International Journal of Health Sciences and Research
[Indexed, Peer-Reviewed Journal]
Volume 16; Issue: 6; June 2026
Website: www.ijhsr.org
Original Research Article *ISSN: 2249-9571*

A Comparison of Phenytoin and Levetiracetam for Prophylaxis of Seizures in the Early Postoperative Period in Traumatic Brain Injury Patients

Eman Aftab[1], Zulfiqar Ali[2], Iqra Nazir[3], Adnan Qadri[4]

[1]Department of Anesthesiology, SKIMS Medical College, Srinagar, Jammu & Kashmir, India.
[2]Department of Anesthesiology, Sher-i-Kashmir Institute of Medical Sciences (SKIMS), Soura, Srinagar, Jammu & Kashmir, India
[3]Department of Anesthesiology, Sher-i-Kashmir Institute of Medical Sciences (SKIMS), Soura, Srinagar, Jammu & Kashmir, India
[4]Department of Anesthesiology, Paras Hospitals, Srinagar, Jammu & Kashmir, India.

Corresponding Author: Dr. Adnan Qadri

DOI: https://doi.org/10.52403/ijhsr.20260616

ABSTRACT

Background: Early post-traumatic seizures worsen secondary brain injury after severe traumatic brain injury (TBI). Phenytoin remains the traditional prophylactic agent, while levetiracetam has gained popularity because of its favorable safety profile.
Methods: This prospective randomized controlled pilot study was conducted in the Neurosurgical ICU of SKIMS, Srinagar between June 2023 and June 2025. Forty-eight adults with severe TBI (GCS ≤8) were enrolled and randomized to receive phenytoin or levetiracetam. Five patients died during the early study period and were excluded from final analysis, leaving 43 patients (21 phenytoin, 22 levetiracetam). Clinical seizure monitoring and EEG assessments were performed during the first seven days after injury.
Results: Baseline demographics, injury severity, Marshall CT scores, and surgical procedures were comparable between groups. Clinical seizures occurred in 9.5% of phenytoin-treated patients and 4.5% of levetiracetam-treated patients. No significant difference was observed in time to first seizure, EEG epileptiform discharges, ICU stay, neurological recovery, adverse effects, or mortality. Adverse effects were numerically more frequent with phenytoin (19%) than levetiracetam (9%).
Conclusions: Levetiracetam demonstrated efficacy comparable to phenytoin for prevention of early post-traumatic seizures and showed a trend toward improved tolerability. Larger multicenter studies are required to confirm these findings.

Keywords: Traumatic brain injury, post-traumatic seizure, prophylaxis of seizures, phenytoin, levetiracetam

INTRODUCTION

Traumatic brain injury (TBI) is a major cause of morbidity and mortality worldwide and remains a significant challenge in critical care practice.[1] The burden is particularly high in low- and middle-income countries. A World Bank report highlighted that India accounts for nearly 10% of global road traffic crash-related deaths despite possessing only 1% of the world's vehicles.[2] Following the primary mechanical insult, TBI evolves through complex secondary

injury mechanisms involving cerebral hypoxia, raised intracranial pressure, neuroinflammation and abnormal electrical activity.[1,3] Post-traumatic seizures (PTS) represent an important complication and are associated with poorer neurological outcomes, prolonged intensive care unit (ICU) stay and increased healthcare utilization.[4,5] PTS are generally classified as immediate, early and late seizures according to the time elapsed following injury.[4,5]

To minimize secondary cerebral injury associated with early seizures, prophylactic antiepileptic therapy has become standard practice in patients with severe TBI. [6] Phenytoin and levetiracetam are the two most commonly used agents. Phenytoin acts primarily through blockade of voltage-gated sodium channels and has long been utilized for prevention of early post-traumatic seizures.[7] Conversely, levetiracetam exerts its effect through binding to synaptic vesicle protein 2A, thereby modulating neurotransmitter release.[8] Compared with phenytoin, levetiracetam possesses favorable pharmacokinetic properties, minimal drug interactions and limited hepatic metabolism.[8,9] Despite widespread use of both agents, uncertainty persists regarding their comparative efficacy and safety. Several systematic reviews and meta-analyses have reported no significant difference between levetiracetam and phenytoin with respect to prevention of early seizures, mortality or overall clinical outcomes. [10-14] However, existing evidence is limited by heterogeneity in study design, small sample sizes and inconsistent methods of seizure detection. Most previous studies have relied primarily on clinically apparent seizures without routine electroencephalographic (EEG) monitoring.[15,16] In critically ill patients receiving sedation and mechanical ventilation, this approach may underestimate the burden of subclinical epileptiform activity.[4,5] Therefore, the present randomized controlled trial was undertaken to compare levetiracetam and phenytoin for prophylaxis of early post-traumatic seizures in patients with severe TBI using both clinical assessment and EEG monitoring. Secondary objectives included comparison of adverse drug reactions, time to first seizure, ICU stay and mortality.

MATERIALS AND METHODS

This prospective, randomized, controlled trial was conducted in the Neurosurgical Intensive Care Unit (NICU) under the Division of Neuroanesthesia and Neurocritical Care at the Sher-i-Kashmir Institute of Medical Sciences (SKIMS), Soura, Srinagar, India. The study was conducted over a two-year period from June 2023 to June 2025. Institutional Ethical Committee clearance was obtained prior to study commencement, and the trial was registered prospectively with the Clinical Trials Registry of India. (Approval No. SKIMS 131/iec-skims/2023-251, dated 05-06-2023).

Study Population

As this was a pilot study, a formal sample size calculation was not initially performed. A convenience sample of 48 adult patients with traumatic brain injury (TBI) was enrolled after obtaining informed, written consent from their legally authorized representatives. After exclusions and dropouts, data for 43 patients were included in the final analysis.

Inclusion Criteria:

Age ≥ 18 years
Confirmed diagnosis of TBI
Admitting Glasgow Coma Scale (GCS) score ≤ 8

Exclusion Criteria:

Patients were excluded if they had a history of epilepsy or seizure disorder, known hypersensitivity to phenytoin or levetiracetam, pre-existing liver or kidney disease, bleeding disorders, or were on anticoagulation therapy. Pregnant or breastfeeding women, patients requiring neuromuscular blockade (which could mask clinical seizures), and those with

independent epileptogenic brain pathologies (e.g., aneurysm, tumor) were also excluded.

Initial Management and Resuscitation

All patients were initially admitted to the Emergency Medicine Department, where primary and secondary surveys were conducted. The airway was secured in patients with a low GCS, inability to maintain airway patency, or signs of respiratory distress. Fluid resuscitation and blood transfusions were administered based on standard operating protocols. Extended Focused Assessment with Sonography in Trauma (E-FAST) and non-contrast computed tomography (NCCT) of the head and spine were performed in all patients with a GCS < 8. Based on clinical and radiological evaluation, patients underwent surgical intervention (e.g., decompressive craniectomy) or were managed conservatively.

Randomization and Intervention

For this study, the "early postoperative period" was strictly defined as the first 7 days following the initial TBI impact, regardless of whether the patient was managed surgically or conservatively.

Patients were randomized in a 1:1 ratio to receive either phenytoin or levetiracetam using a computer-generated random sequence. Allocation concealment was ensured using sequentially numbered opaque sealed envelopes. The treating clinicians were aware of the allocated intervention due to differences in drug administration; however, EEG interpretation and outcome assessment were performed by investigators blinded to treatment allocation.

Group P (Phenytoin): Received an intravenous loading dose of 20 mg/kg, followed by a maintenance dose of 2 mg/kg three times daily.

Group L (Levetiracetam): Received an intravenous dose of 10 mg/kg twice daily.

The assigned antiepileptic drug was initiated intraoperatively by the attending anesthetist (or in the ICU for conservative patients) and maintained for at least 7 days.

Standardized Neurocritical Care

In the NICU, TBI management adhered to standard guidelines. Targets included PaO_2 > 60 mmHg, SpO_2 ≥ 90%, $PaCO_2$ 35–45 mmHg, and serum sodium (Na^+) between 135–145 mEq/L. Hemodynamic goals were maintained with a systolic blood pressure (SBP) ≥ 100 mmHg for patients aged 15–49 or >70 years, and ≥ 110 mmHg for those aged 50–69 years. Decongestants, including mannitol (0.25–0.5 g/kg) and/or 3% hypertonic saline (2–3 ml/kg), were administered based on the severity of cerebral edema. Patients were sedated using a continuous infusion of fentanyl (50–100 mcg/hour) and midazolam (2–5 mg/hour). A daily sedation interruption (sedation vacation) was performed every morning to facilitate neurological assessment.

Clinical and Electroencephalographic (EEG) Monitoring

EEG monitoring in the present study consisted of a one-hour recording obtained during ICU stay. Therefore, the reported EEG findings represent snapshot assessments rather than continuous surveillance. Consequently, non-convulsive seizures occurring outside the recording period may have been missed.

Sample size justification:

This was a pilot randomized controlled trial. Due to the limited number of eligible severe traumatic brain injury patients presenting during the study period, a convenience sample of 48 participants was enrolled. No formal a priori sample size calculation was performed. Therefore, the findings should be interpreted as exploratory and hypothesis-generating.

Statistical Analysis

Statistical analysis was performed using SPSS version 20. Continuous variables were expressed as mean ± standard deviation and compared using the Independent Student's t-

test. Categorical variables were expressed as frequency and percentage and compared using Chi-square test or Fisher's exact test wherever expected cell frequencies were less than five. A p-value <0.05 was considered statistically significant.

RESULTS

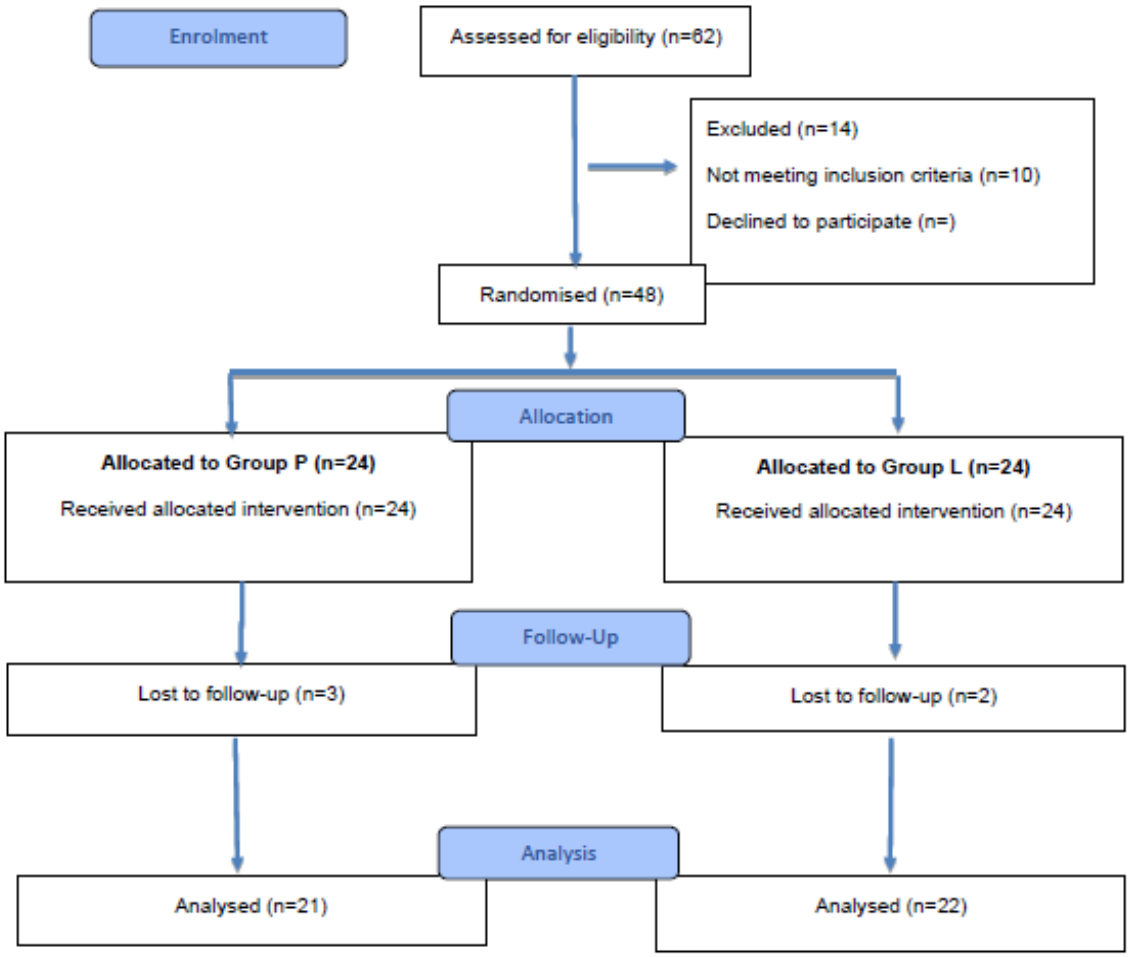

Figure 1: CONSORT flow diagram.

A total of 62 patients with severe traumatic brain injury were assessed for eligibility during the study period as shown in figure 1. Fourteen patients were excluded before randomization, including 10 who did not meet the inclusion criteria and 4 who declined participation. The remaining 48 patients were randomized equally to the phenytoin group (Group P, n=24) and the levetiracetam group (Group L, n=24), and all received the allocated intervention. During follow-up, 5 patients were excluded from the final analysis because of incomplete outcome data or protocol deviations (3 from Group P and 2 from Group L). Consequently, 43 patients (21 in Group P and 22 in Group L) were included in the final analysis.

The baseline demographic profiles of both treatment arms were comparable as shown in table 1. The mean age was 42.19 ± 15.83 years in the phenytoin group and 39.23 ± 13.97 years in the levetiracetam group (p = 0.25). Both groups demonstrated a strong male predominance (90.5% and 86.4%, respectively; p = 0.67). Most patients had no pre-existing comorbidities (52.4% in the phenytoin arm vs. 77.3% in the levetiracetam arm; p = 0.364), with hypertension being the most frequently reported comorbidity when present.

Table 1: Baseline Demographic and Clinical Characteristics

Parameter	Phenytoin (n=21)	Levetiracetam (n=22)	p-value
Age in Years (Mean ± SD)	42.19 ± 15.83	39.23 ± 13.97	0.250
Male	19 (90.5%)	19 (86.4%)	0.670
Female	2 (9.5%)	3 (13.6%)	
RTA	15 (71.4%)	13 (59.1%)	0.396
FFH	6 (28.6%)	9 (40.9%)	
SDH	15 (71.4%)	11 (50.0%)	0.203
EDH	0	2 (9.1%)	
Mixed Lesions	6 (28.6%)	9 (40.9%)	
No Comorbidity	11 (52.4%)	17 (77.3%)	0.364
Baseline GCS 4–5	3 (14.3%)	1 (4.5%)	0.690
Baseline GCS 6–7	10 (47.6%)	10 (45.5%)	
Baseline GCS 8	8 (38.1%)	11 (50.0%)	
Marshall Score 3	4 (19.1%)	2 (9.1%)	0.660
Marshall Score 4	8 (38.1%)	9 (40.9%)	
Marshall Score 5	9 (42.9%)	11 (50.0%)	

Road traffic accidents (RTA) were the primary mechanism of injury across the cohort (71.4% for phenytoin and 59.1% for levetiracetam; p = 0.396), followed by falls from height. Radiologically, subdural hematoma (SDH) was the most common primary lesion. Injury severity was closely matched, with baseline Glasgow Coma Scale (GCS) scores predominantly ≤8 in both cohorts (38.1% vs. 50.0%; p = 0.69), and Marshall CT scores mainly 4 or 5 (p = 0.66). Consequently, surgical intervention profiles were similar, with decompressive craniectomy being the most frequently performed procedure (>90% in both groups; p = 0.212) see table 2.

Both antiepileptic agents demonstrated comparable efficacy in preventing early post-traumatic seizures. Clinically evident seizures occurred in 9.5% of the phenytoin group compared with 4.5% of the levetiracetam group, a difference that was not statistically significant (p = 0.73) as shown table 2. Regarding the timing of the first seizure, the phenytoin group recorded both immediate (9.5%) and early seizures (4.8%). In contrast, the levetiracetam group experienced only early seizures (13.6%) and no immediate seizures, although this temporal difference was not statistically significant (p = 0.25) see table 2.

Table 2: Primary Efficacy Outcomes and EEG Findings

Parameter	Phenytoin	Levetiracetam	p-value
Clinical Seizures Present	2 (9.5%)	1 (4.5%)	0.730
Clinical Seizures Absent	19 (90.5%)	21 (95.5%)	
Immediate Seizures	2 (9.5%)	0	0.250
Early Seizures	1 (4.8%)	3 (13.6%)	
No Seizure	18 (85.7%)	19 (86.4%)	
EEG Discharge Present	1 (4.8%)	3 (13.6%)	0.450
EEG Discharge Absent	20 (95.2%)	19 (86.4%)	
No Adverse Effect	17 (81.0%)	20 (90.9%)	0.210
Deranged LFT	3 (14.2%)	0	
Irritability	0	2 (9.1%)	
Rash	1 (4.8%)	0	

Subclinical seizure activity, evaluated via electroencephalography (EEG), revealed epileptiform discharges in 4.8% of the phenytoin group and 13.6% of the levetiracetam group (p=0.45). Routine EEG analysis consistently demonstrated generalized background slowing (delta/theta activity) across the cohort, secondary to diffuse cerebral edema and continuous fentanyl sedation. Breach rhythms were

universally observed, corresponding to surgical craniectomy sites.

Clinical Course and Mortality

Neurological recovery during the ICU stay was comparable between the two cohorts. The best GCS achieved prior to ICU discharge peaked around 9–10 for the majority of patients in both groups (p=0.294). ICU length of stay varied widely but was most frequently 11–15 days for patients receiving phenytoin and 16–20 days for those receiving levetiracetam (p=0.373). The overall mortality rate was slightly higher in the phenytoin group (28.6%) compared to the levetiracetam group (18.2%); however, this difference did not reach statistical significance (p=0.50) as shown in table 3, indicating a comparable impact on short-term survival.

Table 3: Interventions and Secondary Clinical Outcomes

Parameter	Phenytoin	Levetiracetam	p-value
Decompressive Craniectomy	20 (95.2%)	20 (90.9%)	0.212
Evacuation of EDH	0	2 (9.1%)	
Depressed Skull Elevation	1 (4.8%)	0	
ICU Stay 8–10 days	3 (14.3%)	2 (9.1%)	0.373
ICU Stay 11–15 days	10 (47.6%)	5 (22.7%)	
ICU Stay 16–20 days	6 (28.6%)	9 (40.9%)	
ICU Stay >20 days	2 (9.5%)	6 (27.3%)	
Best GCS 3–8	5 (23.8%)	10 (45.5%)	0.294
Best GCS 9–11	13 (61.9%)	11 (50.0%)	
Best GCS 12–15	2 (9.5%)	1 (4.5%)	
Mortality Yes	6 (28.6%)	4 (18.2%)	0.500
Mortality No	15 (71.4%)	18 (81.8%)	

Safety, Tolerability, and Laboratory Parameters:

Adverse drug reactions were observed more frequently in the phenytoin arm (19.0%) than in the levetiracetam arm (9.0%), though this trend was not statistically significant (p = 0.21). Side effects in the phenytoin group included deranged liver function tests (14.2%) and dermatological rash (4.8%). Conversely, adverse effects in the levetiracetam group were exclusively neurobehavioral, limited to instances of irritability (9.1%). Systematic evaluation of laboratory parameters revealed no significant drug-induced derangements. Complete blood count (CBC) variables, including hemoglobin, total leukocyte count, and differentials, remained comparable between groups ($p > 0.20$). Similarly, biochemical liver profiles including serum bilirubin, alanine aminotransferase (ALT), alkaline phosphatase (ALP), and serum albumin showed no significant intergroup variations (all $p > 0.05$), suggesting that both agents maintained an acceptable hepatic safety profile during the acute phase of treatment.

Table 4: Hematological and Hepatic Laboratory Parameters

Parameter	Phenytoin (Mean ± SD)	Levetiracetam (Mean ± SD)	p-value
Hemoglobin (g/dL)	10.5 ± 1.32	10.8 ± 1.43	0.494
WBC Count	12756.5 ± 3377.7	11733.3 ± 3722.5	0.368
Neutrophils (%)	75.59 ± 10.41	71.31 ± 12.11	0.238
Lymphocytes (%)	16.53 ± 9.09	20.08 ± 9.44	0.233
Eosinophils (%)	0.97 ± 1.29	1.07 ± 1.47	0.820
Monocytes (%)	6.22 ± 1.85	6.92 ± 2.01	0.258
Bilirubin (mg/dL)	0.67 ± 0.18	0.73 ± 0.18	0.071
ALT (U/L)	30.94 ± 10.13	30.76 ± 9.71	0.248
ALP (U/L)	89.03 ± 13.34	89.50 ± 13.07	0.996
Total Protein (g/dL)	6.36 ± 0.57	6.32 ± 0.61	0.276
Albumin (g/dL)	3.29 ± 0.43	3.29 ± 0.38	0.900

DISCUSSION

The primary objective of this study was to compare the efficacy and safety of levetiracetam versus phenytoin for prophylaxis of early post-traumatic seizures in severe traumatic brain injury. Post-traumatic seizures are recognized contributors to secondary brain injury and worse neurological outcomes following severe TBI.[6,7] Our demographic data, which revealed a strong male predominance and identified road traffic accidents as the primary mechanism of injury, aligns with the established epidemiology of severe TBI in low- and middle-income countries.[5] Baseline injury severity, reflected by comparable GCS scores and Marshall CT scores, was well matched between the cohorts, mirroring populations studied by Jones et al.[17] and Szaflarski et al.[18]. Regarding primary efficacy, the incidence of clinically evident seizures was low and statistically indistinguishable between the phenytoin and levetiracetam groups. This is consistent with multiple robust meta-analyses, including those by Xu et al. [19] and Yang et al. [20], which reported no significant superiority of either agent in preventing early post-traumatic seizures.

Crucially, our study incorporated EEG monitoring to detect subclinical seizures, a frequently underdiagnosed complication in sedated and mechanically ventilated patients. [6] Subclinical epileptiform discharges were noted in both treatment groups. The numerically higher but statistically non-significant rate of EEG abnormalities under levetiracetam therapy reflects similar findings reported by Jones et al. [17] While efficacy was comparable, the safety profiles differed. Phenytoin administration was associated with a higher incidence of adverse events, predominantly dermatological reactions and hepatic enzyme derangements. In contrast, levetiracetam-related adverse effects were limited to neurobehavioral symptoms. This observation aligns with findings by Karamian et al. [16] and Xu et al. [19], who highlighted levetiracetam's favorable pharmacokinetic profile and lower potential for drug interactions. ICU stay and mortality did not differ significantly between groups. Mortality rates observed in our study were comparable to those reported by Younus et al. [21] and McGinn et al.[22]. Although Karamian et al. [16] suggested a shorter ICU stay with levetiracetam, this trend was not observed in our cohort.

Strengths and Limitations

A major strength of this study is its inclusion of continuous/snapshot EEG monitoring within a highly homogeneous, severely injured neurosurgical cohort (predominantly undergoing decompressive craniectomy). This allowed for the detection of non-convulsive status epilepticus (NCSE), avoiding reliance on purely clinical observations that are frequently masked by continuous ICU sedation (e.g., fentanyl). However, several limitations must be acknowledged. The small sample size restricts the statistical power required to detect subtle differences in rare outcomes like mortality. As a single-center study, external validity may be constrained by institution-specific critical care protocols. Furthermore, rigorous EEG monitoring in the ICU proved technically challenging; issues such as electrode displacement due to patient movement, sweat artifacts, and interference from the ICU environment limited the feasibility of uninterrupted, prolonged monitoring. Finally, the absence of serum phenytoin drug level monitoring—critical given its narrow therapeutic index—and the limitation to a 7-day follow-up window preclude conclusions regarding late PTS and long-term functional recovery.

CONCLUSIONS

The present pilot randomized study demonstrated comparable efficacy of levetiracetam and phenytoin for prevention of early post-traumatic seizures in severe traumatic brain injury. Although levetiracetam was associated with fewer adverse effects, the observed differences were not statistically significant. Larger

multicentre randomized trials are required before definitive recommendations regarding superiority of either agent can be made.

Declaration by Authors

Ethical Approval: Approved
Acknowledgement: None
Source of Funding: None
Conflict of Interest: The authors declare no conflict of interest.

REFERENCES

1. Saatman KE, Duhaime AC, Bullock R, Maas AI, Valadka A, Manley GT; Workshop Scientific Team and Advisory Panel Members. Classification of traumatic brain injury for targeted therapies. J Neurotrauma. 2008 Jul;25(7):719-38. doi: 10.1089/neu.2008.0586.
2. Vreeburg RJG, van Leeuwen FD, Manley GT, Yue JK, Brennan PM, Sun X, Jain S, van Essen TA, Peul WC, Maas AIR, Menon DK, Steyerberg EW; CENTER-TBI, TRACK-TBI participants and investigators, and the members of the clinical working group of the National Institutes of Health–National Institute of Neurological Disorders and Stroke initiative on classification and nomenclature of traumatic brain injury. Validation of the GCS-Pupil Scale in Traumatic Brain Injury: Incremental Prognostic Value of Pupillary Reactivity with GCS in the Prospective Observational Cohorts CENTER-TBI and TRACK-TBI. J Neurotrauma. 2025 May;42(9-10):798-813. doi: 10.1089/neu.2024.0458.
3. Maas AI, Hukkelhoven CW, Marshall LF, Steyerberg EW. Prediction of outcome in traumatic brain injury with computed tomographic characteristics: a comparison between the computed tomographic classification and combinations of computed tomographic predictors. Neurosurgery. 2005 Dec;57(6):1173-82; discussion 1173-82. doi: 10.1227/01.neu.0000186013.63046.6b.
4. Mohammadifard M, Ghaemi K, Hanif H, Sharifzadeh G, Haghparast M. Marshall and Rotterdam Computed Tomography scores in predicting early deaths after brain trauma. Eur J Transl Myol. 2018 Jul 16;28(3):7542. doi: 10.4081/ejtm.2018.7542.
5. World Bank. Traffic Crash Injuries and Disabilities: The Burden on Indian Society. Accessed January 28, 2024 at: https://documents1.worldbank.org/curated/en/761181612392067411/pdf/Traffic-Crash-Injuries-and-Disabilities-The-Burden-on-Indian-Society.pdf
6. Fordington S, Manford M. A review of seizures and epilepsy following traumatic brain injury. J Neurol. 2020 Oct;267(10):3105-3111. doi: 10.1007/s00415-020-09926-w.
7. Anwer F, Oliveri F, Kakargias F, Panday P, Arcia Franchini AP, Iskander B, Hamid P. Post-Traumatic Seizures: A Deep-Dive Into Pathogenesis. Cureus. 2021 Apr 10;13(4):e14395. doi: 10.7759/cureus.14395.
8. Olanow CW, Finn AL. Phenytoin: pharmacokinetics and clinical therapeutics. Neurosurgery 1981; 8:112–7. doi: 10.1227/00006123-198101000-00022.
9. Glantz MJ, Cole BF, Forsyth PA, et al. Practice parameter: anticonvulsant prophylaxis in patients with newly diagnosed brain tumors. Report of the Quality Standards Subcommittee of the American Academy of Neurology. Neurology. 2000 May 23;54(10):1886-93. doi: 10.1212/wnl.54.10.1886.
10. Patel NC, Landan IR, Levin J, Szaflarski J, Wilner AN. The use of levetiracetam in refractory status epilepticus. Seizure 2006;15(3):137–41. doi: 10.1016/j.seizure.2005.12.003.
11. Gabriel WM, Rowe AS. Long-term comparison of GOS-E scores in patients treated with phenytoin or levetiracetam for posttraumatic seizure prophylaxis after traumatic brain injury. Ann Pharmacother. 2014 Nov;48(11):1440-4. doi: 10.1177/1060028014549013.
12. Michelucci R. Optimizing therapy of seizures in neurosurgery. Neurology 2006; 67: S14–8. doi: 10.1212/wnl.67.12_suppl_4.s14.
13. Meshkini A, Ghojazadeh M, GolbaharHaghighi A, ZareaGavgani V, LotfiSadigh S. Comparison of levetiracetam versus phenytoin for seizure prophylaxis in patients with traumatic brain injury: a meta-analysis. J Anal Res Clin Med. 2015;3(2):118–25. doi:10.15171/jarcm.2015.018
14. Khan NR, VanLandingham MA, Fierst TM, Hymel C, Hoes K, Evans LT, Mayer R, Barker F, Klimo P Jr. Should Levetiracetam

or Phenytoin Be Used for Posttraumatic Seizure Prophylaxis? A Systematic Review of the Literature and Meta-analysis. Neurosurgery. 2016 Dec;79(6):775-782. DOI: 10.1227/NEU.0000000000001445

15. Wang BC, Chiu HY, Luh HT, Lin CJ, Hsieh SH, Chen TJ, Wu CR, Chen PY. Comparative efficacy of prophylactic anticonvulsant drugs following traumatic brain injury: A systematic review and network meta-analysis of randomized controlled trials. PLoS One. 2022 Mar 31;17(3): e0265932. doi: 10.1371/journal.pone.0265932.
16. Karamian A, Farzaneh H, Taheri M, Seifi A. Effectiveness of Levetiracetam versus phenytoin in preventing seizure in traumatic brain injury patients: A systematic review and meta-analysis. Clin Neurol Neurosurg. 2024 May; 240: 108251. doi: 10.1016/j.clineuro.2024.108251.
17. Jones KE, Puccio AM, Harshman KJ, Falcione B, Benedict N, Jankowitz BT et al. Levetiracetam versus phenytoin for seizure prophylaxis in severe traumatic brain injury. Neurosurg Focus. 2008 Oct;25(4): E3. doi: 10.3171/FOC.2008.25.10. E3.
18. Szaflarski JP, Sangha KS, Lindsell CJ, Shutter LA. Prospective, randomized, single-blinded comparative trial of intravenous levetiracetam versus phenytoin for seizure prophylaxis. Neurocrit Care. 2010 Apr;12(2):165-72. doi: 10.1007/s12028-009-9304-y.
19. Xu JC, Shen J, Shao WZ, Tang LJ, Sun YZ, Zhai XF et al. The safety and efficacy of levetiracetam versus phenytoin for seizure prophylaxis after traumatic brain injury: A systematic review and meta-analysis. Brain Inj. 2016; 30(9):1054-61. doi: 10.3109/02699052.2016.1170882.
20. Yang Y, Zheng F, Xu X, Wang X. Levetiracetam Versus Phenytoin for Seizure Prophylaxis Following Traumatic Brain Injury: A Systematic Review and Meta-Analysis. CNS Drugs. 2016 Aug;30(8):677-88. doi: 10.1007/s40263-016-0365-0.
21. Younus SM, Basar S, Gauri SA, Khan AA, Imran M, Abubakar S, Sheikh D, Shehbaz N, Ashraf J. Comparison of Phenytoin versus Levetiracetam in Early Seizure Prophylaxis after Traumatic Brain Injury, at a Tertiary Care Hospital in Karachi, Pakistan. Asian J Neurosurg. 2018 Oct-Dec;13(4):1096-1100. doi: 10.4103/ajns.AJNS_125_17.
22. McGinn RJ, Aljoghaiman MS, Sharma SV. Levetiracetam vs phenytoin prophylaxis in severe traumatic brain injury: Systematic review and meta-analysis. Interdisciplinary Neurosurgery. 2022 Mar 1; 27:101394. https://doi.org/10.1016/j.inat.2021.101394

How to cite this article: Eman Aftab, Zulfiqar Ali, Iqra Nazir, Adnan Qadri. A comparison of phenytoin and levetiracetam for prophylaxis of seizures in the early postoperative period in traumatic brain injury patients. *Int J Health Sci Res.* 2026; 16(6):143-151. DOI: *https://doi.org/10.52403/ijhsr.20260616*

******