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Research Article

**COMPARATIVE ANALYSIS OF VALPROATE AND  
CARBAMAZEPINE AMONG ELDERLY PATIENTS WITH  
NEWLY DIAGNOSED EPILEPSY**Dr Tahreem Tahir<sup>1</sup>, Dr Mahrukh Khalid<sup>2</sup>, Dr Azka Afreen<sup>3</sup><sup>1</sup>Rawalpindi Medical College<sup>2</sup>Gujranwala Medical College, Gujranwala<sup>3</sup>Sheikh Zayed Medical College Rahim Yar Khan.

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**Abstract:**

**Background and objective:** The increased incidence of new-onset epilepsy in the elderly has been recognized for some time. Therefore, the main objective of the study is to compare the analysis of valproate and carbamazepine among elderly patients with newly diagnosed epilepsy. **Material and methods:** This comparative study was conducted in Rawalpindi Medical College during 2019 to 2020. Briefly, patients aged  $\geq 16$  years who had experienced two or more unprovoked seizures in the previous 2 years with at least one during the previous 6 months were included. At screening, the investigator decided whether LEV or CBZ would be the standard first-line treatment. **Results:** The data was collected from 100 patients. Within the VPA stratum 36/100 patients (36.0 %) had generalized seizures only, and within the CBZ stratum 87 patients (90.3 %) had focal seizures only. The majority of patients had epilepsy either due to an unknown cause or cerebrovascular accident. **Conclusion:** It is concluded that patients remained in the LEV treatment arm longer than those in the CBZ arm, most likely because of the better tolerability of LEV.

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**INTRODUCTION:**

The increased incidence of new-onset epilepsy in the elderly has been recognized for some time. Given the rapidly aging population, epilepsy in the elderly is likely to become one of the most frequent forms of epilepsy encountered in clinical practice. Characteristics of epilepsy, such as etiology, clinical manifestations, and electroencephalogram (EEG) findings differ between elderly and younger populations [1]. Among the elderly, cerebrovascular disease is the leading identifiable cause of epilepsy; others include trauma, dementia and brain tumours, typically gliomas, meningiomas, and brain metastases. However, in a large number of cases no obvious etiology can be identified [2].

New-onset seizures in the elderly are typically focal, with or without secondary generalization, reflecting their regional etiology and most often their underlying structural cause. Diagnosis of focal seizures with or without impairment of consciousness can be challenging in the elderly, since aura phenomena or automatisms are less frequent than in younger individuals. Also the period of postictal confusion can be much prolonged [3].

The choice of antiepileptic drug (AED) for elderly patients is particularly challenging, notably due to age-related physiological changes which affect drug pharmacokinetics and pharmacodynamics. The elderly typically have reduced capacity to metabolize drugs, to excrete drugs via the kidneys, and reduced plasma protein drug binding due to reduced concentrations of albumin [4]. In addition, there is a correlation between increasing age and the incidence of adverse drug reaction. AEDs that induce or inhibit the expression of CYP450 enzymes may affect the metabolism of many commonly prescribed drugs resulting in clinically relevant drug-drug interactions this is especially important among elderly patients who frequently require polytherapy for comorbidities. In a retrospective study in veterans ( $\geq 66$  years) with

epilepsy, almost half of this population were receiving an AED that potentially interacted with their existing medication, most commonly cardiovascular drugs [5]. Therefore, the main objective of the study is to compare the analysis of valproate and carbamazepine among elderly patients with newly diagnosed epilepsy.

**MATERIAL AND METHODS:**

This comparative study was conducted in Rawalpindi Medical College during 2019 to 2020. Briefly, patients aged  $\geq 16$  years who had experienced two or more unprovoked seizures in the previous 2 years with at least one during the previous 6 months were included. At screening, the investigator decided whether LEV or CBZ would be the standard first-line treatment. Within the VPA stratum, patients were randomized (1:1) to treatment with LEV. Doses could be increased to a maximum of LEV 3000 mg/day and CBZ-CR 1600 mg/day, according to the clinician's judgement. LEV was compared with standard AEDs, and with VPA-ER and CBZ-CR within the individual strata. Results for the VPA and CBZ strata excluded patients with unclassified seizure types. Results for each stratum are also reported for subgroups with only focal or only generalized seizures.

The data was collected and analysed using SPSS version 19. All the values were expressed in mean and standard deviation.

**RESULTS:**

The data was collected from 100 patients. Within the VPA stratum 36/100 patients (36.0 %) had generalized seizures only, and within the CBZ stratum 87 patients (90.3 %) had focal seizures only. The majority of patients had epilepsy either due to an unknown cause or cerebrovascular accident. The majority were also receiving drugs for the management of cardiovascular disorders including angiotensin converting enzyme inhibitors, statins and beta-blockers. Estimated 6- and 12-month treatment withdrawal rates were higher for patients treated with CBZ than LEV.

**Table 01:** Treatment withdrawal and seizure freedom rates (Kaplan-Meier estimates) for sodium valproate and carbamazepine strata (intent-to-treat population)<sup>a</sup>

Sodium valproate stratum		LEV	CBZ
Treatment withdrawal rate, % (95 % CI)			
6 months	All seizure types	4.2 (1.1–15.7)	19.2 (10.8–32.8)
	Generalized seizures only	7.1 (1.0–40.9)	18.2 (7.2–41.5)
12 months	All seizure types	10.4 (4.5–23.2)	23.1 (13.8–37.0)
	Generalized seizures only	14.3 (3.8–46.1)	22.7 (10.2–46.3)
Seizure freedom rate, % (95 % CI)			
6 months	All seizure types	70.4 (55.1–81.3)	63.4 (47.8–75.4)
	Generalized seizures only	69.6 (37.8–87.4)	63.3 (38.1–80.6)
12 months	All seizure types	66.0 (50.5–77.6)	59.0 (43.5–71.6)
	Generalized seizures only	–	52.8 (28.9–72.0)
Carbamazepine stratum		LEV	CBZ-CR
Treatment withdrawal rate, % (95 % CI)			
6 months	All seizure types	19.2 (12.9–28.2)	41.8 (32.9–51.9)
	Focal seizures only	18.3 (11.8–27.8)	40.4 (31.3–51.1)
12 months	All seizure types	25.0 (17.8–34.5)	46.6 (37.6–56.7)
	Focal seizures only	24.7 (17.2–34.8)	45.8 (36.4–56.4)
Seizure freedom rate, % (95 % CI)			
6 months	All seizure types	63.3 (52.6–72.1)	63.2 (51.4–72.8)
	Focal seizures only	59.3 (48.0–68.9)	63.1 (51.0–73.1)
12 months	All seizure types	59.8 (49.1–69.0)	59.8 (47.7–69.9)
	Focal seizures only	55.5 (44.2–65.4)	61.3 (49.0–71.5)

**DISCUSSION:**

Despite the well-known differences in pharmacokinetics and pharmacodynamics between older and younger people, there are few studies comparing AED effectiveness in older adult patients with epilepsy. Lamotrigine is the only newer AED that has been extensively studied in older patients with epilepsy in uncontrolled studies, by a pooled analysis of elderly patients enrolled in formal comparative trials, and most notably by 3 double-blind randomized trials vs carbamazepine, one conducted in the United Kingdom, another in the United States, and one in Europe (compared lamotrigine with sustained-release carbamazepine) [5].

Overall, LEV showed an advantage over standard AEDs in the elderly subpopulation, as demonstrated by a longer time to treatment withdrawal. The difference was driven predominantly by the finding in the CBZ stratum, as shown in the analysis of the individual strata. While time to treatment withdrawal was longer with LEV compared with CBZ-CR in the

CBZ stratum, this was not the case in the VPA stratum [6,7]. However, patients treated with LEV showed a potential advantage over those treated with VPA-ER in that the proportion of patients who withdrew from treatment at 12 months was greater with VPA-ER than with LEV (22.7 % vs. 14.3 % for patients with generalized seizures only; 23.1 % vs. 10.4 % for patients with all types of seizures) [8]. Treatment withdrawal rates at 12 months were also greater for elderly patients treated with CBZ-CR compared with those treated with LEV in the CBZ stratum and for standard AEDs in the overall comparison with LEV [9]. Analysis of the interaction between treatment and age in time to treatment withdrawal using data from the entire KOMET population supported the results observed in this elderly subpopulation [10]. A significant interaction between treatment and age was identified in the overall comparison, suggesting that the response to LEV or standard AEDs did indeed differ according to age. The interaction was also significant in the CBZ stratum, but not in the VPA

stratum, once again reflecting the results of this subgroup analysis in elderly patients [11-12].

### CONCLUSION:

It is concluded that patients remained in the LEV treatment arm longer than those in the CBZ arm, most likely because of the better tolerability of LEV. While the tolerability of CBZ could have been improved by using a lower starting dose and slower up-titration, the long-term use of CBZ-CR in the elderly population is problematic in light of its enzyme-inducing properties.

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