MEDICAL MANAGEMENT IN ANEURYSMAL SUBARACHNOID HEMORRHAGE

Presented by: Neeraj S Naval
OBJECTIVES

Discuss and review:

- Risk factors; diagnosis; impact of SAH
- Aneurysm early re-rupture prevention
- Various Neuro-protective strategies
- Treatment of complications of SAH such as vasospasm, cerebral salt wasting, stunned myocardium and seizures.
CONFLICTS OF INTEREST

None
2-5% of all Americans have an intracranial aneurysm

10-15% of patients die before reaching the hospital

25% die within 24 h, 30-50% die at 30 days

Mortality rates at high SAH volume centers with specialized NCCUs now decreasing to 25-30%
SAH RISK FACTORS

Smoking (OR 3-5), dose and time dependent

HTN (OR 2.5)

ETOH? (OR 1.5), cocaine

Age (mean 55)

Sex (M:F pre- 3:2, post- 2:3)

Family member with SAH (One 1st degree relative doubles risk, 1-5% risk of SAH by age 70; Two 1st degree relatives, 7-9%, ? Screening)

Intracranial aneurysms/ prior SAH (20-30% multiple)
SAH RISK FACTORS

Systemic disease association

Austosomal dominant Polycystic kidney Disease (10-22%), family Hx: 40% (screening advised)
Ehlers-Danlos syndrome
Marfan syndrome
Pseudoxanthoma Elasticum

Did you know?
22% Higher incidence on Sunday compared to Monday
Higher in April & September
SAH ETIOLOGY

- Trauma (#1)
- Aneurysms
- AVM
- Cav. malformations
- Tumor
- Vasculitis
- Dissection
- Sickle Cell disease
- Perimesencephalic (venous)
MAKING THE DIAGNOSIS
Cohort of 482 patients (Kowalski et al)
Missed diagnosis of SAH in 12% (one out of every 8)
Associated with a smaller hemorrhage and normal mental status
Migraine / tension headache (36%) was the most common misdiagnosis
Failure to obtain CT scan was the most common diagnostic error (73%)
Neurological complications occurring in 40% , 21% experienced a rebleed
KEYS TO DIAGNOSIS

You don’t always get “The worst headache of my life”

Signs of meningeal irritation/ neck stiffness are seen in approximately 75% of SAH but may take several hours to develop.

No localizing signs in 40% of patients

25% of patients experience seizures / loss of consciousness close to the acute onset
KEYS TO DIAGNOSIS

CT scan is **96-100%** sensitive within the first 12 hours, **90%** over 1\(^{st}\) 24 hours, **70-80%** at 3 days, and **50%** at 1 week. (7% decrement per day)

False negative in **anemia, non aneurysmal SAH (spinal AVM), sentinel SAH, unknown time of onset**

**Xanthochromia** usually is seen by **12 hours after the onset of bleeding**; ideally this is measured spectrographically (CSF bilirubin levels within 2 hours of SAH), although many laboratories rely on visual inspection.
HUNT & HESS GRADING SCALE

Grade I - Mild headache with or without nuchal rigidity

Grade II - Severe headache and a nonfocal examination, with or without cranial nerve deficit, no alteration of consciousness

Grade III – Lethargy or mild focal deficits/weakness

Grade IV – Obtundation/ stupour or severe hemiparesis

Grade V - Patient comatose /posturing
## MORTALITY (HUNT & HESS)

<table>
<thead>
<tr>
<th>Grade</th>
<th>1970 (H/H)</th>
<th>1997 (JHU)</th>
<th>2008 (Columbia)</th>
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<tbody>
<tr>
<td>Grade 1</td>
<td>10</td>
<td>1</td>
<td>5</td>
</tr>
<tr>
<td>Grade 2</td>
<td>25</td>
<td>5</td>
<td>5</td>
</tr>
<tr>
<td>Grade 3</td>
<td>40</td>
<td>20</td>
<td>10</td>
</tr>
<tr>
<td>Grade 4</td>
<td>70</td>
<td>40</td>
<td>35</td>
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<tr>
<td>Grade 5</td>
<td>95-100</td>
<td>75</td>
<td>50</td>
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</tbody>
</table>
Grade I : Normal Head CT (CSF diagnosis)

Grade II : < 1mm thickness clot

Grade III : > 1mm thickness of clot in vertical cistern or > 3 x 5mm thick clot in horizontal cisterns

Grade IV : Grade 2/3 with ICH/IVH

Increasing rates of vasospasm from grades 1 to 3 (5 to 35%) and then lower for 4 (5-15%)
MODIFIED FISHER GRADING (CT)

- Alternatives: Modified Fisher (thickness SAH clot, +/- IVH) / Classen grading scales

- MF : 1 Thin SAH - IVH 12%
  2 Thin SAH +IVH ** 20%
  3 Thick* SAH - IVH 20%
  4 Thick* SAH +IVH ** 40%

- * Thick: > 5 mm
- **Blood in lateral ventricles
Address the ABCs

Endotracheal intubation for H/H grade 4,5 (GCS < 8) sometimes 3 for *airway protection*

Intubate to hyperventilate patients if signs of *herniation*

Administer IV crystalloid fluids to maintain volume

Prevent re-rupture of aneurysm

Consider need for external ventricular drainage (EVD)
RE-BLEEDING PREVENTION

Risk of Rebleed 4% in 1\textsuperscript{st} 24h, then 1.5% per day in 1\textsuperscript{st} week

Case fatality rate 50%

Optimal Surgery at either 0-3 days or post 10-14 days but with coiling now available 0-3 days.
EARLY MANAGEMENT (PREVENT RERUPTURE)

Dark, quiet room

Antiemetics for nausea or vomiting.

Cautious Sedation, analgesia

Antihypertensive agents for an SBP greater than 140-160 mm Hg (drips >> IV prn)

? Antifibrinolytics (EACA / tranxemic acid)
BLOOD PRESSURE GOALS

- Ohkuma et al: Systolic arterial pressure >160 mm Hg was a statistically significant risk factor of re-bleeding (odds ratio 3)
- OR of 2 with SBP > 140 compared to SBP < 120
- Unclear if elevated SBP caused the rupture or was related to other factors (Cushings reflex)

- Goals: SBP < 140 in low grade SAH where ICP elevation is not a concern
- SBP < 160 in high grade SAH with hydrocephalus or concern for elevated ICP
Use of antifibrinolytics reduced risk of bleeding by 40% but increased risk of vasospasm/ DIND by 40-50%. No reduction in mortality or poor outcomes.

Conclusion of meta-analysis: NOT Recommended

Limitations: Meta-analysis included trials conducted when surgery used to be delayed for upto 14 days, total doses of tranxemic acid upto 100 gm through phase of vasospasm. Valid for shorter duration?
### Comparison: 01 Antifibrinolytic treatment versus control treatment with or without placebo

**Outcome:** Poor outcome (death, vegetative or severe disability on Glasgow Outcome Scale at 3 months follow-up)

<table>
<thead>
<tr>
<th>Study</th>
<th>Treatment</th>
<th>Control</th>
<th>Peto OR (95% CI Fixed)</th>
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<tr>
<td>01 Trials with control treatment (open studies)</td>
<td>0 / 0</td>
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<td>Not Estimable</td>
<td></td>
<td></td>
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<td>02 Trials with placebo treatment (blind studies)</td>
<td>114 / 299</td>
<td>195 / 233</td>
<td>44.4</td>
<td>1.21 [0.84, 1.74]</td>
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<tr>
<td>Tsemendtsiz 1990</td>
<td>23 / 50</td>
<td>20 / 50</td>
<td>8.5</td>
<td>1.27 [0.58, 2.80]</td>
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<tr>
<td>Vermeulen 1984</td>
<td>112 / 238</td>
<td>114 / 241</td>
<td>46.0</td>
<td>1.01 [0.71, 1.45]</td>
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<tr>
<td>Subtotal(95% CI)</td>
<td>251 / 520</td>
<td>237 / 521</td>
<td>100.0</td>
<td>1.12 [0.88, 1.43]</td>
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<tr>
<td>Test for heterogeneity chi-square = 0.59 df = 2 p = 0.75</td>
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<td>Test for overall effect z = 0.90 p = 0.36</td>
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</table>

### Comparison: 02 Antifibrinolytic treatment versus control treatment with or without placebo

**Outcome:** Rebleeding reported at end of follow up

<table>
<thead>
<tr>
<th>Study</th>
<th>Treatment</th>
<th>Control</th>
<th>Peto OR (95% CI Fixed)</th>
<th>Weight %</th>
<th>Peto OR (95% CI Fixed)</th>
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<tbody>
<tr>
<td>01 Trials with control treatment (open studies)</td>
<td>6 / 30</td>
<td>7 / 29</td>
<td>4.4</td>
<td>0.70 [0.23, 2.26]</td>
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<tr>
<td>Girvin 1973</td>
<td>14 / 39</td>
<td>14 / 41</td>
<td>5.5</td>
<td>2.85 [0.85, 8.50]</td>
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<tr>
<td>Maurice 1978</td>
<td>6 / 39</td>
<td>6 / 39</td>
<td>6.5</td>
<td>0.28 [0.14, 1.06]</td>
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<td>Subtotal(95% CI)</td>
<td>26 / 107</td>
<td>25 / 97</td>
<td>16.4</td>
<td>0.91 [0.48, 1.72]</td>
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<td>02 Trials with placebo treatment (blind studies)</td>
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<td>1.01 [0.56, 1.74]</td>
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<td>Roos 2000</td>
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<td>36.3</td>
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<td>Tsemendtsiz 1990</td>
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<td>12 / 50</td>
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<tr>
<td>Vermeulen 1984</td>
<td>44 / 239</td>
<td>56 / 238</td>
<td>27.7</td>
<td>0.33 [0.21, 0.54]</td>
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<tr>
<td>v. Rossen 1977</td>
<td>5 / 26</td>
<td>4 / 26</td>
<td>3.2</td>
<td>1.24 [0.40, 3.61]</td>
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<tr>
<td>Subtotal(95% CI)</td>
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<td>Total(95% CI)</td>
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<td>184 / 694</td>
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<td>0.55 [0.42, 0.71]</td>
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<td>Test for overall effect z = 4.61 p = 0.00001</td>
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### Comparison: 03 Antifibrinolytic treatment versus control treatment with or without placebo

**Outcome:** Cerebral ischaemia reported at end of follow up

<table>
<thead>
<tr>
<th>Study</th>
<th>Treatment</th>
<th>Control</th>
<th>Peto OR (95% CI Fixed)</th>
<th>Weight %</th>
<th>Peto OR (95% CI Fixed)</th>
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<tbody>
<tr>
<td>01 Trials with control treatment (open studies)</td>
<td>8 / 30</td>
<td>3 / 29</td>
<td>4.2</td>
<td>2.85 [0.79, 10.50]</td>
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<tr>
<td>Girvin 1973</td>
<td>3 / 39</td>
<td>3 / 39</td>
<td>1.7</td>
<td>1.98 [0.25, 15.35]</td>
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<tr>
<td>Subtotal(95% CI)</td>
<td>11 / 69</td>
<td>4 / 56</td>
<td>5.9</td>
<td>2.59 [0.87, 7.75]</td>
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<td>Test for overall effect z = 1.70 p = 0.09</td>
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<tr>
<td>02 Trials with placebo treatment (blind studies)</td>
<td>75 / 229</td>
<td>84 / 233</td>
<td>48.7</td>
<td>0.93 [0.64, 1.37]</td>
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<tr>
<td>Tsemendtsiz 1990</td>
<td>22 / 50</td>
<td>11 / 50</td>
<td>10.3</td>
<td>2.69 [1.17, 6.14]</td>
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<tr>
<td>Vermeulen 1984</td>
<td>59 / 241</td>
<td>36 / 238</td>
<td>35.1</td>
<td>1.10 [1.15, 4.02]</td>
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<td>Subtotal(95% CI)</td>
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<td>131 / 521</td>
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<td>1.34 [1.02, 1.76]</td>
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<tr>
<td>Total(95% CI)</td>
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<td>135 / 577</td>
<td>100.0</td>
<td>1.39 [1.07, 1.82]</td>
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<td>Test for heterogeneity chi-square = 0.17 df = 4 p = 0.057</td>
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<tr>
<td>Test for overall effect z = 2.44 p = 0.01</td>
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</table>
Hillman et al conducted a randomized prospective trial (n > 500)

- Tranxemic acid for < 72 h, 1 gm q6h, max dose 6 gm
- Re-rupture 10.8% control, 2.4% study group (ARR 80%)
- Mortality related to re-rupture significantly decreased
- Vasospasm rates TCD/ symptomatic/ Ct evident infarcts not different
- No difference in overall mortality/ long term outcomes
- Select centers: 4 gm bolus, 1 gm/h till clip/coil
Indication:

- High grade SAH (4/5) for ICP monitoring
- Symptomatic Hydrocephalus (+/- IVH)
- Worsening GCS without e/o re-bleed/ vasospasm
- IVC conventionally used, Lumbar drain alternative
- Late hydrocephalus may develop due to obstruction to CSF outflow, ? Shunt dependent

Caution in SAH with unprotected ruptured aneurysm: Minimal CSF drainage on insertion, Pop off 15-20.
4 Vessel Cerebral angiography

Angiography false negative are negative in 10-20% of patients with SAHs.

Clotted aneurysm, compression by extrinsic clot, local vasospasm.

More common false negatives with posterior circulation aneurysms, aneurysms < 5 mm

If negative, repeat angiography at 1-2 weeks later or consider CTA
CTA
Sensitivity $> 96\%$
50% sensitivity for $< 5$mm Aneurysms
Requires less contrast than DSA
Intervention not simultaneously possible

MRA
Not as good as CTA, no longer recommended except ? Family screening
COMPLICATIONS OF SAH

Re-bleed

Hydrocephalus

Vasospasm: Symptomatic in 20-30%

Stunned Myocardium: Excessive sympathetic stimulation

Neurogenic Pulmonary edema: Increased pulmonary capillary permeability

Hyponatremia: *Cerebral salt wasting* or SIADH.

Seizures: in 6-25% SAH
**VASOSPASM**

**Vasospasm** (DIND) symptomatic (focal or global) in 20-30%, up to 40-70% of patients (TCD).

Symptomatic vasospasm: increased morbidity, 15% mortality

Risk Factors: Fisher grade 3 (MF3/4), High Hunt & Hess grade, young age

Neurologic deficits from cerebral ischemia at days 4-12 post SAH
VASOSPASM

Strokes from DCI after 13 days < 4%

Ultra-early angiographic vasospasm (< 48h) in 10%, TCD in 30%; risks include prior SAH, associated ICH, thick cisternal clot, IVH; only in 3% overt clinical signs

Angiogram correlation with strokes on MRI
Of new strokes visible on MRI, 80% were in setting of severe angiographic vasospasm, 16% in moderate, 3% in mild. 60% cortical, 20% deep, 20% combination
VASOSPASM MECHANISM

**Mechanism 1:** Inflammation/ Reversible Atherosclerosis

Heme breakdown --- free O2 radicals + Endothelin release --- endothelial damage/ vasoconstriction --- intimal and medial thickening.

“Vasospasm” occurs at a microvascular level

**Mechanism 2:** Microembolic theory

**Mechanism 3:** Cortical Depression
DETECTION OF VASOSPASM

**Transcranial Doppler (TCD)**

Based on the principle that the velocity of blood flow in an artery is inversely related to the area of the lumen of that artery

Surveillance tool, ? Definitive diagnosis
MCA-MFV 100 - 120 : mild vasospasm
  120 - 150 : moderate vasospasm
  150 – 200 : severe vasospasm
  > 200 cm/sec : critical vasospasm

- Lindegaards index (MCA/EC-ICA > 3 or > 6)
  (Hyperemia vs vasospasm)
OTHER VASOSPASM CRITERIA (TCD)

- Absolute Δ 50 cm/sec over 24 h
- >3 fold increase from baseline (sensitive)
  < twofold increase (specific)
- B/L comparison with > 40cm/s difference
RELIABILITY OF TCD

Review of 26 studies comparing TCD with Angiography
High PPV in identifying patients with vasospasm in the MCA.

Vora et al: Predictive value of TCD MCA-MFV
1. NPV < 120: 94%
2. PPV > 200: 87%
3. PPV 120-200: 50%.

Suarez et al: Sensitivity and specificity at 80% in “clinically significant” vasospasm

Torbey et al: older patients develop symptomatic vasospasm at lower flow velocities
CT ANGIOGRAM / CT PERFUSION
**CTA/CTP**

**CTA**: Accurate in detecting no spasm or severe cerebral vasospasm in proximal arterial locations, less accurate for distal location and mild-moderate spasm

**CTP**: MTT > 6.4 seconds  
CBF < 25ml/100g/min

**CTA + CTP**: PPV and NPV > 90%
NEWER MODALITIES

TCCS (higher sensitivity and specificity)

Cerebral Microdialysis: glutamate, L/P ratio

SPECT/PET

DWI/PWI

Use clinical exam + TCD/ CTA-CTP/ DSA
TREATMENT OF VASOSPASM (OLD SCHOOL)

Triple-h therapy
Hypervolemic, Hypertensive, Hemodilutional therapy

Hypertensive: MAP goals based on neurological deficits, 20% increase in MAP above baseline

Hypervolemic: CVP 8-12 / PAWP >14 / CI goals >4.5, GEDI > 850

Hemodilution: Improved rheology, decreased viscosity. Hematocrit: 30-35
HEMODYNAMIC AUGMENTATION

Shown to be effective for **Treatment of vasospasm** (Kassel et al > 80% deficits resolved)

**Prophylaxis for vasospasm** Rinkel et al (review of 3 RCT) showed no benefit (Lennihan et al (n 80), Egge et al)

Volume expansion therapy did not improve outcome (Relative Risk (RR) 1.0), nor the occurrence of secondary ischemia (RR 1.1). CBF does not increase significantly in normal brain with triple-h as opposed to in the setting of vasospasm

Heart failure and pulmonary edema, increased risk of re-bleeding and global cerebral edema.
Emerging data that hypertensive but not hypervolemic therapy increases CBF (unless patient is hypo-olemic): *Muench et al*

**Normovolemia vs hypervolemia?**

Controversy about Hb goal (*Anemia associated with worse outcomes*, but **blood transfusions** associated with worse outcomes. Low PBtO2 worsens outcomes, Hb < 9 associated with increased L/P ratios per Oddo et al)

Kramer at al: Anemia worsens outcomes in patients with vasospasm; blood transfusions worsen outcomes in patients with no spasm

**Hb goal > 9 on admission; > 10 in vasospasm**

**Hypertensive therapy is the cornerstone of triple-h therapy**
Normal saline or **Albumin** (volume expander) to achieve volume goals?

Increased mortality with albumin in **post hoc** analysis of TBI patients in SAFE study (but mean ICP 15 vs 12 on insertion)

Improved 3 month outcomes in SAH with albumin (Suarez et al), sequential design, ‘trends’, 2x risk in non-albumin group of hydrocephalus on admission, GCS < 8, h/o HTN)

?? Decreased incidence of significant pulmonary edema with albumin (Mayer et al)

Decreased need for volume resuscitation secondary to decreased urine output / GFR, perhaps useful in **CSW**
PRESSORS VS INOTROPES

MAP/ CPP augmentation: CPP Response to Norepinephrine more predictable than dopamine in head trauma patients

CI augmentation: Comparable increase in mean CBF using Phenylephrine to increase MAP or Dobutamine to increase Cardiac index. Preferred in Stunned myocardium

Conventional HHH failures: Dobutamine used in combination with hypervolemic preload and hypertensive enhancement
Levy et al: Effective in >75% patients who failed to respond to hypervolemic therapy.

Milrinone (tachycardia) vs dobutamine (hypotensive)
INDICATIONS FOR SWAN/ PICCO

1. Refractory vasospasm with trial of inotropic therapy indicated

2. Stunned myocardium where inotropic therapy preferred

3. ?H/o CHF with vasospasm to optimize fluid, pressor management
Both PICCO derived intermittent cardiac output and CCO showed close agreement to Swan-Ganz reference cardiac output (Mutoh et al)

Fluid responsiveness to defined volume loading was predicted better with PICCO-GEDI than with Swan- PCWP/CVP

Patients receiving early goal-directed management using PICCO experienced reduced frequencies of vasospasm and cardiopulmonary complications compared with those managed with Swan Ganz(P<0.05)

Trend towards improved Functional outcomes at 3 months (56% vs 44%) using PICCO (P=0.06).
NEUROINTERVENTION FOR REFRACTORY VSP

Balloon angioplasty + Intra-arterial vasodilators

For Refractory Vasospasm

Former relieves proximal vasospasm; latter acts on the distal vessels (Nicardipine, Verapamil). Effect of IA without TBA short lasting

Papaverine most effective but neurotoxic (seizures, blindness)
VASOSPASM AND PRE AND POST TREATMENT
NEUROPROTECTIVE STRATEGIES

- Ca channel antagonists
- Magnesium
- Statins
- Tirlizad mesylate
- Endothelin Antagonists
- Hypothermia
CA CHANNEL ANTAGONISTS

16 trials conducted for Ca+ channel antagonists in SAH.

**Oral Nimodipine:** Level 1 evidence for its use, 60 mg q4 x 21 days

Relative risk for Symptomatic vasospasm : 0.67
- CT-scan documented cerebral infarction: 0.80
- Poor outcomes (mRS > 3): 0.69
- Angiographically detected cerebral vasospasm: 0.91 (NS)

**Nicardipine**
Relative Risk reduction for Angiographic Vasospasm 21%
RRR for Poor outcomes: 3%
MAGNESIUM

Hypomagnasemia correlates with poor outcomes following SAH

Correlates with higher Hunt & Hess Grades

NMDA blocker, glutamate antagonist, vasodilator; in experimental SAH hypomagnasemia increases vasospasm

MASH Trial (283): Randomized blinded study, study group received 16 gm/day IV, started prior to day 4, continued till day 14

34% reduction in DCI and 23% reduction in poor 3 month outcomes
## STATINS

### a. Overall Incidence of Vasospasm

<table>
<thead>
<tr>
<th>Study ID</th>
<th>Treatment n/N</th>
<th>Control n/N</th>
<th>RR (fixed) 95% CI</th>
<th>Weight (%)</th>
<th>RR (fixed) 95% CI</th>
</tr>
</thead>
<tbody>
<tr>
<td>Lynch</td>
<td>5/19</td>
<td>12/20</td>
<td></td>
<td>24.17</td>
<td>0.44 [0.19, 1.01]</td>
</tr>
<tr>
<td>Tseng</td>
<td>17/40</td>
<td>25/40</td>
<td></td>
<td>51.67</td>
<td>0.68 [0.44, 1.05]</td>
</tr>
<tr>
<td>Oglivy</td>
<td>13/19</td>
<td>12/20</td>
<td></td>
<td>24.17</td>
<td>1.14 [0.71, 1.83]</td>
</tr>
<tr>
<td>Total</td>
<td>35/78</td>
<td>49/80</td>
<td></td>
<td>100.00</td>
<td>0.73 [0.54, 0.99]</td>
</tr>
</tbody>
</table>

### b. Incidence of Vasospasm-Related Delayed Ischemic Deficits

<table>
<thead>
<tr>
<th></th>
<th>Treatment n/N</th>
<th>Control n/N</th>
<th>RR (fixed) 95% CI</th>
<th>Weight (%)</th>
<th>RR (fixed) 95% CI</th>
</tr>
</thead>
<tbody>
<tr>
<td>Tseng</td>
<td>2/40</td>
<td>12/40</td>
<td></td>
<td>63.76</td>
<td>0.17 [0.04, 0.70]</td>
</tr>
<tr>
<td>Oglivy</td>
<td>5/19</td>
<td>7/20</td>
<td></td>
<td>36.24</td>
<td>0.75 [0.29, 1.96]</td>
</tr>
<tr>
<td>Total</td>
<td>7/59</td>
<td>19/60</td>
<td></td>
<td>100.00</td>
<td>0.38 [0.17, 0.83]</td>
</tr>
</tbody>
</table>

### c. Incidence of Mortality

<table>
<thead>
<tr>
<th></th>
<th>Treatment n/N</th>
<th>Control n/N</th>
<th>RR (fixed) 95% CI</th>
<th>Weight (%)</th>
<th>RR (fixed) 95% CI</th>
</tr>
</thead>
<tbody>
<tr>
<td>Tseng</td>
<td>2/40</td>
<td>8/40</td>
<td></td>
<td>70.09</td>
<td>0.25 [0.06, 1.11]</td>
</tr>
<tr>
<td>Oglivy</td>
<td>0/19</td>
<td>3/20</td>
<td></td>
<td>29.91</td>
<td>0.15 [0.01, 2.72]</td>
</tr>
<tr>
<td>Total</td>
<td>2/59</td>
<td>11/60</td>
<td></td>
<td>100.00</td>
<td>0.22 [0.06, 0.82]</td>
</tr>
</tbody>
</table>
STATINS

NNT

Vasospasm 6.25
DIND 5
Mortality 6.7

Simvastatin 80 mg qd / Pravastatin 40 qd x 14 days

Large multicenter trial enrolling (STASH)
STATINS

Before & after (historical control) data: Negative results
Kramer et al (n 150)
Tamargo et al (n 176)
Small prospective trial (Verguewen) negative

Criticisms:
Lynch study: High incidence of vasospasm in control group
Tseng study: non-significant difference in 6 month outcomes, infections 10 fold higher (70%) in placebo
ET antagonists (Clazosentan): robust animal data, preliminary human data shows decreased vasospasm (65% RRR with 15mg/h) but no reduction in poor outcomes (CONSCIOUS -1); CONSCIOUS 2 & 3 enrolling: high risk, less hyperdynamic therapy

Tirilazad mesylate a nonglucocorticoid 21-aminosteroid with no benefit in North American trial

Hypothermia (IHAST): no intra-op benefit
Predictors of seizures following SAH (6-25%):
1. Clot thickness
2. Associated SDH and cerebral infarction
3. Duration of coma after the ictus (high grade SAH)
4. MCA aneurysms/ temporal ICH
5. s/p Craniotomy

No evidence for the effectiveness of routine prophylactic anticonvulsants (epilepsy, outcomes)

Worse cognitive outcomes with PHT following SAH
Potential Indications:

1. Use in patients prior to securing aneurysm?
2. Further use based upon Risk Stratification
3. Grade 4/5 patients: Continuous EEG or prophylaxis
4. Limit duration to 7 days (extrapolation of TBI data)
5. Consider alternatives to PHT (keppra)
CEREBRAL SALT WASTING

CSW involves renal salt loss following brain injury

Mechanisms: 1. Elevated levels of BNP, ANP
2. Decreased sympathetic input to kidneys: decreased proximal Na reabsorption, RAA system suboptimal

Precedes vasospasm by 24 h in 50% cases, concurrent in 75%

Leads to volume loss compared to SIADH which is a euvolemic or hypervolemic condition.
## DDX CSW / SIADH

**CSW**
- Hypovolemic state
- CVP decreased
- Hct increased
- Uric acid Normal / decreased
- FeUrAc increased?
- Urine Na > 40

**SIADH**
- Normo-/ Hyper-
- Increased/ normal
- Decreased/ normal
- Decreased
- Increased
- Urine Na > 20

June 3, 2010
CEREBRAL SALT WASTING: MANAGEMENT

**Fludrocortisone**

Associated with less negative sodium and fluid balance

Reduced need for triple-h therapy.

Hypertonic saline alone has limited usefulness.

No significant change in overall outcomes
Reversible cardiomyopathy seen in 18% SAH

Excessive catecholamine release following SAH

Seen in 36% higher grade H/H (a third of whom have LV dysfunction)

Diffuse ST-T EKG changes, does not respect coronary distribution

Smaller Troponin leaks, usually < 3

TTE: Apical sparing vs Apical ballooning (Tako-Tsubo) pattern ‘damage’ out of proportion to troponin leak

DDX: MI: coronary vascular pattern, high troponins that continue to trend up, TTE damage correlates with troponins
STUNNED MYOCARDIUM / STRESS CARDIOMYOPATHY

Complicates management of vasospasm (triple-h: beta agonist vs beta antagonist, fluids vs lasix)

Consider inotropic support (dobutamine)

Early consideration of balloon angioplasty

Intra aortic balloon counterpulsation
High Grade SAH patients with poor clinical exam

Endpoints more sophisticated than CPP/ ICP like
1. PbtO2 using LICOX with goals > 20-25 mmHg

2. Cerebral Microdialysis: *Increased glutamate* (precedes clinical DCI), *elevated LPR*, decreased glucose poor prognostic indicators

3. cEEG: NCSE/ Decreased apha variability, ADR (? DCI)
Fever, anemia, hyperglycemia independent risk factors

1. Fever in > 50%
Causes of fever: Upto half, no infectious etiology (central), predictors: IVH, High grade.
   Pneumonia: 20-25%, UTI: 13-17%, BSI: 8-10%, Meningitis: 6-8%
   (?surveillance, no routine IVC changes) DVT: 6% (prophylaxis within 24h of admission/ Sx)

2. Anemia

3. Hyperglycemia: Goal of ‘normoglycemia’: brain energy crisis with aggressive BG control (80-120), so recommend 120-160
Based on perimesencephalic location

Good hunt & Hess Grades (1-2), Fisher 2, MF 1

No IVH/ ICH

Venous etiology, ? microaneurysms

Low incidence of recurrence

Low incidence of vasospasm

Outcomes universally good (>90%)

Single angiogram usually sufficient

Ddx: Posterior circulation (basilar) aneurysm
SUMMARY

- Avoid common pitfalls in diagnosis
- Antihypertensive drips prior to securing aneurysm (SBP < 140/ < 160)
- ?Antifibrinolytics
- Consider early seizure prophylaxis, risk stratification
- Maintain goals of euvolemia, normotension early
- DSA / CTA followed by surgical clipping/ endovascular coiling
SUMMARY

- Nimodipine, consider statins and/or magnesium gtt
- TCD daily as surveillance tool, ? CTA/P in high grade (4-8d)
- If symptomatic vasospasm, institute hemodynamic augmentation Pressor +/- inotrope, ? Albumin (CSW), Hb > 10 (>9 if no VSP)
- CVP in most, PICCO > Swan, ? Multimodality Monitoring
- Fludrocortisone/? albumin in CSW, replace ongoing losses
- Neurointerventional if failed triple-h/ stunned myocardium
- DVT prophylaxis, fever control, glycemic control
Thank You