Traumatic Brain Injury in Children

Sumon K Das, MD, FAAP
UMDNJ-RWJMS
New Brunswick, NJ
Epidemiology

- Among children and youth aged 0 to 14 years in the U.S., each year traumatic brain injury (TBI) results in an estimated:
  - 3,000 deaths*
  - 29,000 hospitalizations*
  - 400,000 ER visits* (1 case every 2 minutes!!)

- Unintentional injury is the leading cause of death
  - TBI is the type of injury most often associated with death

- The annual total of TBI-related deaths is:
  - More than 6 times the number of deaths related to HIV/AIDS*
  - 20 times the number of deaths from asthma*
  - 38 times the number of deaths from cystic fibrosis*

*CDC
Epidemiology

- Incidence distributed evenly among three age groups:
  - 0-4 years
  - 5-10 years
  - 11-15 years*
- 5.3 million men, women and children are living with a permanent TBI-related disability in the U.S.
  - *Traumatic Coma Data Bank
Pathophysiology

- Cranial vault is a closed space
  - Brain
  - Blood
  - Cerebrospinal fluid (CSF)
  - Fixed structures

- Intracranial pressure (ICP) is dependent upon volume of brain, blood and CSF
Pathophysiology

- **Primary Injury**
  - Direct disruption of brain parenchyma

- **Secondary Injury**
  - Ischemia, excitotoxicity, energy failure, and cell death cascades
  - Secondary cerebral swelling
  - Axonal injury
INJURY

DIRECT PARENCHYMAL & VASCULAR DISRUPTION AND DEPOLARIZATION

AXONAL & DENDRITIC INJURY

VASCULAR DYSREGULATION

HEMATOMA

↑ CBV

INFLAMMATION & REGENERATION

↑ ICP

ICP

ASTROCYTE SWELLING

NEUROTOXICITY

NECROSIS

APOPTOSIS

VASOGENIC EDEMA

↑ TISSUE OSMOLAR LOAD

BBB

CONTUSION

HEMATICOMA

KS... glutamate

K+ glutamate

O2

AA Cytokines

Ca++

* Kochanek
Posttraumatic Ischemia

- Hypoperfusion (hypotension/hypoxemia)
  - Adelson, 1997: global CBF <20ml/100g/min associated w/ poor outcome
  - Why?
    - Attenuated vasodilatory response
    - Loss of endothelial NO production
    - Increased metabolic demands
Excitotoxicity

- Process by which glutamate and other excitatory AA cause neuronal damage
- Glutamate
  - Most abundant neurotransmitter in the brain
  - Toxic levels produce neuronal death
  - Target for therapy → modification of glutamate receptor interaction
    - Magnesium, glycine site antagonists, hypothermia, pentobarbital
Apoptosis

- Necrosis: cellular and nuclear swelling with dissolution of membranes
- Apoptosis: cell shrinkage and nuclear condensation, DNA fragmentation and formation of apoptotic bodies → “programmed cell death”
Cerebral Swelling

- Delayed phase of metabolic depression
  - Cerebral metabolic rate of oxygen decreased to 1/3 normal
- Peaks between 24-72 hours
Cerebral Blood Volume

- Intracranial hypertension
  - Compromises cerebral perfusion → ischemia
  - Herniation
  - Pathophysiology controversial
    - Increased CBF? relative hyperemia?
    - Hyperglycolysis
    - Edema, rather than hyperemia, may be predominant contributor
Edema

- **Vasogenic:** Edema in the extracellular space as a result of BBB disruption

- **Cellular swelling**
  - Astrocyte swelling from uptake of glutamate → Na and water accumulation
  - Swelling of neurons from ischemia- or trauma-induced ionic pump failure

- **Osmolar swelling:** Dependent on intact BBB or alternative solute barrier
  - Especially important in contusions
  - Possible mechanism
    - Macromolecules are degraded w/in injured brain → osmolar load in contused tissue increases → local accumulation of water
  - Target therapy: mannitol, hypertonic saline
Contusion

Ischemia

Tissue Disruption

NECROSIS

OSMOLAR LOAD

BBB Disruption

BBB Reconstitution

VASOGENIC EDEMA

Secondary Swelling

*Kochanek
Axonal Injury

- Effects particularly devastating in children due to period of developmental axonal connectivity
Secondary Brain Injury

- TBI → hypoperfusion + increased metabolic demands → enhanced vulnerability to secondary insults
## Secondary Brain Injury

### Secondary Insult | Critical Values in TBI | Main Cause
---|---|---
Arterial Hypotension | Systolic BP <65-90mmHg, depending on age | Blood loss, sepsis, cardiac failure, spinal cord injury
Hypoxemia | Arterial O₂ sat <90%, PaO₂ <60mmHg, apnea, cyanosis | Hypoventilation, thoracic injury, aspiration
Hypocapnia | PaCO₂ <35mmHg | Hyperventilation
Fever | Hyperthermia >38.3°C | Infection, stress response, drug fever
Hyponatremia | Serum sodium <135 mOsm/L | Hypotonic fluids, SIADH, salt wasting syndrome
# Secondary Brain Injury

<table>
<thead>
<tr>
<th>Secondary Insult</th>
<th>Critical Values in TBI</th>
<th>Main Cause</th>
</tr>
</thead>
<tbody>
<tr>
<td>Intracranial Hypertension</td>
<td>ICP &gt; 20 mmHg</td>
<td>Mass lesion, cerebral edema caused by vasodilation, and increased cerebral water content</td>
</tr>
<tr>
<td>Cerebral Vasospasm</td>
<td></td>
<td>Traumatic subarachnoid hemorrhage</td>
</tr>
<tr>
<td>Seizures</td>
<td></td>
<td>Cortical injury, metabolic derangement</td>
</tr>
<tr>
<td>Infection</td>
<td></td>
<td>Skull fracture, meningitis, sepsis, pneumonia</td>
</tr>
</tbody>
</table>
# Glasgow Coma Scale

<table>
<thead>
<tr>
<th></th>
<th>Eyes Open</th>
<th>Best Verbal Response in Adults</th>
<th>Best Verbal Response in children &lt; 36 months</th>
<th>Best Verbal Response in infants to pre-school</th>
<th>Best Motor Response</th>
</tr>
</thead>
<tbody>
<tr>
<td>6</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>Obeys commands</td>
</tr>
<tr>
<td>5</td>
<td>-</td>
<td>Oriented &amp; converses</td>
<td>Smiles, interacts</td>
<td>Babbles, gestures</td>
<td>Localizes painful stimuli</td>
</tr>
<tr>
<td>4</td>
<td>Spontaneously</td>
<td>Disoriented &amp; converses</td>
<td>Cries, interacts</td>
<td>Cries for needs</td>
<td>Flexion withdrawal</td>
</tr>
<tr>
<td>3</td>
<td>To verbal command</td>
<td>Inappropriate words</td>
<td>Consolable, moans</td>
<td>Cries, non-specific</td>
<td>Flexion-abnormal</td>
</tr>
<tr>
<td>2</td>
<td>To painful stimuli</td>
<td>Incomprehensible sounds</td>
<td>Irritable, restless</td>
<td>Sounds</td>
<td>Extension</td>
</tr>
<tr>
<td>1</td>
<td>No response</td>
<td>No response</td>
<td>No response</td>
<td>No response</td>
<td>No response</td>
</tr>
</tbody>
</table>
Grading TBI by Glasgow Coma Scale

- **Mild**
  - GCS 13-15

- **Moderate**
  - GCS 9-13

- **Severe**
  - GCS 3-8
Herniation

- **Signs/symptoms**
  - Pupillary dilatation
  - Systemic hypertension
  - Bradycardia
  - Extensor posturing

- **Emergent Treatment**
  - Hyperventilation w/ 100% $O_2$
  - Mannitol or 3% NS
  - Thiopental or etomidate

- **To CT or surgery**

Diagram:
- a: subfalcial (cingulate) herniation
- b: uncal herniation
- c: downward (central, transtentorial) herniation
- d: external herniation
- e: tonsillar herniation
Initial Resuscitation

➢ ABCs

● Airway
  • Neck immobilization
  • If supraclavicular injury, assume cranial and cervical spine injuries

● Breathing
  • limit/avoid BVM ventilation
  • RSI
Intubation of TBI Patients

- **Criteria for Intubation**
  - GCS ≤ 10
  - Decrease in GCS of >3
  - Anisocoria > 1mm
  - Cervical spine injury compromising ventilation
  - Apnea
  - Hypercarbia (PaCO$_2$ >45)
  - Loss of pharyngeal reflex
  - Spontaneous hyperventilation causing PaCO$_2$ <25 mmHg

- **RSI meds**
  - Hemodynamically unstable
    - Etomidate/fentanyl; lidocaine; rocuronium/ vecuronium
  - Hemodynamically stable
    - add benzo or barbiturate
Initial Resuscitation

• Circulation
  • consider 3% NS

• AVOID CEREBRAL HYPOPERFUSION
  • Correct hypoxemia and hypovolemia
Diagnostic Studies

- **Head CT**
  - Clinical correlation
    - Hirsch: CT had high false positive rate in defining increased ICP
  - Reimaging
    - Tabori: routine reimaging did not lead to surgical or medical changes in therapy
    - Reimage for changes in ICP or clinical examination
ICP Monitoring

- **Indications**
  - Initial GCS ≤ 8
  - +/- abnormal head CT
  - Serial neuro exam not possible
- **Risk vs. benefit (i.e. coagulopathy)**
- Has not been studied in RCT
- **Provide adequate anesthesia**
“Presence of open fontanelles and/or sutures in an infant with severe TBI does not preclude the development of intracranial hypertension or negate the utility of ICP monitoring”
Critical pathway for the treatment of established intracranial hypertension in pediatric traumatic brain injury
Management

- CPP = MAP – ICP
- Target CPP
  - >50 mmHg for infants
  - >60 mmHg for children
  - >70 mmHg for adolescents and adults
- In general, threshold ICP >20 mmHg considered unacceptable
  - Autoregulation age dependent
First Step Approach
CSF Drainage

- Compared to mannitol
  - Similar effects on CBF and ICP
  - Greater increase in jugular venous saturation
- Lumbar drainage option if refractory intracranial hypertension and cisterns

OPEN
Osmolar Therapy

- BBB nearly impermeable to mannitol and sodium

- Mannitol
  - Reduces blood viscosity $\rightarrow$ decreases BV diameter $\rightarrow$ decreases CBV
  - Osmotic effect
  - 😵: can accumulate in injured regions causing reverse osmotic effect; ATN/renal failure
  - 0.25 – 1 g/kg bolus dose

- Hypertonic saline
  - Mechanisms similar to mannitol
  - Restoration of cell resting membrane potential
  - Stimulation of ANP release
  - Inhibition of inflammation
  - Enhanced cardiac performance
  - 😵: extrapontine myelinolysis, SAH, renal failure, rebound intracranial hypertension

- Bolus doses 1-2 ml/kg
- Continuous infusion 0.1-1 mL/kg of body weight per hour
  - Minimum dose needed to maintain ICP <20 mmHg
Osmolar Therapy

- Maintain euvolemia
- Monitor serum osmolarity
  - < 320 mOsm/L with mannitol
  - < 360 mOsm/L with hypertonic saline
Positioning, Sedation, Analgesia, Neuromuscular Blockade

- 30° head position → decreased ICP and mean carotid pressure
  - No change in CPP and CBF
  - Improve jugular venous and CSF drainage
- Pain and stress markedly increase cerebral metabolic demands, pathologically increase CBV and raise ICP
- Sedatives/analgesics mitigate aspects of secondary damage
- Narcotics, benzos, barbiturates
  - Barbiturates: decrease ICP, direct neuroprotective effects
    - 😊 - myocardial depression, increased risk of hypotension, prolonged inhibition of synaptic activity in the developing brain during infancy
- Propofol: adequate sedation, no major changes in ICP or CPP
- Intermittent lidocaine for suctioning
- Neuromuscular blockade as needed for refractory hypertension
Anti-seizure Prophylaxis

- Relatively high incidence of post-traumatic seizures (PTS) in head-injured patients
- Increase brain metabolic demands, increase intracranial pressure, and may lead to secondary brain injury
- Phenytoin has been shown to reduce the incidence of early PTS in a single study of children with severe TBI (Lewis)
- Prophylaxis does not reduce incidence of late PTS
Hyperventilation

- Hyperventilation \( \rightarrow \) hypocapnia \( \rightarrow \) cerebral vasoconstriction (dec ICP) \( \rightarrow \) decreased cerebral perfusion \( \rightarrow \) ischemia
  - Mild or prophylactic hyperventilation (Paco\(_2\) < 35 mmHg) should be avoided
  - Moderate hyperventilation (Paco\(_2\) 30–35 mmHg) may be considered for longer periods for refractory intracranial hypertension
    - Chronic hyperventilation depletes brain tissue interstitial bicarbonate buffering and causes cerebral circulation to become hyper-responsive to subsequent increases in Paco\(_2\)
    - respiratory alkalosis \( \rightarrow \) left shift of the hemoglobin-oxygen dissociation curve \( \rightarrow \) impaired delivery of oxygen to tissue
  - Aggressive hyperventilation (Paco\(_2\) < 30 mmHg) may be considered as a second tier option in the setting of refractory hypertension
    - CBF, jugular venous oxygen saturation, or brain tissue oxygen monitoring is suggested
Hypothermia

- **Hyperthermia:** core body temp >38.5°
  - exacerbates neuronal death
- **Hypothermia:** core body temp <35°
  - decrease cerebral metabolism, inflammation, lipid peroxidation, excitotoxicity, cell death, and acute seizures
- **Adult data suggests**
  - Avoid hyperthermia
  - Active cooling for refractory ICH
Second Tier Therapy

SECOND TIER THERAPY

† ICP despite first tier tx?
No surgical lesion on CT?

Working ventriculostomy?
Open cisterns on concurrent CT?

Salvageable patient?
Evidence of swelling on CT?

Consider lumbar drain

Unilateral swelling?

Consider unilateral decompressive craniectomy with duraplasty

Bilateral swelling?

Consider bilateral decompressive craniectomy with duraplasty

Evidence of hyperemia?
No evidence of ischemia?

Consider hyperventilation to a PaCO2 < 30 mm Hg (Consider monitoring CBF, SjO2, AFO2)

Active EEG?
No medical contraindications to barbiturates?

Consider high dose barbiturate therapy

Evidence of ischemia?
No medical contraindications to hypothermia?

Consider moderate hypothermia (32 - 34° C)
Other modalities

- Lumbar CSF drainage: can be helpful if cisterns open
- Decompressive craniectomy
  - Favorable results in patients with secondary deterioration of GCS and/or evolving cerebral herniation within 48 hours after injury
  - Less effective in patients who have experienced extensive secondary brain insults or patients with an unimproved GCS of 3
- Steroids do not improve outcome or lower ICP in severely head-injured adult patients