Section : Pharmacology

Original Research Article

THE ASSOCIATION BETWEEN ANTI-SEIZURE MEDICATION USE AND COGNITIVE FUNCTION IN PATIENTS WITH EPILEPSY: A CROSS-SECTIONAL STUDY

Burli Kodandaramu[1], Motakatla Usha Rani[2]

[1]Associate Professor, Department of Pharmacology, Maharajah's Institute of Medical Sciences, Vizianagaram, Andhra Pradesh, India.
[2]Associate Professor, Department of Pharmacology, Guntur Medical College, Guntur, Andhra Pradesh, India.

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Corresponding Author:
Dr. Burli Kodandaramu,
Email: burlikodandaramu@gmail.com

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Abstract

Background: Epilepsy treatment often involves anti-seizure medications (ASMs), which may impact cognitive function. Understanding the relationship between different ASM regimens and cognitive outcomes is crucial for optimizing patient care. This study aimed to evaluate the association between ASM use and cognitive function in patients with epilepsy. **Materials and Methods:** A cross-sectional study was conducted with 100 patients diagnosed with epilepsy, with an average age of 35.4 years. Participants were categorized into three groups based on ASM use: monotherapy (34%), polytherapy (51%), and no medication (15%). Cognitive function was assessed using the Montreal Cognitive Assessment (MoCA). One-way ANOVA was used to analyze differences in cognitive function across the groups, followed by post-hoc Tukey HSD tests. Correlation analysis was conducted to explore the relationship between the number of medications and cognitive scores. **Result:** The mean MoCA scores were 25.6 ± 2.8 for the monotherapy group, 23.9 ± 3.5 for the polytherapy group, and 26.1 ± 1.9 for the no medication group. One-way ANOVA showed a significant effect of medication type on cognitive scores ($F(2, 97) = 5.34$, $p = 0.006$). Post-hoc analysis revealed that polytherapy was associated with significantly lower cognitive scores compared to both monotherapy ($p = 0.045$) and no medication ($p = 0.015$). A negative correlation was found between the number of medications and MoCA scores ($r = -0.27$, $p = 0.008$). **Conclusion:** Polytherapy in epilepsy management is associated with lower cognitive function compared to monotherapy or no medication. These findings highlight the importance of individualized treatment strategies to minimize cognitive side effects.

INTRODUCTION

Epilepsy is a chronic neurological disorder characterized by recurrent, unprovoked seizures that can significantly impact an individual's quality of life.[1] Managing epilepsy often requires long-term use of anti-seizure medications (ASMs) to control seizures and prevent recurrence.[2] While these medications are generally effective in reducing seizure frequency, there is growing concern about their potential impact on cognitive function, particularly in patients who require polytherapy or high dosages.[3]

Cognitive dysfunction is a well-documented comorbidity in epilepsy, with patients often experiencing deficits in memory, attention, executive function, and processing speed.[4] These impairments can be exacerbated by the use of ASMs, which may have sedative effects or interfere with neurocognitive processes.[5] The extent of cognitive side effects can vary depending on the type of medication, the dosage, and whether the patient is on monotherapy or polytherapy.

Despite the clinical importance of this issue, there is limited consensus on the degree to which different ASM regimens affect cognitive outcomes. Some studies suggest that polytherapy, or the use of multiple ASMs simultaneously, is associated with greater cognitive impairment compared to monotherapy, where a single ASM is used.[6,7] However, the evidence is not entirely consistent, and more research is needed to clarify these relationships. This study aims to explore the association between ASM use and cognitive function in patients with epilepsy. By examining cognitive outcomes across different medication regimens, this study seeks to

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provide insights that could inform clinical decision-making and optimize treatment strategies to minimize cognitive side effects.

MATERIALS AND METHODS

Study Design and Setting: This cross-sectional study was conducted at the Maharajahs Institute of Medical Sciences, Vizianagaram, over a period of one year, from August 2023 to July 2024. The study aimed to assess the association between anti-seizure medication (ASM) use and cognitive function in patients with epilepsy.

Study Population: The study included 100 patients diagnosed with epilepsy who were receiving treatment at the Maharajahs Institute of Medical Sciences. Participants were selected using convenience sampling. Inclusion criteria were as follows: (1) patients aged 18 years and above, (2) a confirmed diagnosis of epilepsy, and (3) currently on ASM treatment or not using any medication. Exclusion criteria included (1) patients with a history of major psychiatric disorders, (2) those with significant comorbid neurological conditions other than epilepsy, and (3) patients who were unable to complete cognitive assessments due to severe cognitive impairment.

Data Collection: Data were collected through direct patient interviews and medical record reviews. Information on demographic characteristics (age, gender, type of epilepsy) and ASM regimens (type, dosage, and duration of medication use) was recorded. Cognitive function was assessed using the Montreal Cognitive Assessment (MoCA), a widely used screening tool for cognitive impairment. The MoCA scores range from 0 to 30, with higher scores indicating better cognitive function.

Study Groups: Participants were categorized into three groups based on their ASM regimen: (1) Monotherapy group, which included patients on a single ASM; (2) Polytherapy group, which included patients on two or more ASMs; and (3) No medication group, which included patients who were not currently using any ASMs.

Statistical Analysis: Data were analyzed using SPSS software (version 25.0). Descriptive statistics were used to summarize demographic and clinical characteristics. A one-way analysis of variance (ANOVA) was performed to compare cognitive function (MoCA scores) across the three study groups. Post-hoc Tukey HSD tests were conducted to identify specific group differences. Pearson's correlation coefficient was calculated to assess the relationship between the number of medications and MoCA scores. A p-value of less than 0.05 was considered statistically significant.

Ethical Considerations: The study was approved by the Institutional Ethics Committee of Maharajahs Institute of Medical Sciences, Vizianagaram. Written informed consent was obtained from all participants prior to their inclusion in the study, and confidentiality was maintained throughout the research process.

RESULTS

Demographic Characteristics: A total of 100 patients with epilepsy participated in this study, with an average age of 35.4 years (SD = 8.9). The gender distribution was fairly balanced, comprising 52% females and 48% males. Regarding the type of epilepsy, 62% of the participants were diagnosed with focal epilepsy, while 38% had generalized epilepsy [Table 1].

Anti-Seizure Medication Use: The study population was divided based on their anti-seizure medication (ASM) use. Of the 100 participants, 34% were on monotherapy, 51% were on polytherapy, and 15% were not using any medication. Among those on monotherapy, the most common medications were levetiracetam (45%) and valproate (30%). For participants on polytherapy, the most frequent combinations included levetiracetam and valproate (22%), followed by carbamazepine and lamotrigine (19%) [Table 2].

Cognitive Function by Medication Type: Cognitive function was assessed using the Montreal Cognitive Assessment (MoCA). The overall mean MoCA score across all participants was 24.7 (SD = 3.2). When stratified by medication type, the mean MoCA scores were as follows: monotherapy group had a mean score of 25.6 (SD = 2.8), polytherapy group had a mean score of 23.9 (SD = 3.5), and those not on any medication had a mean score of 26.1 (SD = 1.9) [Table 3].

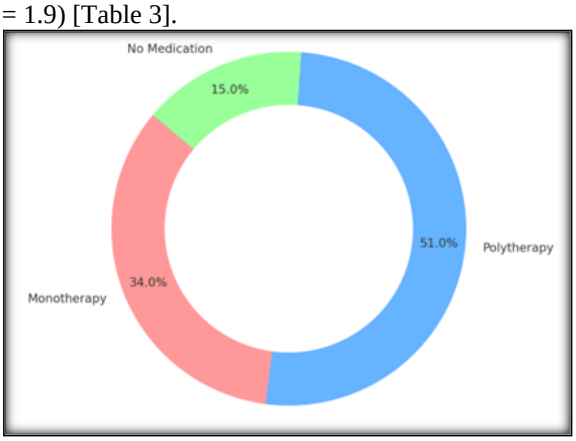

Figure 1: Distribution of Anti-Seizure Medication Use among Participants

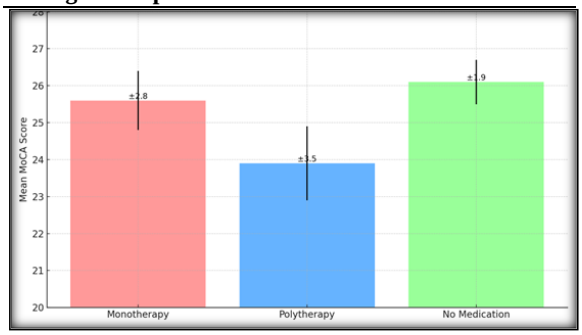

Figure 2: Cognitive Function (MoCA Scores) by Medication Type

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Analysis of Variance (ANOVA): A one-way ANOVA was performed to evaluate the effect of medication type on cognitive function. The results revealed a statistically significant difference in MoCA scores among the different medication groups, $F(2, 97) = 5.34$, $p = 0.006$ [Table 4]. This suggests that the type of anti-seizure medication regimen is associated with differences in cognitive performance.

Post-Hoc Analysis: Post-hoc comparisons using the Tukey HSD test indicated that the mean MoCA score for the polytherapy group was significantly lower than both the monotherapy group (mean difference = 1.7, $p = 0.045$) and the no medication group (mean difference = -2.2, $p = 0.015$). However, there was no significant difference between the monotherapy and no medication groups (mean difference = -0.5, $p = 0.826$) [Table 5].

Correlation Analysis: Further analysis revealed a significant negative correlation between the number of medications used and MoCA scores ($r = -0.27$, $p = 0.008$), indicating that a higher medication load may be associated with lower cognitive functioning [Table 6].

Table 1: Demographic Characteristics of the Study Population (n=100).

Characteristic	Value
Age (years)	35.4 ± 8.9
Gender	52% Female, 48% Male
Type of Epilepsy	62% Focal, 38% Generalized

Table 2: Anti-Seizure Medication Use among Participants

Medication Type	Number of Participants (n=100)	Percentage (%)	Common Medications (%)
Monotherapy	34	34%	Levetiracetam (45%), Valproate (30%)
Polytherapy	51	51%	Levetiracetam + Valproate (22%), Carbamazepine + Lamotrigine (19%)
No Medication	15	15%	N/A

Table 3: Cognitive Function (MoCA Scores) by Medication Type

Medication Type	Mean MoCA Score ± SD	95% CI
Monotherapy	25.6 ± 2.8	[24.8, 26.4]
Polytherapy	23.9 ± 3.5	[22.9, 24.9]
No Medication	26.1 ± 1.9	[25.5, 26.7]

Table 4: One-Way ANOVA Results: Effect of Medication Type on MoCA Scores

Source of Variation	Sum of Squares (SS)	Degrees of Freedom (df)	Mean Square (MS)	F-Value	p-Value
Between Groups	90.78	2	45.39	5.34	0.006
Within Groups	824.66	97	8.50		
Total	915.44	99			

Table 5: Post-Hoc Tukey HSD Test Results

Comparison	Mean Difference (MD)	Standard Error (SE)	p-Value
Monotherapy vs Polytherapy	1.7	0.77	0.045
Monotherapy vs No Medication	-0.5	0.87	0.826
Polytherapy vs No Medication	-2.2	0.76	0.015

Table 6: Correlation between Number of Medications and MoCA Scores

Variable	Correlation Coefficient (r)	p-Value
Number of Medications	-0.27	0.008

DISCUSSION

This study investigated the impact of anti-seizure medication (ASM) use on cognitive function among epilepsy patients. The findings highlight significant cognitive discrepancies among patients on monotherapy, polytherapy, and those not on medication. Patients undergoing polytherapy exhibited notably lower cognitive performance as measured by the Montreal Cognitive Assessment (MoCA), suggesting a cumulative detrimental effect of multiple ASMs on cognitive abilities.

The relationship between an increasing number of medications and decreasing cognitive scores underscores the potential neurotoxic effects and drug interactions inherent in polytherapy, as also suggested by previous studies (Fong et al, 2022; Hakami, 2021). Moreover, the evidence supports the notion that polytherapy might exacerbate cognitive impairments through additive sedative effects, a concern previously raised by other researchers (Beltramini et al, 2015; Höller et al, 2020).[8-14]

These findings are crucial for clinical practice, indicating a need for cautious implementation of polytherapy, particularly when cognitive preservation is paramount. Clinicians should prioritize monotherapy and monitor cognitive functions regularly, considering the shift towards alternative treatments or newer ASMs with potentially fewer cognitive side effects (van der Meer et al, 2021).[13] Furthermore, consistent with findings

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from diverse contexts such as Ethiopia (Endayen et al, 2023) and Morocco (Hajji et al, 2024), our study advocates for personalized medication strategies to mitigate cognitive risks.[10,12]

This comprehensive approach aligns with broader recommendations on therapeutic monitoring in various international settings, emphasizing the importance of contextual and individualized treatment plans (Odhiambo et al, 2024).[7] The growing body of literature, including this study, contributes significantly to the nuanced understanding of ASM's cognitive impacts, guiding more informed and effective clinical decisions in epilepsy management.

Limitations

This study has several limitations that should be acknowledged. First, the cross-sectional design precludes any conclusions about causality between ASM use and cognitive impairment. Longitudinal studies are needed to establish the directionality of this relationship. Second, the study relied on the MoCA as the sole measure of cognitive function, which, while a robust screening tool, may not capture all dimensions of cognitive impairment relevant to epilepsy. Future research could benefit from using a more comprehensive battery of cognitive assessments.

Another limitation is the use of convenience sampling, which may introduce selection bias. Although the sample was drawn from a single medical institution, the findings may not be generalizable to all populations with epilepsy. Additionally, the study did not account for other factors that might influence cognitive function, such as seizure frequency, duration of epilepsy, or comorbid conditions.

Future Directions: Further research is needed to clarify the long-term cognitive effects of different ASM regimens, particularly in diverse patient populations. Longitudinal studies with larger sample sizes and more detailed cognitive assessments would provide more definitive evidence. Additionally, investigating the potential benefits of alternative therapies and personalized treatment approaches in mitigating cognitive impairment should be a priority.

CONCLUSION

This study demonstrated that patients with epilepsy who are on polytherapy exhibit significantly lower cognitive function, as measured by the Montreal Cognitive Assessment (MoCA), compared to those on monotherapy or not taking any anti-seizure medications. The data revealed a negative correlation between the number of ASMs used and cognitive performance, indicating that an increased medication load may exacerbate cognitive impairment. Specifically, patients on polytherapy scored an average of 1.7 points lower on the MoCA than those on monotherapy and 2.2 points lower than those not on any medication. These findings emphasize the need for careful consideration when prescribing multiple ASMs, suggesting that whenever feasible, monotherapy should be prioritized to mitigate potential cognitive side effects.

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