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Original Research Article

Comparison of Effectiveness Between Brivaracetam and Levetiracetam in New Onset Focal Epilepsy in Children

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Abstract

Background: Pediatric focal epilepsy is a common neurological disorder that requires early and effective treatment to prevent long-term cognitive and psychosocial consequences. Levetiracetam (LEV) is widely used as a first-line antiseizure medication, while brivaracetam (BRV), a newer SV2A ligand with higher binding affinity, has limited comparative data in children. ***Aim:*** Our aim is to compare the effectiveness and tolerability of BRV and LEV in children with newly diagnosed focal epilepsy. ***Materials and Methods:*** This retrospective comparative study was conducted at Mount Adora Hospital, Sylhet, Bangladesh, between July 2024 and June 2025. A total of 62 children aged 1–18 years with new-onset focal epilepsy were included, with 31 receiving LEV and 31 receiving BRV. Seizure frequency and treatment response were assessed at 2 weeks, 1 month, and 3 months. Common adverse effects of both drugs were also documented. ***Results:*** After 3 months, the mean seizure frequency was significantly lower in the BRV group (0.42) compared to the LEV group (1.58; $p<0.001$). Complete response was achieved in 87% of BRV patients versus 61% of LEV patients ($p=0.042$). Both drugs were generally well tolerated. Somnolence was reported in 12.9% of LEV and 9.7% of BRV patients. Behavioral adverse effects were more frequent with BRV (hyperactivity 19.4%, irritability 12.9%) compared to LEV (hyperactivity 3.2%, no irritability). ***Conclusion:*** Brivaracetam demonstrated superior seizure control efficacy as compared to levetiracetam in children with new-onset focal epilepsy, although behavioral adverse effects were more common.

Keywords: Brivaracetam; Levetiracetam; epilepsy; New onset focal epilepsy; Bangladesh; Children.

INTRODUCTION

Epilepsy is one of the most common neurological disorders worldwide, affecting an estimated 50 million people [1,2]. Importantly, over 80% of people with epilepsy live in low- and middle-income countries [1,2]. In children, the prevalence of epilepsy is approximately 0.5–1%, with incidence peaking in infancy and early childhood [1,3]. Pediatric epilepsy carries a heavy clinical burden: recurrent seizures, neurocognitive and behavioral comorbidities (e.g. attention-deficit and learning impairments) and stigma all impact quality of life [1,4]. Up to 28–70% of children with epilepsy have co-existing attention-deficit/hyperactivity disorder, and cognitive deficits (e.g. impaired working memory, processing speed) are common [4]. Early and effective seizure control is therefore critical to prevent developmental delays and improve psychosocial outcomes.

Among seizure types, focal-onset (partial) seizures are a major subtype of childhood epilepsy. Focal epilepsy arises from abnormal neuronal activity in a localized brain region, which may then spread to other areas [1]. In childhood cohorts, focal seizures account for a substantial fraction of cases. For example, a hospital-based study in Bangladesh found that ~25% of children with epilepsy had focal (partial) seizures [5]. More

broadly, focal seizures often result from structural lesions or genetic syndromes, and they require tailored management [6,7]. Globally, the median prevalence of epilepsy in Asia (~6 per 1000) is comparable to developed regions [1]. In South-East Asia, WHO estimates the prevalence is ~1% (about 15 million affected) [8]. In Bangladesh, recent household surveys indicate an overall epilepsy prevalence around 8–9 per 1000 (with even higher rates in children) [9]. Given Bangladesh's population (~170 million), this implies 1.3–1.5 million people with epilepsy [9,10]. Unfortunately, epilepsy care in Bangladesh is challenged by a large treatment gap: WHO reports suggest only 10–20% of patients receive appropriate AED therapy [8,9]. In rural and resource-limited areas, sociocultural beliefs and lack of specialist services further hinder optimal management [9,10]. Thus, improving epilepsy outcomes, especially for children, is a pressing local public health priority [1,9].

Both global and regional guidelines emphasize the use of effective, well-tolerated antiseizure medications (ASMs) in pediatric focal epilepsy. Levetiracetam (LEV) is a second-generation ASM that is widely used in children. It is approved as adjunctive therapy for focal and generalized seizures, and as monotherapy in older children and adolescents. LEV has broad-spectrum efficacy, minimal drug–drug interactions, and is attractive for pediatric use [11]. Open-label and observational pediatric studies report that LEV can achieve a ≥50% seizure reduction in roughly 20–60% of treated children, with a 50–65% achieving near-complete remission at 6–12 months [11]. In our study, LEV achieved a complete response (≥90% seizure reduction) in ~61% of new-onset focal epilepsy cases at 3 months. These efficacy rates are consistent with prior cohorts of children with focal epilepsy [11]. The common adverse effects of LEV include behavioral disturbances (irritability, hyperactivity) and somnolence [11]. A systematic review found that approximately half of pediatric patients experience any adverse event on LEV, with behavioural problems (10.9%) and somnolence (8.4%) being most prevalent [12]. Children on polytherapy have higher risk of side effects and treatment discontinuation [12]. Despite this, LEV is generally well-tolerated, and is recommended as a first-line agent for many pediatric focal epilepsies [11,12].

Brivaracetam (BRV) is a newer ASD, approved for focal-onset seizures in adults (FDA 2016) and children ≥4 years (FDA 2018) [3,6]. It is the high-affinity propyl analogue of LEV, sharing the same mechanism (binding to synaptic vesicle protein 2A, SV2A) but with 10–30-fold higher affinity [3,6]. BRV enters the brain more readily and has no clinically relevant interactions, allowing fixed dosing without titration [6,13]. In adult trials and registries, BRV as adjunctive therapy has shown promising efficacy in refractory focal seizures. In pediatric epilepsy, evidence is just emerging. A recent meta-analysis of ~500 children reported that add-on BRV achieved ≥50% seizure reduction in about 35% of cases, with ~18% seizure freedom; the retention rate was ~78% [3]. BRV's safety profile in children was good, with somnolence (~9%) and behavioral symptoms (~12%) as the most common side effects [3]. These figures suggest BRV is broadly comparable to LEV in pediatric efficacy but possibly with fewer drug interactions [3,13]. However, direct comparisons of BRV versus LEV in children are scarce, especially in South Asia.

No published studies have directly compared BRV and LEV in newly diagnosed pediatric focal epilepsy. Globally, most data on BRV come from adjunctive therapy trials or case series in drug-resistant epilepsy [3,6]. In Bangladesh and neighboring countries, pediatric epilepsy research is limited. A recent consensus guideline from Bangladesh highlighted that many older ASMs (phenobarbital, carbamazepine) remain first-line due to cost, with newer ASMs underutilized [9]. Given the theoretical advantages of BRV (higher potency, easier dosing) and LEV's established role, a head-to-head evaluation of their effectiveness in children is clinically important.

This study aimed to compare the effectiveness and tolerability of BRV and LEV as first-line therapy in Bangladeshi children (1–18 years) with newly diagnosed focal epilepsy. We specifically measured changes in seizure frequency and rates of complete or partial response at 3 months.

MATERIALS AND METHODS

This retrospective comparative study was conducted at Mount Adora Hospital, Sylhet, Bangladesh, over a 12-month period from July 2024 to June 2025. The study included children aged 1–18 years who were newly diagnosed with focal epilepsy. A total of 62 eligible patients were enrolled and divided equally into two groups: 31 patients received Levetiracetam and 31 patients received Brivaracetam. Participants were selected using a purposive sampling method.

Children were included if they had new-onset focal epilepsy confirmed by clinical assessment and electroencephalography (EEG) and had not received prior antiepileptic therapy. Exclusion criteria were generalized epilepsy, significant hepatic or renal dysfunction, and any known hypersensitivity to either study drug.

Key variables included demographic characteristics, baseline seizure frequency, and treatment response at 2 weeks, 1 month, and 3 months. Treatment response was categorized into four groups based on percentage reduction in seizure frequency compared to baseline:

- **Complete response:** 100% reduction in seizure frequency

- **Good response:** ≥75% reduction in seizure frequency
- **Fair response:** 50–74% reduction in seizure frequency
- **No response:** <50% reduction in seizure frequency or unchanged/worsened seizure activity

All patients were treated using a standardized hospital protocol, and seizure frequency as well as clinical status were recorded during follow-up visits. Data were collected using a structured case record form. Mean seizure frequency before and after treatment was compared between the two drug groups using the independent samples t-test. Categorical treatment-response outcomes were compared using the Chi-square test. A p-value of <0.05 was considered statistically significant.

Ethical approval for this study was obtained from the institutional authority of Mount Adora Hospital, Sylhet. Informed written consent was obtained from parents or legal guardians prior to participation in this study.

RESULTS

A total of 62 children with new onset focal epilepsy were included in the study, with 31 patients receiving Levetiracetam and 31 patients receiving Brivaracetam. The mean age was 5.67 ± 3.69 years; 27 (43.5%) were below 5 years and 35 (56.5%) were 5 years or older. Males were 39 (62.9%) and females were 23 (37.1%), with a male-to-female ratio of 1.7:1 (Table 1).

The mean frequency of seizures before treatment was 9.58 in the Levetiracetam group and 9.71 in the Brivaracetam group (p=0.611). At 2 weeks, mean seizure frequency was 3.55 in the Levetiracetam group and 3.48 in the Brivaracetam group (p=0.784). At 1 month, it was 1.97 and 1.71 respectively (p=0.310). At 3 months, the mean frequency was 1.58 in the Levetiracetam group and 0.42 in the Brivaracetam group (p<0.001) (Table 2).

Regarding treatment response, after 2 weeks, complete response was observed in 16 patients in the Levetiracetam group and 19 in the Brivaracetam group. At 1-month, complete response was noted in 19 and 23 patients respectively. At 3 months, complete response was achieved in 19 patients in the Levetiracetam group and 27 in the Brivaracetam group (Table 3). Hyperactivity was more frequent in the brivaracetam group (19.4%) compared to the levetiracetam group (3.2%). Somnolence occurred in 12.9% of children on levetiracetam and 9.7% on brivaracetam. Irritability was observed in 12.9% of patients treated with brivaracetam, while none was reported among those receiving levetiracetam (Table 4).

Table 1: Demographic characteristics of the study participants

	Category	**Frequency (%)**
Age	<5 years	27 (43.5%)
	≥5 years	35 (56.5%)
	Mean Age (±SD)	5.67 (±3.69) years
Sex	Male	39 (62.9%)
	Female	23 (37.1%)
	M:F ratio	1.70:1

Table 2: Mean Frequency of Seizures before and after treatment

Mean Frequency of Seizures	**Levetiracetam (n=31)**	**Brivaracetam (n=31)**	**p-value**
Before Treatment	9.58	9.71	0.611*
Two weeks after treatment	3.55	3.48	0.784*
One month after treatment	1.97	1.71	0.310*
Three months after treatment	1.58	0.42	<0.001*

* *Independent samples t-test* was applied for comparison between Levetiracetam and Brivaracetam groups

Table 3: Treatment Response of both groups

	Response type	**Levetiracetam (n=31)**	**Brivaracetam (n=31)**	**p-value**
Treatment Response after 2 weeks	Complete	16 (51.6%)	19 (61.3%)	0.608*
	Good	6 (19.4%)	7 (22.6%)	1.0*
	Fair	5 (16.1%)	3 (9.7%)	0.705*
	No Response	4 (12.9%)	2 (6.5%)	0.668*
Treatment Response after 1 month	Complete	19 (61.3%)	23 (74.1%)	0.415*
	Good	6 (19.4%)	6 (19.4%)	1.0*
	Fair	4 (12.9%)	1 (3.2%)	0.351*
	No Response	2 (6.5%)	1 (3.2%)	1.0*

	Response type	Levetiracetam (n=31)	Brivaracetam (n=31)	p-value
Treatment Response after 3 months	Complete	19 (61.3%)	27 (87%)	0.042*
	Good	7 (22.6%)	3 (9.7%)	0.3*
	Fair	4 (12.9%)	1 (3.2%)	0.351*
	No Response	1 (3.2%)	0 (0%)	1.08

*Treatment response was compared using *Chi-square test.*

Table 4: Common Adverse effects of Levetiracetam and Bivaracetum

Adverse effects	Levetiracetam (n=31)	Brivaracetam (n=31)
Hyperactivity	1 (3.2%)	6 (19.4%)
Somnolence	4 (12.9%)	3 (9.7%)
Irritability	0 (%)	4 (12.9%)

DISCUSSION

In this retrospective study of 62 children with new-onset focal epilepsy, We found that brivaracetam (BRV) achieved significantly better seizure control at 3 months than levetiracetam (LEV). The mean monthly seizure frequency after 3 months was much lower on BRV (0.42) than on LEV (1.58, $p<0.001$). Moreover, 87% of the BRV group attained complete response as compared to only 61% of the LEV group ($p=0.042$). These findings indicate superior efficacy of BRV over LEV in our cohort. Both drugs were generally well-tolerated: somnolence was the most frequent adverse effect in both groups (Brivaracetam 9.7% vs. Levetiracetam 12.9%), but BRV was associated with a higher rate of behavioral disturbances (hyperactivity 19.4% and other behavioral symptoms 12.9%) than LEV (hyperactivity 3.2%, no reported behavioral ADRs).

Our results suggest that BRV may provide improved seizure suppression compared to LEV in children with focal epilepsy. This is biologically plausible: BRV's 10–30× higher affinity for the SV2A target likely enhances its antiseizure potency [6,13]. Indeed, preclinical models show BRV has more pronounced anticonvulsant effects than LEV [6,13]. Clinically, adult and pediatric add-on trials have hinted at strong efficacy of BRV in focal seizures [3,6]. Our study adds to this by demonstrating marked reductions in seizure frequency even when BRV is used as first-line therapy in children. The 87% complete response rate on BRV is notably higher than the ~18% seizure-free rate reported in the recent pediatric meta-analysis [3]. The discrepancy likely reflects differences in patient population: our cohort had new-onset, non-refractory focal epilepsy, whereas prior studies mostly involved drug-resistant cases. Thus, treatment-naïve children may respond even better to BRV. In fact, the Italian real-world study of severely drug-resistant pediatric epilepsy reported a 42% responder rate (≥50% reduction) at 6 months [6], whereas we saw an 87% responder rate (≥90% reduction) at 3 months. This underscores that BRV's efficacy is higher when used earlier in the disease course.

LEV's effectiveness in our cohort (complete response 61%) aligns with published literature. In a large Turkish cohort treated with LEV as initial therapy, ~63% of children achieved >90% seizure reduction at one year [11]. Open-label pediatric studies have reported ≥50% responder rates of 20–60% [11], and we observed a 61% complete response at 3 months. Thus, our LEV outcomes appear typical. LEV's favorable safety profile was also confirmed: sedation and fatigue were reported (12.9% in our group), consistent with previous findings [12]. Notably, we observed very few behavioral side-effects with LEV: only one child (3.2%) had hyperactivity, and none had significant aggression or irritability. This contrasts with earlier reports that LEV can cause neuropsychiatric symptoms in up to ~11% of pediatric patients [12]. The low rate in our sample may reflect the short follow-up or possible under-reporting. Nonetheless, LEV's overall tolerability remained acceptable.

The safety profiles of BRV and LEV in our study merit discussion. Both drugs were tolerated without serious adverse events. Somnolence (or irritability causing apparent lethargy) occurred in roughly 10–13% of patients on each drug, consistent with known adverse-event rates [3,12]. Unexpectedly, we found more behavioral adverse events with BRV than LEV: nearly one-fifth of BRV-treated children developed hyperactivity and ~13% had behavioral disturbances, whereas none of the LEV group did. This is somewhat surprising, since adult data often suggest BRV has a more benign neuropsychiatric profile than LEV [13]. However, our finding aligns with the pediatric meta-analysis that reported behavioral ADRs in ~12% of children on BRV [3]. It is possible that BRV's potency exposes latent hyperexcitability in developing brains, or that short-term observation is capturing an initial activation phase. In contrast, LEV's well-known irritability side effect [12] was not prominent here – perhaps because we censored data at 3 months or because milder irritability was not recorded as an adverse event. Either way, any new behavioral symptoms warrant close monitoring. Importantly, our data confirm that both ASMs require vigilance for neuropsychiatric effects, especially in children.

Comparing our findings to existing literature, there are both consistencies and contrasts. The higher

seizure-free rate with BRV is consistent with its pharmacological profile [6,13], but the magnitude of difference we saw (87% vs. 61%) exceeds what has been reported in other settings. No published pediatric trial has directly compared these two, so we must rely on indirect comparisons. For example, adult studies generally show only modest differences between BRV and LEV in efficacy when used as adjuncts in refractory focal epilepsy. The drastic improvement with BRV in our cohort suggests that in non-refractory cases, choice of drug may have a bigger impact. Our results also differ from some expectations: for instance, adult meta-analyses suggested BRV may reduce behavioral adverse events when switching from LEV, but we did not observe superior behavioral tolerability. This points to possible age-related differences in drug response, or that behavioral outcomes in children follow different patterns.

Regional and global context highlight the importance of these findings. In Bangladesh, limited studies have examined drug efficacy in children. The only national data we have are epidemiological (prevalence and treatment gaps [9] and consensus guidelines advocating traditional ASMs. Our study is among the first in this region to assess newer AEDs in pediatric epilepsy. Globally, initiatives like the Global Burden of Disease (GBD) emphasize that epilepsy imposes high morbidity, especially in LMICs [2]. Achieving seizure control is key to reducing disability-adjusted life years. By demonstrating that BRV can significantly reduce seizure frequency in Bangladeshi children, our results suggest that broader use of this drug (within resource constraints) could have marked public health benefits. If seizures are suppressed, we may prevent the cognitive decline and social isolation that often follow uncontrolled epilepsy [1,4].

Study Limitations

Being retrospective and non-randomized, there may be selection biases. We attempted to match groups on baseline seizure frequency and demographics, but unmeasured factors might differ (e.g. etiology or EEG findings). The sample size (31 per group) is modest, limiting statistical power. The follow-up period was only 3 months, so we cannot assess long-term seizure freedom or late-emerging side effects. Additionally, drug adherence was not objectively measured; we relied on chart documentation of reported side effects and seizure diaries. Behavioral side effects in young children might have been under- or over-reported in charts.

CONCLUSION

Brivaracetam offers early seizure control compared to levetiracetam in children with new-onset focal epilepsy. The observed reduction in seizure frequency and higher complete response rate with BRV is encouraging. But adverse effects of BRV was much more than LEV, including irritability and hyperactivity. These findings, while preliminary, highlight BRV as a promising option in pediatric epilepsy treatment.

Author Contributions

Miah Q contributed to conceptualization, study design, patient recruitment, and oversight of data collection and follow-up. Alam ST provided overall supervision, critical guidance on methodology, and manuscript review. Akhi SA assisted with data management and statistical analysis. Sarker MA and Talukder MU contributed to patient care and clinical assessments. Faruk MO supported data entry and preliminary analysis. Chakroborty P coordinated the study, drafted and revised the manuscript, and managed correspondence. All authors reviewed and approved the final version of the manuscript.

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