Evaluation of High vs Low Dose Levetiracetam for Early Post Traumatic Seizure Prophylaxis in Patients with Traumatic Brain Injury

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Background

Annual Traumatic Brain Injury (TBI) statistics[1]
- 1.5 million TBIs
- 223,000 hospitalizations
- 50,000 deaths

TBI and Seizures
- In the 7 days following a severe TBI, there is a risk of Early Post Traumatic Seizures (EPTS)[2]
- Brain Trauma Foundation Guidelines for Management for Severe TBI recommends 7 days of phenytoin to prevent EPTS[2]

Levetiracetam for EPTS prophylaxis
- Not yet adopted by guidelines[2]
- Mild adverse effect profile
- Lesser need for therapeutic drug monitoring[3]
- Increased tolerability

EPTS prophylaxis at Our Lady of the Lake
- Levetiracetam (preferred)
  - 1000 mg every 12 hours
  - 500 mg every 12 hours
- Fosphenytoin
  - Initial: 20 mg PE/kg
  - Maintenance: 100 mg PE every 8 hours

Objective

To determine if levetiracetam 1000 mg every 12 hours will result in fewer clinical seizures in the 7 days following traumatic brain injury compared to levetiracetam 500 mg every 12 hours

Methods

- Single-center, retrospective, pre/post- levetiracetam protocol implementation, cohort, chart review
- Franciscan Missionaries of Our Lady of the Lake Institutional Review Board (IRB) approved
- January 1, 2018 to December 31, 2021
- Levetiracetam high dose protocol implementation date: July 1, 2020

Patients admitted to trauma service on levetiracetam

Pre-cohort: January 2018 – June 2020 — 500 mg every 12 hours

Post-cohort: July 2020 – December 2021 — 1000 mg every 12 hours

Inclusion criteria
- Patients admitted to the trauma service and initiated on levetiracetam
- Patients diagnosed with TBI per imaging

Exclusion criteria
- Age < 18 years old
- Patients discharged within 48 hours of admission to unit
- Patients with history or development of seizures prior to first dose of levetiracetam
- Anti-epileptic drug use prior to first levetiracetam dose
- Allergies to levetiracetam or contraindication to its use
- Pregnant patients
- Patients with creatinine clearance < 50 mL/min

Statistical Analysis

Chi-Squared: nominal data assessment

Descriptive Statistics: evaluation of sample summarization

Kruskal Wallis: analysis of difference in mean

Logistic Regression: Sample size

Fisher's Exact Test: adjustment for sample size

Results

441 Patients screened for eligibility

341 met exclusion criteria
- Age < 18 years: 4
- Admission < 48 hours: 81
- No TBI on imaging: 15
- Seizures prior to dose: 23
- Seizures history: 62
- Pregnant: 2
- Antiepileptic use: 43
- CrCl< 50 mL/min: 78
- Incarcerated: 12

100 Patients included in analysis

51 patients in pre-protocol implementation

49 patients in post-protocol implementation

Baseline Characteristics	500 mg (N = 51)	1000 mg (N = 49)
Mean age, y ± SD	54 ± 21	44 ± 21
Male, n (%)	38 (74.5)	37 (75.5)
Race, n (%)		
White	30 (58.8)	23 (46.9)
Black	16 (31.4)	22 (44.9)
Mechanism of Injury		
Motor Vehicle Crash	14 (27.5)	23 (46.9)
Fall	22 (43.1)	9 (18.4)
Blunt Force Trauma	8 (15.7)	7 (14.3)

Outcomes	500 mg (N = 51)	1000 mg (N=49)	p-value
Primary Outcome, n (%)			
Seizure Incidence	4 (8)	3 (6)	0.373
Secondary Outcomes, n (%)			
Incidence of loading dose	10 (19.6)	5 (10.2)	-
Treatment duration > 7 days	7 (13.7)	9 (18.4)	0.228
Mortality during admission	12 (23.5)	9 (18.4)	0.525
Secondary Outcomes, days	Mean; (95% CI)	Mean; (95% CI)	
Time to first dose	0.92 (-0.31 - 2.15)	2.3 (-26.7 - 31.35)	0.432
Hospital length of stay	10.8 (8.0 - 13.53)	15.9 (9.07 - 22.7)	0.316
ICU length of stay	7.37 (5.2 - 9.49)	10.26 (5.34 - 15.17)	0.245
Time to seizure onset	1.29 (-1.39 - 3.93)	8.76 (-41.2 - 58.7)	0.086

Discussion

- Study showed seizure incidence consistent with historical findings
- Variances from the 2019 evaluation are likely due to patient selection despite similar inclusion/ exclusion criteria
- Variability in time to drug initiation between groups did not result in a higher seizure incidence
- In the high dose group, patients with lower seizure incidence had a higher TBI severity

Limitations
- Power was not met
- Limited follow-up due to short lengths of stay
- Patients had varying GCS scores during the first 24 hours

Conclusion

High dose levetiracetam may be associated with lower incidence of post-traumatic seizures, however the findings were not statistically significant therefore warranting a larger clinical assessment to establish a dosing protocol

References

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