

Epilepsy and Trauma: Childhood Perspective

Surachai Likasitwattanakul, MD.
Department of Pediatrics
Faculty of Medicine Siriraj Hospital
Mahidol University

Outline

- Introduction
- Classification
- Data on childhood TBI
- Abusive head trauma

Traumatic brain injury (TBI)

- Each year, more than 470,000 children aged 0-14 yrs. visit to ED for TBI
- One of the leading cause of childhood morbidity and mortality

Traumatic brain injury in the US. CDC 2010

Statler KD. Dev Neurosci 2005

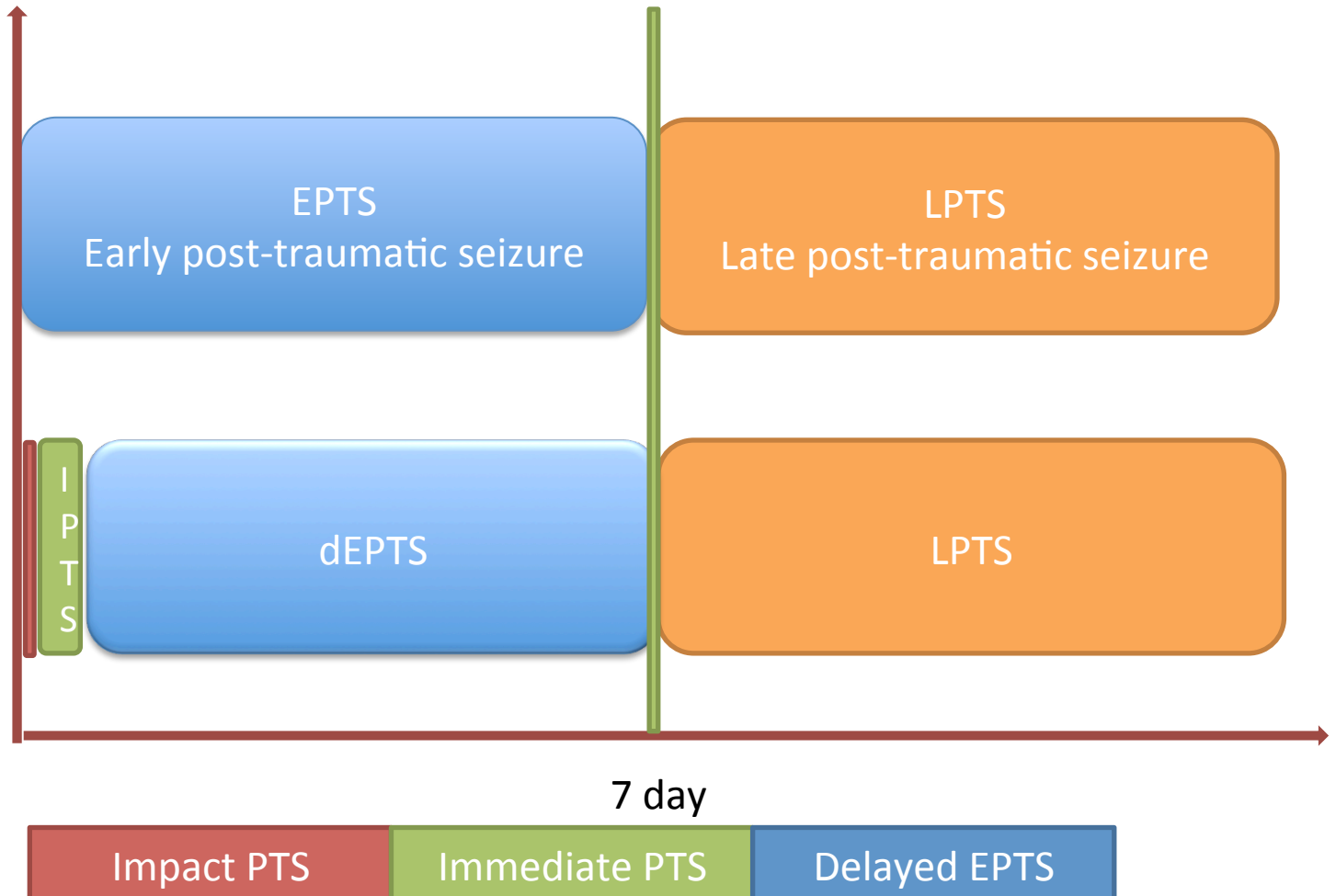
Childhood TBI

- The overall incidence is 5.5-21% (not specifying time, severity, types of seizure)
- Most seizures occur during the first 24 hr. after TBI
- 10-20% of severe TBI have epilepsy after severe TBI

Risk of pediatric EPTS

- Younger age (< 2 yr. old)
- Severe TBI (GSC 3-8) (2-6%, 12-27%, 23-35% in mild, mod., severe TBI)
- Intracranial hemorrhage
- Prolonged loss of consciousness
- Prolonged posttraumatic amnesia
- Depressed or open skull fractures
- **Abusive head trauma (AHT)** (50-65% in AHT to 15-17% in non-AHT)

Suggested classification



Impact PTS

- Occur on impact or within minutes post-injury
- Brief, generalized
- Rapid clearing of mental and neurologic exam
- More common in children
- Result of a concussion (concussive convulsions)
- Not associated with significant intracranial pathology or long-term outcome
- No treatment is needed

Arndt DH, et al. Journal of Child Neurol 2016

Immediate EPTS

- 12-24 hr. after injury (most in first 1-3 hr.)
- Nearly 100% of EPTS occur during period
- Increase incidence with severity
 - 2–6 % in mild TBI
 - 12–27% in moderately severe TBI
 - 3-35 % in severe severe TBI

Statler KD. Dev Neurosci 2005

Issues in management of EPTS

TBI with seizures

- Treatment with AED is warranted in those with seizure to prevent secondary injury

Prophylaxis

- PHT is recommended in children with severe TBI

Problems in children

- Studies of AED in preventing EPTS are not extensively investigated as adult
- The use of PHT use in severe childhood TBI is offered as extrapolation
- Variation of the use of AEDs

Studies of EPTS in childhood

- RCT for seizure prophylaxis in children with PTS with PHT
- 122 patients with moderate to severe TBI received placebo and PTH
 - Primary endpoint PTS within 24 hr. and outcome in 30 days
 - Patient developed seizure **7% with PHT and 5% with placebo**
 - **No difference between groups in survival or neurological outcomes**

Variation of prophylaxis

- 5 pediatric trauma centers in USA.
- 79% received seizure prophylaxis
- 2/5 institutes received 100%
- AEDs used: fosPHT, PHT, LEV, PB

Ostahowski PJ, et al. J Neurosurg Pediatr 2016

Other AEDs

- PB, CBZ, VPA are not extensively studied due to side-effect profiles and pharmacodynamic properties
- LEV is increasingly used in both adult and children with TBI

LEV in childhood EPTS

- 6/34 (17%) developed clinical seizure despite LEV prophylaxis (compared to 10-15% in PHT)

Chung MG, et al. *Pediatr Crit Care Med* 2016

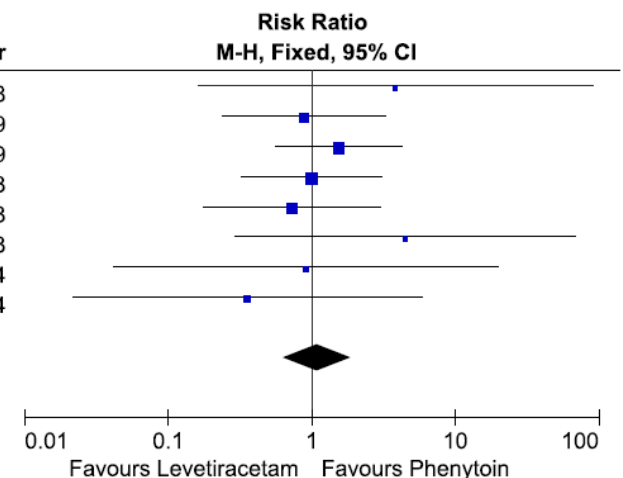
- One phase II study in children demonstrate only 1/20 patients receiving LEV had LPTS
 - Well tolerated and demonstrates the feasibility of pediatric PTE prevention
 - However, the result was not powered to demonstrate efficacy

Pearl PL, et al. *Epilepsia* 2013

Newer AED

- Levetiracetam Versus Phenytoin for Seizure Prophylaxis :A Systematic Review and Meta-Analysis
 - 1614 patients from 11 studies, 1285 in controlled studies
 - LEV was not superior to PHT with regard to early seizure prophylaxis
 - Yang Y, et al. CNS Drugs 2016

Study or Subgroup	Levetiracetam		Phenytoin		Weight	Risk Ratio	
	Events	Total	Events	Total		M-H, Fixed, 95% CI	Year
Jones 2008	1	32	0	41	1.9%	3.82 [0.16, 90.72]	2008
Szaflarski 2009	5	34	3	18	17.1%	0.88 [0.24, 3.28]	2009
Carter 2009	6	36	7	65	21.8%	1.55 [0.56, 4.26]	2009
Inaba 2013	6	406	6	407	26.2%	1.00 [0.33, 3.08]	2013
Caballero 2013	2	18	11	72	19.2%	0.73 [0.18, 2.99]	2013
Kruer 2013	1	20	1	89	1.6%	4.45 [0.29, 68.17]	2013
Anderson 2014	1	22	0	6	3.4%	0.91 [0.04, 20.00]	2014
Gabriel 2014	0	5	3	14	8.7%	0.36 [0.02, 5.92]	2014
Total (95% CI)		573		712	100.0%	1.10 [0.64, 1.88]	
Total events	22		31				
Heterogeneity: Chi ² = 3.13, df = 7 (P = 0.87); I ² = 0%							
Test for overall effect: Z = 0.34 (P = 0.73)							



LPTE

- Risk of PTE followed severe TBI is 10-20%

Statler KD. Devel Neurosci 2006

- Even mild TBI is found to increase risk of PTE (3.7%) in long-term follow-up

Keret A, et al. J Neurosurg Pediatr 2017

LPTE

- Based on existing data, prevention of EPTS do not reduce development of LPTE
- Meta-analysis of highest quality studies fail to show benefit of AED prophylaxis
- This suggests that EPTE is not the sole risk factor for later epilepsy, but rather an association

Schierhout G, et al. Cochrane Database syst Rev 2001

LPTTE in children

- 102 children with TBI with a follow up of 18-96 mo.
 - 9% developed PTE between 8 mo.-5 yr. after injury
 - Increase risk in patients with EPTS, and low GSC

Appleton, RE, et al. J Neurol Neurosurg Psychiatry 2002

- 321 TBI, 47(15%) developed PTE
 - Increase incidence in severe TBI
 - Increase incidence in patient with AHT
 - All kinds of seizure have been encountered including infantile spasm
 - Increase risk of being on more than one AED and intractable epilepsy

Park JT, et al. Ped Neurol 2015

Other issues in TBI in children

- In children with TBI, brain may not be injured by accident but from abusive behavior
- This distinct feature is exclusively seen in small children (less than 5 yr. of age), in particular less than 2 years old

Abusive head trauma (AHT)

- Many names for this condition
 - Shaken baby syndrome
 - Abusive head injury/trauma
 - Inflicted traumatic brain injury
- **Abusive head trauma (AHT)** is a preferred name endorsed by AAP
- This injury is one of the most leading cause of death in non-accidental trauma

Definition: AHT

- An injury to the skull or intracranial contents of an infant or young child (<5 years of age) due to inflicted blunt impact and/or violent shaking. Excluding
 - Unintentional injuries resulting from neglectful supervision
 - Gunshot wounds / stab wounds / penetrating trauma

Pediatric Abusive Head Trauma, CDC 2012

Shaken baby syndrome

- One form of abusive head trauma with a characteristic pattern of injuries that may include retinal hemorrhages, certain fractures (in particular, ribs and the ends of long bones), and recognizable patterns of brain injury.
- AAP consider SBS as a subset of AHT

AHT

- Incidence: 21/100,000 (<1 yr. of age)
12.8/100,000 (< 2 yr. of age)
- In children less than 2 yr. of age, AHT account for most cases of severe traumatic brain injury, with 80% at least was perpetrator
- More than 20% mortality rate and adverse neurodevelopmental outcome

Jayawant S, et al. BMJ 1998

Keenan HT, et al. Pediatrics 2004

Bruce Da, et al. Pediatr Ann 1989

Kesler H, et al. J Neurosurg Pediatr 2008

-Barlow K, Pediatr Rehabil 2004

Diagnosis

- Seizure is the most common presenting symptoms (40-70%) followed by lethargy and unresponsiveness
- Very rarely that the perpetrator would admit the action
- Diagnosis is based on clinical suspicious (not appropriate traumatic history, bruises or other body injuries)
- Neuroimaging studies

Imaging

- Subdural hematoma is considered as a cardinal signs
- Present in almost 90% of the patients but of moderately specific to this condition

- Fanconi M, et al. Eur J Pediatr 2010

- Specificity of SDH for this condition increase when associated with retinal hemorrhage and underlying diffuse parenchymal injury

- Kelly P, et al. Arch Dis Child 2015

Mechanisms of injury

- **Impulsive loading:** non-impact forces generated by alternating angular acceleration and deceleration of the cranial vault
- **Impact loading:** direct application of forces to the head
- Both result in distinct but overlapping injury

Seizure in AHT

- Clinical seizure are common as initial symptoms (40-70%), focal seizures are the most common
- It can be **clinical** (22%) or **subclinical** (47% in those who underwent EEG monitoring)
- Status epilepticus occur in 3-11%

Hasbani DM, et al. Pediatr Crit care Med 2013

Desai BT, et al. Epilepsia 1983

Jennett B. Arch Neurol 1977

Arndt DH, et al. Epilepsia 2013

Electrographic seizure

- Electrographic seizures are common in children with AHT
- In one study, up to 57% of EEG monitoring cases have electrographic seizure and 67% of these have electrographic status epilepticu
- They have no clinical correlation

- Hasbani DM, et al. *Pediatr Crit Care Med* 2013

- Greiner MV, et al. *J of Child Neurol* 2015

- Igarashi A, et al. *Eur J Pediatr Neurol* 2014

Electrographic seizure

- Identification of electrographic seizures direct and change the management in most cases
- These patients need prolonged EEG monitoring either by conventional VDO-EEG, aEEG, or limited channel EEG

Hasbani DM, et al. *Pediatr Crit Care Med* 2013

- Greiner MV, et al. *J of Child Neurol* 2015

- Igarashi A, et al. *Eur J Pediatr Neurol* 2014

Seizure and Epilepsy in AHT

- 404 patients with AHT (95% less than 1 yr.)
- Seizures are presenting symptoms in 73%
- Focal seizures are the most common
- Subclinical seizure in 25%
- 9% died of refractory SE and severe IICP

Bourgeois M, et al. Childs Nerv Syst 2008

Epilepsy and other long-term complication

- Epilepsy occur in 20 - 38% in those who survive and are often intractable
- Infantile spasm in some patients
- Other serious complications
 - Chronic encephalopathies
 - Intellectual disability
 - Behavioral problems

Lind K, et al. Child Abuse Negl 2016

Barlow KM, et al. Pediatrics 2005

Bourgeois M, et al. Childs Nerv Syst 2008

Birca A, Journal of Child Neurol 2014

Summary

- Further studies of TBI exclusively in children are needed in order to delineate the appropriate management
- In children, especially in infant, abusive head trauma should be kept in mind when encounter a case of head trauma
- Both clinical and subclinical seizures are common in AHT
- A long-term follow up in these children are necessary