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Therapeutic drug monitoring of carbamazepine and valproic acid: interindividual variability in epilepsy patients

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ABSTRACT

Aims: Epilepsy is a chronic neurological disorder affecting 1-3% of the global population, characterized by recurrent seizures. Monitoring blood levels of valproic acid and carbamazepine, two commonly used antiepileptic drugs, is essential for effective seizure control. This study aims to analyze the serum concentrations, demographic characteristics and concomitant drug use of patients treated with valproic acid or carbamazepine.

Methods: This retrospective study was conducted at Kırklareli Training and Research Hospital, analyzing the medical records of epilepsy patients treated with valproic acid or carbamazepine. Medical records of 440 epilepsy patients were retrospectively analyzed. Demographic data, concurrent medication use and blood drug levels were recorded, and rates of achieving therapeutic levels were compared.

Results: Of the 440 patients, 378 were treated with valproic acid, and 62 with carbamazepine. In the valproic acid group, 62.2% reached therapeutic levels, with an average concentration of 68.15 µg/ml. In the carbamazepine group, only 27.4% reached therapeutic levels, with an average of 10.07 µg/ml. A statistically significant difference was found between the two groups. A significant association was found between drug interaction counts and non-therapeutic levels in the carbamazepine group ($p<0.05$).

Conclusion: Valproic acid was more likely to be within the therapeutic serum range. Lower therapeutic levels in carbamazepine-treated patients, indicate a need for careful monitoring, dose adjustments and consideration of potential drug interactions. Future studies with larger populations are needed to confirm these findings and support personalized treatment approaches.

Keywords: Epilepsy, carbamazepine, valproic acid, blood-drug level, therapeutic drug monitoring

INTRODUCTION

Epilepsy is one of the most long-standing and prevalent neurological disorders, affecting an estimated 50 million people worldwide. According to the latest definition by the International League Against Epilepsy (ILAE) in 2014, epilepsy is characterized by either two or more unprovoked or reflex seizures occurring more than 24 hours apart or a single unprovoked or reflex seizure with a high probability (at least 60%) of further seizures over the next ten years.[1]

The treatment of epilepsy requires a long-term and continuous approach. Therapeutic options include medical therapy, surgical interventions, and ketogenic diets.[2] Among antiepileptic drugs (AEDs), phenobarbital, phenytoin, ethosuximide, carbamazepine, valproic acid, benzodiazepines, vigabatrin, lamotrigine, topiramate, felbamate, gabapentin, pregabalin, tiagabine, zonisamide, levetiracetam, and oxcarbazepine are used. Carbamazepine and valproic acid are the most used AEDs globally.[3-5] Beyond epilepsy, these two drugs have various other indications. Valproic acid (VPA) is FDA-approved for treating complex partial seizures in pediatric and adult patients aged ten years and older, as well as for monotherapy and adjunctive therapy of various seizure types, including simple and complex absence seizures. It is also used off-label for bipolar disorder-associated manic episodes, migraine prophylaxis, status epilepticus, diabetic peripheral neuropathy, and postherpetic neuralgia.[6] Carbamazepine is used for epilepsy, trigeminal neuralgia, and acute manic and mixed episodes of bipolar disorder; its epilepsy indications include partial seizures with complex symptomatology (psychomotor, temporal lobe), generalized tonic seizures (grand mal), and mixed seizure patterns.[7]

The mechanisms of action of these drugs vary. Carbamazepine blocks voltage-dependent sodium channels, while valproic acid inhibits GABA metabolism, reduces excitatory aspartate and increases inhibitory glycine. It also affects blocking voltage-dependent sodium channels and activating calcium-dependent potassium channels.[6,7] These complex mechanisms necessitate careful monitoring of blood drug levels to ensure therapeutic efficacy and safety.

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The therapeutic efficacy of these drugs can vary depending on individual differences. Many factors, such as age, sex, liver and kidney function, genetic variations, pregnancy, comorbidities, and concomitant medication use, can affect the pharmacokinetics and serum levels of drugs.[8,9] Therefore, monitoring blood levels is not only essential for enhancing treatment efficacy but also critical for preventing adverse effects and enabling personalized dose adjustments.[8]

Extraordinary situations, such as the COVID-19 pandemic, have further complicated access to healthcare and adherence to treatment, thereby increasing the importance of therapeutic drug monitoring.[10] In this context, understanding the relationship between serum levels of antiepileptic drugs and clinical outcomes plays a key role in treatment management.

This study aims to investigate the serum drug levels of epilepsy patients treated with valproic acid or carbamazepine in the Emergency Department of Kırklareli Training and Research Hospital between January 1 and December 31, 2023, and to examine the relationship of these levels with demographic characteristics and concomitant drug use.

METHODS

Data Source

Ethical approval for this retrospective study was obtained from the Kırklareli University Non-interventional Clinical Researches Ethics Committee (Date: 05.07.2024, Decision No: 04). All procedures were carried out in accordance with the ethical rules and the principles of the Declaration of Helsinki.

In this study, data were retrospectively obtained from the files of 440 patients diagnosed with epilepsy who were treated with valproic acid or carbamazepine and admitted to Kırklareli Training and Research Hospital's Emergency Department within the period from January 1 to December 31, 2023. The dataset included demographic characteristics such as gender, age, concurrent medication use and the patients' drug blood levels. Eligibility for participation in the study was determined based on the following criteria: (1) patients clinically diagnosed with epilepsy, (2) patients treated with valproic acid or carbamazepine with drug-level monitoring, and (3) patients over the age of 18 and (4) patients who attended the emergency department.

Since this was a retrospective study using anonymized patient data, the requirement for informed consent was waived by the ethics committee in accordance with national and institutional ethical guidelines.

No specific consent was obtained from participants as data analysis was conducted anonymously. The need for informed consent was disclaimed by the ethics committee due to the retrospective nature of the study, which involved analysis of deidentified patient data from medical records.

Valproic Acid and Carbamazepine Determination

The analysis of Valproic Acid and Carbamazepine was performed using the immunological method on the ROCHE COBAS C503 device.

The therapeutic blood levels for antiepileptic drugs were considered to be 8-12 µg/ml for carbamazepine[11] and 50-100 µg/ml for valproic acid.[12]

Based on these threshold values, patients were categorized into two groups according to their drug levels: therapeutic and non-therapeutic levels. The non-therapeutic group included patients with subtherapeutic and supratherapeutic drug levels.

Drug Interaction Analysis

Drug interaction analyses was conducted using the Drugs.com database. Drugs used by patients with carbamazepine or valproic acid in the database were investigated, and a list containing drug interactions was obtained; these interactions were classified as minor, moderate, major, or no interaction based on their severity.

Statistical Analysis

The analysis of the data obtained from the study was performed using the SPSS version 24 statistical program. The normality of the distribution of continuous variables was tested using the Shapiro-Wilk test. Descriptive statistics were used to describe contin-uous variables [mean (M), standard deviation (SD), minimum (min), median (med), maximum (max)]. The comparison of two independent continuous variables that did not follow a normal distribution was performed using the Mann-Whitney U test. The relationship between two continuous variables that did not follow a normal distribution was analyzed using Spearman's rho correlation analysis. Associations between categorical variables were evaluated using the Chi-square test or, when appropriate, Fisher's exact test. A p-value less than 0.05 was considered to indicate statistical significance.

RESULTS

Among the 440 epilepsy patients treated with carbamazepine and valproic acid included in our study, 378 were prescribed valproic acid, and 62 were prescribed carbamazepine. Regarding gender distribution, 52% (229 patients) were male, and 48% (211 patients) were female. When analyzing the gender distribution by medication, it was found that of the 62 patients treated with carbamazepine, 61.3% (38 patients) were male, and 38.7% (24 patients) were female. Among the 378 patients treated with valproic acid, 50.5% (191 patients) were male, and 49.5% (187 patients) were female (**Table 1**).

Table 1. Demographic profile of the participants

Profile	Total	n (valproic acid)	n (carbamazepine)
Male, n (%)	229	191 (50.5%)	38 (61.3%)
Female, n (%)	211	187 (49.5%)	24 (38.7%)
Mean±SD (years)	43.1	45.5	42.7

SD: Standard deviation

The average age of the 440 epilepsy patients included in the study is 43.1, with those treated with carbamazepine having an average age of 45.5 and those treated with valproic acid having an average age of 42.7. No statistically significant

difference was found in the age distribution between the medication groups and blood drug levels.

Among the 378 patients treated with valproic acid, 235 had therapeutic drug blood levels, whereas only 17 out of the 62 patients treated with carbamazepine had therapeutic drug blood levels. This finding indicates a statistically significant difference in the rates at which valproic acid and carbamazepine achieve therapeutic levels (Table 2).

Table 2. Therapeutic blood drug levels in patients using valproic acid and carbamazepine

Category	Valproic acid	Carbamazepine	p
Therapeutic level	235 (62.16%)	17 (27.42%)	<0.001
Non-therapeutic level	143 (37.83%)	45 (72.58%)	

There is a statistically significant difference in the rates of therapeutic levels between the drugs valproic acid and carbamazepine (p<0.001, Fisher's Exact test).

When considering a therapeutic blood level range for valproic acid of 50-100 µg/ml, it was found that 235 of the 378 patients treated with valproic acid had therapeutic drug levels. Among these patients, 116 were male and 119 were female, with an average drug blood level of 68.15 µg/ml. Additionally, 132 patients had valproic acid levels below 50 µg/ml, with an average drug blood level of 35.51 µg/ml. Of these patients, 67 were male and 65 were female. Furthermore, 11 patients had drug levels above the therapeutic range, with 8 males and 3 females showing an average drug blood level of 152.9 µg/ml (Table 3).

When considering a therapeutic blood level for carbamazepine as 8-12 ug/ml, it was found that 17 out of 62 patients treated with carbamazepine had therapeutic drug blood levels. Among these patients, 13 were male and 4 were female, with an average blood drug level of 10.07 mmol/L. It was observed that 38 patients had carbamazepine levels below 8 ug/ml, with an average drug level of 5.17 ug/ml. Among the patients whose carbamazepine blood levels were below the therapeutic range, 21 were male and 17 were female. For 7 patients, including 3 women and 4 men, the carbamazepine blood levels were above the therapeutic range, with an average drug level of 15.75 ug/ml (Table 3).

In the carbamazepine group, a statistically significant relationship was found between the number of drug interactions and therapeutic drug levels (p=0.0393, Fisher's exact test). Patients who did not reach therapeutic levels had a higher number of total drug interactions compared to those within the therapeutic range. In contrast, no statistically significant relationship was observed between drug interaction counts and therapeutic levels in the valproic acid group (p=0.1354, Fisher's exact test).

Additionally, drug-drug interactions with the potential to alter the serum levels of valproic acid or carbamazepine were recorded. Among the 62 patients in the carbamazepine group, 16 had potential drug-drug interactions that could influence serum carbamazepine levels, of whom 11 were female. In the valproic acid group, 44 out of 378 patients (35 males and 9 females) had potential interactions that could affect valproic acid levels. The frequency of such interactions was significantly higher in the carbamazepine group compared to the valproic acid group (p=0.0048, Fisher's exact test) (Table 4).

DISCUSSION

Therapeutic drug monitoring (TDM) enhances treatment efficacy and reduces drug side effects by considering individual differences. It helps create personalized treatment plans using modern analytical techniques and pharmacokinetic principles.[11-13] Monitoring blood levels of antiepileptic drugs (AEDs) is a crucial method in clinical evaluation, particularly for ensuring effective seizure control, and it has been standard practice since the introduction of AEDs to the market.[14] Factors such as pregnancy, liver and kidney diseases, drug interactions due to polypharmacy, and ageing can affect the efficacy of AEDs. Therefore, therapeutic drug monitoring can assist in dosage adjustments to achieve a seizure-free quality of life.[15]

Valproic acid and carbamazepine are among the most prescribed AEDs globally due to their effectiveness and safety, and monitoring their blood levels is highly important during treatment. In this retrospective study, serum concentrations of valproic acid or carbamazepine and their relationship with patients' demographic characteristics and drug-drug interaction was analyzed in epilepsy patients.

Table 3. Distributions of therapeutic levels of valproic acid and carbamazepine

Drug	Valproic acid			Carbamazepine		
Gender	Therapeutic level	Below therapeutic level	Above therapeutic level	Therapeutic level	Below therapeutic level	Above therapeutic level
Male	116 (60.7%)	67 (35%)	8 (4.3%)	13 (34.2%)	21 (55.3%)	4 (10.5%)
Female	119 (63.6%)	65 (34.7%)	3 (1.7%)	4 (16.7%)	17 (70.8%)	3 (12.5%)
p-value	0.317			0.319		

There is no statistically significant difference in the distribution of therapeutic carbamazepine levels between men and women (p>0.05, Fisher's exact test).

Table 4. Association between therapeutic drug levels and potential drug interactions in the carbamazepine and valproic acid groups

Antiepileptic drug	Total patients (n)	Patients with interactions potentially affecting drug level (n)	Sex distribution of interaction group (M/F)	p-value (Fisher's exact test)	Significant association between interaction count and therapeutic drug level
Carbamazepine	62	16	5/11	0.0048	Yes (p=0.0393)
Valproic acid	378	44	35/9		No (p=0.1354)

In the carbamazepine group, a higher number of drug interactions was associated with non-therapeutic levels (p=0.0393, Fisher's Exact test). No significant association was observed in the valproic acid group (p=0.1354, Fisher's Exact test). Potential interactions affecting serum levels were more frequent in the carbamazepine group (p=0.0048, Fisher's Exact test). M/F: Male/female

The study found that more patients were prescribed valproic acid than carbamazepine. However, there was no statistically significant difference in gender and age distribution between the two drug groups (p>0.05). According to the study results, there was a statistically significant difference in the rates of achieving therapeutic levels between valproic acid (62.16%) and carbamazepine (27.42%), with valproic acid being more likely to reach therapeutic levels. Contrary to our findings, a study by Sharma et al.[16] indicated that 63% of patients treated with carbamazepine achieved therapeutic drug levels, compared to 45.99% of those treated with valproic acid. Another study published in 2020 found that 75.5% of carbamazepine samples and 54.87% of valproic acid samples were within the therapeutic range.[17,18] Previous reports have suggested valproic acid is poorly controlled.[16,19] Our findings align more closely with previously published studies for valproic acid, in which the majority of patients had drug levels within the therapeutic range. This consistency may be partly attributed to the pharmacokinetic characteristics of valproic acid, which are generally more predictable due to its lower potential for hepatic enzyme induction.[20] In contrast, carbamazepine results showed considerable variability, with a significant proportion of patients presenting with subtherapeutic or supratherapeutic levels. This discrepancy may be due to several factors, demographic characteristics of the patients, including potential patient non-compliance, sample size differences, and particularly the high rate of drug-drug interactions associated with carbamazepine, as observed in our dataset.

One of the key findings of this study was the significant impact of drug-drug interactions on therapeutic drug levels, particularly in the carbamazepine group. As reported in the literature, carbamazepine is known to interact with approximately 760 drugs, including 240 major, 487 moderate, and 33 minor interactions,[21] whereas valproic acid interacts with significantly fewer compounds. In our study, patients using carbamazepine who experienced higher rates of drug interactions were less likely to reach therapeutic levels (p=0.0393), suggesting that polypharmacy and drug interactions substantially affect carbamazepine metabolism and clearance.

Additionally, the frequency of potentially interacting drugs that could alter blood drug levels was significantly higher in the carbamazepine group than in the valproic acid group (p=0.0048). This may further explain the lower proportion of patients with therapeutic carbamazepine levels. Moreover, the observation that most of the patients with potential carbamazepine interactions were female may be related to the higher prevalence of comorbidities and consequently increased polypharmacy in women, which could have contributed to the observed variability in carbamazepine serum levels (both below and above the therapeutic range) in this subgroup. In contrast, no statistically significant association was found between drug interaction count and valproic acid serum levels (p=0.1354), indicating that valproic acid may have a more stable pharmacokinetic profile even in the presence of polypharmacy.[22]

These findings underscore the importance of routine therapeutic drug monitoring, especially in patients prescribed carbamazepine. Regular monitoring of serum carbamazepine levels allows timely dose adjustments, ensuring patients reach and maintain therapeutic concentrations. Dose titration should be individualized based on age, weight, renal and hepatic function, and other patient-specific factors. Clinicians should be vigilant in evaluating patients' concurrent medications to anticipate possible pharmacokinetic interactions. Patient education and adherence support are crucial, emphasizing the importance of taking the medication consistently and recognizing potential side effects. The choice of AED, therefore, should take into account not only the patient's seizure type and demographics but also their likelihood of being exposed to interacting drugs. In patients with polypharmacy or higher interaction risk, considering alternative medications or adjusting concomitant therapies can help achieve optimal therapeutic levels. Personalized treatment approaches that incorporate drug interaction risk profiles may lead to better seizure control and fewer adverse outcomes.[23]

Limitations

Our study has several limitations due to its retrospective design. It is possible that not all patients for whom drug levels were requested could be reached. Additionally, vital signs monitoring, physical examination findings, clinical outcomes of patients with non-therapeutic drug levels, seizure frequency, and adverse events were not recorded; therefore, the relationship between therapeutic levels and clinical improvement or deterioration could not be evaluated, and the findings cannot be directly translated into prescribing recommendations. Moreover, information regarding patients' medication use includes only drugs prescribed within the hospital system where the study was conducted. Medications obtained from other hospitals, healthcare institutions, or over-the-counter drugs without prescription were not captured in our data. The choice of the Drugs.com database for drug-drug interaction assessment was based on accessibility and practicality; however, compared to alternative platforms such as Micromedex or Lexicomp, it may have limitations in comprehensiveness and classification of interaction severity. The single-center design may limit the generalizability of the findings, and regional prescribing patterns could have influenced both drug selection and attainment of therapeutic levels. Furthermore, "confounding by indication" should be considered, as patients prescribed carbamazepine may have had more refractory epilepsy types, which could influence serum level outcomes. Despite these limitations, since the data were obtained from the largest and sole central hospital in the city, the results may be representative and provide valuable insights for future studies.

CONCLUSION

This study examined the rates at which valproic acid and carbamazepine, used in treating epilepsy, reach therapeutic serum levels, and how these rates relate to patients' demographic characteristics. We found valproic acid is more likely to reach therapeutic levels than carbamazepine.

However, we also observed that demographic differences among patients treated with carbamazepine and potential drug interactions may be associated with lower serum levels. Therefore, careful monitoring and dosage adjustments are essential, particularly for women who are on carbamazepine therapy. Future studies should aim to validate these findings in larger populations and help develop individualized treatment approaches for antiepileptic drugs.

ETHICAL DECLARATIONS

Ethics Committee Approval

The study was carried out with the permission of the Kırklareli University Non-interventional Clinical Researches Ethics Committee (Date: 05.07.2024, Decision No: 04).

Informed Consent

Because the study was designed retrospectively, no written informed consent form was obtained from patients.

Referee Evaluation Process

Externally peer-reviewed.

Conflict of Interest Statement

The authors have no conflicts of interest to declare.

Financial Disclosure

The authors declared that this study has received no financial support.

Author Contributions

All of the authors declare that they have all participated in the design, execution, and analysis of the paper, and that they have approved the final version.

REFERENCES

1. Banerjee PN, Filippi D, Allen Hauser W. The descriptive epidemiology of epilepsy-a review. *Epilepsy Res.* 2009;85(1):31-45. doi:10.1016/j.eplepsyres.2009.03.003
2. Turkish Neurological Society. In: Dervent A, Ayta S, Çokar Ö, Uludüz D. Approach Guide to Neurological Diseases in Children and Adolescents. 2015. https://noroloji.org.tr/TNDData/Uploads/files/%C3%87ED-2015(1).pdf
3. Hanaya R, Arita K. The new antiepileptic drugs: their neuropharmacology and clinical indications. *Neurol Med Chir (Tokyo).* 2016;56(5):205-20. doi:10.2176/nmc.ra.2015-0344
4. Iorio ML, Moretti U, Colcera S, et al. Use and safety profile of antiepileptic drugs in Italy. *Eur J Clin Pharmacol.* 2007;63(4):409-415. doi:10.1007/s00228-006-0236-6
5. Elendu C, Jeswani BM, Madekwe CC, et al. Clinical and electroencephalographic correlates of carbamazepine-associated hiccups in epileptic patients. *Ann Med Surg (Lond).* 2024;86(7):4015-4034. doi:10.1097/MS9.0000000000002159
6. Rahman M, Awosika AO, Nguyen H. Valproic Acid. [Updated 2023 Aug 17]. In: StatPearls [Internet]. Treasure Island (FL): StatPearls Publishing; 2024 Jan-. Available from: https://www.ncbi.nlm.nih.gov/books/NBK559112/
7. Maan JS, Duong TvH, Saadabadi A. Carbamazepine. [Updated 2023 Jul 10]. In: StatPearls [Internet]. Treasure Island (FL): StatPearls Publishing; 2024 Jan-. Available from: https://www.ncbi.nlm.nih.gov/books/NBK482455/
8. St Louis EK. Monitoring antiepileptic drugs: a level-headed approach. *Curr Neuropharmacol.* 2009;7(2):115-119. doi:10.2174/157015909788848938
9. Akdağ G, Algın Dİ, Erdinç OO. Epileps. *Osmangazi J Med.* 2016;38(Special Issue 1):35-41. doi:10.20515/otd.88853
10. Giza E, Lefkopoulou M, Dimitrakopoulos D, Karachristianou S, Liasidis C. The impact of the COVID-19 pandemic on a Greek cohort of patients with epilepsy. *Hippokratia.* 2021;25(4):145-150.
11. Shared Health – SBGH Lab Manual. Carbamazepine. Available from: https://apps.sbgh.mb.ca/labmanual/test/view?seedId=1397. Accessed August 2025.
12. Tseng YJ, Huang SY, Kuo CH, Wang CY, Wang KC, Wu CC. Safety range of free valproic acid serum concentration in adult patients. *PLoS One.* 2020;15(9):e0238201. doi:10.1371/journal.pone.0238201
13. Zeng L, Yi Q, Huang L, et al. The guideline for therapeutic drug monitoring guidelines development. *J Evid Based Med.* 2022;15(3):272-283. doi: 10.1111/jebm.12486
14. Liu Y, Li J, Xiao S, et al. Revolutionizing precision medicine: exploring wearable sensors for therapeutic drug monitoring and personalized therapy. *Biosensors (Basel).* 2023;13(7):726. doi:10.3390/bios13070726
15. Irving PM, Gecse KB. Optimizing therapies using therapeutic drug monitoring: current strategies and future perspectives. *Gastroenterology.* 2022;162(5):1512-1524. doi:10.1053/j.gastro.2022.02.014
16. Sharma S, Joshi S, Mukherji S, Bala K, Tripathi CB. Therapeutic drug monitoring: appropriateness and clinical utility in neuropsychiatry practice. *Am J Ther.* 2009;16(1):11-16. doi:10.1097/MJT.0b013e31817fd85f
17. French JA, Perucca E. time to start calling things by their own names? The case for antiseizure medicines. *Epilepsy Curr.* 2020;20(2):69-72. doi: 10.1177/1535759720905516
18. Fratoni AJ, Colmerauer JL, Linder KE, Nicolau DP, Kuti JL. A retrospective case series of concomitant carbapenem and valproic acid use: are best practice advisories working? *J Pharm Pract.* 2023;36(3):537-541. doi:10.1177/08971900211063301
19. Al-Balawi RS, Alshehri MA, Alatawi AS, Al Shehri AM, Alshehry MA, Al-Gayyar MMH. Measuring the appropriateness of carbamazepine and valproic acid prescribing and utilization using a newly implemented online system in the Tabuk Region of Saudi Arabia. *Saudi Pharm J.* 2020;28(7):844-849. doi:10.1016/j.jsps.2020.06.008
20. Dalaklioglu S. Evaluating appropriateness of digoxin, carbamazepine, valproic acid, and phenytoin usage by therapeutic drug monitoring. *Clin Lab.* 2013;59(3-4):325-31. doi:10.7754/clin.lab.2012.120425
21. Bowden CL. Valproate. *Bipolar Disord.* 2003;5(3):189-202. doi:10.1034/j.1399-5618.2003.00031.x
22. Marvanova M. Pharmacokinetic characteristics of antiepileptic drugs (AEDs). *Ment Health Clin.* 2016;6(1):8-20. doi:10.9740/mhc.2015.01.008
23. https://www.drugs.com/drug_interactions.html