ICU Management of Subarachnoid Hemorrhage

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Disclosures

• I have no relevant commercial relationship to disclose.

Objectives

• Review the most updated evidence and the clinical applications of therapies for patients with aneurysmal SAH

• Provide recommendations for management of aneurysmal SAH
Subarachnoid Hemorrhage (SAH) Epidemiology

- Traumatic SAH: most common form (240,000 cases/year in US)

- Spontaneous SAH:
  - AVMs
  - ICH-related
  - SA/VA dissections
  - fistula
  - aneurysms
  - dissections
  - fistula
  - aneurysms

- aSAH in US: 10-15 cases/100,000 pop./year
- 30,000 cases/year in US. F:M 3:2
- Mean age at onset: 55 years

Aneurysmal SAH (aSAH)

Presentation
- Thunderclap HA
- Worst headache of life
- Initial LOC (45%)
- Coma/Stupor (10%)
- Meningismus
- Cranial nerve
  - 3rd CN palsy (6%)
  - 6th CN palsy
- Seizures (8%)

Diagnosis
- CT scan sensitive:
  - 99% within 12h
  - 92% within 24h
  - 58% day 5
- Lumbar puncture if high clinical suspicion but negative CT:
  - Xantochromia (6h-2wks)
  - Spectrophotometry for bilirubin
- CTA* or catheter angiography ASAP to identify aneurysm and define its seize and shape
  *98% sensitivity; may miss aneurysms <3 mm

aSAH: Neurosurgical Disease & Systemic Illness

Medical complications strongly influence outcome!
aSAH: A Devastating Event

- High overall mortality: historically ~ 50% (~1 in 8 patients die prior to reaching the hospital. In-hospital > 25%).
- 18% in-hospital mortality in modern neurocritical care era

Contemporary single-center study of 1200 cases of SAH: 12.5 yr study period

- 18% (216/1200) died during hospitalization
- 30% of deaths within 48 h of admission
- 56% by SAH day 7
- 76% by SAH day 14

Survivors:
- Significant long-term disability (> 50%)
- Neurocognitive impairment: 20% at 3 months

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Poor Outcome Predicted by Initial Clinical Severity

<table>
<thead>
<tr>
<th>Hunt and Hess Grading Scale</th>
<th>WFNs Grading Scale</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Grade</strong></td>
<td><strong>Neurologic Status</strong></td>
</tr>
<tr>
<td>1</td>
<td>Mild headache, slight nuchal rigidity</td>
</tr>
<tr>
<td>2</td>
<td>Severe headache, stiff neck, cranial nerve palsy</td>
</tr>
<tr>
<td>3</td>
<td>Drowsy or confused, mild focal neurologic deficit</td>
</tr>
<tr>
<td>4</td>
<td>Stuporous, moderate or severe hemiparesis</td>
</tr>
<tr>
<td>5</td>
<td>Coma, decerebrate posturing</td>
</tr>
</tbody>
</table>

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Grade Neurologic status Mortality GOS

1 | Mild headache, slight nuchal rigidity | 1% | 4
2 | Severe headache, stiff neck, cranial nerve palsy | 5% | 4
3 | Drowsy or confused, mild focal neurologic deficit | 10-20% | 2-4 | 13-14 | 2 \± | 33% | 2
4 | Stuporous, moderate or severe hemiparesis | 30-40% (10%) | 2-4 | 7-12 | 2 \± | 77% | 2
5 | Coma, decerebrate posturing | (70%) |  |  |  |  |  |  |  |
Hospital mortality according to admission Hunt-Hess grade over a 12.5-year study period. Each time epoch represents 300 consecutive admissions.

Who Dies and Why?

Neurocritical Care Focus in aSAH

• Limit acute brain injury from ↑ICP
  - Hydrocephalus
  - Global cerebral edema
• Prevent rebleeding
• Prevent/Treat seizures
• Prevent/Treat delayed cerebral ischemia
• Manage other medical complications:
  - Fever
  - Hyponatremia
  - Neurogenic stunned myocardium/pulmonary edema
Hydrocephalus

- 15% of patients (40% of whom symptomatic)
- Subarachnoid blood impedes CSF flow and/or resorption
  
  - EVD insertion if **symptomatic**, HCP, or in any patient with **poor grade**
    - Outcome relates better to post-EVD insertion HH grade

- 18-26% of patients require VP shunt for persistent HCP

Rebleeding of Unsecured Aneurysm:

- 4-17% rebleed on day 0 (most of rebleeding within first 2-6 h)
  - Cumulative risk 20% at 14 days
- RFs: Poor grade, longer time to Rx, size >10 mm, SBP> 160
- > 70% mortality, odd of survival w/o severe disability 

  **Rebleeding prevention: Early Aneurysm Repair**

- Microsurgical Clipping:
  - Preservation of parent vessels and perforators
  - Permanent obliteration in about 90% of patients
  - Highest complication rate with large and BA aneurysms

- Endovascular Coiling:
  - Obliteration of small-necked aneurysms in 90% of cases
  - Wide neck: coils may migrate and be a source of emboli
  - Rate of thromboembolic events 12.5% (RF size > 10 mm)
  - Risk of coil compaction after several yrs. \(\rightarrow\) rebleeding
Coiling or Clipping?

- Skills of treating interventionalist/neurosurgeon have a great impact on outcome – High Volume Centers!
- Cannot treat all patients with one modality regardless of anatomical, clinical and other factors.
- Coiling can be considered if:
  - Favorable geometry
    - Neck width < 4 mm
    - Dome to neck ratio ≥ 2:1
    - Aspect ratio > 1.6
  - Criteria for coiling of aneurysms without need for adjunctive techniques (e.g. stent placement and balloon remodeling)

Coiling or Clipping?

- Skills of treating interventionalist/neurosurgeon have a great impact on outcome – High Volume Centers!
- Cannot treat all patients with one modality regardless of anatomical, clinical and other factors.
- Coiling can be considered if:
  - High risk cases
    - Posterior circulation Location
      - MCA aneurysms better off with clipping
      - Distal arterial segments aneurysms better off with surgery
    - Poor clinical status, comorbidities, age > 70 years (favor coiling)
    - No large intracerebral hematoma (> 50 ml) with mass effect

Coiling or Clipping?

International Subarachnoid Aneurysm Trial (ISAT) of neurosurgical clipping versus endovascular coiling in 2143 patients with ruptured intracranial aneurysms: a randomised trial

Lancet 2002; 360: 1267-74

- 42 centers (mainly UK, and EU)
- Patients for whom either Rx appropriate
- 2143 patients (out of 9559 assessed) randomized:
  - 88% of patients
  - 90% of aneurysms
  - 97% of aneurysms in MCA ant. circ.
  - < 15% < 10 mm
  - < 10 mm good grade

<table>
<thead>
<tr>
<th>Modality</th>
<th>No. of patients</th>
<th>ISAT (ISAT group)</th>
<th>Coils (coiling group)</th>
<th>ARR 7.4%</th>
</tr>
</thead>
<tbody>
<tr>
<td>MCA</td>
<td>911 (72.2%)</td>
<td>178 (22.4%)</td>
<td>733 (98.9%)</td>
<td></td>
</tr>
<tr>
<td>Ant. circ.</td>
<td>112 (73.0%)</td>
<td>176 (22.4%)</td>
<td>75 (100.0%)</td>
<td></td>
</tr>
<tr>
<td>Posterior</td>
<td>90 (69.0%)</td>
<td>106 (83.4%)</td>
<td>94 (98.9%)</td>
<td></td>
</tr>
<tr>
<td>Posterior</td>
<td>26 (21.0%)</td>
<td>22 (17.9%)</td>
<td>4 (9.6%)</td>
<td></td>
</tr>
<tr>
<td>No clinical aneurysm</td>
<td>68 (56.3%)</td>
<td>55 (44.1%)</td>
<td>13 (22.7%)</td>
<td></td>
</tr>
<tr>
<td>Death</td>
<td>85 (6.7%)</td>
<td>90 (30.3%)</td>
<td>75 (100.0%)</td>
<td></td>
</tr>
<tr>
<td>Dependency</td>
<td>33 (26.5%)</td>
<td>38 (40.2%)</td>
<td>5 (9.6%)</td>
<td></td>
</tr>
</tbody>
</table>

Data as deindexx primary outcomes. P= 0.0039
Coiling associated with

- **Death/Dependency** at 5-year follow-up: ARR 3%
- **Prevalence of epilepsy & cognitive decline** at 1 yr.
- Slightly **rate of late rebleeding** (risks small with either Rx)
  - At the end of 1st year: 2.6% - coiling vs. 1% - surgery
  - Long-term follow-up (mean of 9 yrs): risk still low after >1 yr.


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**Coiling or Clipping?**

International Subarachnoid Aneurysm Trial (ISAT) of neurosurgical clipping versus endovascular coiling in 2143 patients with ruptured intracranial aneurysms: a randomised trial

**Criticisms:**

- Small percentage randomized (only 22% of eligible patients): can results be generalized?
- Clipping by nonsubspecialized neurosurgeons, but minimum case experience required for coiling by interventionalist
- Delay of treatment in clip group (> 14hrs longer than in coil group): pretreatment deaths confounded difference!

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**Coiling or Clipping?**

The Barrow Ruptured Aneurysm Trial: 5-year results

Clinical article

- All eligible SAH (472 out of 725 screened) randomized
- 358 patients actually treated
- Crossover allowed (38% of those assigned to coiling crossed over to clipping)
- Median size of aneurysm 6 mm; 83% anterior circ.
Coiling or Clipping?


No significant difference in poor outcome between groups for anterior circulation aneurysms (n = 339) at any time point.

<table>
<thead>
<tr>
<th>Time Point</th>
<th>0.5</th>
<th>1</th>
<th>2</th>
<th>3</th>
<th>4+</th>
<th>Total</th>
<th>p Value</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Clot in MCA</strong></td>
<td>62</td>
<td>37</td>
<td>21</td>
<td>9</td>
<td>5</td>
<td>140</td>
<td>0.12</td>
</tr>
<tr>
<td><strong>Clot in ACA</strong></td>
<td>61</td>
<td>35</td>
<td>19</td>
<td>8</td>
<td>7</td>
<td>122</td>
<td>0.14</td>
</tr>
<tr>
<td><strong>Clot in VA</strong></td>
<td>61</td>
<td>35</td>
<td>18</td>
<td>9</td>
<td>6</td>
<td>120</td>
<td>0.15</td>
</tr>
<tr>
<td><strong>Clot in ICA</strong></td>
<td>61</td>
<td>35</td>
<td>18</td>
<td>9</td>
<td>6</td>
<td>120</td>
<td>0.15</td>
</tr>
<tr>
<td><strong>Clot in Basal</strong></td>
<td>61</td>
<td>35</td>
<td>18</td>
<td>9</td>
<td>6</td>
<td>120</td>
<td>0.15</td>
</tr>
<tr>
<td><strong>Total</strong></td>
<td>245</td>
<td>147</td>
<td>75</td>
<td>45</td>
<td>28</td>
<td>480</td>
<td>0.10</td>
</tr>
</tbody>
</table>

Values calculated using x² test.

Post hoc analysis.

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But significant benefit in clinical outcomes from coiling for posterior circulation aneurysms (n = 69).

<table>
<thead>
<tr>
<th>Time Point</th>
<th>0.5</th>
<th>1</th>
<th>2</th>
<th>3</th>
<th>4+</th>
<th>Total</th>
<th>p Value</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Clot in MCA</strong></td>
<td>26</td>
<td>15</td>
<td>9</td>
<td>5</td>
<td>1</td>
<td>56</td>
<td>0.03</td>
</tr>
<tr>
<td><strong>Clot in ACA</strong></td>
<td>26</td>
<td>15</td>
<td>9</td>
<td>5</td>
<td>1</td>
<td>56</td>
<td>0.03</td>
</tr>
<tr>
<td><strong>Clot in VA</strong></td>
<td>26</td>
<td>15</td>
<td>9</td>
<td>5</td>
<td>1</td>
<td>56</td>
<td>0.03</td>
</tr>
<tr>
<td><strong>Clot in ICA</strong></td>
<td>26</td>
<td>15</td>
<td>9</td>
<td>5</td>
<td>1</td>
<td>56</td>
<td>0.03</td>
</tr>
<tr>
<td><strong>Clot in Basal</strong></td>
<td>26</td>
<td>15</td>
<td>9</td>
<td>5</td>
<td>1</td>
<td>56</td>
<td>0.03</td>
</tr>
<tr>
<td><strong>Total</strong></td>
<td>104</td>
<td>60</td>
<td>36</td>
<td>20</td>
<td>12</td>
<td>212</td>
<td>0.001</td>
</tr>
</tbody>
</table>

Values calculated using x² test.

Post hoc analysis.

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Clinical article

Robert F. Spetzler, M.D., Cameron G. McDougall, M.D., Scott C. Alves, M.D., Janet M. Zabramski, M.D., Nancy E. Hall, Ph.D., Thomas F. Paty, M.D., Peter Naglia, M.D., and Robert C. Wallace, M.D.

But clipping resulted in significantly better:

- Degree of aneurysm obliteration (87% vs 52% - p<0.0001)
- Rate of aneurysm retreatment (5% vs 13% p = 0.01)

While you might want to read more about the results, the slides provide a basic understanding of the comparisons made between coiling and clipping in the context of anterior circulation aneurysms and posterior circulation aneurysms. The data suggests that clipping may offer advantages in these specific scenarios.
Rebleeding prevention: **Blood Pressure Control**

- No BP target defined in SAH with unsecured aneurysm

*Stroke. 2012; 43: 1711-37*

**Medical Measures to Prevent Rebleeding After aSAH: Recommendations**

1. Between the time of aSAH symptom onset and aneurysm obliteration, blood pressure should be controlled with a titratable agent to balance the risk of stroke, hypertension-related rebleeding, and maintenance of cerebral perfusion pressure (Class I, Level of Evidence B). (New recommendation)

2. The magnitude of blood pressure control to reduce the risk of rebleeding has not been established, but an increase in systolic blood pressure to <160 mm Hg is reasonable (Class III, Level of Evidence C). (New recommendation)

**Impaired cerebral autoregulation in aSAH**

**Prospective – 273 pts:**

**SBP > 150 mm Hg possible RF for prehospitalization rebleeding**

**TABLE 3: Comparison of Systolic Arterial BP in the Rebleed and the Non-Rebleed Groups With Various Cutoff Points**

<table>
<thead>
<tr>
<th>BP, mm Hg</th>
<th>Cutoff</th>
<th>Non-Rebleed Group</th>
<th>Rebleed Group</th>
<th>P</th>
<th>OR (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt;120</td>
<td>120</td>
<td>181</td>
<td>3</td>
<td>0.9999</td>
<td>1.2 (0.3-5.6)</td>
</tr>
<tr>
<td>&gt;120</td>
<td>120</td>
<td>148</td>
<td>21</td>
<td>0.1000</td>
<td>2.1 (0.8-5.2)</td>
</tr>
<tr>
<td>&gt;140</td>
<td>140</td>
<td>108</td>
<td>32</td>
<td>0.1892</td>
<td>2.0 (0.6-7.1)</td>
</tr>
<tr>
<td>&gt;160</td>
<td>160</td>
<td>71</td>
<td>61</td>
<td>0.0001</td>
<td>5.9 (2.4-15.8)</td>
</tr>
</tbody>
</table>

BP indicates blood pressure. Values of P were calculated by use of continuity-corrected χ² analysis. ORs and 95% CIs were calculated by use of conditional logistic regression analysis.

**SBP <160 mm Hg is reasonable**

- Many physicians more comfortable with a SBP < 120-140 mmHg

- But in poor grade SAH excessive ↓BP offset by ↑risk of infarction

**CPP <70 associated with metabolic crisis and brain tissue hypoxia!**

*Stroke. 2011;42(5):1351-1356.*
Rebleeding prevention: Antifibrinolytic therapy


Antifibrinolytic therapy

4 g IV x 1, 1 g/h

DVT: 8 fold

Risk of DVT but not pulmonary embolism

2012 ASA guidelines: short term therapy < 72 hrs reasonable when definitive treatment of the aneurysm is unavoidably delayed and there are no other contraindications (Class IIa, Level of Evidence B)

Delayed Cerebral Ischemia (DCI): Definition

- New [focal neurological signs and/or ▼ in LOC] > 1h
- Appearance of new infarctions on CT or MRI

Risk: starts day 3 post-SAH, peaks day 5-14, ends day 14-21

Vasospasm: 40-60% SAH

Vasospasm have no DCI: 0%

Likely

Microthrombi formation

Cortical spreading ischemia

Microcirculatory spasm
DCI/Vasospasm: Prediction – Radiologic Scales

IVH & thickness of blood on CT most consistent predictors

Fisher Grade

<table>
<thead>
<tr>
<th>Fisher Grade</th>
<th>Modified Fisher Scale</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>No bleeding detected</td>
</tr>
<tr>
<td>2</td>
<td>Diffuse or vertical layers</td>
</tr>
<tr>
<td>3</td>
<td>Localized SAH in any location</td>
</tr>
<tr>
<td>4</td>
<td>THA or SAH with minimal or no SAH</td>
</tr>
</tbody>
</table>

DCI/Vasospasm: Detection

- Neurological examinations
  - GCS Hourly, NIH stroke scale 6 hourly
  - Limb weakness?
  - Aphasia/Neglect?
  - Mutism, LOC?

- Daily Transcranial Doppler Ultrasound

Table 2: Factors influencing MFV (9, 10).

<table>
<thead>
<tr>
<th>Factor</th>
<th>Change in MFV</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age</td>
<td>Increases up to 9–10 years of age then decreases (see [16] for a full range of values)</td>
</tr>
<tr>
<td>Sex</td>
<td>Higher MFV in women than men</td>
</tr>
<tr>
<td>Pregnancy</td>
<td>Decreased in the 3rd trimester</td>
</tr>
<tr>
<td>POCO2</td>
<td>Increases with increasing POCO2</td>
</tr>
<tr>
<td>Mean arterial Pressure (MAP)</td>
<td>Increases with increasing MAP (CBF autoregulation between CBF 30–150 ml/100 g/min)</td>
</tr>
<tr>
<td>Hematocrit</td>
<td>Increases with decreasing hematocrit</td>
</tr>
</tbody>
</table>

DCI/Vasospasm: Confirmatory Studies

- Conventional 4-vessel cerebral angiography
  - Gold standard, allows Rx, but invasive

- CTA
  - Noninvasive
  - Good correlation with angiography
  - Contrast load, radiation exposure!

- CT perfusion:
  - Prolonged mean transit time (MTT) >6.4 more sensitive for vasospasm (92%)
  - Reduced CBF more specific for vasospasm (95%)

Cerebrovasc Dis 2008; 26:163–170
CPT is able to quantify cerebral perfusion parameters: CBF, CBV, MTT. Quantitative cerebral perfusion maps are constructed.

Barrow Quarterly - Volume 17, No. 3, 2001

Decreased CBF in the posterior circulation

Prolonged mean transit time (slow blood flow) through the posterior territories

DSA confirms severe vasospasm (arrows) in the basilar artery

DCI: Detection in Poor-Grade SAH patients

- CTA/CTP \(\rightarrow\) screening for perfusion deficits

Partial Brain tissue PO2 monitoring

Hypoxic \(p\text{tiO}_2 < 10\) mmHg

Correlates with infarction


Microdialysis (markers of ischemia/injury)

\(\uparrow\) in glycerol, glutamate, LPR

Correlates with CBF on PET

J. Neurosurg. 2004; 100:400–406

- Quantitative continuous EEG: \(\alpha/\delta\) ratio from baseline:
  - > 10% in 6 cons. recordings (sensitivity 100%, specificity 76%)
  - > 50% in single recording (sensitivity 89%, specificity 84%)


The Importance of Probe Placement for Focal Neuromonitoring Techniques

- Need to place probe in area at greatest risk for vasospasm. This is difficult!
- Vasospasm generally predicted by CT scan.

<table>
<thead>
<tr>
<th>Author</th>
<th>Year</th>
<th>Area</th>
<th>Risk for Vasospasm</th>
</tr>
</thead>
<tbody>
<tr>
<td>Adams</td>
<td>1997</td>
<td>Y</td>
<td>Y</td>
</tr>
<tr>
<td>Hiras</td>
<td>1998</td>
<td>Y</td>
<td>Y</td>
</tr>
<tr>
<td>Jliner</td>
<td>1999</td>
<td>Y</td>
<td>Y</td>
</tr>
<tr>
<td>Pinto</td>
<td>2002</td>
<td>Y</td>
<td>Y</td>
</tr>
<tr>
<td>Langer</td>
<td>2003</td>
<td>Y</td>
<td>Y</td>
</tr>
<tr>
<td>Prado</td>
<td>2005</td>
<td>Y</td>
<td>Y</td>
</tr>
<tr>
<td>_Machado</td>
<td>2006</td>
<td>Y</td>
<td>Y</td>
</tr>
<tr>
<td>_Costello</td>
<td>2007</td>
<td>Y</td>
<td>Y</td>
</tr>
</tbody>
</table>

- But development of ischemia more variable (both in terms of whether it develops and where)
Multiple Cortical/Deep Infarcts
- 28/57 patients (49%)
- Did not correlate with vasospasm by TCD/angiogram


DCI: Prevention

- Oral Nimodipine 60 mg q4hrs x 21 days  
  - Allen et al Multicenter RCT  
  - No effect on angiographic vasospasm
  - But improves outcome (relative risk of DCI reduced by 0.69)
  
- Volume repletion: EUVOLEMIA!  
  - Hypovolemia is bad: Meticulous attention to input/output
  - Must account for insensible losses (~800 cc/d, higher if fever)
  - Most patients need at least 3 liter/d of IV NS (125 ml/h)
  - Cannot use fluid restriction to treat hyponatremia!

Prophylactic Hypervolemia: Not useful

Randomized trial: 82 patients

- Hypervolemia (albumin for CVP < 8)
  - Versus
  - Normovolemia (albumin for CVP < 5)

Higher CVP target led to:
- Up fluid intake
- Similar fluid balance
- Similar CBF on Xenon CT
- No difference in outcomes

Stroke. 2000;31:383-391
**DCI Prevention: What did not work**

- **Clazosentan**: CONSCIOUS-2 *(Multicenter phase III RCT)*
  - Endothelin receptor antagonist
  - Endothelin 1 is a potent vasoconstrictor
  - 1147 patients randomized to drug vs placebo
  - Effect on angiographic vasospasm
  - But no benefit on outcome

- **IV Magnesium** *(Ca antagonist and NMDAr antagonist)*

  The current evidence does not support routine induction of hypermagnesemia. However, hypomagnesemia should be avoided!

  *Stroke* 2010; 41:921-926  
  *Lancet Neurol.* 2011; 10: 618-625  
  *J Crit Care.* 2013 28, 373-81

**DCI Prevention: What did not work**

- **Statins**
  - Improve vasomotor reactivity via upregulation of endothelial NO synthetasis?
  - 6 small single center RCTs: safe in SAH
  - Mixed results in VSP ppx and outcome improvement

  *Stroke.* 2010;41:e47  

  - 803 pts: Simvastatin 40 mg/d x 21 days VS placebo


  Safe but No benefit: Statins NOT recommended for DCI ppx

Intrathecal Thrombolysis

- Thickness of subarachnoid blood correlates with VSP
- Accelerating subarachnoid blood clearance may prevent VSP?

- t-PA at time of clipping or microcatheter infusion in lumbar cistern/cisterna magna

Meta-analysis of 5 RCTs:
- Decreased poor outcome and VSP w/o hemorrhage
- Methodological flaws!
- Definitive trial required!

Intrathecal Nimodipine

- To achieve high CSF levels of nimodipine w/ plasma levels that do not exceed those associated w/ hypotension (>30 ng/ml)

- Intraventricular administration of Nimodipine slow-release microparticle system EG-1962

NEWTON trial:
- Completed enrollment in NA
- Positive results
- Unpublished yet
- Phase III trial planned

EG-1962 reduced the risk of angiographic vasospasm/DCI by ≈ 50%

<table>
<thead>
<tr>
<th>Vasospasm/DCI</th>
<th>Rescue Therapy</th>
<th>Favorable Outcome After Vasospasm/DCI</th>
</tr>
</thead>
<tbody>
<tr>
<td>EG-1962</td>
<td>18 of 48 (38%)</td>
<td>8 of 16 (50%)</td>
</tr>
<tr>
<td>Oral Nimodipine</td>
<td>11 of 18 (61%)</td>
<td>3 of 11 (27%)</td>
</tr>
</tbody>
</table>

72 patients (WFNS 2-4) randomized to EG-1962 and 18 to nimodipine

DCI Management (Secured Aneurysm)

- Hyperdynamic therapy (not “triple H”)
  - Induced Hypertension (+ Euvolemia) Class IIa, level B
  - CO augmentation (dobutamine, milrinone)
    - In the presence of cardiac dysfunction/NSM

- Endovascular therapy Class IIb, level B
  - IA vasodilator (e.g. verapamil, nicardipine)
    - Rapid onset, short action, may require multiple Rx
  - Transluminal balloon cerebral angioplasty
    - Focal vasospasm of larger vessels
    - Durable, but up to 10% risk of vessel rupture or dissection
DCI: Induced Hypertension

- Phenylephrine, norepinephrine
- No evidence-based standards regarding BP endpoints

Max: SBP < 200-220/ MAP < 150
Initial MAP by 20-35%
Periodic neurological assessments to define BP target
No improvement within 1h? → Endovascular Rx

- If nimodipine causes hypotension:
  - Decrease dose/interval (e.g. 30 mg q2h, or 30 mg q4h)
  - Or discontinue

Seizures

- 1-8% at onset, 5% during hospitalization
- 7% of patients: epilepsy during first yr. after discharge

- May result in rebleeding of unsecured aneurysm
  - Prophylaxis (Levetiracetam) commonly given, for 3–7 days
  - 2012 ASA guidelines: Class IIb; Level of Evidence B
  - If acute seizure, AED continued for 6 months
  - Phenytoin worsens functional outcome: no longer recommended
  - 7-19% of SAH patients
  - cEEG recommended in poor-grade SAH patients

Other medical complications: Hyponatremia

- 20-57% of SAH patients
- Late onset correlates with DCI in poor grade patients

- Never restrict isotonic IVFs! (free water restrict, but give NS)
- NS + salt tablets (2-3 g q6-8h), 3% saline infusion
- Fludrocortisone acetate (0.1 to 0.2 mg PO/IV BID) to promote Na/water retention if excessive diuresis (CSWS)
- Monitor Na q6-12hrs
Other medical complications: Fever

- 41-72% of SAH patients; associated with:
  - ↑ risk of DCI, poor outcome (mRS 4-6), length of stay

Impact of Induced Normothermia on Outcome After Subarachnoid Hemorrhage: A Case-Control Study

40 cons. patients 2003–2005
80 patients 1996–2004

(Columbia University SAH Outcomes Project)

T 37 °C surface or endovascular cooling for first 14 days

mRS 4–6 in 21%

mRS 4–6 in 46%

p= 0.04

Other medical complications: Other medical complications: Other medical complications: Other medical complications:

- • Hypotension
- • Transient ECG abnormalities
- • STE, Troponin: May mimic AMI

2009 meta-analysis: link to DCI, poor outcome and mortality

- Elevated troponin
- LV dysfunction

- Problematic in the face of VSP

- Vasopressor /D CI

- Needs inotropes (1st line)

- Endovascular Rx preferred over induced hypertension

- Intra-aortic balloon pump option (secured aneurysm)

Neurogenic Stunned Myocardium (NSM)

SAH → ICP → Transient Global Ischemia → Catecholamine Surge → LV dysfunction

- Reversible RWMA on echo
- Sometimes apical ballooning on echo
  (Takotsubo cardiomyopathy)

NSM vs AMI

Those with an LV EF <40% and troponin T of <2.8 likely have NSM and not acute MI

Conclusions

• EVD/ICP monitoring in symptomatic HCP/ poor grade
  • CPP > 70 mmHg, ICP < 20 mmHg
• Early repair. SBP < 140-160 with unsecured aneurysm
• Permissive hypertension after securing aneurysm
  • Tolerate spontaneous SBP up to 180-200 mmHg

• To prevent DCI:
  • Nimodipine (60 mg q 4hrs x 21 days; dose & interval if drop in BP)
  • Normovolemia (meticulous maintenance of fluid balance; do not fluid restrict in hyponatremia)
  • Normothermia (target T 37 ° C for first 2 weeks!)

• To treat DCI:
  • Stepwise induced hypertension (and maintain normovolemia!)
  • Inotropes if cardiac dysfunction/NSM
  • Early use of endovascular Rx for refractory cases/NSM