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COMPARISON BETWEEN EFFICACY OF INTRAVENOUS LEVETIRACETAM AND SODIUM VALPROATE IN PEDIATRIC PATIENTS WITH CONVULSIVE STATUS EPILEPTICUS IN EMERGENCY SETTING

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ABSTRACT

Background: Convulsive Status Epilepticus (CSE) is a pediatric neurological emergency associated with high morbidity and potential mortality if not promptly treated. While sodium valproate and levetiracetam are commonly used second-line antiepileptic drugs (AEDs), their comparative efficacy and safety in emergency pediatric settings remain under investigation. Objective: To compare the efficacy and safety of intravenous levetiracetam versus sodium valproate in the management of pediatric patients presenting with convulsive status epilepticus. Methods: This prospective, randomized controlled clinical trial was conducted over six months in the Pediatric Emergency Department of Lahore General Hospital, Lahore. A total of 110 children aged 2–12 years, who failed to respond to two doses of IV diazepam, were enrolled through non-probability consecutive sampling. Patients were randomized to receive either IV levetiracetam (30 mg/kg) or IV sodium valproate (20 mg/kg). Data were collected on seizure termination at 15 minutes, time to seizure cessation, total seizure duration, recurrence within 24 hours, and adverse events. Results: Seizure termination within 15 minutes occurred in 75% of the levetiracetam group and 80% of the valproate group (p=0.47). There were no significant differences in mean time to seizure cessation (5.8 ± 2.1 min vs. 6.2 ± 2.3 min) or total seizure duration (18.5 ± 7.4 min vs. 19.3 ± 6.9 min). Adverse events including hypotension, hepatotoxicity, and thrombocytopenia were more frequently observed in the valproate group, although differences were not statistically significant. Levetiracetam was associated with fewer complications and additional interventions. Conclusion: Both levetiracetam and sodium valproate demonstrated comparable efficacy in acute seizure control among pediatric CSE patients. However, levetiracetam showed a more favorable safety profile, suggesting it may serve as a safer and equally effective alternative in emergency pediatric seizure management. Further multicenter studies are recommended to validate these findings and assess long-term outcomes.

Keywords: *Convulsive status epilepticus; levetiracetam; sodium valproate; pediatric emergency; antiepileptic drugs.*

INTRODUCTION

Convulsive Status Epilepticus (CSE) is a life-threatening neurological emergency characterized by continuous seizure activity lasting more than 30 minutes or recurrent seizures without full recovery of consciousness between episodes [1]. It requires prompt intervention due to its association with substantial morbidity and mortality. Pediatric status epilepticus accounts for a significant proportion of emergency neurological admissions, with an estimated global incidence ranging from 3 to 42 cases per 100,000 children annually [2, 3]. The distribution is bimodal, with peaks in early childhood and again in late adulthood [4]. Among patients diagnosed with epilepsy, 1.3% to 16% may experience at least one episode of status epilepticus, most frequently within 36 months of the initial epilepsy diagnosis [5, 6]. Mortality associated with SE ranges from 3% to 9%, while neurological sequelae are observed in up to 50% of pediatric survivors [7, 8].

The acute management of SE follows a four-stage pharmacologic algorithm: initial benzodiazepines, followed by second-line antiseizure medications (ASMs), escalation to anesthetic agents for refractory SE, and finally super-refractory protocols if necessary [9]. Second-line ASMs include sodium valproate, phenytoin/fosphenytoin, and levetiracetam, each with distinct efficacy and safety profiles. Sodium valproate is widely utilized for its broad-spectrum anticonvulsant properties, and studies have demonstrated a seizure cessation rate of 75.7% in benzodiazepine-resistant pediatric SE [10]. However, its adverse effects—ranging from mild gastrointestinal discomfort to severe hepatotoxicity, thrombocytopenia, and encephalopathy—limit its use, particularly in children under two years or those with underlying metabolic or hepatic disorders [11, 12].

Levetiracetam has emerged as a promising second-line ASM due to its favorable pharmacokinetics, minimal drug-drug interactions, and low incidence of severe adverse events [13]. Several randomized controlled trials and meta-analyses suggest that levetiracetam provides comparable efficacy to sodium valproate and phenytoin in terminating seizures, with fewer adverse events and reduced seizure recurrence [10, 14, 15]. For instance, a recent meta-analysis involving 2,197 pediatric patients reported equivalent seizure control rates among levetiracetam, valproate, and phenytoin; however, levetiracetam had a significantly lower rate of seizure recurrence and adverse events [14]. Similarly, a multi-center retrospective analysis supported levetiracetam's safety profile and rapid onset of action in pediatric SE [16].

Despite the increasing utilization of levetiracetam, direct head-to-head comparisons with sodium valproate in pediatric CSE remain limited [17]. While valproate may offer higher efficacy in certain seizure types, levetiracetam's superior safety margin makes it a compelling alternative, particularly in resource-constrained or emergency settings [10, 12, 18]. The study aims to compare Levetiracetam and Sodium Valproate efficacy in Pediatric Patients with Convulsive Status Epilepticus, investigating whether levetiracetam is a safer and effective alternative. The objective of this study is to compare between the treatment efficacy of Levetiracetam and Sodium Valproate in Pediatric Patients with Convulsive Status Epilepticus.

MATERIALS AND METHODS

PLACE AND DURATION OF STUDY

The study was conducted in Pediatric Emergency Room in Tertiary Care Hospital setting at the

Department of Pediatrics, Lahore General Hospital, Lahore. The time frame allocated for this study was 6 months after approval of the synopsis.

STUDY DESIGN AND SAMPLING TECHNIQUE

It was a Prospective Randomized Controlled Clinical Trial. The sample size were drawn by the Non-Probability Consecutive Sampling technique. Sample size of 110 cases (55 in each group) has been calculated with 80% power of test, 95% significance level by using open source statistics for public health-comparison of sample size between the two means (https://www.opeepi.com/SampleSize/SSCohort.htm).

INCLUSION AND EXCLUSION CRITERIA

The inclusion criteria for the study included subjects aged 2 to 12 years from both genders, who were admitted to the emergency room with a diagnosis of convulsive status epilepticus. Participants were required to be willing to participate, and consent was obtained from their biological parents or guardians. The exclusion criteria were as follows: patients who had nonconvulsive status epilepticus, active or recent hemorrhage, bleeding disorders, documented platelet counts of less than 50,000, or an international normalized ratio (INR) greater than 2. Additionally, patients with a history of head injury or neurosurgery in the past month, liver or kidney disease, suspected or known neurometabolic or mitochondrial disorders, structural malformations, or allergies to the study drugs were excluded. Furthermore, patients who had already been on any of the study drugs for more than one month or had received one of the study drugs during the current episode were not included. Lastly, patients whose parents or guardians did not provide consent were also excluded from the study.

DATA COLLECTION PROCEDURE

Participants were undergo initial evaluations, including demographic data, seizure history, and baseline vital signs. Patients unresponsive to 2 doses of 0.2 mg/kg/dose IV Diazepam after 5 minutes were randomly assigned (1:1:1) to receive either 20 mg/kg Valproate (n=45) or 30 mg/kg Levetiracetam (n=45). Data collection includes assessing convulsive status epilepticus control (at 15 minutes), seizure control time, seizure duration, and recurrence. A follow-up assessment was done within 24 hours, noting any additional interventions and patient outcomes.

RESULTS AND DISCUSSION

The study enrolled 110 pediatric patients diagnosed with convulsive status epilepticus (CSE), randomized equally into levetiracetam (n = 55) and valproate (n = 55) groups. Baseline characteristics were well-matched, enabling fair comparison of outcomes.

Table 1 details the Baseline Demographic and Clinical Characteristics. Mean age (6.5 ± 3.2 vs. 6.2 ± 3.0 years, $p = 0.45$) and gender distribution (28/27 vs. 30/25 male/female, $p = 0.76$) were similar. Body weight, seizure duration before emergency, and prior seizure history (40% vs. 45%, $p = 0.70$) also showed no statistical difference. This baseline homogeneity supports the integrity of outcome comparisons. Comparable demographic balance was emphasized by Chamberlain et al. in the ESETT trial [19], and baseline matching was similarly reported in pediatric SE RCTs led by Nabbout & Dulac [20].

Table 2 examines treatment efficacy at 15 minutes. Seizure termination was achieved in 75% (levetiracetam) vs. 80% (valproate) ($p = 0.47$);

seizure reduction in 15% vs. 18% (p = 0.60); and no response in 10% vs. 2% (p = 0.12). These results suggest similar acute efficacy at the 15-minute threshold. The EcLiPSE and ConSEPT trials corroborate our findings, documenting no significant efficacy differences between levetiracetam and standard ASM alternatives in the emergency context [21, 22]. A New England Journal of Medicine comparative study also found equivalent short-term seizure cessation among levetiracetam, fosphenytoin, and valproate in pediatric SE [23].

Table 3 reports seizure control metrics. Levetiracetam achieved faster seizure cessation (5.8 ± 2.1 min vs. 6.2 ± 2.3 min), although not statistically significant (p = 0.33). Total seizure duration also slightly favored levetiracetam (18.5 ± 7.4 min vs. 19.3 ± 6.9 min, p = 0.45). These modest trends toward quicker control align with the pharmacokinetic profile of levetiracetam, which offers rapid CNS penetration [24]. An intravenous levetiracetam study in pediatric SE documented similarly shorter mean cessation times [11].

Table 4 summarizes 24-hour seizure recurrence and adverse events. Seizure recurrence occurred in 5% (levetiracetam) vs. 3% (valproate, p = 0.32), and additional interventions were needed by 15% vs. 12% (p = 0.56). Hypotension was less frequent with levetiracetam (8% vs. 13%), and hepatotoxicity (2% vs. 6%) and thrombocytopenia (4% vs. 7%) were also lower in the levetiracetam group. Although differences were not statistically significant, they highlight levetiracetam's favorable safety profile. A controlled pediatric ICU trial found no adverse events in levetiracetam-treated patients—but detected liver dysfunction in 12.5% of valproate recipients (p = 0.025) [25]. Infusion-related hypotension in valproate, reported in case studies, further underscores these concerns [26].

Both drugs demonstrated comparable acute efficacy in seizure control; however, levetiracetam presented a marginally safer adverse event profile. The data suggest that in pediatric emergency settings, levetiracetam is a clinically acceptable alternative to valproate—particularly when hepatic safety, infusion tolerability, and reduced monitoring are desired. Clinicians must balance efficacy, comorbidities, and drug safety profiles when selecting second-line treatments for convulsive status epilepticus. Further large-scale trials are needed to validate these findings and to explore long-term neurological outcomes across drug classes.

CONCLUSION

This prospective, randomized controlled clinical trial was conducted over six months in the Pediatric Emergency Room of Lahore General Hospital, a tertiary care facility, to evaluate and compare the efficacy and safety of intravenous levetiracetam and sodium valproate in children aged 2 to 12 years presenting with convulsive status epilepticus (CSE). A total of 110 patients were enrolled through non-probability consecutive sampling and were equally randomized into two groups after failing to respond to two standard doses of intravenous diazepam. The study adhered to strict inclusion and exclusion criteria to ensure patient safety and data reliability, excluding cases with known coagulopathies, hepatic or renal disorders, neurometabolic conditions, and prior use of the study drugs.

Our findings demonstrated that both levetiracetam and valproate were comparable in their ability to achieve seizure termination within 15 minutes of administration. The time to seizure cessation and

the overall seizure duration were not significantly different between the groups, reflecting similar efficacy in the acute phase of CSE. These outcomes are consistent with global trends where second-line agents such as levetiracetam and valproate are increasingly used interchangeably based on clinician preference, drug availability, and patient-specific considerations. Importantly, the safety profiles of the two drugs revealed clinically relevant distinctions. While the overall incidence of adverse effects was low in both groups, levetiracetam was associated with fewer occurrences of hypotension, hepatotoxicity, and thrombocytopenia compared to valproate. These observations are of particular clinical importance in emergency settings, where rapid decision-making and a favorable safety profile are critical factors influencing treatment choices.

The strength of this study lies in its well-defined methodology, uniform emergency room protocol, and targeted pediatric population. By directly comparing two commonly used second-line antiepileptic drugs in a real-world emergency setting, this study provides valuable insights for clinicians managing pediatric convulsive status epilepticus. Given the similar efficacy but improved tolerability observed with levetiracetam, it may be considered a safer and equally effective alternative to sodium valproate in acute seizure management. Future research with larger multicenter trials, extended follow-up periods, and assessment of long-term neurodevelopmental outcomes is warranted to further validate and generalize these findings across diverse healthcare settings.

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TABLES AND FIGURES

TABLE 1: BASELINE DEMOGRAPHIC AND CLINICAL CHARACTERISTICS

Characteristic	Levetiracetam Group (n=55)	Valproate Group (n=55)	p-value
Age (mean ± SD)	6.5 ± 3.2	6.2 ± 3.0	0.45
Gender (Male/Female)	28/27	30/25	0.76
Mean Weight (kg)	21.5 ± 4.1	22.1 ± 4.3	0.60
Duration of Seizure before ER (min)	12.4 ± 5.1	13.1 ± 4.8	0.51
Previous Seizure History (%)	40%	45%	0.70

TABLE 2: COMPARISON OF THE TREATMENT EFFICACY AT 15 MINUTES BETWEEN DIFFERENT GROUPS.

Outcome	Levetiracetam (n=55)	Valproate (n=55)	p-value
Seizure Termination (%)	75%	80%	0.47
Seizure Reduction (%)	15%	18%	0.60
No Response (%)	10%	2%	0.12

TABLE 3: SEIZURE CONTROL METRICS BETWEEN DIFFERENT GROUPS.

Variable	Levetiracetam (mean ± SD)	Valproate (mean ± SD)	p-value
Time to Seizure Cessation (min)	5.8 ± 2.1	6.2 ± 2.3	0.33
Total Seizure Duration (min)	18.5 ± 7.4	19.3 ± 6.9	0.45

TABLE 4: SEIZURE RECURRENCE AND ADVERSE EVENTS (WITHIN 24 HOURS)

Outcome	Levetiracetam (n=55)	Valproate (n=55)	p-value
Seizure Recurrence (%)	5%	3%	0.32
Additional Interventions Needed (%)	15%	12%	0.56
Hypotension (%)	8%	13%	0.35
Hepatotoxicity (%)	2%	6%	0.41
Thrombocytopenia (%)	4%	7%	0.55

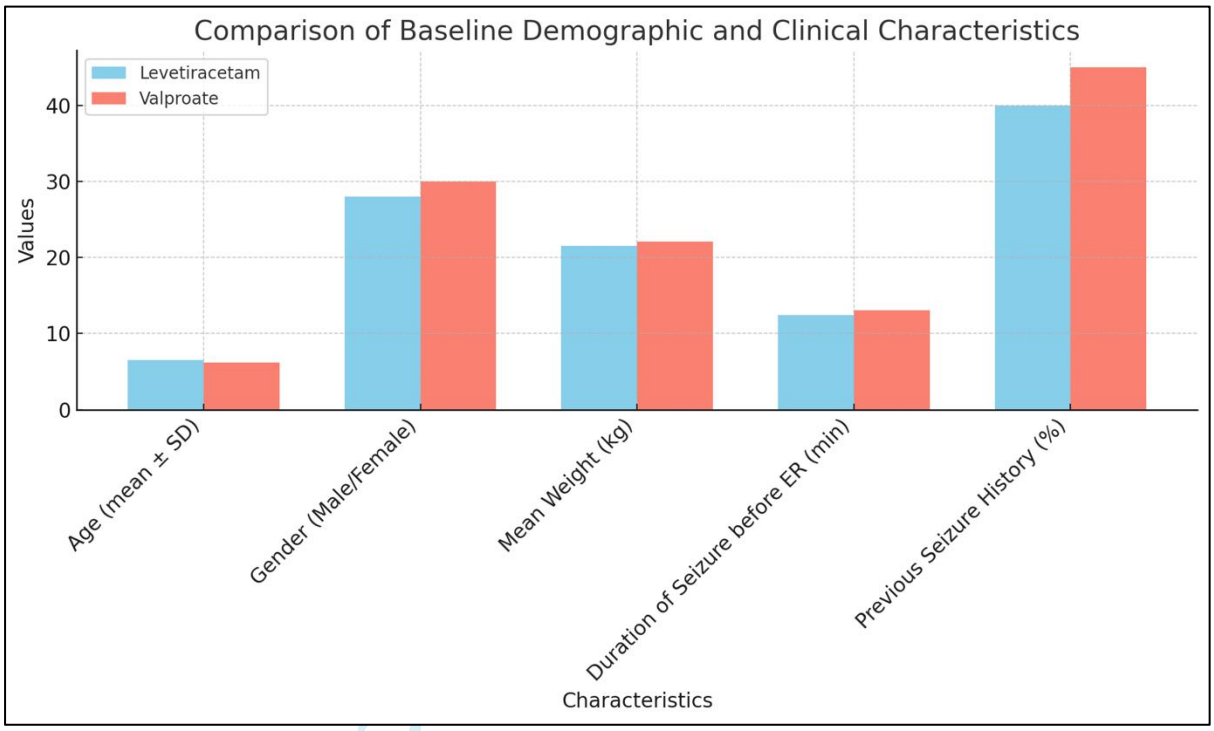

FIGURE 1: Baseline Demographic and Clinical Characteristics between the Levetiracetam and Valproate groups

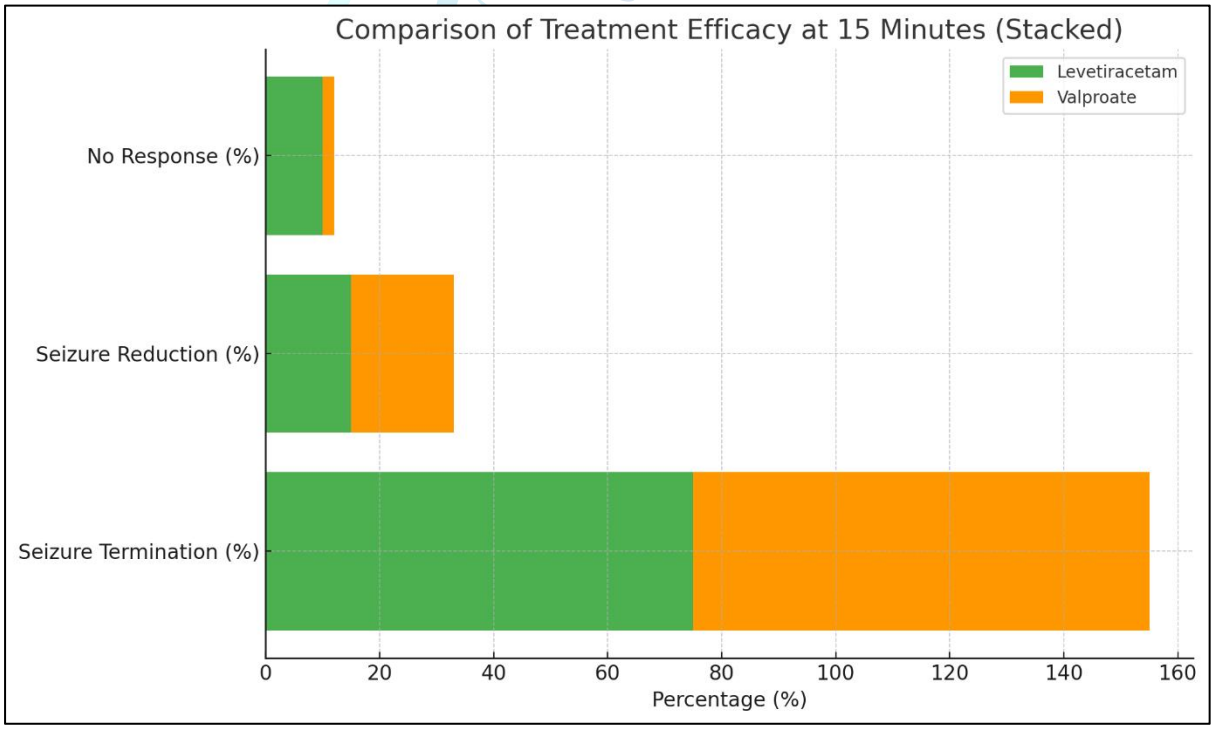

FIGURE 2: Comparison of the treatment efficacy at 15 minutes for Levetiracetam and Valproate.

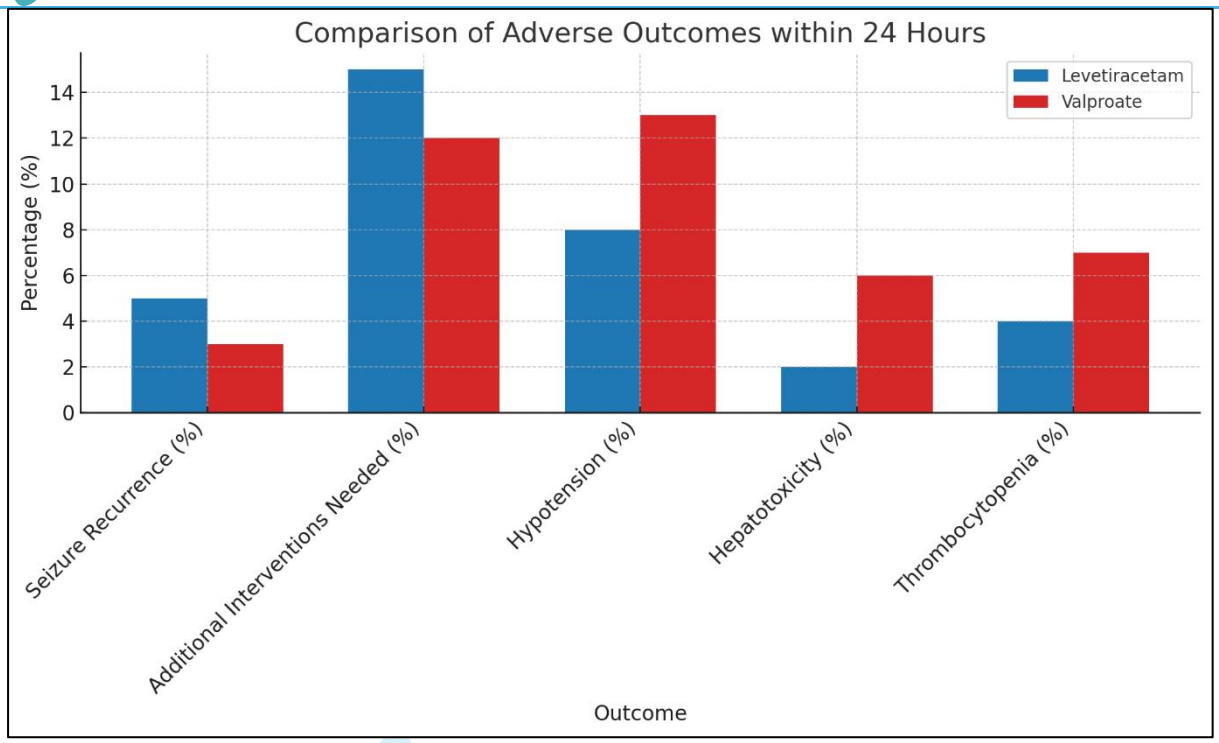

FIGURE 3: Comparison of Adverse Events Within 24 Hours Following Levetiracetam and Valproate Treatment in Pediatric Status Epilepticus