Progesterone for the Treatment of Traumatic Brain Injury

TBI Management Guidelines

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Page 0911 for any questions
Introduction

These guidelines are a template for the care of TBI patients at sites participating in the multicenter clinical trial ProTECT III. We recognize the existence of legitimate treatment variability within this heterogeneous population of patients, and thus the following guidelines do not circumvent clinical acumen. However, treatment variability has undermined several notable clinical trials in TBI, and the NIH has required that this trial attempt to limit this variability. These guidelines are based on the 2007 Brain Trauma Foundation guidelines and consensus opinion from 31 academic US medical centers.

Physiologic Goals for TBI Patients

<table>
<thead>
<tr>
<th>Pulse Ox ≥ 90%</th>
<th>ICP &lt; 20</th>
<th>Na+ 135-145*</th>
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</thead>
<tbody>
<tr>
<td>PaO2 ≥ 100</td>
<td>PbtO2 ≥ 15</td>
<td>INR ≤ 1.4</td>
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<tr>
<td>PaCO2 35-45</td>
<td>CPP ≥ 60</td>
<td>PLTS ≥ 75,000</td>
</tr>
<tr>
<td>SBP ≥ 100</td>
<td>pH 7.35-7.45</td>
<td>Hgb ≥ 8</td>
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<tr>
<td>Temp 36-38.3°</td>
<td>Glucose 80-180</td>
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*Hypertonic Saline Therapy: Nat+ range: 145 mmol/L (minimum) to 160 mmol/L (maximum)

Oxygenation and Ventilation

1. Avoidance of Hypoxia – episodes of hypoxia are one of the most common and most deleterious secondary insults in TBI patients
   - Keep SpO2 > 90% in non-intubated patients
   - Keep PaO2 > 100 mmHg in intubated patients, except during ventilator weaning
2. Ventilation – hyperventilation should be avoided due to the risk of cerebral ischemia
   - Target PCO2 is 35-45 mmHg
   - Therapeutic hyperventilation should only be used for brief periods when there is: (1) acute neurological deterioration that coincides with cerebral herniation and (2) for refractory elevated ICP (see Tier 2 under ICP management)

Cerebral Perfusion

3. Cerebral Perfusion Pressure (CPP) – this is a critical parameter to maintain as episodes of hypotension are a significant cause of secondary insults to the injured brain
   - Maintain CPP ≥ 60 mmHg in patients with ICP monitoring
   - Adequate resuscitation – it is critical that endpoints of resuscitation are met (CVP>10, lactate<2.5, SvO2>65, base deficit>-3)
4. Blood Pressure – these goals are aimed at maintaining CPP
   - SBP goal > 100 mmHg (acceptable range 100 – 180 mmHg)
   - Vasopressors may be used if euvoletic and CPP<60mmHg but not to push the CPP>70 mmHg

Anemia and Coagulopathy

5. Anemia – an adequate hemoglobin is important for oxygen delivery to the brain; the target is 8 g/dl or above in this trial
6. Coagulation – For anticipated ventriculostomy placement or intracranial surgery, platelets should be maintained > 75,000 and the INR < 1.4
### ICP Monitoring and Management

7. **Indications** – All patients with signs and symptoms of increased ICP and/or GCS ≤ 8 should receive a ventriculostomy ± PbtO2 monitoring if their head CT is abnormal
   - Ventriculostomy should additionally be considered for patients with a normal head CT that have 2 or more of the following: age>40, motor posturing, and SBP<100mmHg
   - Intraparenchymal pressure monitors without ventriculostomy are discouraged

8. **Increased ICP is defined as ≥ 20 mmHg** – The following general measures and management tiers for intracranial hypertension represent an increasing level of therapeutic intensity; tier 1 measures should generally be performed before progressing to more intensive therapies. Because increasing ICP may be an early sign of an expanding surgical lesion, a repeat head CT should be considered.

#### Management of Increased ICP

<table>
<thead>
<tr>
<th>General Measures</th>
<th>Consider repeat head CT</th>
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<tbody>
<tr>
<td></td>
<td>Craniotomy for surgical lesions</td>
</tr>
<tr>
<td></td>
<td>Treat fever, hypotension, hypoxia, and hypercarbia</td>
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<tr>
<td></td>
<td>Adjust c-collar</td>
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</tbody>
</table>

**Tier 1**

<table>
<thead>
<tr>
<th>Adequate analgesia and sedation</th>
<th>Elevate HOB 30° and adjust c-collar</th>
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<tbody>
<tr>
<td>Drain EVD to 10 cmH2O*</td>
<td>Mannitol 0.25-1 gram IV*</td>
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</table>

*Return EVD to transduce once drained. Hypertonic saline preferred if patient is hypovolemic

**Tier 2**

<table>
<thead>
<tr>
<th>Repeat Mannitol (0.25-1 g/kg) q6hr*</th>
<th>3% Saline 250ml over 30min q6hr*</th>
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<tbody>
<tr>
<td>PCO2 goal 30-35 mmHg</td>
<td>Neuromuscular Paralysis</td>
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</table>

**Tier 3**

<table>
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<tr>
<th>Decompressive hemi or bilateral craniectomy</th>
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<tr>
<td>Barbiturate or Propofol Coma</td>
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<tr>
<td>Hypothermia</td>
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Adjunctive ICU Measures

10. **Antiseizure Prophylaxis** – phenytoin is recommended prophylaxis for TBI patients
   - 20 mg/kg loading dose followed by 300mg daily; adjust to therapeutic level
   - Stop phenytoin after 7 days if no seizure activity

11. **Stress Ulcer Prophylaxis** – TBI patients requiring mechanical ventilation should receive prophylaxis per ICU pharmacy guidelines
12. **DVT Prophylaxis** – TBI patients are at high risk of DVT/PE and should receive prophylaxis
   - All should be placed on SCDs upon admission
   - Prophylactic subcutaneous UFH (5000 units q8 hours) or LMWH (40mg daily) may be started in select patients with 24hr head-CT stability and Neurosurgical/Trauma staff approval

13. **Serum Electrolytes and Hyperosmolar Therapy**
   - Q6 hr electrolytes and serum osmolality should be followed with hyperosmolar therapy
   - Mannitol should be held for serum osm>320 or osmolar gap>20 (measured – calculated osm)
   - The Na goal increases to 145-160 mmol/L with **hypertonic** therapies
   - 23.4% saline may be used (30mL over 20 minutes q6hr)
   - Hold hypertonic saline treatment for Na > 160

14. **Nutritional Support**
   - Early enteral feeding should be initiated at 10 ml/hr as soon as feasible and increased to goal
   - Nonparalyzed TBI patients require 140% and paralyzed require 100% of basal caloric expenditure

**Contact the ProTECT III Team:**

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