Variation in seizure prophylaxis in severe pediatric traumatic brain injury

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OBJECTIVE Posttraumatic seizure is a major complication following traumatic brain injury (TBI). The aim of this study was to determine the variation in seizure prophylaxis in select pediatric trauma centers. The authors hypothesized that there would be wide variation in seizure prophylaxis selection and use, within and between pediatric trauma centers.

METHODS In this retrospective multicenter cohort study including 5 regional pediatric trauma centers affiliated with academic medical centers, the authors examined data from 236 children (age < 18 years) with severe TBI (admission Glasgow Coma Scale score $\leq$ 8, ICD-9 diagnosis codes of 800.0–801.9, 803.0–804.9, 850.0–854.1, 959.01, 950.1–950.3, 995.55, maximum head Abbreviated Injury Scale score $\geq$ 3) who received tracheal intubation for $\geq$ 48 hours in the ICU between 2007 and 2011.

RESULTS Of 236 patients, 187 (79%) received seizure prophylaxis. In 2 of the 5 centers, 100% of the patients received seizure prophylaxis medication. Use of seizure prophylaxis was associated with younger patient age ($p < 0.001$), inflicted TBI ($p < 0.001$), subdural hematoma ($p = 0.02$), cerebral infarction ($p < 0.001$), and use of electroencephalography ($p = 0.023$), but not higher Injury Severity Score. In 63% cases in which seizure prophylaxis was used, the patients were given the first medication within 24 hours of injury, and 50% of the patients received the first dose in the prehospital or emergency department setting. Initial seizure prophylaxis was most commonly with fosphenytoin (47%), followed by phenytoin (40%).

CONCLUSIONS While fosphenytoin was the most commonly used medication for seizure prophylaxis, there was large variation within and between trauma centers with respect to timing and choice of seizure prophylaxis in severe pediatric TBI. The heterogeneity in seizure prophylaxis use may explain the previously observed lack of relationship between seizure prophylaxis and outcomes.

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KEY WORDS seizures; antiepileptic medications; traumatic brain injury; pediatrics; epilepsy; trauma

TRAUMATIC brain injury (TBI) is a serious health problem among children in the United States, resulting in over 250,000 emergency department (ED) visits and up to 13,500 hospitalizations annually.²³ Post-traumatic seizures are a common complication associated

with TBI, particularly in cases of severe TBI.^{17,18,21} Since they can cause hypoxia, increased intracranial pressure, increased metabolite production, and higher metabolic demands, seizures may result in secondary brain injury that can have detrimental long-term developmental effects.^{1,12}

ABBREVIATIONS AIS = Abbreviated Injury Scale; ED = emergency department; EEG = encephalography; ICU = intensive care unit; ISS = Injury Severity Score; OR = operating room; PEGASUS = Pediatric Guideline Adherence and Outcomes; PICU = pediatric ICU; TBI = traumatic brain injury.

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Therefore, prevention and expedient management of seizures is an important aspect of the care of critically injured children with TBI.

Seizures after TBI can occur early (0–7 days postinjury) or late (8 or more days postinjury).^{13,18,22} Early seizure prophylaxis may be associated with a reduced incidence of early posttraumatic seizures which may lead to less secondary neurological insult and better postdischarge outcomes. Observational studies suggest that decreased posttraumatic seizures may have a survival benefit in patients treated with phenytoin in the acute phase.^{10,17,18,22,24} These findings served as the rationale for the 2012 Brain Trauma Foundation Guidelines, which detail acute care recommendations for children with severe TBI. While the Guidelines recommend phenytoin as the seizure prophylaxis medication of choice to prevent early seizures,^{1,16} there were only a small number of studies that were eligible to serve as evidence (3 Level III studies for the 2003 Guidelines, and only 1 Level III study for the 2012 updated Guidelines) for this recommendation. Moreover, recommendations pertaining to seizure prophylaxis such as time of medication initiation and choice of medication were not specifically considered, leaving these decisions to provider discretion.

The specific mechanisms by which seizure prophylaxis may or may not affect cerebral outcomes is not yet known. The recent Pediatric Guideline Adherence and Outcomes (PEGASUS) study, which examined the relationship between adherence to the 2003 Brain Trauma Foundation Guidelines and patient outcomes, reported a relationship between guideline adherence and favorable patient outcomes.²⁵ In this study, there was no relationship between seizure prophylaxis examined in the intensive care unit and outcomes. However, this study was not powered to examine the effects of seizure prophylaxis use on outcomes and hence may have resulted in the null findings. Therefore, we aimed to examine the characteristics of seizure prophylaxis use in the PEGASUS cohort. Given the lack of strong evidence in the Guidelines and our observed lack of association between seizure prophylaxis use and outcomes, we hypothesized that there would be a wide variation in the use of seizure prophylaxis at various locations as well as the choice of medication used for seizure prophylaxis both within and between leading pediatric trauma centers.

Methods

This study was approved by the University of Washington institutional review board.

Data Set and Study Population

This study is a focused analysis of a data set collected from 2007 to 2012 for the PEGASUS study.²⁵ Data were collected retrospectively and includes 236 records from 5 urban pediatric trauma centers affiliated with academic medical centers located in 5 different U.S. states. The pediatric trauma centers that contributed patient data are the University of Washington's Harborview Medical Center, Seattle, WA; Children's Hospital of Pittsburgh, Pittsburgh, PA; Ann and Robert H. Lurie Children's Hospital of Chi-

cago, Chicago, IL; Harbor University of California, Los Angeles Medical Center, Torrance, CA; and Nationwide Children's Hospital, Columbus, OH. Each center was able to contribute data on 30 to 50 pediatric patients with severe TBI. All patients were under 18 years of age and presented with severe TBI as defined by an ICD-9-CM code indicating TBI, Glasgow Coma Scale Score of less than 9, a minimum head Abbreviated Injury Scale (AIS) score ≥ 3 , and history of trauma. Eligible patients were also required to be in the intensive care unit (ICU) and intubated for at least 48 hours and have an abnormal head CT upon admission (subdural hematoma, intracranial hemorrhage, intraventricular hemorrhage, cerebral infarction, diffuse axonal injury).²⁵

Seizure Prophylaxis Post-TBI

The following seizure prophylaxis data were abstracted: patient demographics, injury and treatment characteristics, seizure prophylaxis used (single and multiple [serial administration] medications used), time from trauma center admission to first use of seizure prophylaxis, overall seizure prophylaxis use among the participating centers, and seizure prophylaxis of choice by trauma center and treatment location (prehospital, ED, operating room [OR], and pediatric ICU [PICU]). Since the hour of initiation of seizure prophylaxis was not recorded, time to first seizure prophylaxis medication use was used as an approximation based on the date of injury and first seizure prophylaxis used. When examining types of seizure prophylaxis used, only those patients actually receiving at least 1 dose of medication for seizure prophylaxis were included in the analysis. For the purpose of this study, "prophylactic" refers to seizure prophylaxis that was administered with the intent to prevent seizures.

Statistical Analysis

Descriptive statistics were used to characterize clinical characteristics of the cohort. Frequencies and percentages were calculated for the data collected and were compared within each center and between centers. Patient and injury characteristics were examined in bivariate analyses with the cases stratified by seizure prophylaxis and by number of seizure medications using chi-square tests for categorical variables and t-tests for continuous variables. Statistical significance was defined as $p < 0.05$. Univariate regression analysis was performed, with adjustments made to correct for the clustering effect between study centers.

Results

Clinical Characteristics and Seizure Prophylaxis

The clinical characteristics of the entire cohort of 236 patients have been previously described.²⁵ In brief, the average age was 8.0 years and the majority of the patients were male (69%). One hundred and seventy (72%) of 236 patients had extracranial injuries. All patient records from each of the 5 centers in the PEGASUS dataset had information pertaining to seizure prophylaxis. Of the 236 patients treated at the 5 participating centers, 187 (79%) received at least 1 seizure prophylaxis medication, while

21% did not receive any seizure prophylaxis. A comparison of the characteristics of patients who did and did not receive seizure prophylaxis medication is provided in Table 1. In 2 of the 5 centers, 100% of the patients with severe TBI received seizure prophylaxis medication.

Seizure prophylaxis was associated with younger age (mean age 7.0 [SD 6.0]), inflicted injury (30%), presence of subdural hematoma or cerebral infarction on CT scan (70% and 19%, respectively), and use of electroencephalography (EEG, 66%). Overall, neither greater Injury Severity Score (ISS) nor head AIS score was associated with seizure prophylaxis use. The majority of patients who did not receive seizure prophylaxis had an admission motor Glasgow Coma Scale (GCS) of 1 ($p < 0.001$).

Time and Location of Seizure Prophylaxis

Time from injury to first seizure prophylaxis use is given

in Fig. 1. Over half (63%) of the patients receiving any seizure prophylaxis were given an initial dose within 24 hours. In almost 95% of patients, seizure prophylaxis was initiated within 72 hours of injury.

The location of seizure prophylaxis initiation varied by center and within each center. Of the 187 patients who received at least 1 prophylactic dose of antiseizure medication, approximately 44% received the first dose in the PICU. Seizure prophylaxis was initiated in the OR in 11 patients in 4 (60%) of 5 centers. Collectively, about half of the patients treated with seizure prophylaxis received their first dose of antiseizure medication in the prehospital or ED setting (Fig. 2).

Choice of Seizure Prophylaxis by Center and Location

The choice of initial seizure prophylaxis varied with-

TABLE 1. Clinical characteristics associated with any seizure prophylaxis medication use*

Variable	Total	Seizure Prophylaxis Medication Used		p Value†
		Yes	No	
No. of patients	236	187 (79.2)	49 (20.8)	
Mean age in yrs [SD]	8.0 [6.3]	7.0 [6.0]	12.1 [5.4]	<0.001
Male sex	163 (69.1)	128 (68.5)	35 (71.4)	0.532
Mean GCS score at admission [SD]	4.61 [1.82]	4.95 [1.84]	3.35 [1.01]	<0.001
Motor GCS score at admission				<0.001
1	118 (50)	75 (40.1)	43 (87.8)	
2	11 (4.7)	11 (5.9)	0 (0.0)	
3	21 (8.9)	18 (9.6)	3 (6.3)	
4	43 (18.2)	41 (21.8)	2 (4.2)	
5	39 (16.5)	39 (20.7)	0 (0.0)	
6	4 (1.7)	3 (1.6)	1 (2.1)	
Mechanism of injury				<0.001
Nonaccidental trauma	58 (24.6)	56 (30.0)	2 (4.1)	
Accidental trauma	178 (75.4)	131 (70.0)	47 (95.9)	
Head AIS score				0.052
3	28 (11.9)	23 (12.3)	5 (10.2)	
4	84 (35.6)	73 (39.0)	11 (22.5)	
5	121 (51.3)	89 (47.6)	32 (65.3)	
6	3 (1.3)	2 (1.1)	1 (2.0)	
Mean ISS [SD]	28.3 [12.8]	25.7 [11.2]	38.2 [13.8]	0.01
Head CT				
Epidural hematoma	40 (17.0)	31 (16.6)	9 (18.4)	0.74
Subdural hematoma	157 (66.5)	131 (70.1)	26 (53.1)	0.02
Subarachnoid hemorrhage	108 (45.8)	82 (43.9)	26 (53.1)	0.574
Intracerebral hemorrhage	74 (31.4)	52 (27.8)	22 (44.9)	0.001
Intraventricular hemorrhage	47 (19.9)	31 (16.6)	16 (32.7)	<0.001
Cerebral edema	127 (53.8)	101 (54.0)	26 (53.1)	0.925
Cerebral infarction	39 (16.5)	36 (19.3)	3 (6.1)	<0.001
Contusion	94 (39.8)	78 (41.7)	16 (32.7)	0.336
Diffuse axonal injury	70 (29.7)	48 (25.7)	22 (44.9)	0.029
Surgery performed	151 (64.0)	118 (63.1)	33 (67.4)	0.499
EEG performed	136 (57.6)	123 (65.8)	13 (26.5)	0.023

* Values are numbers of patients (%) unless otherwise indicated.

† Univariate regression analysis adjusted for clustering effect of centers. Boldface type indicates statistical significance.

FIG. 1. Bar graph showing the time to initiation of seizure prophylaxis medication after TBI in 187 children across 5 centers.

in and between centers and treatment locations (Fig. 3, Supplementary Fig. 1). Across all centers, 4 different antiseizure medications were used for initiation of seizure prophylaxis. Fosphenytoin was the most commonly used (47%), and phenytoin was the second most used (40%). There was within-center variation in initial seizure prophylaxis choice, with 4 of 5 centers using at least 3 different antiseizure medications for initial prophylaxis. Center 5 differed from the other 4 centers with regard to location of initiation of seizure prophylaxis and choice of initial seizure prophylaxis, with over 95% of the patients receiving phenytoin as the first drug of choice and over 80% receiving their first dose of antiseizure medication in the ED. The most variation with regard to choice of prophylactic seizure medication use within centers occurred at Centers 1, 3, and 4, where all 4 different antiseizure medications were used. There was also variation in drug

choice across treatment locations (Supplementary Fig. 1). Phenytoin, fosphenytoin, and phenobarbital were used in all locations, while levetiracetam was limited to the PICU. Phenytoin was favored as the initial seizure prophylaxis medication in the ED and OR (used in 68% and 82% of cases, respectively) but was only used in 12% of cases in the PICU, where fosphenytoin was the favored (used in 64% of cases).

Use of Single Versus Multiple Seizure Prophylaxis Medications

The clinical characteristics of patients receiving single versus multiple types of seizure prophylaxis were similar (Table 2). Twenty-three (12%) of 187 patients receiving any seizure prophylaxis were given multiple types during their treatment. Subdural hematoma and intraventricular hemorrhage were each associated with use of multiple

FIG. 2. Bar graph showing the location of initiation of seizure prophylaxis medication after TBI in 187 children by center.

FIG. 3. Stacked bar graph showing the choice of initial seizure prophylaxis medication after TBI by center in 187 children.

prophylactic antiseizure medications. Use of any seizure prophylaxis medication, age, mechanism of injury, and overall injury severity were not significantly associated with the use of multiple seizure prophylaxis types.

Between-centers analysis of seizure prophylaxis use and associated factors are shown in Table 3. In all centers except Center 4, most patients (70%–92%) were treated with a single antiseizure medication for seizure prophylaxis. There was a statistically significant difference in use and choice of prophylactic antiseizure medications by center ($p < 0.001$), both overall and when compared with associated factors (age, inflicted TBI, cerebral infarction, any encephalography [EEG]).

Electroencephalography was performed in 136 (58%) of 236 cases. Of the 187 patients who received seizure prophylaxis, 123 (66%) underwent EEG. Of the 49 patients who did not receive seizure prophylaxis medication, 13 (28%) underwent EEG; 9 (69%) of these 13 patients were from Center 4. There was a wide variation in EEG utilization among those patients who received seizure prophylaxis (14%–100% of patients across the 5 centers). Centers 1 and 2 had higher EEG utilization rates with increased use of seizure prophylaxis, while Centers 3, 4, and 5 had lower EEG utilization.

Change in Seizure Prophylaxis Use

There was wide variation in choice of seizure prophylaxis for the 23 patients who received multiple types of seizure prophylaxis. Change from phenytoin to fosphenytoin was the most common (48%). A total of 7 drug combinations including multiple drug types were used for seizure prophylaxis across the 5 centers.

Discussion

The Brain Trauma Foundation Guidelines for children with severe TBI recommend the use of phenytoin for early seizure prevention.¹⁶ However, this recommendation is

largely based on a single Level III study published in 1993 that reported a decrease in early seizure rates among those children treated with phenytoin.¹⁷ As a result, the Guidelines do not address the specifics of seizure prophylaxis, such as timing, choice, or which patients should be considered the appropriate recipients of seizure prophylaxis. The main findings of this study are as follows: 1) Although fosphenytoin was the most commonly used medication for initiation of seizure prophylaxis, there was large variation in seizure prophylaxis use within and between centers and across treatment locations. 2) The majority of patients received initial seizure prophylaxis early after severe TBI. 3) The use of multiple types of seizure prophylaxis medications was associated with intraventricular hemorrhage and diagnosis of subdural hematoma.

Some of our results on seizure prophylaxis support previous work showing that younger patients and those with inflicted TBI have higher rates of seizure.^{4,6,18,20,21} Surprisingly, in this study, those patients with a lower ISS were more likely to receive seizure prophylaxis, and this is in contrast to previous studies that have found patients with more severe injury to be at risk for seizure, indicating that measures for seizure prophylaxis would have been used in this group.^{2,5,18,21} In our study, fosphenytoin was the most common initial seizure prophylaxis, which is contradictory to the current recommendations. While phenytoin is the recommended medication according to the Guidelines, studies evaluating the efficacy and cost-effectiveness of the 2 medications do not unanimously support equivalent use. Phenytoin has been linked with a higher incidence of postinfusion sequelae, such as rash and Stevens-Johnson syndrome.^{11,15} However, fosphenytoin is up to 18 times more expensive per dose than phenytoin. Levetiracetam has only been researched as a potential option for seizure prophylaxis,^{7,8,13,14,19} and initial studies have found it as effective as phenytoin but without similar side effects or the need to check drug levels in the blood.^{7,8,13,14,19,22} Even with

TABLE 2. Clinical characteristics associated with single versus multiple seizure prophylaxis medication*

Variable	Total	Single Medication	Multiple Medications	p Value†
No. of patients	187	164 (87.7)	23 (12.3)	
Mean age in yrs [SD]	7.0 [6.0]	7.0 [6.0]	7.0 [6.3]	0.977
Male sex	128 (68.5)	114 (69.5)	14 (60.9)	0.514
Mean GCS score at admission [SD]	4.9 [1.8]	5.0 [1.8]	4.5 [1.7]	0.285
Motor GCS score at admission				0.2775
1	75 (40.1)	64 (39.0)	11 (47.8)	
2	11 (5.9)	8 (4.9)	3 (13.0)	
3	18 (9.6)	17 (10.4)	1 (4.4)	
4	41 (21.9)	38 (23.2)	3 (13.0)	
5	39 (20.9)	34 (20.7)	5 (21.7)	
6	3 (1.6)	3 (1.8)	0 (0.0)	
Mechanism of injury				0.332
Nonaccidental trauma	56 (30.0)	48 (29.3)	8 (34.8)	
Accidental trauma	131 (70.0)	116 (70.7)	15 (65.2)	
Head AIS score				0.2049
3	23 (12.3)	22 (13.4)	1 (4.4)	
4	73 (39.0)	63 (38.4)	10 (43.5)	
5	89 (47.6)	78 (47.6)	11 (47.8)	
6	2 (1.1)	1 (0.6)	1 (4.4)	
Mean ISS [SD]	25.6 [11.2]	25.4 [10.8]	27.2 [13.4]	0.159
Head CT				
Epidural hematoma	31 (16.6)	29 (17.7)	2 (8.7)	0.242
Subdural hematoma	131 (70.1)	111 (67.7)	20 (87.0)	0.008
Subarachnoid hemorrhage	82 (43.9)	73 (44.5)	9 (39.1)	0.64
Intracerebral hemorrhage	52 (27.8)	46 (28.1)	6 (26.1)	0.807
Intraventricular hemorrhage	31 (16.6)	24 (14.6)	7 (30.4)	0.007
Cerebral edema	101 (54.0)	86 (52.4)	15 (65.2)	0.181
Cerebral infarction	36 (19.3)	29 (17.7)	7 (30.4)	0.184
Contusion	78 (41.7)	68 (41.5)	10 (43.5)	0.779
Diffuse axonal injury	48 (25.7)	45 (27.4)	3 (13.0)	0.337
Surgery performed	118 (63.1)	99 (60.4)	19 (82.6)	0.17
EEG performed	123 (65.8)	105 (64.0)	18 (78.3)	0.075
GOS score at discharge				
1 (death)	26 (13.9)	21 (12.8)	5 (21.7)	0.169
2 (vegetative state)	13 (7.0)	12 (7.3)	1 (4.4)	
3 (moderate disability)	84 (44.9)	75 (45.7)	9 (39.1)	
4 (mild disability)	49 (26.2)	43 (26.2)	6 (26.1)	
5 (baseline function)	15 (8.0)	13 (7.9)	2 (8.7)	

GOS = Glasgow Outcome Scale.

* Values are numbers of patients (%) unless otherwise indicated.

† Boldface type indicates statistical significance.

this benefit, levetiracetam may not be used as commonly due to its higher cost relative to phenytoin.¹³

Most patients received seizure prophylaxis within 24 hours of hospital admission and over half received the first dose of medication in the prehospital or ED setting, early in severe TBI care. This is important because studies have reported that first posttraumatic seizures are common within 24 hours of injury.^{5,15} However, although most patients received seizure prophylaxis early, the prehospital

setting had a large variation in type of seizure prophylaxis used. The Pediatric Guidelines do not address seizure prophylaxis in the prehospital or OR setting despite the fact that seizure prophylaxis choice may be particularly important early after severe TBI. Interestingly, our study indicates lack of uniformity in seizure prophylaxis choice within and between centers, and also for any given patient at a given pediatric trauma center, demonstrating the lack of consensus as to seizure prophylaxis choice. This pat-

TABLE 3. Variation in seizure prophylaxis medication use and significantly associated factors by center*

Group & Variable	Total	Center 1	Center 2	Center 3	Center 4	Center 5	p Value†
All patients	236	50 (21.2)	42 (17.8)	40 (17.0)	56 (23.7)	48 (20.3)	<0.001
No seizure prophylaxis medication	49 (20.8)	0 (0.0)	2 (4.8)	11 (27.5)	36 (64.3)	0 (0.0)	
Single medication type	164 (69.5)	40 (80.0)	35 (83.3)	28 (70.0)	17 (30.4)	44 (91.7)	
Multiple medication types	23 (9.8)	10 (20.0)	5 (11.9)	1 (2.5)	3 (5.4)	4 (8.3)	
Patients receiving any seizure prophylaxis medication	187 (79.2)	50 (100.0)	40 (95.2)	29 (72.5)	20 (35.7)	48 (100.0)	
Mean age in yrs [SD]	7.0 [6.0]	8.5 [5.6]	3.2 [4.7]	4.3 [5.3]	9.5 [6.2]	9.0 [5.9]	<0.001
Nonaccidental trauma	56 (30.0)	13 (26.0)	21 (52.5)	13 (44.8)	1 (5.0)	8 (16.7)	<0.001
Subdural hematoma	131 (70.1)	36 (72.0)	29 (72.5)	24 (82.8)	15 (75.0)	27 (56.3)	0.134
Cerebral infarction	36 (19.3)	13 (26.0)	10 (25.0)	2 (6.9)	7 (35.0)	4 (8.3)	0.017
EEG performed	123 (65.8)	50 (100.0)	38 (95.0)	14 (48.3)	8 (40.0)	13 (27.1)	<0.001
Patients receiving multiple seizure prophylaxis medications	23 (9.8)	10 (20.0)	5 (11.9)	1 (2.5)	3 (5.4)	4 (8.3)	
Subdural hematoma	20 (87.0)	9 (90.0)	5 (100.0)	1 (100.0)	2 (66.7)	3 (75.0)	0.631
EEG performed	18 (78.3)	10 (100.0)	5 (100.0)	0 (0.0)	1 (33.3)	2 (50.0)	0.01
Nonaccidental trauma	8 (34.8)	4 (40.0)	3 (60.0)	1 (100.0)	0 (0.0)	0 (0.0)	0.129

* Values are numbers of patients (%) unless otherwise indicated.

† Boldface type indicates statistical significance.

tern reflects not only variation in institutional practice but also variation in practice between clinicians of different disciplines. The observed change in seizure prophylaxis may be problematic if therapeutic levels are not able to be achieved due to this change.

Electroencephalographic monitoring is becoming increasingly common for patients with TBI due to the recognition of the occurrence of subclinical seizures.^{3,4,9,20} In one study, subclinical seizures, confirmed by EEG, occurred in 16.1% of patients admitted to a PICU with TBI, with 7.5% of the patient population experiencing only subclinical seizures.⁴ Our study suggests that there was a large variation in EEG utilization across centers, which may suggest differences in institutional practice, provider discretion, and lack of uniform guidelines. It is likely that patients in whom EEG was performed were more likely to receive seizure prophylaxis, although we do not know which occurred first as we do not have additional data on timing of EEG. More patients received seizure prophylaxis than underwent EEG in our cohort, which suggests that seizure prophylaxis was started based on multiple factors, such as younger age, nonaccidental trauma, and/or CT findings, or started empirically depending on provider discretion, which may explain the wide intercenter and intracenter variability in seizure prophylaxis.

There are some limitations to this study. First, data were collected specifically for the PEGASUS study to assess pediatric guideline adherence rather than the specifics of seizure prophylaxis. Second, we did not have information pertaining to actual seizure rates or EEG data, seizure prophylaxis complications, or side-effects of prophylactic seizure medication use in this population. Third, while information is available pertaining to the specific seizure prophylaxis that was initiated in a particular location, the duration of use of each drug was not recorded. Therefore, we focused on the initial seizure prophylaxis administered

rather than the total number of doses throughout treatment. Finally, although combining data for phenytoin and fosphenytoin would have reduced the variability in our data set, we did not combine the data for these two drugs because they are 2 distinct medications with different patterns of clinical use.

Conclusions

In conclusion, this study describes the wide variation in the use of seizure prophylaxis medications in children with severe TBI. Although the current Pediatric Guidelines recommend only phenytoin for use in early seizure prevention, we found large variation in choice of seizure prophylaxis not only between centers but also across treatment locations within centers. The lack of understanding of specific mechanisms by which early seizure prophylaxis may benefit outcomes may explain the heterogeneity in use of seizure prophylaxis medications and the previously observed lack of relationship in the PEGASUS study. Study of the most efficacious seizure prophylaxis medication is warranted in pediatric TBI.

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Conception and design: Vavilala, Ostahowski, Kannan. Acquisition of data: Ostahowski. Analysis and interpretation of data: Vavilala, Ostahowski, Kannan, Qiu. Drafting the article: Ostahowski, Kannan. Critically revising the article: Ostahowski, Wainwright, Mink, Groner, Bell, Giza, Zatzick, Ellenbogen, Boyle, Mitchell. Statistical analysis: Qiu.

Supplemental Information

Online-Only Content

Supplemental material is available with the online version of the article.

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