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ORIGINAL RESEARCH
Pediatric Cardiology

Levetiracetam compared with carbamazepine as monotherapy in children with focal epilepsy

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ABSTRACT

Objective: Carbamazepine (CBZ) has traditionally been used as a first-line agent for pediatric focal epilepsy, yet tolerability issues and potential drug–drug interactions have encouraged the broader use of newer antiseizure medications, including levetiracetam (LEV). Robust head-to-head data comparing LEV with CBZ as initial monotherapy in children remain scarce. In this study, LEV monotherapy was compared with CBZ, a well-established treatment for focal epilepsy, and its efficacy in seizure control and tolerability were evaluated.

Material and Methods: In this prospective, randomized clinical study, 80 children aged 2–14 years with newly diagnosed focal epilepsy meeting International League Against Epilepsy criteria were allocated to LEV (n=37) or CBZ (n=43) monotherapy. Seizure frequency, treatment response, drug resistance, and adverse events were evaluated at baseline and at 3, 6, and 12 months.

Results: Baseline demographic and clinical variables were comparable between groups. Seizure frequency declined significantly over time in both treatment arms. At 3 months, a numerically greater reduction was observed in the LEV group, although the between-group difference was not statistically significant ($p>0.05$); outcomes were similar at 6 months. By 12 months, seizure reduction was achieved in all patients receiving CBZ and in 86.7% of those receiving LEV, without a significant difference between groups ($p=0.155$). Drug resistance rates decreased across follow-up and did not differ significantly at 12 months. Adverse events occurred more often with CBZ, most notably somnolence and cutaneous reactions, whereas behavioral effects, particularly irritability, were more frequent with LEV. No serious hematologic or renal toxicity and no persistent hepatic adverse events were detected.

Conclusion: As initial monotherapy for newly diagnosed focal epilepsy in children, LEV and CBZ show comparable seizure-control efficacy. LEV may offer better overall tolerability, although behavioral symptoms require close surveillance. Both agents represent reasonable first-line options, with selection individualized according to patient-specific risk–benefit considerations.

Keywords: Carbamazepine; children; focal epilepsy; levetiracetam; monotherapy; randomized clinical trial.

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Fokal epilepsili çocuklarda monoterapi olarak levetirasetam ve karbamazepinin karşılaştırılması

ÖZET

Amaç: Karbamazepin (CBZ), pediatrik fokal epilepside geleneksel olarak birinci basamak tedavi olarak kullanılmaktadır; ancak tolere edilebilirlik sorunları ve olası ilaç–ilaç etkileşimleri, levetirasetam (LEV) dahil olmak üzere daha yeni nöbet ilaçlarının kullanımını teşvik etmiştir. Çocuklarda başlangıç monoterapisi olarak LEV ile CBZ'yi doğrudan karşılaştıran güçlü veriler ise sınırlıdır. Bu çalışmada, LEV monoterapisi, fokal epilepside iyi tanımlanmış bir tedavi olan CBZ ile karşılaştırılmış, nöbet kontrolündeki etkinliği ve tolere edilebilirliği değerlendirilmiştir.

Gereç ve Yöntemler: Bu prospektif, randomize klinik çalışmada, Uluslararası Epilepsi ile Savaş Birliği kriterlerine göre yeni tanı almış, fokal epilepsili 2–14 yaş arasındaki 80 çocuk LEV (n=37) veya CBZ (n=43) monoterapisi almak üzere randomize edilmiştir. Nöbet sıklığı, tedavi yanıtı, ilaç direnci ve advers olaylar başlangıçta ve 3., 6. ve 12. aylarda değerlendirilmiştir.

Bulgular: Başlangıçtaki demografik ve klinik özellikler açısından gruplar benzerdi. Nöbet sıklığı her iki tedavi kolunda da zaman içinde anlamlı biçimde azaldı. Üçüncü ayda LEV grubunda sayısal olarak daha belirgin bir azalma gözlenmiş olmakla birlikte, gruplar arasındaki fark istatistiksel olarak anlamlı değildi (p>0,05); altıncı ayda da benzer sonuçlar elde edildi. On ikinci ay sonunda CBZ alan tüm hastalarda ve LEV alan hastaların %86,7'sinde nöbet sıklığında azalma sağlandı; ancak iki grup arasında anlamlı fark saptanmadı (p=0,155). Takip süresince ilaç direnci oranlarında azalma görüldü ve 12. ayda gruplar arasında anlamlı farklılık bulunmadı. Advers olaylar CBZ grubunda daha sık gözlenmiş olup, özellikle somnolans ve kutanöz reaksiyonlar ön plandaydı. LEV grubunda ise irritabilite başta olmak üzere davranışsal yan etkiler daha sık bildirildi. Hiçbir hastada ciddi hematolojik ya da renal toksisite ve kalıcı hepatik advers etki saptanmadı.

Tartışma: Yeni tanı almış pediyatrik fokal epilepside başlangıç monoterapisi olarak levetirasetam ve karbamazepin benzer nöbet kontrolü etkinliği göstermektedir. Levetirasetam genel tolere edilebilirlik açısından bazı avantajlar sağlayabilir; ancak davranışsal yan etkiler açısından dikkatli izlem gereklidir. Her iki ajan da birinci basamak tedavi seçeneği olarak değerlendirilebilir ve tedavi seçimi hasta özellikleri ile risk–yarar dengesi göz önünde bulundurularak bireyselleştirilmelidir.

Anahtar Kelimeler: Çocuk; fokal epilepsi; karbamazepin; levetirasetam; monoterapi; randomize klinik çalışma.

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INTRODUCTION

Epidemiological data suggest that approximately 4–10% of children experience at least one seizure (febrile or afebrile) by 16 years of age. The cumulative lifetime incidence of epilepsy is estimated at around 3%, with more than half of all cases presenting during childhood. The annual prevalence ranges between 0.5% and 1.0% (1). The primary goal of epilepsy management in children is to achieve sustained seizure freedom while preserving normal growth, neurodevelopment, and overall systemic maturation (2).

Antiseizure medications (ASMs) are commonly categorized into first-generation and newer-generation agents (3, 4). Despite the availability of numerous ASMs, nearly half of patients fail to achieve sufficient seizure control with initial monotherapy, and approximately 35% eventually require alternative or more effective treatment strategies (4). In addition, the broad pharmacological profiles of many ASMs and their potential for significant adverse effects make long-term management challenging. Therefore, there remains a continued need for therapies that provide improved efficacy while maintaining better tolerability.

Since its introduction to clinical practice in the early 2000s, levetiracetam (LEV) has been widely used as a newer-generation ASM with broad efficacy and reported safety in various epilepsy syndromes (5, 6). Among first-generation ASMs, carbamazepine (CBZ) has long been considered a first-line treatment for focal epilepsy. However, due to its considerable adverse-effect profile and frequent drug–drug interactions, its use as long-term monotherapy for focal seizures has become less favored in recent years (7, 8). By keeping voltage-gated sodium channels in an inactivated configuration for longer, CBZ decreases high-frequency, repetitive firing in postsynaptic neurons, which underlies its antiepileptic activity. In addition, it inhibits presynaptic neurotransmitter release, leading to suppression of synaptic transmission (9, 10). Common adverse effects of CBZ include somnolence, nausea, vomiting, ataxia, and headache, as well as hepatic and hematological complications, which are typically dose-dependent and more frequently observed during the initial treatment period. Accordingly, regular clinical assessments and laboratory follow-up are required (11).

Levetiracetam was first introduced in 1999 as an effective second-generation ASM and was initially approved as adjunctive therapy for focal seizures in adolescents (12). Its mechanism of action involves binding to synaptic vesicle protein 2A, thereby modulating neurotransmitter release through inhibition of calcium mobilization from intracellular neuronal stores (13). Data derived from double-blind, placebo-controlled studies indicate the efficacy of LEV in both adult and pediatric populations (14, 15). Nevertheless, its safety and efficacy in infants remain less clearly established (16). Although LEV monotherapy or add-on therapy has been associated with mental health-related adverse effects, including mood symptoms, irritability, and paranoid ideation, in a subset of adult patients, it has also been reported to decrease seizure burden and improve quality of life (13, 17). Major advantages of LEV include twice-daily dosing, a favorable tolerability profile, minimal drug–drug interactions, and no requirement for routine serum level monitoring, all of which support its widespread use in epilepsy management (18).

A growing body of literature has focused on LEV monotherapy in childhood epilepsies, including both focal and generalized seizure types (19). Smaller studies have suggested that LEV may be effective when transitioning patients from polytherapy to monotherapy (20). However, randomized controlled trials (RCTs) directly comparing LEV and CBZ monotherapy in children with focal seizures remain limited. Available evidence suggests that LEV monotherapy demonstrates efficacy comparable to that of other ASMs, particularly CBZ, while potentially offering a more favorable adverse-effect profile. Nevertheless, larger-scale RCTs have been recommended to more accurately assess both efficacy and tolerability (21, 22).

In light of the limited number of comparative studies and the clinical importance of selecting the most appropriate ASM for focal seizures in childhood, we conducted this prospective, randomized study to evaluate and compare the efficacy and adverse-effect profiles of LEV and CBZ as monotherapy.

MATERIAL AND METHODS

Ethical Approval

Ethical approval for this study was obtained from the Şişli Etfal Training and Research Hospital Ethics Committee on May 11, 2009 (approval no. 71). The study was conducted in accordance with the ethical principles of the Declaration of Helsinki.

Study Population and Eligibility Criteria

This study enrolled 80 children aged 2–14 years with newly diagnosed focal epilepsy. All participants had experienced at least two unprovoked seizure events, with an interval of over 24 hours between episodes, and fulfilled the diagnostic criteria of the International League Against Epilepsy (ILAE) (23). Additional inclusion criteria were a normal brain magnetic resonance imaging (MRI) study and confirmation of the diagnosis by electroencephalography (EEG).

Exclusion criteria comprised seizure types not classified as focal according to ILAE definitions, a history of brain injury within the preceding 3 months, known renal, hepatic, or hematological disorders, prior use of antiseizure or psychiatric medications, and refusal to participate by parents or legal guardians.

Enrollment and Baseline Assessment

Patients were selected based on clinical history and neurological examination. Participation was voluntary, and written informed consent was obtained from parents or legal guardians before enrollment. Following neurological examination and EEG evaluation, children with unprovoked seizures were identified. At study entry, a structured questionnaire was completed to collect demographic data and seizure-related characteristics, including seizure type, seizure frequency, seizure duration, and the presence of adverse effects.

All patients underwent baseline EEG, complete blood count (CBC), liver function tests (LFTs), serum creatinine (Cr), and blood urea nitrogen (BUN) assessments as part of the standard clinical evaluation.

Randomization and Treatment Protocol

After confirming eligibility, participants were randomized to one of two treatment groups: the levetiracetam group (LEV; n=37) or the carbamazepine group (CBZ; n=43). In both groups, medications were administered twice daily in either syrup or tablet form, according to the child's age and parental preference.

In the CBZ group, treatment was initiated at a dose of 10 mg/kg/day and increased by 10 mg/kg/day at weekly intervals until the standard maintenance dose of 30 mg/kg/day was reached and maintained. In the LEV group, treatment was similarly initiated at 10 mg/kg/day and titrated weekly by 10 mg/kg/day to a standard dose of 30 mg/kg/day. The maximum allowed doses were 40 mg/kg/day for LEV and 35 mg/kg/day for CBZ (24, 25).

The treatment strategy consisted of dose titration until seizure freedom was achieved. Parents were informed in advance about potential adverse effects and were instructed to maintain a seizure diary documenting seizure characteristics, seizure frequency, seizure duration, medication adherence, and possible adverse events (e.g., somnolence, agitation, nausea, and dermatological reactions).

Follow-up and Outcome Assessment

Parents were advised to contact the study team immediately in the event of serious adverse effects outside scheduled visits. Physical examinations were carried out at each follow-up visit to evaluate potential adverse effects, and routine laboratory tests (CBC and liver and renal function tests) were repeated. Seizure diaries were reviewed at each visit, and relevant data were recorded.

Patients who required discontinuation of treatment due to serious adverse effects or at the treating physician's discretion were withdrawn from the study. After the 3rd-, 6th-, and 12th-month visits, physical examination findings, EEG results, seizure frequency, and adverse-effect rates were compared between the two treatment groups.

Table 1. Comparison of groups according to demographic characteristics

	Levetiracetam (n=37)	Carbamazepine (n=43)	p
Age, (Mean±SD)	8.66±3.45	8.02±3.52	0.417*
Body weight (kg) (Mean±SD)	25.63±10.72	26.09±11.01	0.852*
Gender, n (%)			0.591**
Female	15 (40.5)	20 (46.5)	
Male	22 (59.5)	23 (53.5)	

SD: Standard deviation; *: Student's t-Test; **: Chi-Square Test.

Seizure characteristics, seizure frequency, seizure duration, and adverse effects were evaluated at baseline and at the 3-, 6-, and 12-month follow-up visits. The analyses were conducted using a per-protocol approach, including only patients with available data at the relevant follow-up visit.

Statistical Analysis

Statistical analyses were performed using NCSS 2007 (Number Cruncher Statistical System) and PASS 2008 (Utah, USA). Continuous variables are summarized as mean±standard deviation. Between-group comparisons of independent samples were carried out using Student's t test for normally distributed data and the Mann–Whitney U test when distributional assumptions were not satisfied. Within-group (paired) comparisons were assessed with the paired t test for normally distributed variables and the Wilcoxon signed-rank test for non-normally distributed variables. Categorical variables were compared using Pearson's chi-square test, Fisher's exact test, or, where applicable, the McNemar test. All tests were two-tailed, and statistical significance was set at $p<0.05$.

RESULTS

Study Population and Baseline Characteristics

A total of 80 children were enrolled during the study period and subsequently randomized to the levetiracetam (LEV, n=37) or carbamazepine (CBZ, n=43) groups. During the follow-up period, some patients had missing data or were lost to follow-up; therefore, analyses were performed using the data available at the relevant time points. No statistically significant between-group differences were observed in terms of baseline demographic or clinical characteristics.

Based on clinical history, a broad spectrum of focal seizure types was observed, including focal aware seizures, focal seizures with impaired awareness, focal motor seizures, focal non-motor seizures, and focal to bilateral tonic–clonic seizures. In some patients, precise seizure classification was not possible because seizures were infrequent, occurred exclusively during sleep, were unwitnessed, or were reported by unreliable observers. Nevertheless, no specific epilepsy syndrome or structural abnormality was identified in any patient, including those classified as non-responders.

Table 2. Treatment outcome measures

Seizure frequency	Levetiracetam n (%)	Carbamazepine n (%)	p
Month 3			0.061
Decrease	36 (97.3)	36 (83.7)	
Increase	1 (2.7)	1 (2.7)	
No change	0 (0)	6 (14.0)	
Month 6			0.962
Decrease	30 (81.1)	35 (81.4)	
Increase	4 (10.8)	4 (9.3)	
No change	3 (8.1)	4 (9.3)	
Month 12			0.155
Decrease	26 (86.7)	26 (100)	
Increase	3 (10.0)	0 (0)	
No change	1 (3.3)	0 (0)	

Chi-Square Test.

Patient Characteristics

Prior to the initiation of monotherapy, patients had been treated exclusively with benzodiazepines for acute postictal management, and no other antiseizure medications had been administered. The two treatment groups were comparable with respect to baseline demographic characteristics (Table 1). However, only 70% of the patients were able to complete the 12-month evaluation.

Treatment Efficacy

Seizure incidence between scheduled follow-up visits was compared between treatment groups at 3, 6, and 12 months (Table 2). At the 3-month assessment, patients receiving LEV showed a numerically greater reduction in seizure frequency than those treated with CBZ; however, the between-group difference did not reach statistical significance ($p>0.05$). By month 6, seizure frequency had decreased to a comparable degree in both groups ($p>0.05$). At 12 months, a reduction in seizure frequency was observed in 26/30 patients (86.7%) in the LEV group and in 26/26 patients (100%) in the CBZ group; however, the observed difference did not achieve statistical significance ($p=0.155$).

Table 3. Evaluation of treatment resistance

Drug resistance	Levetiracetam n (%)	Carbamazepine n (%)	p
Month 6			0.240*
Absent	29 (%78)	39 (%90)	
Present	8 (%22)	4 (%10)	
Month 12			0.407*
Absent	28 (%93)	26 (%100)	
Present	2 (%7)	0 (%0)	
Treatment Outcomes at Month 6 vs. Month 12			0.317**

*: Chi-Square Test; **: McNemar Test.

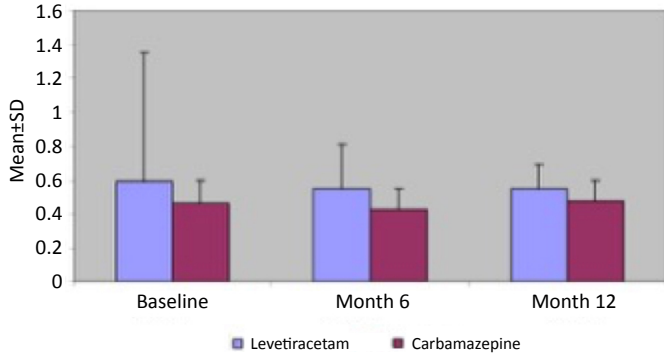

Figure 1. Distribution of serum creatinine levels.

Because of loss to follow-up and missing data, the number of evaluable patients differed across follow-up visits, particularly at month 12.

Assessment of Treatment Resistance

In this study, treatment resistance was defined based on clinical management decisions, specifically discontinuation of the drug or the addition of another medication to the treatment regimen.

The evaluation of treatment resistance is presented in Table 3. No statistically significant difference was observed between the LEV and CBZ groups in terms of the distribution of treatment resistance at 6 months (p=0.240). Similarly, no significant difference was found between the groups at 12 months (p=0.407). In the within-group analysis, the distribution of treatment resistance between the 6- and 12-month assessments was compared using the McNemar test, and no significant change was detected (p=0.317).

Although the proportion of patients classified as treatment-resistant appeared lower at 12 months than at 6 months, this comparison should be interpreted cautiously because the number of patients with available follow-up data differed between time points.

Treatment-related Adverse Events

No hematological or renal complications were reported in either group. Hepatic complications were observed as elevations in liver enzyme levels exceeding three times the upper limit of normal during the first month of treatment. Liver function tests returned to normal within one week after discontinuation of the medication.

Transient liver enzyme elevations were observed during the first month in some patients and resolved after drug discontinuation. No persistent hepatic, hematological, or renal complications were detected during long-term follow-up. Serum creatinine levels remained stable throughout the study period in the LEV group. In the CBZ group, a mild but statistically significant decrease in creatinine levels was observed at 6 months; however, this difference became clinically negligible by the 12-month follow-up (Fig. 1). Overall, both medications appeared safe with respect to long-term renal function.

In the LEV group, irritability was the most commonly reported adverse event, affecting 36% of patients at the 12-month assessment. Inattention and social withdrawal were infrequent throughout follow-up and were no longer observed in the LEV group by month 12. At 3, 6, and 12 months, the distribution of psychological adverse effects differed significantly between the LEV and CBZ groups (p<0.05) (Table 4).

DISCUSSION

Levetiracetam (LEV) has emerged as a promising first-line antiseizure medication for newly diagnosed epilepsy due to its rapid and sustained efficacy in both adults and children with focal-onset seizures, favorable tolerability profile, predictable

Table 4. Distribution of behavioral adverse effects during follow-up

	3-month		6-month		12-month	
	LEV (n=37)	CBZ (n=43)	LEV (n=37)	CBZ (n=43)	LEV (n=30)	CBZ (n=26)
Irritability	13 (35.1)	6 (13.9)	12 (32.4)	3 (6.9)	11 (36.6)	2 (7.6)
Inattention	1 (2.7)	1 (2.3)	1 (2.7)	1 (2.3)	0 (0)	1 (3.8)
Social withdrawal	1 (2.7)	1 (2.3)	1 (2.7)	1 (2.3)	0 (0)	0 (0)
p	**0.036**		**0.007**		**0.021**	

Fisher's exact test. LEV: Levetiracetam; CBZ: Carbamazepine.

pharmacokinetics, absence of enzyme-inducing properties, and limited potential for clinically relevant drug interactions. Despite these advantages, data regarding the efficacy and safety of LEV as monotherapy in childhood epilepsies remain limited, as most available studies have evaluated LEV primarily as adjunctive therapy. Consequently, evidence supporting its use as initial monotherapy in pediatric focal epilepsy is still relatively scarce (26–29).

In this study, we evaluated levetiracetam (LEV) and carbamazepine (CBZ) as first-line monotherapy in children with newly diagnosed focal epilepsy, with particular emphasis on seizure-related outcomes and tolerability. Overall, seizure control achieved with LEV was comparable to that observed with CBZ. Although seizure control appeared numerically higher in the LEV group across the first 3 months, the observed between-group difference did not achieve statistical significance.

Consistent with our findings, previous studies have reported that LEV and CBZ monotherapies demonstrate comparable efficacy and are generally well tolerated for treating pediatric focal epilepsy. In contrast, one study suggested that LEV may be more effective than CBZ in achieving seizure control in childhood focal epilepsies, which is not in agreement with our results (30). Moreover, a randomized controlled clinical trial conducted in adult patients observed no statistically significant efficacy difference between LEV and CBZ as therapy for focal seizures; however, seizure freedom was achieved more rapidly and was sustained for longer durations in adults (31). These more rapid and pronounced treatment responses in adults may be attributable to age-related differences in metabolic rates and physiological characteristics when compared with pediatric populations (21, 32).

Several studies conducted in both adult and pediatric populations have suggested that LEV monotherapy may be effective even at relatively low doses in controlling focal seizures (33–35). In our cohort, treatment with LEV was initiated at 20 mg/kg/day, with dose escalation permitted up to 40 mg/kg/day until seizure freedom was achieved. Notably, none of the patients required discontinuation of LEV due to serious adverse events.

A retrospective chart review evaluating treatment failure rates among children and adolescents receiving LEV, valproate, or oxcarbazepine monotherapy reported higher failure rates with LEV as initial treatment compared with the other agents. This was attributed to insufficient efficacy in generalized and focal epilepsies, respectively. In addition, findings from the SANAD study did not support the use of LEV or zonisamide as first-line treatment in focal epilepsy, instead recommending lamotrigine as the preferred initial therapy. Another study involving 52 patients aged 6 months to 16 years with partial or generalized epilepsy noted a >50% seizure-frequency reduction in roughly half of the cohort and a 25–50% reduction in the remaining half, while in two patients, the drug was withdrawn because of adverse reactions (36–38). The heterogeneity of these results may be explained by methodological differences across studies. In particular, the retrospective design of many studies precluded randomization, and the wide range of LEV doses used in focal epilepsy (27.1–108 mg/kg/day) limited meaningful comparisons of treatment efficacy. In contrast, in our study, a reduction exceeding 50% in seizure frequency was attained by 97.3% of patients at 3 months, 81.1% at 6 months, and 86.7% after one year of follow-up in the LEV group. These findings support LEV as an effective and safe monotherapy option in childhood focal epilepsy. Long-term follow-up revealed low resistance rates and high overall response rates with both medications. Although resistance appeared slightly higher in the LEV group early in treatment, this difference was no longer evident by the 12-month follow-up.

A population-based real-world study using linked healthcare databases from Ontario reported an incidence of acute kidney injury of 30 cases per 10,000 patient-months within the first 30 days after LEV initiation. Similarly, a large claims-based study in the United States demonstrated only a marginal increase in the risk of acute renal failure following LEV initiation compared with other antiseizure medications in previously untreated patients (39, 40) Both LEV and CBZ appeared to be safe with respect to gastrointestinal and renal function during long-term use. Neither medication exerted a clinically significant effect on serum creatinine levels in our cohort.

LEV is generally well tolerated, with behavioral changes and irritability being the most commonly reported adverse effects. The lowest incidence of adverse effects has been reported at doses around 40 mg/kg/day. Psychomotor slowing has been described at higher doses (approximately 65 mg/kg/day) and has been shown to resolve with dose reduction to 50 mg/kg/day. Previous studies have reported significantly higher rates of irritability in LEV-treated patients compared with those receiving CBZ, whereas somnolence has been more frequently observed in the CBZ group (21, 30, 38). In our study, behavioral changes and irritability were also the most frequently observed adverse effects in the LEV group, and the distribution of psychological adverse effects at 3, 6, and 12 months differed significantly between treatment groups ($p<0.05$). As the maximum LEV dose used in our cohort was 30 mg/kg/day, psychomotor slowing was not observed. Importantly, none of our patients discontinued treatment due to adverse effects, underscoring the importance of close behavioral monitoring during LEV therapy.

The strengths of this study include its randomized design, the relatively limited number of randomized clinical trials conducted in pediatric focal epilepsy, the use of a single standardized CBZ formulation, and the achievement of homogeneity between treatment groups. However, several limitations should be acknowledged, including the inability to measure serum levels of the study drugs LEV and CBZ and the lack of systematic assessment of psychological variables such as depression and anxiety. Future prospective research with larger cohorts, extended follow-up, and a more comprehensive assessment of psychological outcomes is needed to support stronger, more definitive clinical conclusions.

CONCLUSION

Our study demonstrates that LEV and CBZ monotherapies exhibit comparable efficacy and safety profiles in children recently diagnosed with focal epilepsy. The favorable tolerability and absence of serious adverse effects associated with LEV support its use as a safe treatment option in pediatric patients. Although careful monitoring for behavioral adverse effects is recommended, both medications appear to be safe with respect to renal and hepatic function during long-term use. Larger, long-term prospective investigations are required to corroborate our observations and build on these results.

Ethics Committee Approval: This study was approved by the Ethics Committee of Şişli Etfal Training and Research Hospital (Date: May 11, 2009, Decision No. 71).

Informed Consent: Written informed consent was obtained from the patient(s) and/or their legal guardian(s) for participation and publication.

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