Objectives

• Review the new Brain Injury Guidelines.

• Discuss the uses, actions, doses, and side effects of medications used in treatment of patients with traumatic brain injury.

Traumatic Brain Injury (TBI)¹

• Blow or jolt to the head or penetrating head injury that disrupts the function of the brain.

• Range from mild (concussion) to severe.

• Can cause long term or permanent damage.
The Numbers

- 2.5 million ED visits, hospitalizations or death.
- Contributes to about 30% of all injury deaths.
- Over the past decade (2001–2010), rates of TBI-related ED visits increased by 70%.
- 5.3 million Americans live with TBI related disability.
- Economic costs estimated to be $76.5 billion (direct & indirect costs).

Brain Injury Guidelines

- Released September 2016
- 189 publications used for evidence

Decompressive Craniectomy

- Level I
  - Insufficient evidence to support a recommendation
- Level II A
  - Bi-frontal DC is not recommended to improve outcomes
    - It does help reduce ICP and to minimize days in ICU.
  - A large frontotemporoparietal DC is recommended for reduced mortality and improved neurologic outcomes in patients with severe TBI.
**Crani's**

- Craniectomy
- Craniotomy

---

**Craniectomy Before & After**

---

**Prophylactic Hypothermia**

- **Level I & II A**
  - Insufficient evidence to support a recommendation
- **Level II B**
  - Early (within 2.5 hours), short-term (48 hours post-injury) prophylactic hypothermia is not recommended to improve outcomes in diffuse injury.
Hyperosmolars

- No level I, II, III
- Although hyperosmolar therapy may lower intracranial pressure, there was insufficient evidence about effects on clinical outcomes to support a specific recommendation, or to support use of any specific hyperosmolar agent, for patients with severe traumatic brain injury.
- Decreases ICP through reducing blood viscosity which improves the microcirculation blood flow, & decreases cerebral blood volume & ICP.
- Mannitol
  - Diuretic effect is undesirable if patient is already hypotensive
  - Attention needs to be paid to replacing lost intravascular volume (dose 0.25 g/kg to 1g/kg).
  - Avoid arterial hypotension
- Hypertonic Saline (3%)
  - Can be hazardous to the hyponatremic patient

<table>
<thead>
<tr>
<th>Mechanism of Action</th>
<th>Hypertonic Saline 3% (3, 7.5, and 23.7% available)</th>
<th>Mannitol (Osmitrol®)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Appropriate Use</td>
<td>Treatment of ↑ ICP</td>
<td>Treatment of ↑ ICP</td>
</tr>
<tr>
<td>Adverse Drug Reactions</td>
<td>Hypertension, Hyperchloremia, Heart failure, Central pontine myelinolysis</td>
<td>Hypotension, Thrombophlebitis, Renal dysfunction, Heart failure</td>
</tr>
<tr>
<td>Usual Single Dose</td>
<td>1.3 mL/kg BOLUS</td>
<td>0.25-1 gram/kg BOLUS to 1g/kg (0.22 in-line filter required)</td>
</tr>
<tr>
<td>Contraindications</td>
<td>None</td>
<td>Renal Failure, Pulmonary Edema</td>
</tr>
</tbody>
</table>

Cerebrospinal Fluid Drainage

- Level I & II
  - There was insufficient evidence to support a Level I or II recommendation for this topic.
- Level III
  - An EVD system zeroed at the midbrain with continuous drainage of CSF may be considered to lower ICP burden more effectively than intermittent use.
  - Use of CSF drainage to lower ICP in patients with an initial GCS <6 during the first 12 hours after injury may be considered.
Ventilation Therapy

• Level I & II A
  – There was insufficient evidence to support a Level I or II A recommendation for this topic.
• Level II B
  – Prolonged prophylactic hyperventilation with partial pressure of carbon dioxide in arterial blood (PaCO2) of 25 mm Hg or less is not recommended.

Ventilator Therapy

Recommendations from the 3rd edition not supported by evidence meeting current standards

• Hyperventilation is recommended as a temporizing measure for the reduction of elevated intracranial pressure (ICP).
• Hyperventilation should be avoided during the first 24 hours after injury when cerebral blood flow (CBF) is often critically reduced.
• If hyperventilation is used, jugular venous oxygen saturation (SjO2) or brain tissue O2 partial pressure (BtpO2) measurements are recommended to monitor oxygen delivery.

Anesthetics, Analgesics, & Sedatives

• No Level I or II A
• Side effects include hypotension, decreased cardiac output, increased intrapulmonary shunting, which leads to hypoxia.
• May cause paradoxical rise in CPP which negates benefit of decreased ICP.
• Diligent observation and close monitoring of dose & duration of administration
Propofol/Diprivan3,4 (1/2)

- Level IIB
  - Not recommended for improvement in mortality or 6 month outcomes
  - High doses can cause significant morbidity
  - Good for control of ICP
- Class-Other general anesthetic
- Use-Induction & maintenance of anesthesia & sedation of mechanically ventilated adult patients in the ICU.
  - Dose-ICU sedation 5mcg/kg/minute for at least 5 minutes.
  - Increase by 5-10mcg/kg/minute every 5-10 minutes until desired effect achieved.
- Side Effects- Hyperkalemia, metabolic acidosis, myocardial failure, rhabdomyolysis & death

Propofol/Diprivan4 (2/2)

- No dosage adjustments needed for those with hepatic or renal impairment.
- Extravasation may cause local pain, swelling, blisters, and tissue necrosis.
- Geriatric patients more sensitive so start with slower infusion rates.
- Similar outcomes to Midazolam.

Nimodipine/Nimotop5

- Class-Calcium antagonists with cerebral activity
- Use-Thought to work by relaxing narrowed blood vessels in the brain near the area of bleeding so blood can flow more easily, reducing brain damage. **Only used for SAH.**
- Dose- 60 mg PO q4 hours for 21 days.
  - Start therapy within 96 hours of SAH
  - IV dosing not available in the US
- Reduce does by 50% in hepatic impairment with close monitoring of BP & HR. No dose adjustments for renal.
- Side Effects-Diarrhea, headache, diaphoresis, palpitations, hypertension, cardiac arrest…
Precedex (Dexmedetomidine)\(^6\)
- **Class**: Sedative
- **Use**: Sedation of mechanically vented ICU patients
- **Dose**: 1 mcg/kg IV loading infusion over 10 minutes
  - Followed by a maintenance infusion of 0.2-0.7 mcg/kg/hour IV for up to 24 hours.
- **Side Effects**: Nausea, vomiting, dizzy, diarrhea, anxiety, hypernatremia, confusion, hypotension, pulmonary edema, hypoglycemia…

Fentanyl/Sublimaze\(^7\)
- **Class**: Opioid analgesic
- **Use**: Sedation for mechanically ventilated patient
- **Dose**: 25-50mcg/hour IV infusion
  - Titrate to desired effect
  - Goal CPOT <3, RASS -1 to 0
- **Dose adjustment** with renal impairment, use caution in hepatic impairment
- **Side Effects**: Dyspnea, urinary retention, nausea, delirium, muscle rigidity, respiratory depression…

Barbituates\(^3\)
- **Level II B evidence**
- **No recommended for induction of burst suppression measured by EEG or prophylaxis against development of intracranial hypertension**
- **High doses are recommended to control elevated ICP**
  - Essential to have hemodynamic stability before & during drug therapy.
  - High doses have more favorable outcomes over low doses.
  - Extreme Caution for doses >5mg/kg/hour or when any dose used >48 hours in critically ill patients
- **Drug results in drop in blood pressure in 1/4 patients which offsets the effects of ICP lowering on CPP**
Pentobarbital/Nembutal

- **Class:** Barbiturate
- **Use:** Induce coma for increased ICP
- **Dose:** 15 to 20 mg/kg IV loading dose slowly over 1 to 2 hours for mechanically ventilated patient.
  - Follow with maintenance infusions at 1 to 2 mg/kg/hour IV and titrate by 0.5 to 1 mg/kg/hour as needed, based on serum pentobarbital concentration and clinical response.
  - Reduced doses for hepatic & renal impairment
- **Side Effects:** Anxiety, irritability, confusion, hypoventilation, seizures, bronchospasm...

Fioricet (Butalbital, APAP, & Caffeine)

- **Class:** Analgesic
- **Use:** To treat headache/pain related to traumatic brain injury
- **Dose:** 50mg/325mg/40mg tablets or capsule 1-2 PO q4 hours PRN
- **Side Effects:** Rash, dizzy, nausea, hot flash, constipation, flatulence, tremor...

Steroids

- **Level I**
  - Not recommended
  - Increases mortality
**Nutrition**

- No Level I
- Level II A
  - Provide enough nutrition to reach basal caloric replacement by 5th day & at most 7th day post injury to decrease mortality.
- Level II B
  - Transpyloric (jejunal) feeding to decrease incidence of VAP and to reduce gastric residual

**Infection Prevention**

- No Level I
- Level II A
  - Use of providine-iodine oral care is NOT recommended.
  - May cause increased risk of ARDS
  - Early tracheostomy
  - Decreases the number of mechanical ventilator days
- Level III
  - Use of antimicrobial impregnated catheters for EVD
- Prophylactic antibiotics after intubation
  - No evidence to support it
  - Associated with more severe infections

**VTE-BIG**

- No Level I or II
- Level III
  - LMWH or low dose unfractionated Heparin may be used in combination with mechanical prophylaxis.
  - Both increase the risk for expansion of intracranial hemorrhage.
- Parkland protocol
VTE-Eastern Association for the Surgery of Trauma guidelines

- Low Dose Heparin
  - No Level I or II
  - Level III Safety not established. Decision should be made on a case by case basis.
- Low Molecular Weight Heparin
  - No Level I
  - Level II use in injuries requiring prolonged bedrest
    - Pelvic fractures, complex lower extremity fractures, & spinal cord injuries with motor paralysis
  - Level III- Injury severity score >9 should have LMWH as primary method of VTE prophylaxis.
    - Not sufficiently studied on TBI patients with ICH.

Lovenox (Enoxaparin)

- Best when used in combination with mechanical prophylaxis (SCD’S)
- Class-Fractionated Heparin (LMWH)
- Use-To prevent formation of blood clots
- Dose-30-40 mg BID prophylactic dose
- Side Effects-dizzy, headache, nosebleed, bleeding gums, red/dark urine...
**Low Dose Heparin**
- **Class:** Anticoagulant
- **Use:** To prevent and treat DVT and PE
- **Dose:** 5,000 units subcutaneously every 8 to 12 hours
- **No dosage adjustments needed for hepatic or renal failure but patients with hepatic disease have an increased risk for bleeding.**
- **Side Effects:** Vomiting, headache, fever, bleeding, erythema, bronchospasm, and skin necrosis...

**Seizures**
- **No level I**
- **Level II A**
  - Phenytoin or valproate not recommended for preventing late post traumatic seizures (PTS).
  - Phenytoin decreases incidence of early PTS within 7 days of injury.
  - Insufficient evidence to support Keppra over Phenytoin

**Keppra (Levetiracetam)**
- **Class:** Anticonvulsant
- **MOA:** Unknown
- **Use:** Seizure prophylaxis in TBI patients
  - 7 days with no seizure at time of injury
  - 10 days if seizure activity noted
- **Dose:** 1 gram BID
- **Side Effects:** Nausea, vomiting, anxiety, rash, cough, hostility, constipation, hypertension, hallucinations, lethargy...
Phenytoin
- Class: Anti-convulsant
- Use: Seizure prophylaxis in head trauma & TBI
- Dose: Loading dose is 10 to 20 mg/kg IV with Max of 1,000 mg.
  - Maintenance dose is 4 to 6 mg/kg/day IV, divided into 2 or more doses.
  - Do not exceed an IV administration rate of 50 mg/minute
  - Use IV route only when oral phenytoin administration is not possible
- Dosage adjustments may be required in hepatic & renal impairment.
  - May have increased fraction of “free” phenytoin.
- Side Effects: headache, dizziness, drowsiness, confusion, cerebral edema, coma...

Other Drugs
- Benzodiazepines
- Phenergan
- Zofran
- Risperdal
- Amantadine

Benzodiazepines & Phenergan
Contraindicated in TBI patients!!!
**Zofran/Ondansetron hydrochloride**

- **Class:** Serotonin/5HT3 Antagonist
- **Use:** Prevention & treatment of nausea & vomiting
- **Dose:** 4-8 mg PO/IV PRN
- **Side Effects:** Headache, chills, blurred vision, dyspnea, laryngospasm

---

**Risperidone (Risperdal)**

- **Class:** Serotonin-Dopamine Antagonist Antipsychotics
- **Use:** Treat behavioral disturbances in TBI patients
- **Dose:** 2-3 mg PO daily
- **Side Effects:** Nausea, vomiting, headache, epistaxis, drowsy, chest pain, orthostatic hypotension, confusion, urinary retention, seizures, cough

---

**Amantadine (Symmetrel)**

- **Class:** Other systemic antivirals
- **Use:** Accelerates recovery in severe TBI, particularly in diffuse, frontal or right sided brain injury.
- **Dose:** 100-300mg PO daily
- **Side Effects:** Dizzy, Nausea, vomiting, weakness, rash, tremor, confusion, hypertension, urinary retention, seizures, dizzy
Intracranial Pressure Monitoring

- Level I and II A
  - There was insufficient evidence to support a recommendation for this topic.
- Level II B
  - Management of severe TBI patients using information from ICP monitoring is recommended to reduce in-hospital and 2-week post-injury mortality.

Cerebral Perfusion Pressure Monitoring

- Level I
  - There was insufficient evidence to support a recommendation for this topic.
- Level II B
  - Management of severe TBI patients using guidelines-based recommendations for CPP monitoring is recommended to decrease 2-week mortality.

Advanced Cerebral Monitoring

- Level I and II
  - There was insufficient evidence to support a recommendation for this topic.
- Level III
  - Jugular bulb monitoring of arteriovenous oxygen content difference (AVDO2), as a source of information for management decisions.
  - May be considered to reduce mortality and improve outcomes at 3 and 6 months post-injury.
Blood Pressure Thresholds

- Level I and II
  - There was insufficient evidence to support a recommendation for this topic.
- Level III
  - Maintaining SBP at ≥100 mm Hg for patients 50 to 69 years old or at ≥110 mm Hg or above for patients 15 to 49 or over 70 years old may be considered to decrease mortality and improve outcomes.

Intracranial Pressure Thresholds

- Level I & II A
  - There was insufficient evidence to support a recommendation for this topic.
- Level II B
  - Treating ICP above 22 mm Hg is recommended because values above this level are associated with increased mortality.
- Level III
  - A combination of ICP values and clinical and brain CT findings may be used to make management decisions.

Cerebral Perfusion Pressure Thresholds

- Level I & II A
  - There was insufficient evidence to support a recommendation for this topic.
- Level II B
  - The recommended target cerebral perfusion pressure (CPP) value for survival and favorable outcomes is between 60 and 70 mm Hg. Whether 60 or 70 mm Hg is the minimum optimal CPP threshold is unclear and may depend upon the patient’s autoregulatory status.
- Level III
  - Avoid aggressive attempts to maintain CPP >70mmHg with fluids.
  - Pressors may be considered due to risk of adult respiratory failure.
References (1/2)


References (2/2)

References (3/4)


References (4/4)


