Pediatric Guidelines Committee

TBI Workgroup

Post Traumatic Seizures in Pediatric TBI patients

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1) What are the categories of post traumatic seizure (PTS) in pediatric traumatic brain injury (TBI) patients?

Consistent definitions in the literature include:

Early PTS occurs within 7 days of injury.[1] An early PTS can be further divided into:

- **Impact seizures**- occur upon impact or within minutes following the injury.[1]
- **Immediate PTS-** occurs within the first 24 hours following injury.[1]
- **Delayed early PTS-** occurs on days 2 to 7 following injury.[1]

Late PTS occurs beyond 7 days of injury.[1]

Nonconvulsive seizures are defined as electrographic seizures (seen on electroencephalography [EEG]) without obvious clinical seizure activity.[2]

Nonconvulsive status epilepticus is defined as either a nonconvulsive seizure that lasts longer than 30 minutes or multiple periods of nonconvulsive seizure which result in seizure activity exceeding 30 minutes during a 1 hour period.[2]

Post Traumatic Epilepsy (PTE) is defined as recurrent, unprovoked seizures at least 1 week after a TBI.[3]

2) What are the risk factors or criteria associated with early PTS and PTE?

Risk factors for PTS include abusive head trauma (AHT), younger age (most commonly < 2 years although 1-7 years was also highlighted), certain races, intracranial hemorrhage, severe TBI, prolonged loss of consciousness, prolonged posttraumatic amnesia, retained bone and metal fragments, and depressed or open skull fractures.[1,4]

A retrospective study utilizing data from both the National Trauma Data Bank and Pediatric Health Information Systems database found that PTS in children following *severe* TBI had the greatest correlation with a **triad** of 1) younger age, 2) injury by abuse/assault, and 3) presence of subdural hematoma.[5]

A single-center retrospective study on patients with mild TBI, examined possible risk factors for either PTS or PTE and found that the rate of PTE following mild TBI was 3.1%, which is eight times higher than

the epilepsy rate in the general population.[6] No association was found between the development of PTE and either immediate PTS or computed tomography (CT) findings associated with the injury.[6]

The same group also examined pediatric TBI patients with moderate and severe TBI, and they noted that PTS-alone *did not* correlate with future PTE. However, PTE was seen more often in patients following severe TBI (as compared with moderate TBI) and in patients who had both a skull fracture and additional intracranial pathology on the initial CT.

3) What is the importance of preventing PTS in pediatric patients?

Pediatric PTS is associated with adverse outcomes including increased likelihood of in-hospital complications and discharge to specialized or intermediate care facilities.[4] Additionally, PTS may contribute to secondary cerebral injury due to increased oxygen demands, elevated intracranial pressure, and release of neurotransmitters.[5,7]

4) Can children that have had a PTS be safely be discharged from the ED?

In a secondary analysis of the Pediatric Emergency Care Applied Research Network (PECARN) TBI study, investigators focused on patients with PTS.[8] A total of 42,424 children met criteria for analysis, and 536 of those patients had PTS with 15 having recurrent seizures (defined as a second seizure within 1 week of the Emergency visit). Of the 536 patients with PTS, 466 had a CT performed. For patients with any pathology noted on CT, the frequency of recurrent seizures was 15.5%. For patients with no pathology noted on CT, the reported frequency of recurrent seizures varied with initial GCS: 6% in patients with GCS scores 3-13, 3.6% in patients with a GCS score of 14, and 0.3% in patients with a GCS score of 15. From these data, the authors make the recommendation that patients with PTS who have a GCS score of 15 and no pathology noted on CT can be "safely considered for discharge from the ED."[10]

5) Who would benefit from continuous EEG monitoring?

In one study examining patients < 3 years with TBI as a result of AHT, researchers found that for patients who underwent continuous EEG, nonconvulsive seizures and nonconvulsive status epilepticus were highly prevalent (rates of 57% and 30%, respectively).[2] Additionally, presenting with altered mental status at admission correlated with the occurrence of nonconvulsive seizures.[2] As such, clinicians should consider continuous EEG in patients with suspected AHT, especially in those with altered mental status.

Additional risk factors for PTS that might warrant consideration for continuous EEG include: age < 2 years, presence of a depressed or open skull fracture, presence of intracranial hemorrhage, severe TBI, GCS ≤ 8, or loss of consciousness/amnesia lasting > 30 minutes.[1]

6) What is the recommendations for anti-epileptic drugs (AEDs) in pediatric severe TBI?

According to the Brain Trauma Foundation Guidelines for Management of Pediatric Severe Traumatic Brain Injury (3rd Edition), prophylactic treatment with AEDs is suggested to reduce the incidence of early

PTS (within 7 days of injury).[9] This was rated Level III evidence, and the guideline authors note that there was insufficient evidence to recommend Levetiracetam (Keppra) over Phenytoin (Dilantin) based on either efficacy in preventing early PTS or toxicity.[9]

A study done in 2020 evaluated the prevalence of early post traumatic seizures after children were given prophylactic Levetiracetam (Keppra) after severe TBI.[10] Sample size was small (n=44); however, children treated with prophylactic AEDs had a 9% incidence of early PTS, as compared to a previously reported 18% rate.[10]

7) Why not prescribe AEDs for all pediatric patients with TBI?

Knowing which patients need prophylactic AEDs is important because the risk of side effects from these drugs is not negligible. Potential adverse effects, a narrow therapeutic index, and highly variable pharmacokinetic properties can occur with use of phenytoin.[11] Levetiracetam was FDA approved in 2006 as an AED with fewer documented adverse effects, as compared with other AEDs. There are no significant drug interactions, and unlike many other AEDs, it does not cause CYP450 enzymatic induction or inhibition.[11] However, as noted above, there is insufficient evidence to support its use over phenytoin in preventing PTS in children.[9]

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