Medical Management of Intracranial Hypertension

Joao A. Gomes, MD FAHA
Head, Neurointensive Care Unit
Cerebrovascular Center
Anatomic and Physiologic Principles
Intracranial compartments

- **Brain** 80% (1,400 cc)
- **CSF** 75-150 cc (10%): 50% intraventricular and 50% subarachnoid compartment
- **Blood** 75-150 cc (10%): 70% venous, 30% arterial
Monro-Kelly doctrine

- An increase in the volume of one compartment must be accompanied by an approximately equal decrease in the volume of the other compartments to maintain normal ICP
Compensation

- Shift of CSF from the intracranial to the spinal thecal compartment
- Dural sinus collapse and arterial vasoconstriction: decreased CBV
- Brain herniation
The graph illustrates the relationship between cerebral blood flow (mL/100 g/min) and mean arterial blood pressure (mmHg). The x-axis represents the mean arterial blood pressure ranging from 0 to 180 mmHg, while the y-axis represents cerebral blood flow from 0 to 80 mL/100 g/min.

- **Autoregulation**: This region shows a stabilized cerebral blood flow range from 60 to 80 mL/100 g/min, which remains relatively constant across a wide range of mean arterial blood pressure (40 to 140 mmHg).
- **Impaired dilatation, arterial collapse, ischemia**: Cerebral blood flow decreases as mean arterial blood pressure decreases below 60 mmHg.
- **Endothelial damage, hyperemia, vasogenic edema**: Cerebral blood flow increases as mean arterial blood pressure increases above 140 mmHg.

This graph highlights the importance of maintaining normal blood pressure to ensure adequate cerebral blood flow.
Cerebral Perfusion Pressure

- CBF determinations difficult to perform.
- CPP is a helpful guide to estimate adequacy of cerebral circulation.
- CPP is the “blood pressure” of the brain
- CPP = MAP - ICP
- Normal CPP 60-100
- CPP < 30 - 40 typically leads to ischemia
Compliance: pressure-volume response

- CSF added to the craniospinal space
- Pressure-volume curve follows a hyperbolic function (rather than linear)
- Reflection of the elastic properties of the craniospinal system (elastance)
Compliance: zones I, II, III

• Ratio of the change in volume to the resulting change in pressure ($\Delta V/\Delta P$)
• Measure of the distensibility of the intracranial cavity
• Zone II: normal ICP, poor compliance
ICP Monitoring
C Intracranial pressure monitoring by ventricular catheter

Catheter

Lateral ventricle

Collecting system

Monitor

Cleveland Clinic
ICP waveforms

- The choroid plexus is credited as the site of transfer of the arterial pulse to the CSF.
- Pressure gradient exists along the craniospinal axis in a rostro-causal fashion (about 60% lower in the lumbar space).
- Facilitates the movement of CSF from the ventricles into the subarachnoid space.
Intraventricular monitoring

- **Percussive wave** (P1): choroidal plexus pulse
- **Tidal wave** (P2): intracranial compliance
- **Dicrotic wave** (P3): closure of aortic valve
- Poor compliance: peaked P2
A Trial of Intracranial-Pressure Monitoring in Traumatic Brain Injury
Pathophysiology
<table>
<thead>
<tr>
<th>Condition</th>
<th>Mass Effect</th>
<th>Edema</th>
<th>Vasodilatation</th>
<th>Disturbed Circulation of CSF</th>
</tr>
</thead>
<tbody>
<tr>
<td>Traumatic brain injury</td>
<td>+</td>
<td>+</td>
<td></td>
<td>+</td>
</tr>
<tr>
<td>Subarachnoid hemorrhage</td>
<td>+</td>
<td>+</td>
<td></td>
<td>++</td>
</tr>
<tr>
<td>Cerebral venous thrombosis</td>
<td>+</td>
<td></td>
<td></td>
<td>+</td>
</tr>
<tr>
<td>Anoxic–ischemic encephalopathy</td>
<td>+</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Brain tumor</td>
<td>+</td>
<td>+</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Brain infarction after acute occlusion of middle cerebral artery</td>
<td>+</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Spontaneous intracerebral hematoma</td>
<td>+</td>
<td>+</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Abscess</td>
<td>+</td>
<td>+</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Meningitis</td>
<td>+</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Idiopathic intracranial hypertension</td>
<td>+</td>
<td></td>
<td></td>
<td>+?</td>
</tr>
<tr>
<td>Acute liver encephalopathy</td>
<td>+</td>
<td></td>
<td>+</td>
<td></td>
</tr>
<tr>
<td>Acute hypoosmolar syndromes</td>
<td>+</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Hypertensive encephalopathy</td>
<td>+</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Reye’s syndrome</td>
<td>+</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Craniosynostosis†</td>
<td>+</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
Treatment
Figure 2. Algorithm for the Treatment of Increased Intracranial Pressure (ICP). CSF denotes cerebrospinal fluid.
Principles of Treatment

• General
  - Avoid shivering, agitation or fever
  - Euvolemia to slight hypervolemia
  - Pressors as needed to maintain CPP
  - Facilitate venous outflow (head elevation > 30 degrees, midline position)
• **Specific**
  - Controlled hyperventilation (PaCO2 25-30 mmHg)
  - External CSF drainage
  - Osmotic therapy
  - Metabolic suppression (propofol, barbiturates)
  - Decompressive surgery
  - Hypothermia
ICP Treatment Algorithm

Insert ICP monitor and maintain CPP >65 mm Hg (ventriculostomy preferred)

Yes

ICP >20-25 mm Hg?

Yes

CSF drainage (if available)
Sedation/Analgesia

No

ICP >20-25 mm Hg?

Yes

Hypertonic saline (23.4% 30 cc bolus)
Mannitol bolus (0.5-1.0 g/kg)

No

ICP >20-25 mm Hg?

Yes

Consider mild hyperventilation \( (P_aCO_2 \ 30-35 \text{ mm Hg}) \); further sedation; neuromuscular blockade

No

ICP >20-25 mm Hg?

Yes

Stepwise withdrawal of ICP therapies

No

ICP >20-25 mm Hg?

Consider repeat CT scan

Yes

Second-tier therapies such as hypothermia, decompressive craniectomy, barbiturate coma.
<table>
<thead>
<tr>
<th>Therapy Steps</th>
<th>Levels of Evidence</th>
<th>Treatment</th>
<th>Risk</th>
</tr>
</thead>
<tbody>
<tr>
<td>8</td>
<td>Not reported</td>
<td>Decompressive craniectomy</td>
<td>Infection or delayed hematoma, Subdural effusion, Hydrocephalus and syndrome of the trephined</td>
</tr>
<tr>
<td>7</td>
<td>Level II</td>
<td>Metabolic suppression (barbiturates)</td>
<td>Hypotension and increased number of infections</td>
</tr>
<tr>
<td>6</td>
<td>Level III</td>
<td>Hypothermia</td>
<td>Fluid and electrolyte disturbances and infection</td>
</tr>
<tr>
<td>5</td>
<td>Level III</td>
<td>Induced hypocapnia</td>
<td>Excessive vasoconstriction and ischemia</td>
</tr>
<tr>
<td>4</td>
<td>Level II</td>
<td>Hyperosmolar therapy, Mannitol or hypertonic saline</td>
<td>Negative fluid balance, Hypernatremia, Kidney failure</td>
</tr>
<tr>
<td>3</td>
<td>Not reported</td>
<td>Ventricular CSF drainage</td>
<td>Infection</td>
</tr>
<tr>
<td>2</td>
<td>Level III</td>
<td>Increased sedation</td>
<td>Hypotension</td>
</tr>
<tr>
<td>1</td>
<td>Not reported</td>
<td>Intubation, Normocarbic ventilation</td>
<td>Coughing, ventilator asynchrony, ventilator-associated pneumonia</td>
</tr>
</tbody>
</table>

Cleveland Clinic
Brain shrinkage due to acute hypernatremia

Takeshi Machino, MD; and Toshihiro Yoshizawa, MD, PhD, Ibaraki and Tsukuba, Japan
23.4% Hypertonic Saline

- “Bullet”
- Standard dose: 30 mL (120 mEq - 8008 mOsm/L) given over 15-20 minutes
- May repeat once at discretion of MD (i.e. another dose of 30 mL)
- MD or APRN/PA may administer 23.4% slow via central line if indicated at 2 cc/min
- Appropriate for initial or adjunct emergency treatment of acute intracranial hypertensive crisis or herniation
Hypertonic saline versus mannitol for the treatment of elevated intracranial pressure: A meta-analysis of randomized clinical trials

Hooman Kamel, MD; Babak B. Navi, MD; Kazuma Nakagawa, MD; J. Claude Hemphill III, MD, MAS; Nerissa U. Ko, MD
Efficacy and Dose-Response Relationship of 23.4% Hypertonic Saline Administration and Intracranial Pressure (ICP) in Patients with Elevated ICP

Background

- 23.4% hypertonic saline (HTS) is used for treatment of elevated intracranial pressure (ICP).
- Pharmacokinetic/pharmacodynamic studies are limited and dose-response curves in humans have not been reported.
- HTS 23.4% is traditionally dosed in 30 cc increments rather than based on patient’s weight regardless of disease severity.
- We hypothesize that there is a correlation between weight-based dosing (mOsm/Kg) and ICP reduction.

Study Objectives

- Describe the onset, duration of action and maximum ICP lowering effect following administration of 23.4% HTS in critically ill patients with ICP crisis.
- Develop a dose-response curve for 23.4% HTS.

Research Design and Methods

- Retrospective chart review of patients admitted to the Neurocritical care unit from August 2010 to August 2011 who developed ICP crisis (>20 mm Hg sustained for >5 minutes) and were treated with 23.4% HTS.
- Only data for the first ever treatment with HTS were collected.
- Patient demographics, onset and duration of action, lowest ICP achieved and use of adjunctive therapies were recorded.
- Descriptive statistics and correlation analysis were performed.
- IRB approval and granted per institution policy.

Results

<table>
<thead>
<tr>
<th>Total number of patients</th>
<th>N=19</th>
</tr>
</thead>
<tbody>
<tr>
<td>Male gender, n (%)</td>
<td>9 (47)</td>
</tr>
<tr>
<td>Age (years)*</td>
<td>52 ± 18</td>
</tr>
<tr>
<td>Weight (kg)*</td>
<td>98 ± 26</td>
</tr>
<tr>
<td>ICU LOS (days)*</td>
<td>20 ± 28</td>
</tr>
<tr>
<td>GCS Pre*</td>
<td>6.6 ± 3</td>
</tr>
<tr>
<td>GCS Post*</td>
<td>8.7 ± 4</td>
</tr>
<tr>
<td>GCS change*</td>
<td>2 ± 2</td>
</tr>
<tr>
<td>Concomitant hypothermia and pentobarbital coma, n (%)</td>
<td>13 (68)</td>
</tr>
<tr>
<td>Sodium pre</td>
<td>136 ± 6</td>
</tr>
<tr>
<td>Sodium post</td>
<td>146 ± 6</td>
</tr>
<tr>
<td>Admission diagnosis, n (%)</td>
<td></td>
</tr>
<tr>
<td>SAH</td>
<td>10 (52)</td>
</tr>
<tr>
<td>ICH</td>
<td>6 (32)</td>
</tr>
<tr>
<td>Other</td>
<td>3 (16)</td>
</tr>
</tbody>
</table>

Conclusions

- 23.4% HTS was associated with a 67% reduction in ICP values in critically ill neurology/neurosurgery patients.
- Time to clinical endpoint of ICP <20 mmHg was 41 minutes and in 75% of patients the duration of action was 127 minutes.
- An improvement of 2 points in GCS was also observed.
- The first description of a dose-response curve for 23.4% HTS in humans is reported.
- While most patients received 2-4 mOsm/Kg of HTS, additional benefit may be derived from doses as high as 7 mOsm/Kg.

Limitations

- Retrospective study.
- Small number of patients.
- Confounding factors: hypothermia, hyperventilation, pentobarbital therapy.
- Heterogeneous group of patients with different severities.
- Some patients received concomitant hypertonic therapy (i.e. mannitol) within few hours prior to HTS.
- Lack of continuous ICP documentation.

Bibliography


ICP Change Over Time

Total number of patients: N=19

<table>
<thead>
<tr>
<th>Male gender, n (%)</th>
<th>9 (47)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (years)*</td>
<td>52 ± 18</td>
</tr>
<tr>
<td>Weight (kg)*</td>
<td>98 ± 26</td>
</tr>
<tr>
<td>ICU LOS (days)*</td>
<td>20 ± 28</td>
</tr>
<tr>
<td>GCS Pre*</td>
<td>6.6 ± 3</td>
</tr>
<tr>
<td>GCS Post*</td>
<td>8.7 ± 4</td>
</tr>
<tr>
<td>GCS change*</td>
<td>2 ± 2</td>
</tr>
<tr>
<td>Concomitant hypothermia and pentobarbital coma, n (%)</td>
<td>13 (68)</td>
</tr>
<tr>
<td>Sodium pre</td>
<td>136 ± 6</td>
</tr>
<tr>
<td>Sodium post</td>
<td>146 ± 6</td>
</tr>
<tr>
<td>Admission diagnosis, n (%)</td>
<td></td>
</tr>
<tr>
<td>SAH</td>
<td>10 (52)</td>
</tr>
<tr>
<td>ICH</td>
<td>6 (32)</td>
</tr>
<tr>
<td>Other</td>
<td>3 (16)</td>
</tr>
</tbody>
</table>
23.4% HTS was associated with a 67% reduction in ICP values in critically ill neurology/neurosurgery patients.

Time to clinical endpoint of ICP <20 mmHg was 41 minutes and in 75% of patients the duration of action was 127 minutes.

An improvement of 2 points in GCS was also observed.

The first description of a dose-response curve for 23.4% HTS in humans is reported.

While most patients received 2-4 mOsm/Kg of HTS, additional benefit may be derived from doses as high as 7 mOsm/Kg.
HTS: side effects

- CPM
- SDH
- CHF
- Acid-base abnormalities
- Coagulopathies
- Hypotension with rapid infusion (decreases SVR)
Multimodal Monitoring
Partial Pressure of $O_2$ Brain Tissue

It is a closed polarographic $p_{bt}O_2$ probe with reversible electrochemical reactions.

This new type of chemistry virtually eliminates drifting of the probe’s sensitivity and zero point
Partial Pressure Oxygen in Brain

What are we measuring?

Microvascular delivery and local cellular consumption

Licox
ICP/CPP Management

Unrelated to oxygenation ...
Pupillometer
<table>
<thead>
<tr>
<th></th>
<th>Right</th>
<th>Left</th>
<th>Diff</th>
</tr>
</thead>
<tbody>
<tr>
<td>NPi</td>
<td>4.5</td>
<td>0</td>
<td></td>
</tr>
<tr>
<td>Size</td>
<td>1.88 mm</td>
<td>3.59 mm</td>
<td>L &gt; R 1.71</td>
</tr>
<tr>
<td>MIN</td>
<td>1.61 mm</td>
<td></td>
<td></td>
</tr>
<tr>
<td>CH</td>
<td>14%</td>
<td></td>
<td></td>
</tr>
<tr>
<td>CV</td>
<td>0.57 mm/s</td>
<td></td>
<td></td>
</tr>
<tr>
<td>MCV</td>
<td>0.91 mm/s</td>
<td></td>
<td></td>
</tr>
<tr>
<td>LAT</td>
<td>0.23 sec</td>
<td></td>
<td></td>
</tr>
<tr>
<td>DV</td>
<td>0.19 mm/s</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
Decompressive Hemicraniectomy
Early decompressive surgery in malignant infarction of the middle cerebral artery: a pooled analysis of three randomised controlled trials

Katayoun Vahedi, Jeannette Hofmeijer, Eric Juettler, Eric Vicaud, Bernard George, Ale Algra, G Johan Amelink, Peter Schmiedek, Stefan Schwab, Peter M Rothwell, Marie-Germaine Bausser, H Bart van der Worp, Werner Hacke, for the DECIMAL, DESTINY, and HAMLET investigators

Figure 1: Distributions of the scores on the mRS and death after 12 months for patients treated with or without decompressive surgery
Multimodal Monitoring: the key?
Cleveland Clinic

Every life deserves world class care.