MEDICAL PROBLEMS IN THE NEUROCRITICALLY ILL

Karthik Mahadevan
Introduction

• This is NOT a comprehensive review of the topic
• I have chosen topics that I thought were relevant to understanding pathophysiology, and attempted to address some common presentations
As we do a better job of managing Neurological/ neurocritical problems, medical problems and complications increase in relative importance....
Spectrum of Neurointensive Care

- Traumatic Brain Injury
- Subarachnoid Hemorrhage
- Intracranial Hemorrhage
- Ischemic Stroke
- Anoxic Brain Injury
- Infections- Meningitis, Encephalitis etc
The spectrum of medical problems and complications in neurocritically ill

- In conjunction with presenting symptom. Neurotrauma patients with pulmonary contusion or aspiration pneumonia
- Medical illness secondary to neurologic process. Neurogenic pulmonary edema, cardiac arrhythmias, ALI, SIRS
- Medical problems as complications of therapy. Infections, GI bleed, side effects of hypothermia, DVT/PE
MEDICAL COMPLICATIONS FREQUENTLY AFFECT OUTCOME IN ACUTE BRAIN INJURY
Medical complications are a frequent cause of death in Subarachnoid Hemorrhage

Medical complications of aneurysmal subarachnoid hemorrhage: A report of the multicenter, cooperative aneurysm study. Solenski, Nina; Haley, E; Kassell, Neal; Kongable, Gail; Germanson, Terry; Truskowski, Laura; Torner, James

Medical complications of aneurysmal subarachnoid hemorrhage: A report of the multicenter, cooperative aneurysm study.

Solenski, Nina; Haley, E; Kassell, Neal; Kongable, Gail; Germanson, Terry; Truskowski, Laura; Torner, James


<table>
<thead>
<tr>
<th>Medical Complication</th>
<th>No.</th>
<th>%</th>
<th>95% CI</th>
<th>% Severe</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pulmonary</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Pulmonary edema</td>
<td>104</td>
<td>23</td>
<td>19–27</td>
<td>6</td>
</tr>
<tr>
<td>Pneumonia</td>
<td>102</td>
<td>22</td>
<td>19–27</td>
<td>5</td>
</tr>
<tr>
<td>Atelectasis</td>
<td>72</td>
<td>16</td>
<td>13–20</td>
<td>1</td>
</tr>
<tr>
<td>ARDS</td>
<td>17</td>
<td>4</td>
<td>2–6</td>
<td>35</td>
</tr>
<tr>
<td>Pulmonary embolism</td>
<td>1</td>
<td>&lt;1</td>
<td>&lt;1–1</td>
<td>100</td>
</tr>
<tr>
<td>Other&lt;sup&gt;b&lt;/sup&gt;</td>
<td>10</td>
<td>2</td>
<td></td>
<td>40</td>
</tr>
<tr>
<td>Cardiac</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Arrhythmia</td>
<td>160</td>
<td>35</td>
<td>31–40</td>
<td>5</td>
</tr>
<tr>
<td>Cardiac failure</td>
<td>16</td>
<td>4</td>
<td>2–6</td>
<td>0</td>
</tr>
<tr>
<td>Metabolic</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Electrolyte disturbance</td>
<td>127</td>
<td>28</td>
<td>24–32</td>
<td>2</td>
</tr>
<tr>
<td>Hepatic dysfunction</td>
<td>111</td>
<td>24</td>
<td>21–29</td>
<td>4</td>
</tr>
<tr>
<td>Renal dysfunction</td>
<td>33</td>
<td>7</td>
<td>5–10</td>
<td>15</td>
</tr>
<tr>
<td>Diabetes insipidus</td>
<td>30</td>
<td>7</td>
<td>5–9</td>
<td>7</td>
</tr>
</tbody>
</table>

CI, confidence interval; ARDS, adult respiratory distress syndrome.

<sup>a</sup>First occurrence within days 0 through 14 after subarachnoid hemorrhage (n = 455 patients);<sup>b</sup>includes hypoxia or apnea not otherwise explained.
Frequency of medical complications in SAH with poor outcome
Fig. 3. Attributable risk of individual predictors to poor outcome (mRS 4–6) and mortality (based on Nagelkerke $R^2$ values). *(From Wartenberg KE, Schmidt JM, Claassen J, et al. Impact of medical complications on outcome after subarachnoid hemorrhage. Crit Care Med 200634:617; with permission.)*
Brain Injury and MODS

Acute Brain Injury

Multi organ Dysfunction Syndrome
Inflammatory response in acute brain injury is a double edged sword

- Cytokines are released immediately after injury.
- They induce a pro-inflammatory state.
- This upregulates the anti-inflammatory mechanism (compensatory anti-inflammatory response).
- MODS is due to excessive or maladaptive activation of immune response.
- Immune suppression from CARS increases susceptibility to infections.
Pro inflammatory response to brain injury

Fig. 1. Primary shear injury and secondary ischemic lesion causes a cascade of cellular events, finally resulting in tissue damage and the development of cerebral inflammation. (Picture redrawn and modified from Keel M et al, 2005, and Reilly P et al, 1997.)
Anti inflammatory Mechanisms

Compensatory Anti Inflammatory Response Syndrome
SIRS/ MODS

Medical Complications
SAH and SIRS
“SIRS burden” is related to higher rate of vasospasm
Acute Lung Injury
The development of acute lung injury is associated with worse neurologic outcome in patients with severe traumatic brain injury

- 137 patients with isolated TBI during 4 y
- 31% developed ALI/ARDS
- **ALI/ARDS not correlated with GCS or other intracranial complication**
- Mortality: 38% with ALI/ARDS . 15% without ALI/ARDS
- ALI/ARDS was an independent mortality factor
FEVER

Independent variable affecting outcome and a marker of poor outcome
Fever in Acute Brain Injury

- Worsening of brain edema and ICP
- Exacerbation of ischemic injury
- Increased O2 consumption
- Depressed level of consciousness
- Increased risk of vasospasm
- Increased LOS /ICU stay
- Death and poor functional outcome
Fever is associated with poor outcomes

In the pooled analyses covering 14,431 patients with stroke and other brain injuries, fever is consistently associated with worse outcomes across multiple outcome measures. *(Stroke. 2008;39:3029-3035.)*
Fever- Management

- Temperature should be measured frequently
- Infections should be sought and treated
- Antipyretics should be used as the first step – but effective in about a 1/3\textsuperscript{rd} of patients.
- Acetaminophen is drug of choice
- Surface cooling should be considered when antipyretics are ineffective (shivering may offset some of the benefits)
Acetaminophen Vs Ibuprofen in stroke patients

Dippel et al. BMC Cardiovascular Disorders 2003 3:2
Hyperglycemia is associated with poor outcome in SAH
Fever and hyperglycemia

- Both fever and hyperglycemia may be part of systemic inflammatory response from acute brain injury
- There is a lot of data showing that these are associated with poor outcomes
- There are no large high quality clinical trials showing an outcome benefit from controlling temperature or glucose in neurocritically ill patient
- General principles in hyperglycemia in the ICU should be used. (Goal of ~140-150). Hypoglycemia should be avoided. Glucose >200mg/dL is associated with infections
- Reduce glucose variability
- Routine use of acetaminophen is recommended to keep temps at or below normal. Consider surface cooling but balance against shivering risk
Pulmonary Complications

- Pneumothorax
- Pulmonary Contusions
- Acute Lung Injury
- Aspiration Pneumonia
- Neurogenic Pulmonary Edema
- Pulmonary Embolism
- Hypercarbic respiratory failure in neuromuscular failure
Pulmonary Edema

- Neurogenic or Neuro cardiogenic (Takostubo)
- Pathophysiology not completely defined-
  Syndrome of sympathetic outflow, probably
  starting in the “NPE trigger zones” of the
  hypothalamus
- “Leaky” pulmonary endothelium, stunned
  myocardium (neuro-cardiogenic, neuro-
  hemodynamic, blast theory, pulmonary venule
  adrenergic hypersensitivity)
- Early and late forms (12-48 hrs) described and is
  a diagnosis of exclusion
- Treatment: supportive care, positive pressure
  ventilation
SAH → ICP

Sympathetic activation

- Pulmonary vasoconstriction
  - Pulmonary venous pressure
- Shift of blood from systemic to pulmonary circulation
- Systemic vasoconstriction
  - Systemic pressure
  - Left ventricular compliance
- Left atrial pressure

- Pulmonary blood volume

Pulmonary capillary pressure

- Pulmonary capillary permeability

- Neurogenic pulmonary edema
Cardiac

- LV dysfunction- “stress cardiomyopathy”
- Cardiac arrhythmias
- EKG changes and troponin elevation can mimic coronary syndromes
- Traumatic injury to cardiac structures-
- Cardiac problems may be related to underlying ischemic heart disease (acute MI with embolic CVA), electrolyte abnormalities etc.
Infectious Complications

- Presenting with CNS infection - Meningitis, Encephalitis, Brain Abscess
- Nosocomial
  - Pneumonia – VAP
  - Line Sepsis
  - EVD related infections (most common in 1st week)
And Others

- GI – UGI bleed, ileus etc
- Hematologic- Coagulopathy, Anemia
- Endocrine – Hyperglycemia
- DVT/ PE
Therapeutic Hypothermia

Complications
Side effects of therapeutic Hypothermia

- Immunosuppression (Incidence of Pneumonia)
- Problems of shivering
- Problems of rewarming and ICP-control
- Cardiovascular
- Coagulopathy
- Devices related side effects
Hypothermia in severe stroke: side effects

<table>
<thead>
<tr>
<th>Condition</th>
<th>Count</th>
<th>Percentage</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pneumonia</td>
<td>24/50</td>
<td>(48%)</td>
</tr>
<tr>
<td>Sepsis</td>
<td>3/50</td>
<td>(6%)</td>
</tr>
<tr>
<td>Pancreatitis</td>
<td>3/50</td>
<td>(6%)</td>
</tr>
<tr>
<td>Cardiac failure</td>
<td>1/50</td>
<td>(2%)</td>
</tr>
<tr>
<td>Severe coagulopathy</td>
<td>2/50</td>
<td>(4%)</td>
</tr>
<tr>
<td>Platelet count &lt;100 cts/nl</td>
<td>35/50</td>
<td>(70%)</td>
</tr>
<tr>
<td>Cardiac arrhythmia</td>
<td>31/50</td>
<td>(62%)</td>
</tr>
<tr>
<td>Severe hypotension (MAP&lt;50 mm Hg)</td>
<td>2/50</td>
<td>(4%)</td>
</tr>
</tbody>
</table>
Shivering

- ‘Last resort’ response – metabolically inefficient
- Increases heat production by 2-5 x – much heat dissipated to environment.
- Increased oxygen consumption
- Core versus surface cooling?
Infectious Complications after hypothermia

<table>
<thead>
<tr>
<th>Treatment group</th>
<th>Duration of cooling</th>
<th>Pneumonia rate</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>Ventilated</td>
<td></td>
<td><strong>hypothermia</strong></td>
<td>control</td>
</tr>
<tr>
<td>N=100</td>
<td>24 to 72 hours</td>
<td>54% (54/100)</td>
<td>47% (8/17)</td>
</tr>
<tr>
<td>N=10</td>
<td>12-72 hours</td>
<td>30% (3/10)</td>
<td>0% (0/10)</td>
</tr>
<tr>
<td>Non-ventilated</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>N=81</td>
<td>6-24 hours</td>
<td>50% (14/28)</td>
<td>10% (3/30)</td>
</tr>
</tbody>
</table>

Cardiovascular effects of hypothermia

- Decrease heart rate
- Blood pressure increased/unchanged
- Cardiac output reduced (but VO2 decreased)
- Increased contractility; decreased diastolic function.
- Increased systolic time interval, which is compounded with pacing
Effects on ICP during rewarming

Rewarming and ICP-Control

![Graph showing effects on ICP during rewarming with hypothermia at 33°C and normothermia at 37.5°C, with data points indicating ICP in mm Hg over time. The graph includes a legend for dead (sad face) and survivor (happy face) with a temperature range from 0 to 50 mm Hg.]
Other effects of hypothermia

- Hyperglycemia: reduced insulin secretion and sensitivity
- Renal function: cold induced diuresis
- Electrolyte excretion
- Reduced gut motility
- Reduced drug clearance
- Device related
  - Skin lesions
  - **Thrombosis** (4-5% endovascular cooling)
  - Infections
  - Necrosis, ...
Hypothermia side effects

- Important to recognize and treat
  - Counter warming
  - Shivering protocols
  - Empiric Antibiotics
  - Hemodynamic management
  - Electrolyte challenges
“I Can’t Breathe”

- 59 Y O with lupus presented with a few day history of abdominal pain, diarrhea to ED
- She had a flu like illness with headaches, sinus congestion and at presentation was short of breath.
- Admitted to ICU with hypoxia and possible pneumocystis pneumonia
- In 2 hours after presentation ....
CENTRAL LINE PLACEMENT
SEMI-UPRIGHT
RIGHT
What is the diagnosis?