Instructional Course #34

Review of Neuropharmacology in Pediatric Brain Injury

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Micah Baird MD
Outline of Course

1. Introduction
   John Pelegano MD

2. Neuropharmacologic Agents to Increase Arousal
   Jilda Vargus-Adams MD, MSc

3. Neuropharmacologic Agents for Agitation / Cognition
   Micah Baird MD

4. Brief Break

5. The Unusual Story of Zolpidem
   John Pelegano MD

6. Audience’s Clinical Experiences, Questions & Answers
   Jilda Vargus-Adams MD, MSc
I have nothing to disclose
Medications in this Presentation

- Most, it not all, of the medications discussed have not been tested in pediatric populations.
- Most, if not all, the medications discussed are being used off-label in pediatric populations.
Definition of Traumatic Brain Injury

Traumatic brain injury occurs when an external mechanical force causes brain dysfunction

(Mayo Clinic)
Definition of Traumatic Brain Injury

When an external force traumatically injures the brain

(Wikipedia)
Mild Traumatic Brain Injury

An injury to the head as a result of blunt trauma or acceleration/deceleration forces that result in one or more of the following conditions:

– Any period of observed or self-reported:
  • Transient confusion, disorientation, or impaired consciousness
  • Dysfunction of memory around the time of injury
  • Loss of consciousness lasting less than 30 minutes
Mild Traumatic Brain Injury (cont.)

- Observed signs of neurological or neuropsychological dysfunction, such as:
  
  • Seizures acutely following injury to the head
  
  • Symptoms among infants and very young children;
    - Irritability, Lethargy, or Vomiting
  
  • Symptoms among older children and adults;
    - Headache, Dizziness, Irritability, Fatigue, Poor Concentration when identified soon after injury, support the diagnosis of mild TBI, but cannot be used to make the diagnosis in the absence of loss or altered consciousness.

(CDC)
Definition of TBI Severity

- This definition combines 3 elements commonly seen in rankings of the severity of TBI’s.

1. Rating of Initial Responsiveness (i.e. GCS)
2. Degrees of Post-Traumatic Amnesia (PTA)
3. Duration of Loss of Consciousness (LOC)
# Definitions of Degrees of Traumatic Brain Injury

<table>
<thead>
<tr>
<th></th>
<th>GCS</th>
<th>PTA</th>
<th>LOC</th>
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<tbody>
<tr>
<td>Mild</td>
<td>13–15</td>
<td>&lt;1 day</td>
<td>0–30 minutes</td>
</tr>
<tr>
<td>Moderate</td>
<td>9–12</td>
<td>&gt;1 to &lt;7 days</td>
<td>&gt;30 min but &lt;24 hours</td>
</tr>
<tr>
<td>Severe</td>
<td>3–8</td>
<td>&gt;7 days</td>
<td>&gt;24 hours</td>
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TBI’s in the United States 2002 – 2006

- 52,000 Deaths
- 275,000 Hospitalizations
- 1,365,000 Emergency Department Visits
- ??? Receiving Other Medical Care or No Care *
Variation of TBI by Age

Children, older adolescents, and adults ages 75 years and older are the most likely groups to sustain a TBI.
In every age group, TBI rates are higher for males than females.
Falls are the leading cause of TBI. Rates are highest among ages 0 to 4 and ages 75 and older.
Etiology of TBI in 0 - 14 Year Olds

- Struck by/against
- Unknown/Other
- Motor Vehicle-Traffic
- Falls
- Assault
Incidence Studies of TBI’s in Children\textsuperscript{2}
TBI Severity in Males by Age

0-4 Years: 469
5-9 Years: 262
10-14 Years: 363
15-17 Years: 423

TBI's per 100,000 Population

0 50 100 150 200 250 300 350 400 450 500

0-4 Years: Mild - 12.5
5-9 Years: 3
10-14 Years: 10
15-17 Years: 20.9

Mild  Moderate, Severe or Fatal
TBI Severity in Females by Age

<table>
<thead>
<tr>
<th>Age Range in Years</th>
<th>TBI's per 100,000 in Population</th>
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</thead>
<tbody>
<tr>
<td>0-4 Years</td>
<td>352</td>
</tr>
<tr>
<td>5-9 Years</td>
<td>156</td>
</tr>
<tr>
<td>10-14 Years</td>
<td>152</td>
</tr>
<tr>
<td>15-17 Years</td>
<td>174</td>
</tr>
</tbody>
</table>

- **Mild**: Blue line
- **Moderate, Severe or Fatal**: Red line
Predictors of TBI Outcomes in Peds

It is very difficult to study pediatric TBI outcomes as:

1. Pre-morbid level of functioning for each child is often different, even for the same age and normal development.

2. Children w/TBI’s may be innately different from peers
   - For example, children w/ ADHD are more prone to TBI’s
     - 1.8 times the risk of concussion
     - 1.7 times the risk of intracranial injury
Predictors of TBI Outcomes in Peds (cont.)

It is very difficult to study TBI outcomes as:

3. A Child’s recovery is influenced by their family’s coping abilities

4. It is difficult to consistently quantify severity of injury given variations in the type/location/extent/degree of CNS injury.
Factors that Influence Recovery from Pediatric TBI’s

• Poor outcomes are more prevalent in children with more severe injury, however measured.

  – Glasgow Coma Scale (GCS) – at presentation
    • GCS ≤ 8 - Severe TBI
    • GCS 9 – 12 - Moderate TBI
    • GCS ≥ 13 - Mild TBI

  – Time to Follow Commands (TFC)

  – Duration of post-trauma amnesia (PTA)
    • < 24 hrs from injury – better outcomes
    • > 2 weeks from injury – poorer outcomes
Factors that Negatively Influence Recovery from Pediatric TBI’s

- Younger children, particularly preschoolers
- Multiple skull fractures
- Open head injuries
- Infants with inflicted injuries
- Diffuse brain injury
- Poor behavioral outcomes are more likely in families with poor coping skills, low SES, and in children with pre-morbid behavior problems.
Factors that Negatively Influence Recovery from Pediatric TBI’s

• Acute clinical signs consistent with a poor prognosis:
  – Increased intracranial pressure
  – Fever during acute recovery
  – Seizures
  – Abnormal metabolic markers
  – Unstable blood pressure
  – Poor neurologic exam at presentation
  – Spike waves on EEG
Case History #1 (RS)

• RS was a 16 year old female when struck by a hit-and-run driver. She was found unresponsive in a snow bank.
• In the E.D. she had agonal respiration, core body temp of 93.5, fixed and dilated pupils, absent corneal reflexes, GCS 4.
• X-rays revealed a large left subdural hematoma, hemoperitoneum and right tibial fracture.
• She was taken to the OR for craniotomy, terminal ileocecal resection, ORIF of the tibial fracture.
Case History #1 (RS)

- In the PICU she had an IVC filter, a tracheostomy, G-tube and autonomic dysfunction (increased HR, temp, BP nl)
- Her clinical status gradually improved to GCS 7 over 2-3 weeks. At transfer to rehab, family reported spontaneous eye opening, inconsistent blink to command, some spontaneous but non-purposeful movements and vocalizations but no words.
- While in rehab a CT scan 48 days post-injury revealed dilated ventricles and a VP shunt was placed.
- After a few months of neurosensory stimulation there was no change in her status and she was admitted to our facility for discharge planning now 5 months post-injury.
Case History #1 (RS)

- Physical exam upon admission:
  - open craniotomy (slightly sunken)
  - eyes open but with bilateral ptosis, no visual tracking, sluggishly reactive pupils and intermittent nystagmus.
  - blink to threat & corneal reflexes were present
  - expressionless face
  - spontaneous non-purposeful left ankle movement (no other movement)
  - no response to auditory stimuli
  - no speech, no communication effort, no vocalizations
  - generalized extension in response to painful stimuli

Impression: GCS 7, Severe TBI, Possible Minimally Responsive State
References


References


- Koepsell, Rivara, Vavilala, Wang, Temkin, Jaffe, Durbin “Incidence and Descriptive Epidemiologic Features of TBI in King County, WA: Pediatrics (2013)