Critical Care Management of Acute Ischemic Stroke
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Disclosures
• Nothing to disclose

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Overview
• Update on acute revascularization
• Acute supportive care
• Blood pressure management
• Post-stroke cerebral edema
• ICU care after stroke

Pathophysiology
• Time dependent
• Focal ischemia is different from global ischemia
• Energy failure-> Ca++ entry and cell death
• Glutamate toxicity
• Apoptosis

TIME IS BRAIN
Role of Time – IV rtPA

Most Recent Pooled Analysis of IV rtPA Trials

- NINDS Part 1
- NINDS Part 2
- ATLANTIS A
- ATLANTIS B
- ECASS II
- ECASS III
- EPITHET

Lees et al., Lancet, 2010

Revascularization Therapy with IV tPA

- Tissue plasminogen activator (t-PA)
  - IV t-PA is approved in US for AIS within 3 hours of symptom onset (OR 1.9; 95% CI 1.2-2.9)
  - 3 to 4.5 hour window is effective (ECASS-III)

Complications with IV tPA

- Bleeding
  - 6.4% vs. 0.6% in clinical trials
  - no mortality difference
  - Registry data shows improved safety (1.6% bleeding rate)
  - Increased risk if not adhering to NINDS trial protocol
  - Earlier treatment associated with better outcomes, less complications
- Angioedema (1.3-5.1%)
  - Swelling of lips, tongue self-limited
  - Rx: IV ranitidine, diphenhydramine, methylprednisolone
- Post-MI myocardial rupture (rare)
- Treatment of tPA-related bleeding
  - Transfuse blood
  - 10 units cryoprecipitate
  - 2 units FFP
  - 10 units platelets
  - PCC
  - Factor VIII
  - Aminocaproic acid (Amicar)
  - 1g/kg IV, followed by 1g/hr for 24 hours
  - Tranexamic acid
  - 10 mg/kg IV followed by 1 mg/kg/hr for 24 hours
Revascularization without IV tPA

- **IA Lytics**
  - PROACT-II trial supports benefit from IA pro-urokinase; t-PA is used off label

- **Mechanical Embolectomy**
  - Devices do open vessels and have FDA clearance to open vessels
  - 2 ongoing, 1 completed study to establish clinical efficacy (MERCI, PENUMBRA, IMS-3)
  - Stent retriever trials: Solitaire and Trevo (SWIFT, TREVO) show improved efficacy

Rescue therapy after IV tPA

**Interventional Management of Stroke (IMS-III)**

- NIH sponsored, randomized, prospective trial of IV t-PA vs. IV t-PA + endovascular
  - 656 stroke events
  - CT scan performed
  - IA t-PA
  - EKOS t-PA
  - MERCI
  - Penumbra
  - Solitaire
  - Outcome: 90-Day mRS

58 study centers
6 years

Broderick et al., NEJM, March 2013
Acute stroke interventions

- **IV tPA**
  - Proven efficacy
  - Better outcome earlier in all subgroups

- **IA lytics**
  - Proven efficacy
  - Unapproved for IA tPA
  - Earlier is better, <6 hours

- **Embolectomy**
  - Stent retrievers better
  - Solitaire, Trevo, Merci Penumbra all able to recanalize vessels
  - No clinical efficacy data

- **Recue therapy**
  - New trial data no benefit
  - Ongoing trials with new devices

Stroke Revascularization 2013

Acute supportive care post stroke

- **Airway, ventilation, oxygenation**
  - Common saturation <96%
  - Especially with underlying cardiac, pulmonary disease
  - Airway obstruction, aspiration, atelectasis, pneumonia
  - Hypoventilation, Cheyne-Stokes

- To intubate or not??
  - Poor outcome in >50% at 30 days

- **Cardiac monitoring**
  - 24 hours continuous for Afib and other rhythms
  - In cryptogenic stroke, cardiac event monitors

- **Hypotension**
- **Hypovolemia**
- **Hyperthermia**
- **Hypoglycemia**

HTN after Acute Stroke

- Acute HTN is common after acute stroke
- Current guidelines suggest treatment for SBP > 220 mmHg or DBP > 120 mmHg or if evidence of end-organ damage
- With thrombolytic therapy, goal BP < 180/105 mmHg
- Risk of acute deterioration with aggressive reduction of BP
- Blood pressure reduction within 24 hours is associated with poor outcome
  - OR 1.89 per 10% decrease (p=0.047) of poor outcome at 3 months

*Neurology 2003; 61:1047-51*
Blood pressure goals

- Optimal blood pressure after acute stroke is controversial
- Treat blood pressure cautiously in acute ischemic stroke
  - t-PA limit <185/110 mmHg
  - Lower BP by 15% if exceeds 220/120 mmHg
  - Choice of BP agent is controversial
    - Labetolol and nicardipine don’t raise ICP

Table 6. Potential Approaches to Arterial Hypertension in Acute Ischemic Stroke Patients Who Are Candidates for Acute Reperfusion Therapy

<table>
<thead>
<tr>
<th>Patient characteristics</th>
<th>Management of BP during and after IAP after acute reperfusion therapy to maintain BP at or below 160/100 mmHg</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mild SBP every 15 minutes for 2 hours from the start of IAP therapy, then every 30 minutes for 4 hours, then every 90 minutes for 18 hours</td>
<td>Manage BP to &lt;160/100 mmHg using either SBP or DBP as appropriate. Increase BP to maintain BP at or below 160/100 mmHg using pressors and observe for symptom resolution.</td>
</tr>
<tr>
<td>Moderate SBP every 15 minutes for 2 hours from the start of IAP therapy, then every 30 minutes for 4 hours, then every 90 minutes for 18 hours</td>
<td>If SBP &gt;160-200 mmHg or diastolic SBP &gt;100-120 mmHg:</td>
</tr>
<tr>
<td>Labetolol 5 mg IV followed by continuous infusion 0.5-1 mg/min, or nicardipine 1 mg IV. Increase up to desired effect over 1.5-2 hours every 5-15 minutes, maximum 15 mg/h.</td>
<td>If BP is not controlled or claudication BP &gt;180 mmHg, consider inhibitors of platelet aggregation.</td>
</tr>
</tbody>
</table>


Ischemic Stroke Penumbra

Induced Hypertension

- Remains experimental
- Consider in specific cases
  - Hypotension unresponsive to fluid resuscitation
  - Fluctuating neurological symptoms with hemodynamic changes
  - Increase BP by 10-20% using pressors and observe for symptom resolution
  - Potential to incorporate perfusion imaging
Induced Hypertension

**For**
- May increase pial-pial blood flow
- Increase perfusion to the ischemic penumbra
- Is probably safe

**Against**
- Requires ICU care and central line access
- May cause coronary or gut ischemia
- Could cause cerebral vasoconstriction

Induced Hypertension is Safe

- Retrospective safety study in acute stroke patients
  - 33 controls vs. 30 treated with neosynephrine
  - 10/30 treated patients had BP threshold
  - No increased cardiac morbidity

Evidence for Induced Hypertension

- Koenig, et al. (2006)
  - 100 patients randomized to either induced HTN or standard therapy
  - Used perfusion MRI to select patients with ischemic penumbra (mismatch DWI/PWI)
  - Non-significant decrease in NINDS scores at discharge in treated group, but with longer LOS, ICU time
  - No difference in adverse events

Volume expansion/Hemodilution

- Volume expansion with Dextran, hetastarch, albumin
- No benefit in meta-analysis
- ALIAS: High dose albumin trial stopped
- Awaiting trial data
- Treatment of hypotension with isotonic fluids and pressors
- Devices to augment BP with counterpulsation in trials only
- Vasodilators and hemodilution not recommended
Cerebral Edema

- Severe, life-threatening complication after acute ischemic stroke
- Occurs in 10-20% of anterior circulation strokes
  - Carries a 50-80% mortality when associated with distal carotid or proximal MCA occlusion
- Posterior fossa strokes can present with hydrocephalus and brainstem compression
  - Should be treated with early suboccipital decompression if brainstem is compressed

Malignant Cerebral Edema

- Typically pattern occurs 3-5 days post-infarct, and generally subsides in 2 weeks
- Rarely, edema can occur within 24 hours with signs of early herniation
- Difficult to predict which patients are at risk
  - Evidence of >50% MCA infarct within 12 hours
  - Early sulcal effacement and midline shift
  - Reperfusion injury after thrombolysis
  - Perfusion maps potentially helpful; DEFUSE study

Medical Management

- HOB 30 degrees
- Hyperventilation
  - Goal pCO2 25-30 mmHg
  - Transient, temporizing measure
- Hyperosmolar therapy
  - Mannitol
  - Hypertonic saline
- Hypothermia (33-34 degrees Celsius)
- No role for corticosteroids
Osmolar Therapy

- **Mannitol**
  - Typically bolus over 20 min (0.25-0.5 g/kg every 4-6 hours)
  - Monitor for hypotension and hypovolemia
  - Can precipitate renal failure
  - Less effective at serum osms >320 mmol/dl
- **Hypertonic saline**
  - Infusion of 3% NaCl to maintain serum sodium gradient
  - Bolus of 23.4% NaCl over 20 minutes very effective
  - Less side effects of hypotension, renal failure

Hemicraniectomy in Ischemic Stroke

- Decompressive surgery to decrease mass effect and tissue shift after ischemia is controversial.
- Evidence of benefit in patient populations such as trauma, SDH, mass lesions and posterior fossa strokes
- Meta-analysis showed reduced mortality and improved outcomes with hemicraniectomy for hemispheric strokes

European Pooled Trial

- Prospective pooled analysis of 3 trials of decompressive surgery in malignant MCA infarction
- **DECIMAL, DESTINY, HAMLET**
  - Age 18-60
  - Treatment initiated within 48 hrs of stroke onset
  - Randomized to surgery or conservative Rx
  - N=93 patients
  - Reduced mortality 78-29%

Antithrombotic Therapy for Stroke

- Avoid routine use of IV heparin, IIb/IIIa agents
- Aspirin alone is the only proven strategy within the first 24-48 hours
- Dural sinus thrombosis and arterial dissection may specifically benefit from heparin
Secondary Prevention

- Antiplatelet
  - ASA within 24-48 hours of onset
  - Clopidogrel or asa+persantine first line by discharge
- Anticoagulants
  - Warfarin for atrial fibrillation
  - Target specific oral anticoagulants: dabigatran, rivaroxiban, apixiban

Low molecular weight heparin

- LMWHs and heparinoids reduce the risk of venous thromboembolic events
  - DVT OR 0.27 (CI 0.08-0.96)
  - PE OR 0.34 (CI 0.17-0.69)
- No significant reduction in death and disability OR 0.87 (CI 0.72-1.06)
- Significant increase in major systemic hemorrhages (OR 2.17) but not ICH (OR 1.7)

General ICU Care

- Airway
- Blood pressure, cardiac monitoring
  - Afib 24 hours
- Temperature
  - Treat fever with antipyretics
  - Cooling blankets, endovascular treatments not proven to change outcome
  - Hypothermia is experimental at present
- Infection
  - No antibiotic prophylaxis, but early treatment
  - Avoid foley catheters

Glucose management

- Glucose
  - Treat hypoglycemia (glucose <60 mg/dl) immediately
  - Keep serum glucose 140-180 mg/dL
  - Infusion vs. sliding scale insulin is controversial

*Stoke Hyperglycemia Insulin Network Effort*
**Nutrition**

- Assess and document swallowing EARLY
- Discourage rule of NPO X 24 hour as a standard
- NG tube is preferred if swallowing is unsafe
- Start feeds as soon as possible

**DVT prophylaxis**

- 10% PE related deaths
- Compression devices unless DVT present
- Both SQ unfractioned heparin and LMWH are safe and effective to prevent venous clot and likely PE
- PREVAIL trial favors LMWH over heparin SQ
- Early mobilization: AVERT trial within 24 hours

**Stroke Centers**

- System approach for stroke shown to improve outcomes
- Pre-printed orders, leadership, QA, connection to community/EMS
- JC accreditation and auditing
- Comprehensive stroke centers with endovacular capability certification started

**Guidelines**

*Stroke*

Guidelines for the Early Management of Patients With Acute Ischemic Stroke: A Guideline for Healthcare Professionals From the American Heart Association/American Stroke Association


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