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Research Article

A Comparison of Seizure Prophylaxis in Brain Traumatic Injury: Sodium Valproate versus Levetiracetam

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Abstract

Introduction: Literature is rife with discordant results regarding the use of antiepileptic drugs for prophylaxis of Post-traumatic epilepsy. This study was conducted in Isfahan hospitals to compare the effectiveness of Sodium Valproate and Levetiracetam in preventing early seizures in patients with traumatic brain injuries.

Method: A total of 160 patients with traumatic brain injury treated in Kashani Hospital (Isfahan, Iran) from 2024 to 2025 were enrolled and divided into group A (n=80) and group B (n=80) according to random sampling. The medication was continued for 3 months after the injury.

Result: There were no statistically significant differences in demographic and clinical information between the two groups (P>0.05). We failed to determine a significant relationship between the antiepileptic drug used and the initial EEG (P=0.584) and seizure activity (P= 0.680) between the two drug groups. However, a significant correlation between the antiepileptic drug used and seizure activity was found at subsequent follow-ups (10, 180 days); patients who took levetiracetam had a decreased incidence of seizure activity at follow-ups. There was no significant correlation between the GCS score, both initially and on two follow-ups, and the antiepileptic drug used.

Conclusion : Logically, it would seem that the long-lasting high risk of epilepsy after brain injury might be reduced if prophylactic antiepileptic drugs are administered. Looked specifically at prophylactic antiepileptic drugs post-TBI and reported a better safety profile, with a lower adverse drug reaction rate, for Levetiracetam versus Sodium Valproate.

Keywords: Seizure, Prophylaxis, Brain Traumatic Injury, Sodium Valproate, Levetiracetam.

Introduction

Traumatic Brain Injury (TBI) has recently become a significant global concern due to the rising number of cases resulting in long-term disability and impacting healthcare systems [1]. This injury can lead to various adverse effects, ranging from simple seizures to debilitating chronic epilepsy [2].

Seizures following trauma are typically categorized into immediate, early, and late seizures [3]. Immediate seizures refer to those occurring at the time of or within a few minutes after the impact [4]. Seizures occurring within one week after the head injury are termed early seizures, while late seizures occur more than one week after the injury [5].

Approximately 25% of individuals who experience early seizures after trauma may develop additional seizures months or years later. Medications used to control seizures are called antiepileptic drugs (AEDs) [6]. These drugs may also be utilized for other issues, such as chronic pain, restlessness, or mood instability [7].

The selection of appropriate treatment depends on the specific brain injury of the patient. A study aimed at identifying the characteristics of brain injuries associated with the development of seizures revealed that the increased risk of seizures after TBI heavily depends on the injury's severity and the time since the injury occurred [8]. Factors such as age over 65, skull fractures, subdural hematoma, and loss of consciousness

or amnesia lasting more than one day have been identified as significant risk factors for subsequent seizures [9]. Different age groups also exhibit varying results among TBI patients, with children being more prone to early seizures while adolescents and adults are more susceptible to late seizures [10].

In 1978, the Food and Drug Administration (FDA) introduced Valproic Acid (VPA) as a frontline or adjunctive treatment for various types of epilepsy, widely used for seizure management [11]. Subsequent research findings indicated that Valproic Acid significantly reduces the occurrence and severity of seizures in most patients, albeit with common side effects such as gastrointestinal, neurological, and hematological symptoms [12]. These side effects are often reduced over time or mitigated through proper dosage adjustment. Other drug-related side effects include headaches, abdominal pain, drowsiness, dizziness, depression, appetite changes, light sensitivity, and more [11].

In 2000, the Food and Drug Administration approved the use of Levetiracetam as an adjunctive treatment for focal, myoclonic, and primary generalized seizures. This drug chemically differs from other antiepileptic drugs. However, it offers desirable safety profiles, unique mechanisms of action, and minimal drug interactions, making it an attractive therapeutic choice for seizure management [13].

Given the extensive use of Sodium Valproate and Levetiracetam in various hospital emergency departments for trauma patients, this current study was conducted in Isfahan hospitals to compare the effectiveness of Sodium Valproate and Levetiracetam in preventing early seizures in patients with traumatic brain injuries.

Methods

A total of 160 patients with traumatic brain injury treated at Kashani Hospital (Isfahan, Iran) from 2024 to 2025 were enrolled and divided into group A (n=80) and group B (n=80) by random sampling.

This study was approved by the Ethics Committee of Isfahan University of Medical Sciences (IR.MUI.MED.REC.1401.378). Patients who participated in this research had complete clinical data. Patients and their family members (Severe TBI) were informed of this study and signed an informed consent form.

Inclusion criteria were TBI patients admitted to the hospital with a time from injury to presentation of <12 h, GCS scores of 9–12 (moderate), GCS scores <8 (severe), and age >18 years.

Exclusion criteria included any previous history of brain injury, brain tumor, cerebral infarct or spontaneous intracerebral hemorrhage, hemodynamically unstable patients, GCS scores of >12 and age <18 years, coincidence of thoracic and abdominal trauma, known hypersensitivity to any anticonvulsant, any treatment, or condition contraindicated for the drugs used in the study. Furthermore, pregnant patients and patients with more than 12 hours between TBI and admission were excluded.

Patients were randomly divided into two groups (A and B) by a random allocation software. Group (A) patients were given Sodium Valproate for seizure prophylaxis, whereas Group (B) patients received levetiracetam.

Patients were initiated on a protocol of intravenous (IV) levetiracetam monotherapy or Sodium Valproate for early seizure prophylaxis based on standardized hospital-wide clinical protocols. Therapy was initiated within 12 h of injury.

Data were collected using a predesigned pro forma in both groups.

Group A: 250 mg of sodium valproate was administered intravenously every 12 hours and then orally (PO) after the patient was PO (able to take the drug orally).

Group B: 500 mg was administered intravenously every 12 hours and then orally after the patient was able to take the drug orally. The medication was continued for 3 months after the injury.

The stated doses were administered for a period of three months following the receipt of the effective dose of the drug.

Data were analyzed using IBM SPSS (IBM Corporation, Armonk, New York, United States) version 16.0 for Windows. Continuous variables such as age are expressed as mean and standard deviation, whereas categorical variables such as gender are given in frequency and percentage. Data analysis was done to

determine if there are any significant differences between the two cohorts with respect to abnormal EEG findings and seizure activity. The chi-square test was utilized to compare the two medication groups in terms of their age, gender, and GCS scores, and Fisher's exact test was utilized to determine any differences between the two groups in terms of the EEG findings and seizure activity, respectively. $P < 0.05$ was considered statistically significant.

Results

The study population consisted of 160 patients, of whom 151 were males and 49 were females, with a mean age of 44.91±10.84 years. The most prevalent Trauma Mechanism was Motor Vehicle Crashes in 48% of patients. Table 1 shows the patients' demographic and clinical information collected at admission. There were no statistically significant differences in the demographic and clinical information of patients between the two groups (P>0.05).

There is no significant correlation between mode of trauma mechanism and GCS (P>0.05) (Table 2).

We failed to determine a significant relationship between the antiepileptic drug used with the initial EEG (P = 0.584) and seizure activity (P = 0.680) in between the two drug groups. However, a significant correlation of the anti-epileptic drug used was found with seizure activity on subsequent follow-ups (10, 180 days); patients who took levetiracetam had decreased incidence of seizure activity on follow-ups. There was no significant correlation between the GCS score both initially and on two follow-ups with the antiepileptic drug used (Table 3).

Table 1. Demographic Information of the Patients

Variable	Group A (n=80)	Group B (n=80)	P value
Sex, (Male: Female), n (%)	62 (77.5)/ 18 (22.5)	59 (73.75) / 21 (26.25)	0.591
Age, year, (mean±SD)	45.62±10.34	44.43±11.18	0.448
BMI, (mean±SD)	25.01±1.80	24.91±1.90	0.716
GCS, n (%) Moderate (9-12)/ Severe (3-8)	66 (82.5)/ 14 (17.5)	56 (70)/ 24 (30)	0.079
Trauma Mechanism, n (%)			
Falls	16 (20)	23 (28.75)	0.100
Motor Vehicle Crashes	47 (58.8)	39 (48.75)	
Struck by objects	10 (12.5)	11 (13.75)	
Other	7 (8.8)	7 (8.75)	
Location Of Injury, n (%)			
Temporal	7 (8.8)	18 (22.5)	0.750
Parietal	36 (45)	48 (60)	
Occiput	25 (31.3)	10 (12.5)	
Frontal	8 (10)	2 (2.5)	
Diffuse	4 (5)	2 (2.5)	
Type of bleeding, n (%)			
Subdural hematoma	5 (6.3)	9 (11.25)	0.240
Contusion	20 (25)	19 (23.75)	
Subarachnoid hemorrhage	34 (42.5)	30 (37.5)	
Intracerebral hemorrhage	4 (5)	3 (3.75)	
Intraventricular hemorrhage	3 (3.8)	7 (8.75)	
Epidural hematoma	14 (17.5)	12 (15)	

Other: Sports, Violence, Self-harm.

Table 2. Various characteristics such as trauma mechanism, GCS, and loss of consciousness after injury in the patient population

Trauma Mechanism	loss of consciousness		GCS		
	yes	no	Moderate	Severe	Total
Falls	10	31	24	15	39
Motor Vehicle Crashes	21	53	65	21	86
Struck by objects	11	15	14	7	21
Other	4	15	9	5	14
Total	46	114	112	48	160

P value: 0.664

Table 3. Correlation of electroencephalographic findings and seizure activity and Glasgow Coma Scale score (initially and on follow up) with the drug used

EEG finding	Group A (n=80)	Group B (n=80)	P value 1* P value 1#	P value 2
Initially				
Abnormal EEG/ Seizure Activity GCS, (mean±SD)	2 / 7 (28.5) 10.5±2.12	2 / 8 (25) 11.5±0.7	0.584*	0.592
Seizure activity (24-48 h) GCS, (mean±SD)	7 / 80 (8.75) 10.14±1.34	8 / 80 (10) 9.34±2.79	0.680	0.410
follow up 10 day				
Abnormal EEG/ Seizure Activity GCS, (mean±SD)	6/ 11 (55.5) 11.34±0.55	3/ 5 (60) 10±1	0.095*	0.067
Seizure activity (7-10 day) GCS, (mean±SD)	11 / 80 (13.75) 11.66±0.57	5/ 80 (6.25) 9.2±1.92	0.014	0.080
follow up 180 day				
Abnormal EEG/ Seizure Activity GCS, (mean±SD)	5 / 10 (50) 10±1	2 / 5 (40) 7±2.82	0.084*	0.170
Seizure activity (10-180 day) GCS, (mean±SD)	10/ 80 (12.5) 9.5±2.82	5/ 80 (6.25) 10±1	0.028	0.480

P value 1*: EEG between two groups, P value 1#: Seizure activity between two groups, P value 2: GCS between two groups

Discussion

TBI is one of the main causes of long-term neurological disability, and the increased risk of seizures that follows plays an important role as a source of further impairment [1]. It is also a predictor of epilepsy in the future. Classically, AEDs are used to reduce the incidence of primary post-traumatic stress (PTS), but different studies have been full of conflicting results regarding the use of these drugs for the prevention of Post-traumatic epilepsy (PTE) and PTS [14].

It seems reasonable that the high long-term risk of epilepsy after brain injury may be reduced if prophylactic AEDs are administered [15].

Also, the results of the studies indicated that in severe TBI, prophylactic antiepileptics (AEDs) reduced the incidence of initial PTS, but did not lead to long-term improvement. In some studies, compared to phenytoin, Levetiracetam had fewer side effects and better safety for reducing seizures after traumatic brain injury [14,16,17].

In the present study, the use of both Levetiracetam and sodium valproate had an effective role in reducing abnormal EEG findings, but Levetiracetam was significantly more successful in reducing seizures.

The results of Liou (2020) study, after examining patients in Taiwan, indicated that AED prophylaxis was ineffective in preventing seizures, because the seizure rate was not significantly different in patients who received the drug or not [18].

Fordington (2020) [3] showed in a study that there is no relationship between the initial use of antiseizure medication (ASM) and the risk of epilepsy at 18 or 24 months in adults with TBI.

DJohn (2020) [19] also examined 412 TBI patients in the United States. The results showed that inappropriate use of Levetiracetam is common in patients hospitalized with non-severe TBI, and many patients continue Levetiracetam after discharge. Patients with mild and moderate TBI probably do not need seizure prophylaxis

with Levetiracetam, so education about the appropriate indication and duration of Levetiracetam use in patients with TBI is essential.

The results of Zaman (2017) [20] study in Texas also revealed that despite existing guidelines to stop seizure prophylaxis after TBI, some patients remain on AED treatment and may be inappropriately exposed to potential drug side effects

Conclusion

Literature is rife with discordant results regarding the use of AEDs for prophylaxis of PTE and PTS. AEDs have been classically prescribed to reduce the incidence of early PTS. Logically, it would seem that the long-lasting high risk of epilepsy after brain injury might be reduced if prophylactic AEDs are administered. looked specifically at prophylactic AEDs post-TBI and reported a better safety profile, with a lower adverse drug reaction rate, for Levetiracetam versus Sodium Valproate.

Conflict of Interest Disclosures

The authors declare no conflict of interest.

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Authors' Contributions

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Ethical Statement

The current study was approved by the Isfahan University of Medical Sciences Ethics Committee with the code of IR.MUI.MED.REC.1401.378.

Declaration of Generative AI and AI-assisted technologies

During the preparation of this work, the authors did not use Chatgpt to write the manuscript.

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