Levetiracetam Dosing Based on Glasgow Coma Scale Scores in Pediatric Traumatic Brain Injury Patients

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Abstract

Introduction Severe traumatic brain injury (TBI) increases the risk of early posttraumatic seizures (EPTS). Guidelines suggest the use of prophylactic antiseizure agents, including levetiracetam. This study aims to evaluate the feasibility of using levetiracetam dosing based on Glasgow Comas Scale (GCS) scores with higher doses used for more severe TBI.

Methods Patients 6 months to 18 years old admitted to Penn State Hershey Children's Hospital (PSHCH) with a TBI who received levetiracetam for EPTS prophylaxis with at least one documented GCS score were included. Patients were divided into two cohorts: before and after implementation of the pediatric TBI Cerner PowerPlan at PSHCH which standardized levetiracetam dosing based on GCS scores. Primary outcome was appropriate dosing of levetiracetam based on GCS. Secondary outcomes included seizure occurrence and adverse effects.

Results Eighty-five patients were included: 42 in the pre-PowerPlan group and 43 in the post-PowerPlan group. Overall, 46 (54%) patients received the appropriate levetiracetam dose based on GCS (pre-PowerPlan, $n = 19$ [45%] vs. post-PowerPlan $n = 27$ [63%], $p = 0.104$). Sixty-four percent of severe TBI patients received appropriate levetiracetam dosing after implantation of the PowerPlan compared with 28% prior to the PowerPlan ($p = 0.039$). Three patients in each group experienced a seizure while on levetiracetam. Two patients experienced agitation and somnolence attributed to levetiracetam.

Conclusion Levetiracetam dosing based on GCS scores in pediatric TBI patients is a novel approach, and dosing accuracy may be increased with use of a PowerPlan. Additional large-scale studies are needed to evaluate efficacy and safety of this approach prior to widespread implementation.

Keywords
- seizures
- levetiracetam
- traumatic brain injury
- critical care

Introduction

Early posttraumatic seizures (EPTS), defined as a seizure within 7 days of injury, are a common complication of patients presenting with traumatic brain injury (TBI).[1] EPTS are associated with complications that affect neurological development and impact quality of life.[2] Multiple risk factors have been found to contribute to the development of

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Table 1 Levetiracetam dosing guidelines at Penn State Health Children's Hospital for patients aged 6 months to 18 years with traumatic brain injury

GCS score	Dose
14–15	10 mg/kg every 12 hours (maximum dose 1,500 mg)
9–13	40 mg/kg loading dose (maximum dose 3,000 mg) 20 mg/kg every 12 hours (maximum dose 1,500 mg)
≤8	60 mg/kg loading dose (maximum dose 3,000 mg) 30 mg/kg every 12 hours (maximum dose 1,500 mg)

Abbreviations: GCS, Glasgow Coma Scale; kg, kilogram; mg, milligram.

EPTS including severe TBI, defined as a Glasgow Coma Scale (GCS) score less than 9.[3–6]

Utilization of antiseizure medications have also been found to be a protective factor against EPTS,[3] and current guidelines suggest the use of a prophylactic antiseizure agent, which include either levetiracetam or phenytoin. However, guidelines cannot recommend one agent over the other.[7] Prior studies have found conflicting results when comparing both agents, with one study noting that levetiracetam was more efficacious than phenytoin while others noting no difference between the agents.[8,9]

Given the relatively benign adverse event profile of levetiracetam, minimal drug interactions, and lack of therapeutic drug monitoring needed, providers may opt to choose levetiracetam over other agents.[10–12] Prophylactic levetiracetam for TBI was evaluated in several studies which have found mixed results for efficacy. Some studies showed favorable results in reducing seizures while others found that it was similar to placebo; however, all of these studies were small and various dosing regimens were utilized.[5,9,13] There are no current consensus recommendations on the dose to utilize for EPTS, and doses have ranged between 5 and 60 mg/kg.[5,13,14]

In February 2022, the Penn State Hershey Children's Hospital (PSHCH) implemented standardized dosing of levetiracetam based on GCS score for seizure prophylaxis in pediatric TBI patients; this standardized dosing was then incorporated into a TBI Cerner PowerPlan (►**Table 1**). No prior studies, to our knowledge, have evaluated the use of levetiracetam in pediatric TBI patients based on GCS scores. The aim of this study, therefore, was to evaluate the feasibility of levetiracetam dosing for preventing of EPTS based on GCS scores in pediatric TBI patients.

Methods

Development of Levetiracetam Dosing Guidelines at Penn State Hershey Children's Hospital

A lack of standardized levetiracetam dosing for EPTS prophylaxis for pediatric TBI patients at PSHCH was identified in 2021. Based on the increased risk of EPTS with more severe TBI, lack of consensus about recommended levetiracetam dosing for prevention of EPTS, and concern about adverse effects of higher doses of levetiracetam, guidelines were established at PSHCH using existing literature and expert consensus between pediatric neurosurgeons, pediatric trauma surgeons, pediatric neurologists, and pediatric intensivists that standardized levetiracetam dosing based on GCS. Patients less than 6 months of age were excluded because of concerns regarding reliability of GCS in this population as well as the preference of some providers for antiseizure medications other than levetiracetam (e.g., phenobarbital). Prior to development of the guidelines and PowerPlan, there was no standardized or intended levetiracetam dosing for any pediatric TBI patients, including those with severe TBI. After the implementation of the guidelines and PowerPlan, dosing for patients under 6 months remained at the discretion of the attending neurosurgeon.

Study Design

This was a retrospective, Institutional Review Board exempt study conducted at PSHCH, a level 1 pediatric trauma center and 136 pediatric bed hospital.

Patient Characteristics

Patients were included in the study if they were at least 6 months of age and less than 18 years of age, presented to PSHCH with a TBI, received levetiracetam for EPTS prophylaxis, and had at least one documented GCS score. Initial GCS scores were collected at three different time points (if available): as reported on the scene of the injury by Emergency Medical Services (EMS), in the PSHCH Emergency Department (ED), and by the admitting service after hospital admission. Patients were excluded if they had a history of a known seizure disorder or if they received an antiseizure medication at any point in time (including benzodiazepines being used to treat seizures) prior to receiving levetiracetam for EPTS. We included patients who received medication with antiseizure effects for purposes including sedation or agitation. Patients were separated into two cohorts: those who received levetiracetam for a TBI prior to implementation of the TBI PowerPlan and those who received levetiracetam for a TBI after implementation of the TBI PowerPlan.

Study Outcome

The primary outcome of this study was appropriate levetiracetam dosing according to the PSHCH GCS-based recommendations after implementation of the PowerPlan. Secondary outcomes included occurrence of seizures within the first 7 days of traumatic injury, occurrence of adverse events, utilization of the PowerPlan, time to first levetiracetam dose, and duration of levetiracetam therapy.

Data Collection

Study data were collected and managed using Research Electronic Data Capture (REDCap) tools hosted at Penn State Milton S. Hershey Medical Center and Penn State College of Medicine. REDCap is a secure, web-based application designed to support data capture for research studies. Baseline demographics collected included the following: age, sex, race, ethnicity, mechanism and classification of injury, initial

GCS scores as noted above, level of care (either Pediatric Intensive Care Unit, Pediatric Intermediate Care Unit, or floor status), levetiracetam dose, and concomitant medications administered with antiseizure effects. The primary outcome of appropriate levetiracetam dosing was based on GCS upon admission, or if unavailable, based on GCS in the ED. Dose of levetiracetam was deemed appropriate if both the loading dose, if applicable, and the maintenance dose were based on the PSHCH guidelines. For patients who received their first dose of levetiracetam dose outside of PSHCH, the dose was deemed appropriate if the ordered maintenance dose was based on the PSHCH guidelines irrespective of the dose received at the outside facility. For the secondary outcome of seizure occurrence, seizure data collected included both clinical seizures and subclinical seizures as noted on electroencephalogram (EEG). An adverse event was recorded if levetiracetam was specified as the cause or a potential cause of an adverse event as noted in the medical record. Time to first levetiracetam dose was calculated based on time of presentation to the PSHCH ED or, if unavailable, as the documented admission time. Time to first dose was not calculated for patients who received their first dose of levetiracetam prior to arrival at PSHCH.

Statistical Analysis

Statistical analysis was conducted with IBM SPSS Version 29. A chi-square test was performed for categorical data. Mann–Whitney U test was utilized for quantitative data.

Results

Medical records of 97 patients admitted between April 2021 and January 2023 to PSHCH were reviewed and met the initial inclusion criteria. Forty-nine of these patients were in the pre-PowerPlan cohort and 48 patients were in the post-PowerPlan cohort (►**Fig. 1**). Of the 49 patients in the pre-PowerPlan group, 7 met the exclusion criteria. Of the 47 patients in the post-PowerPlan group, 5 met the exclusion criteria. A total of 85 patients were included in the analysis; 42 in the pre-PowerPlan group and 43 in the post-PowerPlan group. Baseline demographics are reported and there were no significant differences in age, race, or ethnicity between

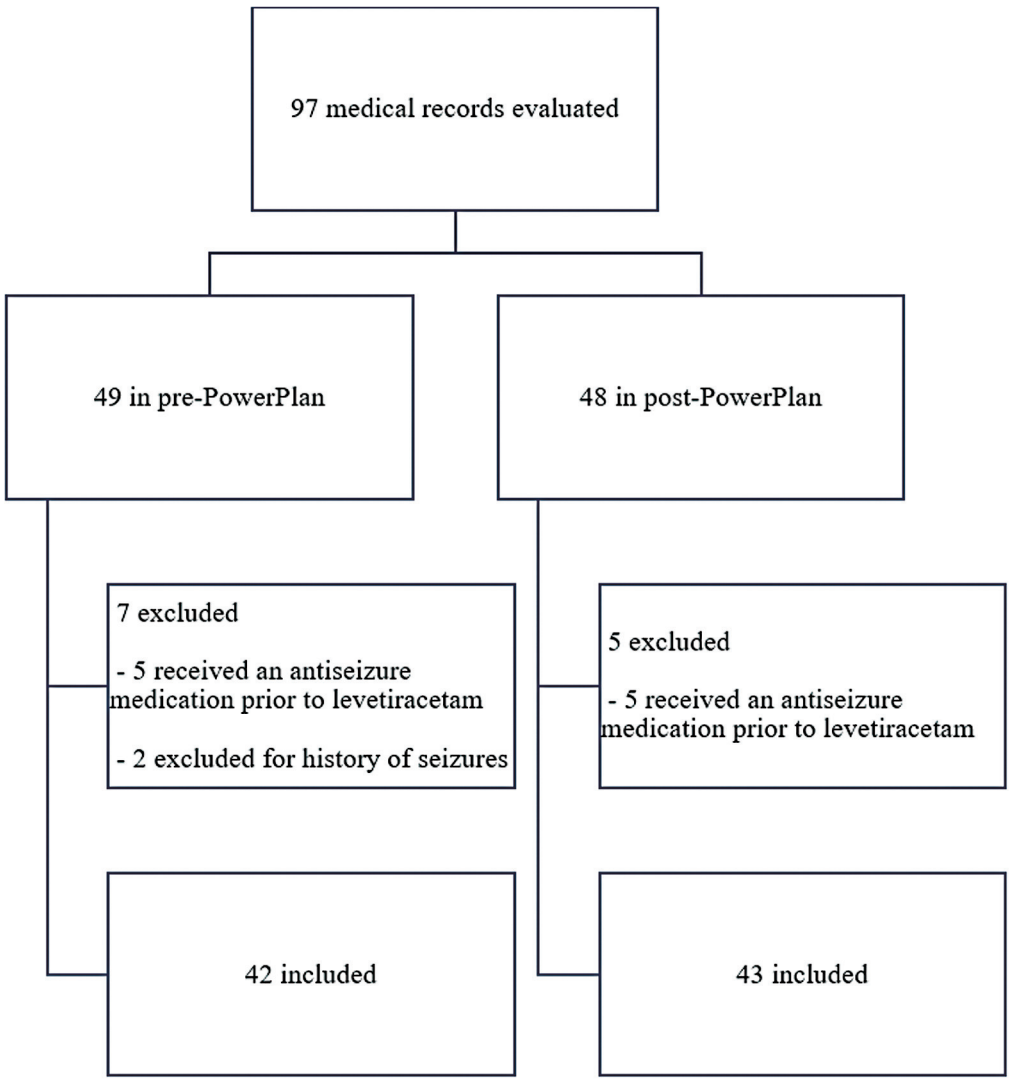

Fig. 1 Patient selection.

the two groups (►**Table 2**). There were more males in the post-PowerPlan group ($n = 33$, 77%) compared with the pre-PowerPlan group ($n = 19$, 45%; $p = 0.039$). While the post-PowerPlan group had higher median levetiracetam loading doses (40 mg/kg, interquartile range [IQR] 35–60 vs. 30 mg/kg, IQR 14–57) and maintenance doses (17 mg/kg, IQR 10–21 vs. 11 mg/kg, IQR 10–21), this did not reach statistical significance. Of note, there was one patient in the pre-PowerPlan group who only received a loading dose of levetiracetam. The majority of patients ($n = 48$, 56%) experienced multiple types of cranial injury. While there were no differences noted in type of injury between the groups, the occurrence of subarachnoid hemorrhage trended toward significance in the post-PowerPlan versus pre-PowerPlan group ($n = 13$, 30% vs. $n = 6$, 14%, $p = 0.078$). No significant differences were found in the median GCS scores reported at the three time points. No significant differences were found in concomitant antiseizure medication administration between the two groups.

Primary and secondary outcomes are noted in ►**Table 3**. Based on current PSHCH levetiracetam dosing recommendations, 45% of patients in the pre-PowerPlan group and 63% of patients in the post-PowerPlan group were dosed appropriately based on initial GCS documented after admission or, if not available, initial GCS documented in the ED ($p = 0.104$). There was a significant increase in patients with severe TBI receiving appropriate levetiracetam dosing after implementation of the PowerPlan (28 vs. 64%, $p = 0.039$). In the post-PowerPlan group, only 23% of the patients received levetiracetam that was specifically ordered through the PowerPlan itself, rather than manually entering the doses.

No statistical difference in seizure occurrence was found between the two groups; three patients in each group experienced a seizure while on levetiracetam for EPTS prophylaxis ($p = 0.976$). A comparison of the patients who experienced seizures in each group is noted in ►**Table 4**. Based on GCS score on admission, all six patients had a severe TBI and all six patients were considered underdosed based on the current levetiracetam dosing at PSHCH. In the pre-PowerPlan cohort, one patient did not receive a loading dose while one patient received a 10 mg/kg loading dose and the other received a 40 mg/kg loading dose. All three patients received a maintenance dose of 20 mg/kg. In the post-PowerPlan cohort, one patient did not receive a loading dose, while one patient received a 20 mg/kg loading dose and the other received a 30 mg/kg loading dose. Two of three patients received a 20 mg/kg maintenance dose while the remaining patient received a 30 mg/kg maintenance dose.

One patient in each group experienced an adverse event attributed to levetiracetam. The patient in the pre-PowerPlan group was noted to be agitated while the patient in the post-PowerPlan group was found to be somnolent. Both of these patients were considered to be underdosed based on the current PSHCH PowerPlan dosing guidelines. There was no significant difference in time to first dose of levetiracetam or duration of levetiracetam therapy between the two groups.

Discussion

TBI remains a significant pediatric public health problem with high mortality and morbidity, including EPTS.[2,15,16] While levetiracetam is a commonly used prophylactic antiseizure medication after TBI, there is no consensus on weight-based standardized dosing, and the reported range of dosing utilized is wide.[5,13,14] Thus, guidelines were established at PSHCH using existing literature and expert consensus between pediatric neurosurgeons, pediatric trauma surgeons, pediatric neurologists, and pediatric intensivists that standardized levetiracetam dosing based on GCS. Patients with lower GCS scores and thus more significant injury and higher risk of EPTS[1,3–6] would receive higher levetiracetam doses. This study aimed to evaluate the feasibility of varied levetiracetam dosing based on GCS, and, to our knowledge, is the first study to do so.

Overall, while there was no difference noted in appropriate levetiracetam dosing after implementation of the PowerPlan, there was a trend toward significance (45 vs. 63%, $p = 0.104$). There was no significant change in levetiracetam dosing for mild and moderate TBI patients prior to and after introduction of the PowerPlan, but there was a significant increase in appropriate dosing for severe TBI patients (28 vs. 64%, $p = 0.039$). Even after implementation of the PowerPlan, only 63% of patients received the correct dosing according to the guidelines, and usage of the PowerPlan was low. We believe that low use of the PowerPlan can largely be attributed to technical issues within Cerner that have since been addressed and expect utilization of the PowerPlan to improve over time, but this is a clear limitation of this study.

GCS scores can change over relatively short periods of time and are affected by sedative and paralytic medications; choosing which GCS to base levetiracetam dosing on is a challenge and limitation to this approach. The most accurate GCS score would be the score following resuscitation unaffected by medication administration, but it can be difficult to identify which score most accurately reflects that patient's underlying brain injury via retrospective chart review. Our data collection included GCS scores documented by EMS at the scene of the injury, upon arrival to the PSHCH ED, and after admission to the hospital. The hospital admission score was used (when available) because it was felt to represent the GCS most closely after resuscitation, but the effect that medication administration may have had on this score was not determined. It is possible that patients were dosed with levetiracetam based on what treating clinicians felt was their most accurate GCS score that was not reflected accurately in this analysis. Choosing the most appropriate GCS score to use to determine levetiracetam dosing is an overall challenge with these guidelines. Since the completion of this study, the GCS score after resuscitation in the ED trauma bay at PSHCH unaffected by medication administration is used to determine levetiracetam dosing.

There were no differences in seizure occurrence for levetiracetam based on dosing standardized to GCS scores compared with previous provider preferred dosing of levetiracetam. Notably, seizure occurrence was lower in our

Table 2 Patient characteristics

Characteristic[a]	Total ($n = 85$)	Pre-PowerPlan ($n = 42$)	Post-PowerPlan ($n = 43$)	*p*-Value
Age, years	9 [4–15]	9.5 [4–15]	7 [3–13]	0.184
Sex, male, *n* (%)	52 (61)	19 (45)	33 (77)	0.039
Race, *n* (%)				
White	64 (75)	30 (71)	34 (79)	0.414
Black	4 (5)	1(2)	3 (7)	0.317
Asian	1 (1)	1(2)	0 (0)	0.309
Other	16 (19)	10 (24)	6 (14)	0.245
Ethnicity, *n* (%)				
Hispanic or Latino	11 (13)	5 (12)	6 (14)	0.778
Non-Hispanic or Latino	71 (84)	34 (81)	37 (86)	0.527
Other	3 (4)	3 (7)	0 (0)	0.074
Levetiracetam weight-based loading dose, mg/kg[b]	$n = 27$, 39 [26–60]	$n = 13$, 30 [14–57]	$n = 14$, 40 [35–60]	0.413
Levetiracetam weight-based maintenance dose, mg/kg[c]	$n = 84$, 13 [10–21]	$n = 41$, 11 [10–21]	$n = 43$, 17 [10–21]	0.309
Mechanism of injury, *n* (%)				
Fall	38 (45)	17 (41)	21 (49)	0.438
Motor vehicle accident	28 (33)	16 (38)	12 (28)	0.318
Pedestrian versus motor vehicle	6 (7)	4 (10)	2 (5)	0.381
Gunshot wound	4 (5)	1 (2)	3 (7)	0.317
Other	7 (8)	4 (10)	3 (7)	0.669
Injury classification, *n* (%)[d]				
Skull fracture	49 (58)	24 (57)	25 (58)	0.926
Subdural hemorrhage	41 (48)	20 (48)	21 (49)	0.911
Epidural hemorrhage	16 (19)	9 (21)	7 (16)	0.544
Subarachnoid hemorrhage	19 (22)	6 (14)	13 (30)	0.078
Intraparenchymal hemorrhage	10 (12)	5 (12)	5 (12)	0.968
Other	15 (18)	10 (24)	5 (12)	0.141
Level of care, *n* (%)				
Pediatric intensive care unit	53 (62)	28 (67)	25 (58)	0.417
Pediatric intermediate care unit	24 (28)	12 (29)	12 (28)	0.946
Pediatric floor	8 (9)	2 (5)	6 (14)	0.147
GCS score[e]				
Initial at scene of injury	$n = 76$, 13 [4–15]	$n = 36$, 11 [4–14]	$n = 40$, 13 [6–15]	0.246
Initial in emergency department	$n = 78$, 14 [3–15]	$n = 42$, 13 [3–15]	$n = 36$, 14 [3–15]	0.464
Initial after hospital admission	$n = 76$, 13 [3–15]	$n = 36$, 10 [3–15]	$n = 40$, 14 [3–15]	0.302
Concomitant medications with antiseizure effects, *n* (%)				
Midazolam	33 (39)	17 (40)	16 (37)	0.757
Propofol	23 (27)	12 (29)	11 (26)	0.756
Pentobarbital	5 (6)	2 (5)	3 (7)	0.664
Gabapentin	7 (8)	5 (12)	2 (5)	0.224
Lorazepam	4 (5)	2 (5)	2 (5)	0.981
Diazepam	1 (1)	0 (0)	1 (2)	0.320

Abbreviations: GCS, Glasgow Coma Scale; kg, kilogram; mg, milligram.
[a]Data are presented as median [interquartile range], unless otherwise indicated.
[b]Per Penn State Health Children's Hospital (PSHCH) dosing guidelines, not every patient receives a loading dose. Patients who received a dose outside of PSHCH were not included.
[c]One patient in the pre-PowerPlan group only received a loading dose.
[d]Injury classification was separated into isolated injuries. More than half of all patients had multiple types of injury.
[e]Not all patients had GCS scores documented at every time point.

Table 3 Primary and secondary outcomes

Outcome[a]	Total ($n=85$)	Pre-PowerPlan ($n=42$)	Post-PowerPlan ($n=43$)	*p*-Value
Appropriate levetiracetam dose based on GCS, *n* (%)	46 (54)	19 (45)	27 (63)	0.104
Appropriate levetiracetam dose based on GCS category[b]				
14–15	28/45 (62)	12/20 (60)	16/25 (64)	0.783
9–13	4/8 (50)	2/4 (50)	2/4 (50)	1.000
≤8	14/32 (44)	5/18 (28)	9/14 (64)	0.039
Adverse events, *n* (%)	2 (2)	1 (2)	1 (2)	0.987
Agitation	1 (1)	0 (0)	1 (2)	
Somnolence	1 (1)	1 (2)	0 (0)	
Time to first dose, hours[c]	$n=74$, 5 [3–8]	$n=38$, 6 [3–8]	$n=36$, 4 [3–9]	0.552
Duration of therapy, days	4 [2–7]	5 [2–7]	3 [2–7]	0.420

Abbreviation: GCS, Glasgow Coma Scale.
[a]Data are presented as median [interquartile range], unless otherwise indicated.
[b]Reported as number of patients who received the appropriate levetiracetam dose/total number of patients with that respective GCS score (%).
[c]Did not include patients who received a dose prior to arrival at Penn State Health Children's Hospital.

Table 4 Characteristics of patients with seizure occurrence

Characteristic[a]	Total ($n=6$)	Pre-PowerPlan ($n=3$)	Post-PowerPlan ($n=3$)
Seizure type, *n* (%)			
Clinical	2 (33)	1 (33)	1 (33)
Subclinical	4 (67)	2 (67)	2 (67)
Injury classification, *n* (%)			
Skull fracture	4 (67)	2 (67)	2 (67)
Subdural hemorrhage	5 (83)	2 (67)	3 (100)
Epidural hemorrhage	1 (17)	1 (33)	0 (0)
Subarachnoid hemorrhage	2 (33)	1 (33)	1 (33)
Intraparenchymal hemorrhage	1 (17)	1 (33)	0 (0)
GCS score			
Initial at scene of injury	6 [4–9]	5 [4–5]	5 [3–7]
Initial in emergency department	5 [3–8]	3 [3]	3 [3–8]
Initial after hospital admission	3 [3–7]	3 [3]	3 [3]
Levetiracetam weight-based loading dose, mg/kg[b]	$n=4$, 30 [12–40]	$n=2$, 25 [9–25]	$n=2$, 30 [20–30]
Levetiracetam weight-based maintenance dose, mg/kg	20 [19–23]	19 [18–19]	20 [20]
Number of rescue medications	2 [1–2]	1 [0]	2 [0]
Rescue medication utilized, *n* (%)			
Fosphenytoin	3 (50)	2 (67)	1 (33)
Phenobarbital	3 (50)	0 (0)	3 (100)
Lorazepam	2 (33)	1 (33)	1 (33)
Midazolam	1 (17)	1 (33)	0 (0)
Dosed appropriately based on GCS, *n* (%)	0 (0)	0 (0)	0 (0)
Seizure time from injury in days	3 [2–4]	4 [2–4]	2 [1–2]

Abbreviations: GCS, Glasgow Coma Scale; kg, kilogram; mg, milligrams.
[a]Data are presented as median [interquartile range], unless otherwise indicated.
[b]One patient in each group did not receive a levetiracetam loading dose.

study (7% overall) compared with previously published studies.[5,9,13] The majority of patients ($n = 45$, 53%) in this study had mild TBI so were not at high risk of developing EPTS. Additionally, only 7.1% of patients had an EEG completed, so it is likely that subclinical seizures were not identified contributing to our overall low seizure incidence and this study's limitations. The six patients in our study who seized all had severe TBI and were underdosed based on dosing recommendations.

Patients less than 6 months of age were excluded from this study because they are not included in GCS-based levetiracetam dosing guidelines at PSHCH. This age group is at higher risk for EPTS and abusive head trauma, which independently can increase the risk of seizures.[17–20] Excluding this population at particularly high risk of EPTS from this study likely contributed to the overall lower rate of EPTS we observed.

Since levetiracetam dosing is neither standardized nor commonly reported in the literature for TBI patients, it is difficult to know if our study population received more or less levetiracetam compared with other TBI patients. Levetiracetam was associated with an overall low incidence of reported adverse effects in our population; given that even the "high-dose" levetiracetam used was still within the accepted standard dosing range, this is likely not surprising. Commonly reported adverse effects of levetiracetam include somnolence, nervousness, irritability, dizziness, asthenia, and nasopharyngitis.[21] Higher doses of levetiracetam have been shown to decrease seizure occurrence overall while adverse events often occur independent of dose.[21–25] As severe TBI patients that receive the highest levetiracetam doses are presumably intubated and sedated, dose-related adverse effects may be difficult to detect in this population.

Interestingly, there were significantly more females in the pre-PowerPlan group compared with the post-PowerPlan group. Surveillance data have indicated that males are more likely to sustain a TBI compared with females.[26] The significance of this finding is not clear.

Our study had several limitations in addition to those already discussed. It was a retrospective chart review which relies on accurate documentation. The sample size was small, as was the occurrence of both seizures and adverse events, so we cannot comment on the efficacy or safety of GCS-based levetiracetam dosing based solely on this study; additional larger studies with the use of continuous EEG to detect subclinical seizures are required before any conclusions about the potential widespread use of this dosing regimen can be drawn. Some variables may have become statistically significant with a larger sample size. It was challenging to accurately collect time of patient arrival to first dose of levetiracetam, and patients who received levetiracetam prior to their arrival at PSHCH had to be excluded from this calculation. Duration of levetiracetam therapy was not easily elucidated as many of the mild or moderate TBI patients were discharged on levetiracetam, and there was no documentation to determine adherence to regimen. Additionally, since many TBI patients can experience somnolence or agitation due to the nature of the injury, it was difficult to determine if these adverse events were because of levetiracetam. Thus, it is possible that patients experienced adverse events that were not specifically attributed to levetiracetam in the electronic medical record (EMR). For the pre-PowerPlan group, there was no standardized dose of levetiracetam, and as a result, it was difficult to make a direct comparison of our current dosing protocol to previous practices. Patients who were considered appropriately dosed who received their first dose of levetiracetam, may have received an incorrect loading dose that would have either been considered overdose or underdosed based on our current PowerPlan. Additionally, it was difficult to control for confounding variables, including the use of concomitant medications with antiseizure effects. The exclusion of patients that received an antiseizure medication for seizures prior to levetiracetam administration may have excluded patients that were most likely to develop EPTS and thus skewed our results.

Conclusion

Levetiracetam dosing based on GCS scores in pediatric TBI patients is a novel approach, and dosing accuracy may be increased with use of a PowerPlan. Additional large-scale studies are needed to evaluate efficacy and safety of this approach prior to widespread implementation.

Conflict of Interest

None declared.

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