Intracranial Pressure

Santiago Ortega Gutierrez, MD
Neurocritical care fellow
Columbia University

Disclosures

• Recipient of 2011-2012 SPOTRIAS NINDS-NIH funded research fellowship

Topics to cover

• Physiopathology
  – Components of ICP
  – Monroe-Kellie doctrine
  – CBF-ICP relationship

• ICP monitoring
  – Devices
  – Waveform analysis

• Treatment of ICP: Columbia Stepwise Protocol

Intracranial Pressure

Intracranial components
Total volume approx. 1500 cc

• 75-80% Parenchyma
• 10% CSF
• 10% Blood

Monroe-Kellie Doctrine:

– Intracranial tissue compartments are normally in a state of volume equilibrium, which under normal physiologic conditions results in a constant ICP of 8 to 10 mmHg.
ICP - Intracranial volume curve: Demonstrates that as volume increases, an exponential rise in pressure is observed as a result of displacement of CSF and blood volume.

Monroe-Kellie Doctrine

- Disturbance of volume equilibrium disrupts the pressure equilibrium
- Pressure = force/area
- Pathologically elevated ICP represents the force required to displace blood and CSF from the intracranial space in order to accommodate new volume

**Causes of Increased ICP:**

- **Space Occupying Lesion:** Hematoma, Tumor, Abscess
- **Increased CSF:** Hydrocephalus
- **Inc. Blood Volume (Vasogenic edema):** Trauma, Tumor, Abscess, Hypertensive encephalopathy
- **Inc. Brain Volume (Cytotoxic edema):** Infarction, Ischemia

**Clinical Signs**

- Increased ICP
  - Depressed level of consciousness
  - Pressor response
  - Projectile vomiting
  - CN 6 palsies
- Brainstem herniation
  - CN 3 palsy
  - Motor posturing
  - Lower extremity rigidity
  - Loss of lateral EOMs
  - Hyperventilation

**ICP/CPP Management**
Clinical Applications

- No reliable quantitative measure complex relationships between intracranial compliance, cerebral autoregulation and intracranial pressure
- ICP waveform analysis provides a method by which qualitative assessments can be made

ICP Monitoring Techniques

ICP Waveform

- Normal pulse have three peaks:
  - Percussion wave (P1)
    - Representative of arterial input
    - Unclear how arterial pulsations are transmitted via choroid plexus to the CSF and parenchyma
  - Tidal wave (P2)
    - Representative of retrograde venous pulsation / intracranial volume
  - Dicrotic wave (P3)
    - Follows the dicrotic notch
    - Representative of venous drainage
ICP Waveform

**ICP Waveform patterns**

- **Pathologic waves (Lundberg waves)**
  - **A waves** (Plateau waves)
    - Rapid rise in ICP from normal levels to peak at levels ~50 mmHg for 5 - 20 min followed by spontaneous reduction
    - May be associated with Cushing Reflex
  - **B waves**
    - Sharply peaked waves to levels ~30 mmHg with rapid fall within seconds but repeated q 1 - 2 minutes
    - Classically associated with change in respiratory pattern
  - **C waves**
    - Rhythmic elevations 5-6/min to lesser levels
    - Associated with fluctuating blood pressures

**Lundberg A and B waves**

**ICP/CPP Treatment Thresholds**

- **Guideline**
  - ICP treatment should be initiated at an upper threshold of 20 mm Hg.
  - Option: Cerebral Perfusion Pressure should be maintained at a minimum of 50 mm Hg.
Universal Measures
- Cardiopulmonary homeostasis and euvolemia
- Identify cause(s) of raised ICP or reduced CPP
  - Head positioning
  - Subclinical seizures
  - Ventilatory pattern (elev PCO₂, dec PaO₂)
  - Fever (1°C rise in core temp can inc metabolic rate by 10%)
  - Glycemic control
  - Raised intrathoracic or intraabdominal pressures

IAP/ITP - ICP relationship
- Clinical study where TBI patients were randomized to receive set weights placed on abdomen
- Changes in IAP, ITP, ICP measured pre-post intervention

Fever and ICP
- Fever results in an increase in the metabolic rate and hence CBF/CBV leading to increased ICP
- Presence and duration of fever independently associated with poor outcome

Hyperglycemia and ICP
- Hyperglycemia post brain injury leads to lactic acidosis and subsequent cerebral edema
- ? Clinically meaningful definition of hyperglycemia

Surgery
Two options
1. External ventricular drainage of CSF
   - Most reliable method of assessing global ICP
   - Indications
     - Hydrocephalus or extensive IVH
     - Many institutions considered 1st line therapy
   - Up to 6 – 10% risk of infection
2. Decompressive Craniectomy
   1. Compartmental ICP
   2. Diffuse ICP
Craniectomy

Currently considered for patients failing maximal medical therapy (really?)
Animal studies demonstrate significant reduction in ICP and increased compliance
Clinical studies:
• Mostly retrospective
  • Results indicate resultant decreased ICP, improved brain oxygenation and compliance
  • Survival and functional outcome data inconsistent
  • Lack of standardized indications, timing, technique

Craniectomy

• Adequate bone window and duroplasty to allow for outward swelling without vascular compromise
• Most often accompanied by anterior temporal lobectomy
• Bone is stored on abdominal wall for 3 months

Sedation and Analgesia

• Adequate sedation and pain control are important first steps in managing raised ICP
• Agents reduce ICP by primary reduction in CMR and subsequently CBF
• Not for primary treatment of raised ICP
• Goal: adequate control without obscuration of clinical examination
Propofol

Substituted phenol with rapid anesthetic but no analgesic properties

Mechanism of action
- Reduces ICP by dose dependent coupled fall in CBF and CMR
- CBF reduction secondary to decreases in CMR
- In head injured patients, CMR may be reduced disproportionately more than CBF
- Direct anticonvulsant action via GABA dependent chloride channels
  - Dosing: Bolus - 0.3 mg/kg Q 5 min
    Infusion - 0.3 mg/kg/h to 3 mg/kg/h

Adverse effects
- Dose dependent systemic hypotension, bradycardia, and cardiac depression
- Liver dysfunction / elevated triglycerides
- Chemical pancreatitis
- Prolonged half-life with continuous infusions
- Propofol-infusion syndrome

Propofol Infusion Syndrome

Benzodiazepines

Mild effect on CMR and CBF
- No clinical trials assessing efficacy
- Potential Adverse effects:
  1. Reduction in CPP by systemic hypotension
  2. Rise in PCO2 by respiratory depression
  3. Prolonged sedation with long-term use
    - Midazolam is preferred agent due to water solubility and shorter half-life
      (Dose: Bolus 0.3 to 0.6 mg/kg
       Infusion – 0.02 to 0.10 mg/kg/hr)

Opioids

Mild effect on CMR and CBF
Clinical trials equivocal for ICP control
Use as adjunctive therapy

Adverse effects
- Increase in PCO2 secondary to respiratory depression (when ventilation not controlled)
- Cerebrovasodilation in response to decreased MAP (when bolus injection rather than continuous infusion utilized and autoregulation intact)
- Prolonged sedation with long-term use

Diagram showing CPP optimization: Dopamine infusion resulting in increased MAP and CPP, and decreased ICP
4. Hyperventilation

- Reduces ICP by vasoconstriction induced by alkalosis
- Fall in ICP parallels the fall in CBV
- Theoretically
  - Corrects brain/CSF lactic acidosis
  - Increases $O_2$ metabolism and normalize glucose uptake
  - Reverses hyperemia (post-traumatic) and restore autoregulation

Adverse effects

- Prolonged vasoconstriction +/- hypotension results in reduction in CBF to ischemic levels
- Effects are temporary after which lower PCO2 levels are required to achieve ICP control

Randomized Clinical Trial

**Design**
- Prophylactic HV (PaCO2 25 ± 2 mm Hg) to severe TBI patients (GCS <= 8) applied for first 5 days (± THAM)
- CBF not measured

**Results**
- 14% of treatment group had ICP > 20 mmHg on admission
- HV group demonstrated largest fluctuation in ICP
- GCS 4 and 5 had significantly worse outcomes at 3 and 6 months
- Worse outcomes avoided in THAM + HV group

Summary

PaCO2 levels below 28 mmHg are acceptable only as an emergency measure, for up to 30 minutes, until more definitive therapy is initiated.
**Mannitol**

**Other Mechanisms of Action**
- Reduce RBC rigidity
- Free radical scavenger
- Reduce CSF production

**Adverse effects**
- Hyperosmotic prerenal renal failure
- Electrolyte disturbances (hypokalemia)
- Dehydration and hypotension
- Expansion of ICH

**Mannitol Dosing**

**NICU Mannitol Protocol**
- Only indicated for ICP-directed care
- Dosage: 0.5 – 1.0 g/kg IV Q4-6 hrs PRN raised ICP
- GOAL: osmotic gradient of 10 – 20 mOsm
  \[
  \text{Osm}_{\text{calc}} = 2 \times \text{Na} + \text{glc}/18 + \text{bun}/2.8
  \]
  \[
  \text{Osm gap} = (\text{Osm}_{\text{calc}} - \text{Osm}_{\text{meas}})
  \]
- Normovolemia maintained (CVP 5 – 8)
- No absolute [Na⁺] or Osm contraindication; however, effectiveness diminished with Na⁺ > 160 mEq / 310 mOsm

**Hypertonic saline**

**Mechanism of Action**
- Osmotic effect
- Anti-inflammatory effects
- Modulation of neuroendocrine system (ANP, VSP)
- Maintain BBB integrity via membrane stabilization
- Improve regional cerebral blood flow (rCBF)

**Hypertonic saline**

**Osmotic effect**
- Via properties of sodium chloride
  1. Low permeability across BBB
  2. Hi reflection coefficient (1.0)
- Hyperosmolar concentrations
  Create a gradient to pull water from interstitial and intracellular spaces into the intravascular compartment

<table>
<thead>
<tr>
<th>Osmotic Agent</th>
<th>Sodium Content (mmol/L)</th>
<th>Osmolality (mmol/L)</th>
</tr>
</thead>
<tbody>
<tr>
<td>20% Mannitol</td>
<td>N/A</td>
<td>1375</td>
</tr>
<tr>
<td>0.9% NaCl</td>
<td>154</td>
<td>308</td>
</tr>
<tr>
<td>3% NaCl</td>
<td>513</td>
<td>1026</td>
</tr>
<tr>
<td>23.4% NaCl</td>
<td>4004</td>
<td>8008</td>
</tr>
</tbody>
</table>
**Hypertonic saline**

**Adverse effects**
- CNS
  - Central pontine myelinolysis
  - Seizures
  - Rebound cerebral edema
  - SDH or ICH

- Systemic
  - CHF
  - Hypokalemia
  - Hyperchloremic acidosis
  - Coagulopathy
  - Phlebitis
  - Renal failure

**Clinical Evidence**
- Many case series, retrospective studies, and a few prospective randomized studies demonstrate HS effective in lowering ICP
- Lack of uniformity in indications, timing, dosage
- Better understanding of safety and dose-response curve
- Eventually RCT of Mannitol v. HS (equiosmolar)

**23.4% NaCl**
Quereshi et al
- Case series of 8 patients refractory to diuretics (lasix, mannitol), hyperventilation treated with 30 cc 23.4% NaCl

**NICU Hypertonic Saline Guidelines**
- **Dosing:**
  - 3%NaCl: 125 - 250 cc bolus Q 6 hours PRN raised ICP or continuous infusion @ 0.5 – 1.0 cc/kg/hr
    - Hold for Na>160
  - 23.4% NaCl: 30 cc bolus Q 6 hours PRN raised ICP
    - Hold for Na>160

**METABOLIC THERAPY**
- Primary reduction of cerebral metabolic rate for oxygen (CMRO₂)
- Secondary reduction of cerebral blood flow (CBF) and cerebral blood volume (CBV)
6. Barbiturates

- Free radical scavenger and reduces lipid peroxidation
- Direct increase in vasomotor tone
  - underlying electrical brain activity and CO₂ reactivity must be in place

Barbiturates

Adverse effects

- Hypotension / cardiac suppression
- Gastric Stasis
- Mucous Plugging
- Anergy
- Hypothermia
- Prolonged coma
- Inability to diagnose brain death by clinical criteria

Clinical Trials

Randomized Controlled Trial (Eisenberg, 1988)

- Barbiturate therapy after other medical therapies failed
- Adequate ICP controlled in 30 % of barbiturate treated group
  v. 16% of no-barbiturate treated group
- Patients failing to respond to barbiturate therapy had higher mortality/morbidity

Other uncontrolled trials have demonstrated similar effect on ICP control and morbidity/mortality

Prophylactic use has been shown to provide no benefit (Ward, 1985; Schwartz, 1984)

Dosing

- Thiopental
  - 250 mg IV bolus reduces ICP in seconds with duration of only 15 – 20 min
  - Some advocate use as a test to determine responders
  - Multiple repetitive dosing results in prolonged half-life
- Pentobarbital
  - Loading dose 3 - 5 mg/kg over 30 min
  - 50 – 200 mg IV bolus for raised ICP
  - Half life: 15 to 48 hours (bolus); up to 190 hrs (infusion)
  - End point: ICP control for 24 – 36 hours
  - Pupillary responses first to recover with motor responses last

7. Hypothermia

Actions

- Reduces ICP primarily via a reduction in CMR and resultant decreased CBF
- Reduce release of excitatory neurotransmitters
- Inhibition of inflammatory cascade
- Attenuate the opening of blood-brain barrier

Adverse Effects

- Rebound intracranial hypertension
- Increased risk of sepsis
- Cardiac ischemia/ arrhythmias
- Coagulation abnormalities

Hypothermia

Clinical Evidence

- Supporting evidence in small, single center RCTs (Shiozaki, 1993; Clifton, 1995; Marion, 1997)
- Large, multicenter RCT (Clifton, 2001)
  - 392 patients randomized to hypothermia (33 C) v normothermia
  - Cooling initiated within 6 hours of onset of injury
  - Cooling maintained for 48 hours
Hypothermia

Table 4. Rates of Poor Outcome and Death Six Months after Severe Brain Injury in Patients Treated with Induction of Hypothermia or Normothermia.


Summary

- Adequately provides control of ICP
- Unclear whether leads to improved outcomes
- Currently goal is to maintain normothermia
- Newer techniques to induce hypothermia may make it more feasible, reduce morbidity