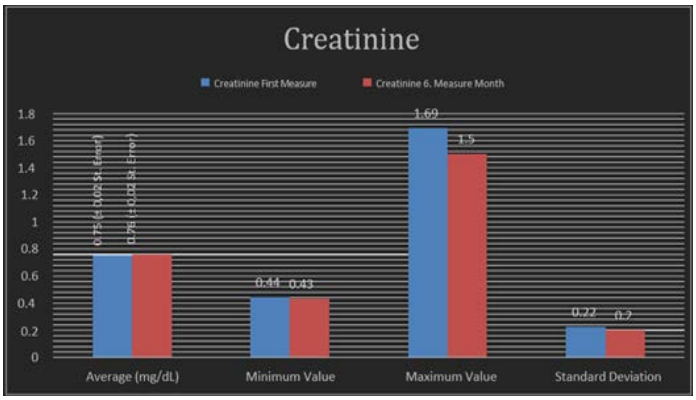

Figure 4. Creatinine changes based on two measurements in six months period

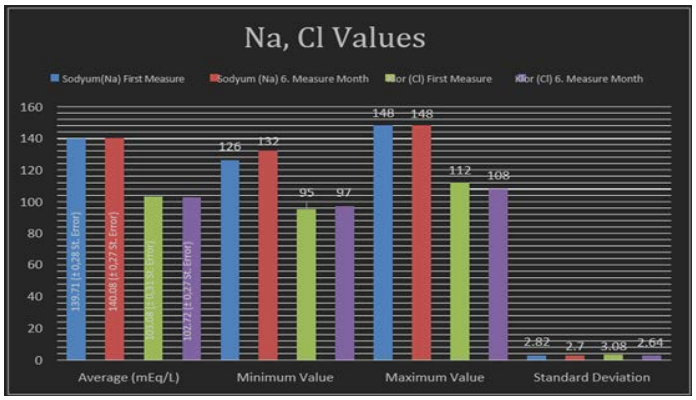

Figure 5. Na^{+} and Cl^{-} variations based on two measurements in six months period

observed very low for measurements at both different times (Figure 5, Table 1).

K^{+} and Ca^{+2} Values

The mean values of K^{+} and Ca^{+2} measured twice in a six-month period have been analyzed. The average K+ and Ca+2 values were 4.45 mEq/L - 9.13 mg/dL on average in the first measurement taken with patients using pregabalin, this value was not changed for K+ in the sixth month and was as 9.35 mg/dL for Ca^{+2}. In the six-month period, the minimum values between patients were 2.70 mEq/L - 8.00 mg/DL respectively for K^{+} and Ca^{+2} for the first measurement, and the first maximum values for the two electrolytes were 5.80 mEq/L - 10.30 mg/dL respectively. In the sixth month measurement, the minimum values for K^{+} and Ca^{+2} were 3.20 mEq/L - 7.10 mg/dL respectively, while the maximum values were 5.70 mEq/L - 12.80 mg/dL respectively. The standard error rate was also calculated and observed very low for measurements at both different times (Figure 6, Table 1).

Mg^{+2} and P^{+3} Values

The values, the arithmetic average and the concentration changes of Mg^{+2} and P^{+3} which were measured twice in the six-month period have been examined. Average Mg^{+2} and P^{+3} values were average 2.09 mg/dL - 3.38 mg/dL on the first measurement taken with patients using pregabalin, and this value was calculated at 2.1 mg/dL - 3.26 mg/dL respectively in the sixth month. In the six-month period, the minimum values between patients were 1.36 mg/dL - 1.10 mg/dL respectively for Mg^{+2} and P^{+3} for the first measurement, and the first maximum values for the two electrolytes were 3.9 mg/dL - 5.30 mg/dL respectively. In the sixth month measurement, the minimum values for Mg^{+2} and P^{+3} were 1.20 mg/dL - 2.20 mg/dL respectively, and the maximum values were 3.60 mg/dL - 5.80 mg/dL respectively. The standard error rate was also calculated and observed very low for measurements at both

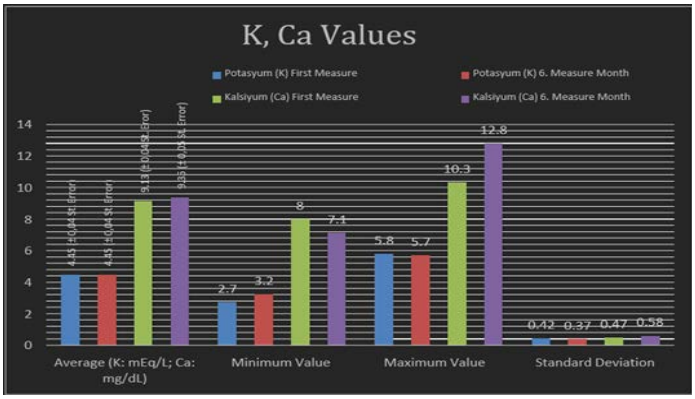

Figure 6. K^{+} and Ca^{+2} variations based on two measurements in six months period

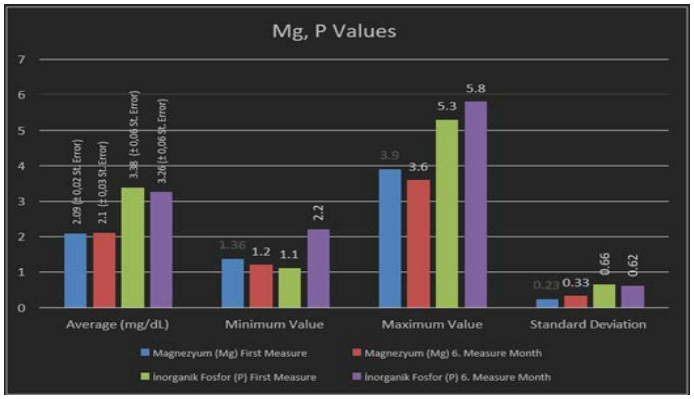

Figure 7. Mg^{+2} and P^{+3} variations based on two measurements in the six months period

different times (Figure 7, Table 1).

DISCUSSION

The general reference range of the GFR is 90 mL/min/1.73 m^2 for men and women starting from the age range of 20. In the age of 80, this average value is 68 mL/min/1.73 m^2 for men and 49 mL/min/1.73m^2 for women. The average normal GFR value is typically 60- 120 mL/min/1.73 m^2 (13). Considering the average age of patients in the study, it was not observed that the use of pregabalin had both quantitative and statistically significant effects on GFR.

Urea is mainly in the liver, but also expressed at low levels in other tissues. Urea is produced by urea cycle enzymes and its metabolic process may effect by diseases, hormones, and diets. Urea is eliminated through urine especially. Blood urea nitrogen (BUN) use to estimate renal function (14). High concentrations of substances excreted by the kidney, such as urea, creatinine, and uric acid, cause uremia as a result of renal failure (15). In order for substances such as creatinine and urea to be eliminated from the body in a controlled manner, GFR must occur without any problems (16). Although the reference range of each laboratory is different, the normal urea value is accepted between 10-40 mg/dL in laboratory tests. In our study, the averages of urea values obtained from the patients were observed within this range. Therefore, we can argue that pregabalin does not have a significant effect on urea, therefore, it does not make a significant difference in the urea marker in terms of renal functions.

Uric acid is the end product of purine metabolism by action of xanthine oxidase or xanthine dehydrogenase. It is found in the blood and excreted in the urine. Normal blood uric acid levels range between 2.4-6.0 mg/dL in adult women and 3.4-7.0 mg/dL in adult men. Studies since the 1950s have found that high serum uric acid levels are associated with various diseases such as hypertension, atherosclerosis, vascular pathologies, hyperinsulinemia and renal failure. It has been proven that uric acid plays an important role in evaluation of renal functions (17).

Pregabalin has a bioavailability of more than 90%. It is well absorbed orally and completely excreted in urine without hepatic metabolism. Pregabalin toxicity has been reported in very few patients with chronic kidney disease (CKD) or without CKD. Although rare, neurotoxicity has been reported, especially in patients undergoing hemodialysis. It has been observed that this situation can be prevented by adjusting the drug dose. Therefore, caution should be exercised when using this drug in patients with CRF and its dose should be adjusted according to renal function (18). Considering the mean values calculated over a 6-month period, our retrospective study results are within the range of values presented by the literature. This indicates that the use of pregabalin has no effect on uric acid, one of the markers of renal function, in patients unaffected by CKD.

Plasma creatinine may be within the normal range even in the presence of significant nephropathy. Therefore, plasma creatinine alone is not a reliable measure of renal function. Creatinine is an ideal endogenous substance for measuring GFR. Plasma creatinine is a product of the metabolism of creatinine and phosphocreatine in skeletal muscle. Serum creatinine levels are usually stable in people with stable renal function. Creatinine is freely filtered in the glomerulus and reabsorption does not occur. In advanced renal failure, an increase in serum creatinine levels is expected. The general reference range for plasma creatinine level is 0.6 mg/dL and 1.3 mg/dL (19). The results of the mean creatinine values calculated in the study are within the normal value ranges. This shows that use of pregabalin does not make a significant difference when looking at the measured values over a 6-month period. The maximum creatinine values are thought to be associated with diet.

The kidneys help maintain electrolyte concentrations by filtering water-electrolytes from blood and excreting the excess in urine. Thus, it provides the balance of electrolyte-water excretion. Serum electrolytes alone are not sufficient to assess renal function, but become significant when compared with other markers of renal function (20). No significant difference was found when compared to the average values of the current study with reference ranges given in the literature for serum electrolytes Na^{+}, Ca^{+2}, Cl^{-}, K^{+}, P^{+3} and Mg^{+2}.

In oral bioavailability adjustments, plasma clearance of pregabalin is essentially equivalent to renal clearance. This indicates that pregabalin undergoes almost zero nonrenal elimination. Since pregabalin is eliminated renally, it affects renal function pharmacokinetics (21). Based on this information, we retrospectively examined the patients with different diagnoses using various doses of pregabalin, as a result of the evaluation of their 6-month measurements, we see that they preserved their normal kidney functions. The data obtained are consistent with the knowledge that almost all elimination of pregabalin is renal. Renal insufficiency occurring at any time will affect the efficacy, elimination and excretion of this drug during use. Therefore, we can say that the use of pregabalin in our study did not have an adverse effect on kidney functions as a result of measuring the clearances and serum values of the substances.

Limitations

During our study, the very low GFR of 3 patients detected while scanning the patient's epicrisis was not included in the statistical evaluations, considering that these patients might have developed a possible CKD. There was no difference in the mean values.

CONCLUSION

In the study, the mean of GFR, creatinine, urea, uric acid and serum electrolytes Na^{+}, Ca^{+2}, Cl^{-}, K^{+}, P^{+3} and Mg^{+2} concentrations, which are markers of renal function values, were examined retrospectively in the adult patient group using pregabalin. As seen in the literature, the renal function values we obtained show a normal distribution between certain reference intervals. In addition, this study may lead to the investigation of the effects of pregabalin on other organs. Since the included patient group was heterogeneous and the number of patients was sufficient for general organ function evaluation, it was observed that pregabalin did not have an effect that would significantly alter renal function. It can be thought that this study forms the basis for new studies to be planned prospectively. It may be useful to observe the renal effects of all drugs with retrospective scans in terms of toxicity and adverse effects, not only for pregabalin. Thus, drug safety can be increased with interdisciplinary approaches by providing information that may be beneficial to drug research and development institutions.

Etik Kurul: Approval for the study was granted by the Ethics Committee for Pharmaceutical and Non-Medical Device Research, under decision number 2019/1747, and all procedures in the study were conducted in accordance with the ethics committee protocol.

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REFERENCES

1. Yamanoglu T. Chronopharmacology of the Interaction Between Pregabalin and Morphine (PhD Thesis), Gazi University, Ankara, 2015.
2. Ben-Menachem E. Pregabalin pharmacology and its relevance to clinical practice. Epilepsia 2004;45 Suppl 6:13-8.
3. Moore RA, Straube S, Wiffen PJ, et al. Pregabalin for acute and chronic pain in adults. Cochrane Database Syst Rev 2009; 8;(3):CD007076.
4. Dworkin RH, Kirkpatrick P. Pregabalin. Nat Rev Drug Discov 2005;4(6):455-6.
5. Kavoussi R. Pregabalin: From molecule to medicine. Eur Neuropsychopharmacol 2006;16 Suppl 2:S128-33.
6. Taylor DM, Barnes TR, Young AH. The Maudsley Prescribing Guidelines in Psychiatry. 13th edition. Hoboken, NJ: Wiley, 2019.
7. Sinha N. Pregabalin. The Essence of Analgesia and Analgesics. Anticonvulsant-Type Analgesics. Sinatra RS, Jahr JS, Watkins-Pitchford JM ed. 2010; 72 (6).
8. Perucca E. Clinically relevant drug interactions with antiepileptic drugs. Br J Clin Pharmacol 2006;61(3):246-55.
9. Naidoo S, Meyers AM. Drugs and the kidney. S Afr Med J 2015;105(4):2683.
10. Jung YJ, Lee DY, Kim HW, et al. A Case Report of Syndrome of Inappropriate Antidiuretic Hormone Induced by Pregabalin. Electrolyte Blood Press 2016;14(2):31-4.
11. Johnson DW. Evidence-based guide to slowing the progression of early renal insufficiency. Intern Med J 2004;34(1-2):50-7.
12. Stevens LA, Coresh J, Greene T, et al. Assessing kidney function--measured and estimated glomerular filtration rate. N Engl J Med 2006;354(23):2473-83.
13. Fenton A, Montgomery E, Nightingale P, et al. Glomerular filtration rate: new age- and gender- specific reference ranges and thresholds for living kidney donation. BMC Nephrol 2018;19(1):336.
14. Wang H, Ran J, Jiang T. Urea. Subcell Biochem 2014;73:7-29.
15. Matovinović MS. 1. Pathophysiology and Classification of Kidney Diseases. EJIFCC 2009;20(1):2-11.
16. Yang HC, Zuo Y, Fogo AB. Models of chronic kidney disease. Drug Discov Today Dis Models 2010;7(1-2):13-9.
17. Iseki K, Oshiro S, Tozawa M, et al. Significance of hyperuricemia on the early detection of renal failure in a cohort of screened subjects. Hypertens Res 2001;24(6):691-7.
18. Lee DW, Lee HJ, Kim HJ, et al. Two cases of pregabalin neurotoxicity in chronic kidney disease patients. NDT Plus 2011;4(2):138.
19. Traynor J, Mactier R, Geddes CC, et al. How to measure renal function in clinical practice. BMJ 2006;333(7571):733-7.
20. Shrimanker I, Bhattarai S. Electrolytes. 2023 Jul 24. In: StatPearls [Internet]. Treasure Island (FL): StatPearls Publishing; 2024.
21. Bockbrader HN, Radulovic LL, Posvar EL, et al. Clinical pharmacokinetics of pregabalin in healthy volunteers. J Clin Pharmacol 2010;50(8):941-50.