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Short communication

Effects of Valproate, Carbamazepine, and Levetiracetam Monotherapy on Liver Enzyme Levels in Children with Epilepsy: A Retrospective Observational Study

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ABSTRACT
Antiseizure medications (ASMs) are widely used in childhood epilepsy, and some are associated with alterations in liver enzyme levels, making biochemical monitoring an important component of follow-up. The aim of this study was to evaluate and compare the effects of valproate, carbamazepine, and levetiracetam monotherapy on aspartate aminotransferase (AST/GOT), alanine aminotransferase (ALT/GPT), and gamma-glutamyl transferase (GGT) in children with epilepsy. This retrospective observational study was conducted at the outpatient clinic of Tripoli University Hospital, Libya, from January 2023 to March 2026. It included 120 children aged 1 to 14 years at diagnosis (76 females, 44 males) with normal baseline GOT, GPT, and GGT, treated with valproate (n=45), carbamazepine (n=40), or levetiracetam (n=35) monotherapy and followed for 6 to 24 months. Enzyme results were classified as normal or elevated according to age- and sex-specific reference ranges. Groups were compared using the chi-square or Fisher's exact test. Liver enzyme abnormalities were found in 15 of 45 children (33.3%) on valproate, 19 of 40 (47.5%) on carbamazepine, and 4 of 35 (11.4%) on levetiracetam. GOT elevation was the most frequent abnormality with valproate (8 children), while GOT and GGT elevations were equally frequent with carbamazepine (6 children each). No GGT elevation occurred with levetiracetam, and the four affected children had mild GOT (2) or GPT (2) elevations. The difference in the overall frequency of abnormalities between groups was statistically significant (chi-square, p=0.003). Mild liver enzyme elevations occurred in all three groups, least often with levetiracetam, which had no GGT elevations. Because of the retrospective design and limited sample size, these findings should be confirmed in larger prospective studies that account for dose, duration, and clinical liver injury.
Keywords. *Childhood Epilepsy, Valproate, Carbamazepine, Levetiracetam, Liver Function Tests.*

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Introduction

Liver function is commonly assessed using AST/GOT, ALT/GPT and GGT [1]. Changes in these markers may indicate hepatic irritation or injury, but isolated enzyme elevations do not necessarily indicate clinically significant liver damage [1]. Antiseizure medications are the mainstay of treatment in childhood epilepsy and are often continued for years. Valproate is known to be associated with hepatic adverse effects, and monitoring of liver biochemistry is clinically important, particularly at treatment initiation and in patients with additional risk factors [2,3].

Recent studies have further emphasized the importance of routine liver enzyme monitoring in pediatric patients receiving these medications [9,13]. Carbamazepine induces hepatic enzymes, so some biochemical changes, particularly in GGT, may reflect enzyme induction rather than hepatocellular injury [4,5]. Levetiracetam is generally regarded as having a favorable hepatic safety profile [6,7].

Comparing liver enzyme levels in children receiving different antiseizure medications may help inform clinical monitoring and treatment decisions. Local data from Libya are limited. This study therefore aimed to describe and compare liver enzyme findings in children treated with these three drugs as monotherapy [8]. This study was conducted to evaluate and compare the effects of valproate (Depakin), carbamazepine (Tegretol), and levetiracetam (Keppra) monotherapy on GOT, GPT, and GGT levels in children with epilepsy during follow-up after treatment initiation.

Patients and Methods

Study Design and Setting

This was a retrospective observational study conducted at the outpatient clinic of Tripoli University Hospital, Tripoli, Libya. Data were collected for the period from January 2023 to March 2026.

Study Population

The study included 120 children diagnosed with epilepsy, aged 1 to 14 years at diagnosis (76 females and 44 males). All had normal GOT, GPT, and GGT levels before starting antiseizure medication. Follow-up after treatment initiation ranged from 6 to 24 months.

Treatment Groups

- Group A: valproate (Depakin) monotherapy, 45 children.
- Group B: carbamazepine (Tegretol) monotherapy, 40 children.

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• Group C: levetiracetam (Keppra) monotherapy, 35 children.

Inclusion Criteria

1. Children aged 1 to 14 years at epilepsy diagnosis.
2. Diagnosis of epilepsy and outpatient follow-up at Tripoli University Hospital.
3. Treatment with valproate, carbamazepine, or levetiracetam as monotherapy.
4. Normal liver enzyme levels before treatment initiation.
5. At least 6 months of follow-up after treatment initiation.

Exclusion Criteria

1. Pre-existing liver disease or liver injury before treatment.
2. Elevated GOT, GPT, or GGT before starting antiseizure medication.
3. Treatment with more than one antiseizure medication.

Data Collection

Clinical and laboratory data were retrospectively reviewed, including age, sex, antiseizure medication, baseline liver enzyme results, follow-up duration, and subsequent GOT, GPT, and GGT measurements. Results were categorized as normal or elevated according to the laboratory reference ranges applicable to each child's age and sex.

Statistical Analysis

Categorical variables are summarized as frequencies and percentages. The frequency of liver enzyme abnormalities was compared across the three groups using the chi-square test, or Fisher's exact test when expected cell counts were small. A p-value below 0.05 was considered statistically significant.

Results

A total of 120 children were included: 45 (37.5%) in the valproate group, 40 (33.3%) in the carbamazepine group, and 35 (29.2%) in the levetiracetam group. There were 76 females (63.3%) and 44 males (36.7%).

Table 1. Distribution of the study population by treatment group

Group	Medication	n	%
A	Valproate (Depakin)	45	37.5%
B	Carbamazepine (Tegretol)	40	33.3%
C	Levetiracetam (Keppra)	35	29.2%
Total	—	120	100%

For valproate and carbamazepine, each child appears in one category, so the counts sum to the group size. For levetiracetam, four children in total had abnormalities (35 minus 31 with normal results), which equals its isolated GOT (2) plus isolated GPT (2) elevations, with no concurrent elevation.

Table 2. Liver enzyme findings by treatment group

Finding	Valproate (n=45)	Carbamazepine (n=40)	Levetiracetam (n=35)
Elevated GOT	8	6	2
Elevated GGT	2	6	0
Elevated GPT	3	4	2
Concurrent GOT and GPT elevation	2	3	0
Normal liver enzymes	30 (66.7%)	21 (52.5%)	31 (88.6%)

**In the levetiracetam group, four children had mild enzyme elevations: GOT in 2 and GPT in 2.*

In the valproate group, GOT elevation was the most frequent abnormality (8 children), followed by GPT (3), GGT (2), and concurrent GOT and GPT elevation (2). In the carbamazepine group, GOT and GGT elevations were each seen in 6 children, GPT in 4, and concurrent GOT and GPT in 3. In the levetiracetam group, no GGT elevation was recorded; four children had mild elevations (GOT in 2, GPT in 2), and 31 of 35 (88.6%) had normal enzymes, the highest proportion of the three groups.

Table 3. Overall frequency of liver enzyme abnormalities

Group	Any abnormality, n (%)	Normal, n (%)
Valproate (n=45)	15 (33.3%)	30 (66.7%)
Carbamazepine (n=40)	19 (47.5%)	21 (52.5%)

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Levetiracetam (n=35)	4 (11.4%)	31 (88.6%)
Total (N=120)	38 (31.7%)	82 (68.3%)

The difference between groups was statistically significant (chi-square = 11.3, df = 2, p = 0.003).

Discussion

This retrospective study evaluated liver enzyme findings in children receiving valproate, carbamazepine, or levetiracetam monotherapy. The frequency and pattern of biochemical abnormalities differed between treatment groups, with the highest proportion of abnormal results in the carbamazepine group (47.5%), followed by valproate (33.3%) and levetiracetam (11.4%).

In the valproate group, GOT elevation was the most frequently reported individual abnormality. Valproate is known to be associated with hepatic adverse effects, and monitoring of liver biochemistry is clinically important, particularly during treatment initiation and in patients with additional risk factors [2,3].

In the carbamazepine group, GOT and GGT elevations were each reported in six children. Carbamazepine can induce hepatic enzymes, and some biochemical changes may reflect enzyme induction rather than hepatocellular injury [4,5]. This is consistent with previous findings suggesting that isolated GGT elevations in patients on carbamazepine are often transient and related to enzyme induction [11,14]. The clinical significance of an isolated GGT elevation should therefore be interpreted together with other liver tests, symptoms and the degree of elevation.

In the levetiracetam group, no GGT elevations were reported, and 31 of 35 children had normal enzymes. This is consistent with the generally favorable hepatic safety profile of levetiracetam [6,7], as supported by recent systematic reviews highlighting its safety in pediatric populations [12], although the sample size is limited and the absence of GGT elevations in this cohort does not establish that the drug carries no risk of liver injury.

Strengths and limitations

An important strength is the availability of baseline liver enzyme results before treatment, allowing later abnormalities to be assessed against pretreatment values. Limitations include the retrospective design, possible missing measurements, differences in follow-up duration, and variation in testing frequency. The magnitude of elevation, drug dose, time to onset, and clinical manifestations were not analyzed, and isolated biochemical abnormalities could not be distinguished from clinically significant drug-induced liver injury. The sample size was small, and the groups were not randomized, so confounding by indication, age, and treatment duration cannot be excluded. Pairwise and adjusted analyses were not possible with the available aggregate counts.

Conclusion

Mild liver enzyme elevations were observed with all three antiseizure medications, most often with carbamazepine and valproate and least often with levetiracetam, in which no GGT elevations occurred. These findings support routine liver enzyme monitoring in children on these drugs. Larger prospective studies with dose, duration, magnitude of elevation, and clinical outcomes are needed before drawing firm conclusions about comparative hepatic safety.

Conflict of interest

The author declares no conflict of interest.

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