ONLINE FIRST

ORIGINAL ARTICLE

Comparison between Efficacy of Levetiracetam Versus Valproic Acid in Pediatric Patients with Status Epilepticus: A Randomized Controlled Trial

Atifa Mazhar[1*], Javaria Rasheed[1], Fakhta Hafeez[1], Suleman[1]

1Department of Pediatric Medicine, Nishtar Medical University & Hospital, Multan, Pakistan
Correspondence: *atifa.m.hashmi@gmail.com*
doi: 10.22442/jlumhs.2026.01512

ABSTRACT

OBJECTIVE: To compare the efficacy of levetiracetam versus valproic acid in children with status epilepticus.

METHODOLOGY: This randomized controlled trial was conducted at the Department of Pediatric Medicine, Nishtar Hospital, Multan, from June-November 2025. Children aged 2–14 years with status epilepticus were enrolled. They were randomly allocated to receive intravenous levetiracetam (20 mg/kg loading, 60 mg/kg/day maintenance) or valproic acid (15 mg/kg loading, 20 mg/kg/day maintenance). The primary outcome was sustained seizure control for ≥24 hours, and the secondary outcome was immediate cessation within 15–30 minutes. Data were analyzed using SPSS v26, with $p<0.05$ considered significant.

RESULTS: In a total of 138 pediatric patients, 69 (50.0%) were males, and 69 (50.0%) were females. The median age was 7.9 years (IQR 4.9–11.1), with 36 (26.1%) children aged 2–5 years, 76 (55.1%) aged > 5–12 years, and 26 (18.8%) aged 13–14 years. Median duration of seizure onset before treatment was 36.5 minutes (IQR 24.0–48.3); overall median duration of epilepsy diagnosis was 1.7 years (IQR 0.8–2.7). Sustained seizure control was achieved in 111 (80.4%) patients overall, with 59 (85.5%) in the levetiracetam group, and 52 (75.4%) in the valproic acid group ($p=0.133$). Immediate cessation of seizures after drug infusion was documented in 92 (66.7%) patients overall, including 47 (68.1%) receiving levetiracetam and 45 (65.2%) receiving valproic acid ($p=0.718$).

CONCLUSION: Intravenous levetiracetam and valproic acid are equally efficacious in achieving both immediate cessation and sustained control of seizure activity in pediatric patients with status epilepticus.

KEYWORDS: Children, levetiracetam, seizures, status epilepticus, valproic acid.

Trial Registration: *NCT07052136 (clinicaltrials.gov)*

INTRODUCTION

Epilepsy is a chronic neurological condition that predisposes affected individuals to recurrent seizures. Following an episode of seizure, a postictal state occurs that manifests clinically as a period of confusion and altered alertness that resolves spontaneously[1]. Status epilepticus is a serious medical emergency that is defined as "seizure activity that lasts longer than 5 minutes, or having more than 1 seizure within 5 minutes, without returning to a normal level of consciousness between seizure episodes"[2]. Among every 100,000 children, 20 develop status epilepticus per year[3]. To treat status epilepticus effectively, the airway, respiration, and circulation must be evaluated and managed at the same time as antiepileptic medication is given. The main objective of treatment is to end seizure activity as soon as possible[4]. Benzodiazepines are the first-line agents to be used, but when these fail to abolish status epilepticus, additional drugs are required. For this purpose, both levetiracetam and valproic acid are appropriate, but which is the best choice as the next step remains a topic of debate.

A study reported that when it comes to a comparison of valproic acid versus levetiracetam, the frequency of achievement of immediate cessation of seizure activity was higher in the levetiracetam group as compared to the valproic acid group (94% vs 83%, respectively)[5]. Another study reported that although the frequency of immediate cessation of seizure activity was higher in the levetiracetam group as compared to the valproic acid group (72.5% vs 57.5%, respectively), when it came to the frequency of sustained control of seizure activity, valproic acid was better than levetiracetam (68.4% vs 66.7%, respectively). Still, the difference was statistically insignificant ($p=0.872$)[6]. In another study, the frequency of sustained control of seizure activity was higher in the valproic acid group than in the levetiracetam group (92% vs 78%, respectively)[7]. In contrast, another study found that the frequency of sustained control of seizure activity was higher in the levetiracetam group than in the valproic acid group (68.1% vs 47.2%, respectively)[8].

Early and sustained control of seizures is paramount in status epilepticus to save the life of the patient, and this warrants use of the best drug based on evidence. Since there is a significant degree of variability in results of previous studies to decide which drug amongst levetiracetam and valproic acid is the better choice, it is imperative to conduct further trials so that an evidence-based decision can be made regarding the best and preferred choice of drug to be used in status epilepticus in case of failed response of benzodiazepines. This study was done to compare the efficacy of levetiracetam versus valproic acid in pediatric patients with status epilepticus.

METHODOLOGY

This randomized controlled trial (NCT07052136 at clinicaltrials.gov) was conducted at the Department of Pediatric Medicine, Nishtar Hospital, Multan, from June 2025 to November 2025, after obtaining approval from the Institutional Ethical Review Board (letter number: 3605/NUM, dated: 10-03-2025). Inclusion criteria were children aged 2 to 14 years of either gender with a previously established diagnosis of generalized tonic-clonic epilepsy who presented with benzodiazepine refractory convulsive status epilepticus. Patients with focal seizures, those already using levetiracetam or valproic acid, and those with a history of hypersensitivity to either drug were excluded. Children presenting with a first-ever episode of status epilepticus without a previous diagnosis of epilepsy were not eligible for inclusion. Status epilepticus was defined as tonic–clonic seizure activity lasting longer than five minutes or the occurrence of more than one seizure within five minutes without regaining normal consciousness between episodes. A sample size of 139 (69 in each group) was calculated using the WHO sample size calculator software with a level of significance of 95%, with 80% power, and anticipated proportion of patients achieving sustained control of seizures in the levetiracetam group as 68.1%, and with valproic acid as 47.2% [8].

After obtaining informed consent from parents or guardians, all eligible patients were enrolled using non-probability consecutive sampling. Baseline characteristics including age, gender, duration of diagnosis of generalized tonic–clonic epilepsy, socioeconomic status, area of residence (urban or rural), body mass index (BMI), and duration of seizure onset were recorded. Socioeconomic status was determined using the World Bank classification based on monthly household income, where families with income ≤11,605 PKR were considered low-income, 11,606–45,395 PKR as lower-middle, 45,396–140,461 PKR as upper-middle, and above 140,461 PKR as high-income[9]. Obesity was determined by calculating BMI, obtained by dividing weight in kilograms by the square of height in meters, with both measured barefoot and bareheaded. According to WHO BMI-for-age percentiles, children with BMI ≥85th and <95th percentile were classified as overweight, while those with BMI ≥95th percentile were classified as obese.

All eligible patients initially received intravenous lorazepam 0.1 mg/kg as first-line therapy according to the institutional status epilepticus protocol. Failure of first-line benzodiazepine therapy was operationally defined as persistence or recurrence of convulsive seizure activity within 5 to 10 minutes after administration of an adequate weight-based dose of intravenous lorazepam. Patients fulfilling this criterion were considered to have benzodiazepine refractory convulsive status epilepticus and were subsequently randomized to receive intravenous levetiracetam or valproic acid as second-line therapy. A total of 138 patients were randomly assigned in a 1:1 ratio to the levetiracetam or valproic acid group using a paper lottery method. The allocation sequence was prepared before patient enrolment using identical folded slips containing the treatment assignments, with 69 slips for each group. The slips were thoroughly mixed and placed in an opaque container. After confirmation of eligibility and enrolment, one slip was drawn for each participant to determine treatment allocation. The allocation remained concealed from the enrolling investigator until the participant had been enrolled and the treatment assignment was revealed. The levetiracetam group received intravenous levetiracetam at a loading dose of 20 mg/kg infused over 15 minutes, followed by a maintenance dose of 60 mg/kg/day in two divided doses over 24 hours. The valproic acid group received intravenous valproic acid at a loading dose of 15 mg/kg infused over 15 minutes, followed by 20 mg/kg/day in two divided doses over 24 hours. Standard pediatric seizure protocols were applied to all patients, and their progress was monitored continuously. The primary outcome was sustained control of seizure activity, defined as complete cessation of seizures (no seizure activity on EEG and regain of consciousness) maintained for at least

24 hours following drug administration. The secondary outcome was immediate cessation of seizure activity, defined as complete clinical cessation of convulsive seizure activity during 15-30 minutes after completion of the study drug infusion, based on continuous clinical observation during this period. Participants and the treating clinical team were aware of the assigned intervention because the study drugs had different dosing regimens and administration requirements. A consultant paediatrician who was not involved in randomization or treatment administration performed the outcome assessment and remained unaware of treatment allocation at the time of assessment.

Data were analyzed using IBM-SPSS Statistics, version 26.0. Continuous variables were presented as mean with standard deviation (SD) or median with interquartile range (IQR) as appropriate, while categorical variables were expressed as frequencies and percentages. Stratification was performed for age, gender, duration of disease, and duration of seizure onset to control for potential effect modifiers. Post-stratification comparisons between groups for sustained seizure control and immediate cessation of seizure activity were done using the Chi-square test or Fisher's exact test, with $p<0.05$ considered significant.

RESULTS

In a total of 138 pediatric patients, 69 (50.0%) were males, and 69 (50.0%) were females. The median age was 7.9 years (IQR 4.9–11.1), with 36 (26.1%) children aged 2–5 years, 76 (55.1%) aged > 5–12 years, and 26 (18.8%) aged 13–14 years. Based on BMI, 92 (66.7%) children were within the normal range, 14 (10.1%) were overweight, and 32 (23.2%) were obese. Regarding socioeconomic status, 90 (65.2%) belonged to the lower category, 38 (27.5%) to the middle category, and 10 (7.2%) to the upper category. The median duration of seizure onset before treatment was 36.5 minutes (IQR 24.0–48.3), and the overall median duration of epilepsy diagnosis was 1.7 years (IQR 0.8–2.7). **Table I** shows a comparison of baseline demographic and clinical characteristics of children between study groups, and no statistically significant differences were found (p>0.05 for all variables).

Table I: Comparison of baseline characteristics between groups (N=138)

Characteristics		Total	Levetiracetam (n=69)	Valproic Acid (n=69)	P-value
Gender	Male	69 (50.0%)	34 (49.3%)	35 (50.7%)	0.865*
	Female	69 (50.0%)	35 (50.7%)	34 (49.3%)	
Age (years)	2 to 5	36 (26.1%)	16 (23.2%)	20 (29.0%)	0.585*
	>5 to 12	76 (55.1%)	41 (59.4%)	35 (50.7%)	
	13-14	26 (18.8%)	12 (17.4%)	14 (20.3%)	
Age (years), median (IQR)		7.9 (4.9-11.1)	8.8 (4.7-11.0)	7.6 (4.3-11.7)	0.327^
Residence	Urban	76 (55.1%)	39 (56.5%)	37 (53.6%)	0.732*
	Rural	62 (44.9%)	30 (43.5%)	32 (46.4%)	
Body mass index categories	Normal	92 (66.7%)	45 (65.2%)	47 (68.1%)	0.848*
	Overweight	14 (10.1%)	8 (11.6%)	6 (8.7%)	
	Obese	32 (23.2%)	16 (23.2%)	16 (23.2%)	
Socioeconomic status	Lower	90 (65.2%)	42 (60.9%)	48 (69.6%)	0.349*
	Middle	38 (27.5%)	20 (29.0%)	18 (26.1%)	
	Upper	10 (7.2%)	7 (10.1%)	3 (4.3%)	
Duration of onset of seizures (minutes), median (IQR)		36.5 (24.0-48.3)	35.0 (24.0-47.0)	37.0 (24.5-50.0)	0.355^
Duration of diagnosis (years), median (IQR)		1.7 (0.8-2.7)	1.5 (0.8-2.8)	1.9 (0.8-2.7)	0.868^

**Chi-square test; ^Mann-Whitney U test*

of the primary treatment outcome, sustained seizure control was achieved in 111 (80.4%) patients overall, with 59 (85.5%) in the levetiracetam group and 52 (75.4%) in the valproic acid group, with no statistically significant difference (p=0.133). The secondary outcome of immediate cessation of seizures after drug infusion was documented in 92 (66.7%) patients overall, including 47 (68.1%) receiving levetiracetam and 45 (65.2%) receiving valproic acid (p=0.718), and the details are shown in **Table II**.

Table II: Comparison of primary and secondary outcomes

Outcomes		Total (%)	Levetiracetam (n=69)	Valproic acid (n=69)	Relative risk (95% CI)	Risk difference (95% CI)	P-value
Sustained seizure control	Yes	111 (80.4%)	59 (85.5%)	52 (75.4%)	1.1 (1.0 to 1.3)	10.1% (-3.0 to 23.3)	0.133*
	No	27 (19.6%)	10 (14.5%)	17 (24.6%)	-	-	
Immediate cessation of seizures achieved	Yes	92 (66.7%)	47 (68.1%)	45 (65.2%)	1.0 (0.8 to 1.3)	2.9% (-12.8 to 18.6)	0.718*
	No	46 (33.3%)	22 (31.9%)	24 (34.8%)	-	-	

**Chi-square test applied. Relative risk was calculated for achievement of the respective outcome, with the valproic acid group as the reference category. The "No" category represents the complementary outcome; therefore, separate effect estimates were not calculated.*

Stratified analysis of effect modifiers with respect to sustained seizure control showed that no significant association was found with respect to study groups in gender (p=0.909), age groups (p=0.790), residence (p=0.986), BMI categories (p=0.726), socioeconomic status (p=0.425), duration of onset of seizures (p=0.305), or duration of diagnosis (p=0.920), and the details are given in **Table III**.

Table III: Stratification of effect modifiers with respect to sustained seizure control (N=111)

Variables		Levetiracetam (n=59)	Valproic Acid (n=52)	P-value
Gender	Male	29 (53.7%)	25 (46.3%)	0.909*
	Female	30 (52.6%)	27 (47.4%)	
Age (years)	2 to 5	16 (51.6%)	15 (48.4%)	0.790*
	>5 to 12	33 (55.9%)	26 (44.1%)	
	13-14	10 (47.6%)	11 (52.4%)	
Residence	Urban	33 (53.2%)	29 (46.8%)	0.986*
	Rural	26 (53.1%)	23 (46.9%)	
Body mass index categories	Normal	39 (50.6%)	38 (49.4%)	0.726*
	Overweight	6 (60.0%)	4 (40.0%)	
	Obese	14 (58.3%)	10 (41.7%)	
Socioeconomic status	Lower	37 (50.7%)	36 (49.3%)	0.425*
	Middle	16 (53.3%)	14 (46.7%)	
	Upper	6 (75.0%)	2 (25.0%)	
Duration of onset of seizures (minutes), median (IQR)		36.0 (24.0-46.5)	38.5 (24.5-50.0)	0.305^
Duration of diagnosis (years), median (IQR)		1.5 (0.9-2.8)	1.9 (0.8-2.8)	0.920^

*Numbers are given among children who had sustained seizure control. Percentages are calculated row-wise. *Chi-square test; ^Mann-Whitney U test*

Stratified analysis of effect modifiers with respect to immediate cessation of seizures showed that no significant association was found with respect to study groups in gender (p=0.996), age groups (p=0.406), residence (p=0.855), BMI categories (p=0.452), socioeconomic status (p=0.108), duration of onset of seizures (p=0.179), or duration of diagnosis (p=0.705), and the details are given in **Table IV**.

Table IV: Stratification of effect modifiers with respect to immediate cessation of seizures (N=92)

Variables		Levetiracetam (n=47)	Valproic Acid (n=45)	P-value
Gender	Male	23 (51.1%)	22 (48.9%)	0.996*
	Female	24 (51.1%)	23 (48.9%)	
Age (years)	2 to 5	11 (47.8%)	12 (52.2%)	0.406*
	>5 to 12	28 (57.1%)	21 (42.9%)	
	13-14	8 (40.0%)	12 (60.0%)	
Residence	Urban	27 (51.9%)	25 (48.1%)	0.855*
	Rural	20 (50.0%)	20 (50.0%)	
Body mass index categories	Normal	29 (48.3%)	31 (51.7%)	0.452*
	Overweight	5 (62.5%)	3 (37.5%)	
	Obese	13 (54.2%)	11 (45.8%)	
Socioeconomic status	Lower	27 (43.5%)	35 (56.5%)	0.108*
	Middle	17 (65.4%)	9 (34.6%)	
	Upper	3 (75.0%)	1 (25.0%)	
Duration of onset of seizures (minutes), median (IQR)		36.0 (26.0-44.0)	42.0 (25.0-54.0)	0.179^
Duration of diagnosis (years), median (IQR)		1.5 (0.8-2.9)	1.7 (0.7-2.9)	0.705^

*Numbers are given among children who had immediate cessation of seizures. Percentages are calculated row-wise. *Chi-square test; ^Mann-Whitney U test*

DISCUSSION

In this study, sustained seizure control was achieved in 80.4% of the cohort, including 85.5% receiving levetiracetam, and 75.4% receiving valproic acid (p=0.133). Immediate cessation of seizures within 15 to 30 minutes was achieved in 66.7% overall, with 68.1% with levetiracetam, and 65.2% in the valproic acid group (p=0.718). These results indicate that both agents were effective in terminating convulsive activity and maintaining seizure control, with no meaningful statistical difference in efficacy. A study analyzed 1213 patients across six randomized controlled trials, and the pooled analysis revealed comparable efficacy between levetiracetam and valproate in clinical seizure termination, reporting 63.6% versus 64.1% respectively with a relative risk of 1.03 (p=0.55)[10]. Regional data studying 110 children with convulsive status epilepticus, and randomized to receive phenytoin, valproate, or levetiracetam following failure of benzodiazepines, found seizure control at 15 minutes achieved in 94% of patients receiving levetiracetam, and 83% receiving valproate (p=0.38)[5]. Their findings substantiate that both levetiracetam and valproic acid provide comparable seizure termination rates when used as second-line therapy in pediatric populations. The comparable effect between both agents is consistent with the pharmacological rationale, as both act via modulation of neuronal excitability and synaptic neurotransmission but through distinct mechanisms which may converge in achieving similar clinical control during prolonged seizures.

In contrast, some others reported slightly higher efficacy of valproate when compared with levetiracetam[7]. In that study, conducted among 150 pediatric patients with status epilepticus, seizures were controlled at 24 hours in 92% receiving valproate, and 78% receiving levetiracetam. While their difference did not reach statistical significance (p=0.115), valproate appeared to induce faster recovery of consciousness, with a mean time of 75.0 minutes compared with 120.8 minutes in the levetiracetam group (p<0.0001). Differences in the timing of outcome assessment may explain differences between the present study and others[7]. They evaluated seizure control at 24 hours, while the current study used two defined outcomes, immediate control and sustained control at 24 hours, thus capturing both short- and longer-term response profiles[7]. Differences in the loading and maintenance doses, as well as prior exposure to other antiepileptic agents, may have influenced the observed clinical response.

The equivalence in sustained seizure control between the two drugs in the present trial is consistent with another study, where authors studied patients with generalized convulsive status epilepticus[11]. In contrast, local data found a significantly greater reduction in seizure frequency with levetiracetam in children with early childhood epilepsy[12]. Their trial demonstrated efficacy in 89.7% receiving levetiracetam versus 58.6% receiving valproate (p<0.05). The discrepancy from the present findings may stem from the different clinical context, as that study examined chronic epilepsy management over four weeks rather than acute status epilepticus. The sustained intracellular mechanisms that mediate seizure recurrence prevention differ from those governing acute seizure termination, explaining why levetiracetam showed higher efficacy in long-term seizure frequency reduction but not in acute status control. In children followed for six months, levetiracetam achieved seizure control in 85% and valproate in 73% (p=0.037), reflecting better long-term tolerability and adherence to levetiracetam but comparable immediate therapeutic effectiveness[13]. The current results also align with the findings of Isguder and collaborators, who investigated refractory status epilepticus and found no difference in response between the two drugs. However, liver dysfunction was observed in 12.5% of patients receiving valproate, while none occurred with levetiracetam (p=0.025)[14].

The median duration of seizure onset before treatment in this cohort was 36.5 minutes, which reflects realistic emergency presentation times in tertiary care settings within Pakistan. This duration aligns with patterns observed in other studies where median prehospital duration of convulsive activity ranged between 30 and 45 minutes[15,16]. The comparable response to treatment despite variation in seizure duration underscores the pharmacodynamic efficiency of both agents when administered promptly following benzodiazepine failure. The comparable distribution of socioeconomic and anthropometric characteristics between groups further strengthens internal validity, minimizing confounding and suggesting that differences in nutritional or socioeconomic factors did not bias the outcomes[17-20]. These findings may suggest that the effectiveness of both levetiracetam and valproic acid remains relatively consistent across different patient subgroups encountered in routine pediatric practice.[21] From a clinical perspective, this consistency is valuable because status epilepticus requires urgent treatment decisions, often before detailed investigations or complete clinical information become available.[22,23] The comparable efficacy across these subgroups indicates that neither drug requires preferential selection based solely on baseline demographic characteristics, allowing clinicians to individualize therapy according to contraindications, anticipated adverse effects, drug availability, and institutional treatment protocols.

The findings of this study also have practical implications for resource-limited healthcare settings where rapid access to second-line antiepileptic medications may be influenced by local availability and cost. Since both levetiracetam and valproic acid demonstrated similar rates of immediate seizure termination and sustained seizure control, treatment delays associated with waiting for a specific agent may be avoided. Prompt administration of an available, evidence-based second-line medication is likely to have greater clinical importance than the choice between these two drugs. Early seizure control reduces the duration of ongoing neuronal excitation, limits the risk of progression to refractory status epilepticus, and may decrease the need for intensive care interventions, mechanical ventilation, and prolonged hospitalization. These findings therefore support the incorporation of either intravenous levetiracetam or valproic acid into standardized pediatric status epilepticus treatment pathways, particularly in tertiary care hospitals serving large populations with variable resource availability.

This study also carries certain limitations. The sample size, while adequate for primary comparison, may not be sufficient to detect subtle differences in subgroup analyses, such as variations in efficacy across nutritional or socioeconomic strata. The absence of long-term follow-up limits the ability to evaluate seizure recurrence beyond the acute period, which would be valuable in assessing sustained therapeutic impact.

CONCLUSION

Intravenous levetiracetam and valproic acid are equally efficacious in achieving both immediate cessation and sustained control of seizure activity in pediatric patients with status epilepticus. The comparable outcomes across demographic and clinical variables further suggest that treatment selection can be tailored based on individual tolerance, comorbidity profile, and resource considerations.

Ethical permission: Nishtar Medical University & Hospital, Multan, Pakistan ERC approval letter No. 3605/NUM.
Conflict of interest: There is no conflict of interest between the authors.
Financial Disclosure / Grant Approval: No funding agency was involved in this research.
Data Sharing Statement: The corresponding author can provide the data supporting the findings of this study on request. Privacy or ethical restrictions bound us from sharing the data publicly.

AUTHOR CONTRIBUTION

Mazhar A: Data collection, responsible for data integrity, drafting, proofreading, critical revisions, approved for publication.
Rasheed J: Conception and design, drafting, proofreading, critical revisions, approved for publication.
Hafeez F: Literature review, data analysis, proofreading, critical revisions, approved for publication.
Suleman: Data collection, data synthesis, proofreading, critical revisions, approved for publication.

ACKNOWLEDGEMENTS: The authors are thankful to Muhammad Aamir Latif (RESnTEC) for his valuable assistance in the trial registration of this research.

REFERENCES

1. Pottkämper JCM, Hofmeijer J, van Waarde JA, van Putten MJ. The postictal state - What do we know? Epilepsia. 2020; 61(6): 1045-1061. doi: 10.1111/epi.16519.
2. Alshehri RS, Alrawaili MS, Zawawi BMH, Alzahrany M, Habib AH. Pathophysiology of Status Epilepticus Revisited. Int J Mol Sci. 2025; 26(15): 7502. doi: 10.3390/ijms26157502.
3. Wasim A, Al Maawali SS, AlJabri AS, Al Amrani F, Ahmad F, Mansi A et al. Aetiology and Outcome of Childhood Convulsive Status Epilepticus: A tertiary care experience in Oman. Sultan Qaboos Univ Med J. 2024; 24(3): 367-374. doi: 10.18295/squmj.8.2024.050
4. Mullhi R, Hayton T, Midgley-Hunt A, Trimble M, Chaudhary UJ, Samarasekera S et al. Guidance for: The acute management of status epilepticus in adult patients. J Intensive Care Soc. 2025; 26(2): 249-262. doi: 10.1177/17511437251321338
5. Vignesh V, Rameshkumar R, Mahadevan S. Comparison of phenytoin, valproate and levetiracetam in pediatric convulsive status epilepticus: a randomized double-blind controlled clinical trial. Indian Pediatr. 2020; 57(3): 222-27.
6. Prasad R, Panghal A, Singh A, Mishra OP, Singh TB. Levetiracetam versus sodium valproate in refractory convulsive status epilepticus in children: an open randomized trial. Acta Sci Neurol. 2021; 4(4): 65-71. doi: 10.31080/ASNE.2021.04.0339.
7. Nazir M, Tarray RA, Asimi R, Syed WA. Comparative efficacy of IV phenytoin, IV valproate, and IV levetiracetam in childhood status epilepticus. J Epilepsy Res. 2020;10(2):69-73. doi: 10.14581/jer.20011
8. Naseer A, Sharif S, Khan S, Aamer M. Comparison between efficacy of levetiracetam and sodium valproate in pediatric patients with statusepitepticus. Pak Pediatr J. 2022; 46(1): 25-30.
9. The World Bank. World Bank country classifications by income level for 2024-2025. Available from: https://blogs.worldbank.org/en/opendata/world-bank-country-classifications-by-income-level-for-2024-2025
10. Wang S, Wu X, Xue T, Song Z, Tan X, Sun X et al. Efficacy and safety of levetiracetam versus valproate in patients with established status epilepticus: A systematic review and meta-analysis. Heliyon. 2023; 9(2): e13380. doi: 10.1016/j.heliyon.2023.e13380.
11. Nene D, Mundlamuri RC, Satishchandra P, Prathyusha PV, Nagappa M, Bindu PS, et al. Comparing the efficacy of sodium valproate and levetiracetam following initial lorazepam in elderly patients with generalized convulsive status epilepticus (GCSE): A prospective randomized controlled pilot study. Seizure. 2019; 65: 111-117. doi: 10.1016/j.seizure.2019.01.015.
12. Khan MI, Sabahat A, Mohammad EN, Khan MJU, Waqas M, Gul M et al. Comparative efficacy of levetiracetam and sodium valproate in the treatment of early childhood epilepsy. Insight J Health Rehab. 2025; 3(4): 204-249. doi: 10.71000/ek18t176.
13. Latif Z, Mukhtar M, Rohan A, Shah WF, Aslam Z, Akbar M et al. Comparison of Levetiracetam Versus Sodium Valproate as a Monotherapy in Early Childhood Epilepsy. Cureus. 2025; 17(7): e87574. doi: 10.7759/cureus.87574.
14. İşgüder R, Güzel O, Ceylan G, Yılmaz Ü, Ağın H. A Comparison of Intravenous Levetiracetam and Valproate for the Treatment of Refractory Status Epilepticus in Children. J Child Neurol. 2016; 31(9): 1120-6. doi: 10.1177/0883073816641187.
15. Kimura M, Ito H, Sota R, Taketani T. Active Seizures on Arrival at the Hospital During Ambulance Transfers in Children: A Five-Year Record Review. Cureus. 2026; 18(1): e102705. doi: 10.7759/cureus.102705.

16. Amengual-Gual M, Sánchez Fernández I, Vasquez A, Abend NS, Anderson A, Arya R et al. Pediatric status epilepticus management by Emergency Medical Services (the pSERG cohort). Seizure. 2023; 111: 51-55. doi: 10.1016/j.seizure.2023.07.010. Epub 2023 Jul 16
17. Muthiah N, Rothenberger S, Abel TJ. Socioeconomic status and healthcare utilization disparities among children with epilepsy in the United States: Results from a nationally representative sample. Sci Rep. 2023; 13(1): 21776. doi: 10.1038/s41598-023-48668-3.
18. Fong SL, Thuy Le MA, Lim KS, Khosama H, Ohnmar O, Savath S et al. Affordability of newer antiseizure medications in Asian resource-limited countries. Epilepsia. 2023; 64(8): 2116-2125. doi: 10.1111/epi.17668.
19. Contreras-García IJ, Cárdenas-Rodríguez N, Romo-Mancillas A, Bandala C, Zamudio SR, Gómez-Manzo S et al. Levetiracetam Mechanisms of Action: From Molecules to Systems. Pharmaceuticals (Basel). 2022; 15(4): 475. doi: 10.3390/ph15040475.
20. Trinka E, Höfler J, Zerbs A, Brigo F. Efficacy and safety of intravenous valproate for status epilepticus: a systematic review. CNS Drugs. 2014; 28(7): 623-39. doi: 10.1007/s40263-014-0167-1.
21. Mahajan I, Kumar P, Jain A, Bansal U, Singh V, Rathoria E. Sodium Valproate Versus Levetiracetam in Pediatric Generalized Epilepsy: A Comparative Study. Cureus. 2025; 17(12): e100114. doi:10.7759/cureus.100114.
22. Punia V. From Guideline to Lifeline: Turning Status Epilepticus Management Evidence Into Improved Outcomes. Epilepsy Curr. 2025; 26(2): 119-121. doi: 10.1177/15357597251389974.
23. van der Meer P, Dirven L, Fiocco M, Vos M, Kouwenhoven M, van den Bent M et al. NCOG-45. First-line antiepileptic drug treatment in glioma patients with epilepsy: Levetiracetam versus valproic acid. Neuro Oncol. 2020; 22(Suppl 2): ii139. doi: 10.1093/neuonc/noaa215.583.