THERAPEUTIC HYPOTHERMIA FOR ACUTE SPINAL CORD INJURIES

Marc Grossman, MD FACEP CPHM
Asst. Medical Director, Miami Dade Fire Rescue

Benjamin Abo, DO EMTP
Assistant to the Assistant

DISCLOSURE

- None

SPINAL CORD INJURIES (SCI) IN THE US

- Incidence: 12,000/yr
- Prevalence: 320,000
- Cost: $12 billion/yr
  - Direct costs of initial hospitalization/follow-up
    - Quadriplegic - $300K
    - Paraplegic - $150K
  - Does not include indirect costs such as lost wages, etc.

Spinal Cord Medicine 2nd Ed
SPINAL CORD INJURIES IN THE US

- Incidence: 12,000/yr
- Prevalence: 320,000
- Cost: $12 billion/yr
- Estimated lifetime costs by age at injury

<table>
<thead>
<tr>
<th>Severity of Injury</th>
<th>25 yrs old</th>
<th>50 yrs old</th>
</tr>
</thead>
<tbody>
<tr>
<td>High Tetraplegia AIS A-MC</td>
<td>$4.5 million</td>
<td>$2.5 million</td>
</tr>
<tr>
<td>Paraplegia AIS A-D</td>
<td>$2.2 million</td>
<td>$1.5 million</td>
</tr>
<tr>
<td>Incomplete Motor at any level AIS D</td>
<td>$1.5 million</td>
<td>$1.1 million</td>
</tr>
</tbody>
</table>

Data: Spinal Cord Injury Facts and Figures at a Glance published February 2012 by the National SCI Statistical Center, Birmingham, AL.

In the news

New York Times: December 4, 2008 City Pushes Cooling Therapy for Cardiac Arrest. By ANEMONA HARTOCOLLIS
CAUSES OF SCI SINCE 2005

- Vehicular, 39.2%
- Falls, 28.3%
- Violence, 14.6%
- Sports, 8.2%
- Other/Unk, 9.7%

SC/NERVE INJURY BY LEVEL ('97-'11)

N=275

ACUTE SCI PATHOPHYSIOLOGY

- Primary Injury = mechanical insult
  - Acute compression
  - Impaction
  - Laceration
  - Shear
  - Missile injury
ACUTE SCI PATHOPHYSIOLOGY

- Secondary Injury Mechanisms (SIMs)
  - Vascular changes
  - Electrolyte shifts
  - Neurotransmitter accumulation
  - Free radicals
  - Endogenous opioids
  - Edema
  - Inflammation
  - Loss of energy metabolism

- Hyperthermia aggravates multiple SIMs

SCI: SYSTEMS APPROACH

- Prevention
- Emergency Medical Services
- Trauma Center Protocols
- Critical Care Management
- Rehabilitation
- Post-hospitalization programs

ASIA IMPAIRMENT SCALE

- A = Complete
  - No motor or sensory S4-S5
- B = Incomplete
  - Sensory only
- C = Incomplete
  - Motor preserved
  - >½ key muscles below have muscle grade <3
- D = Incomplete
  - Motor preserved
  - >½ key muscles below have muscle grade >3
- E = Normal
SPINAL SHOCK

- No motor, sensory or reflex
- Flaccid below level of injury
- Not to be confused with neurogenic shock
  - BP
  - HR
  - Temp

TREATMENT STRATEGIES

- Medical
- Surgical
- Experimental

NEUROPROTECTION AFTER SCI: THE BIG 4

- Preventing / Minimizing SIMs
  - Maintain temp
  - Medicate hypothermic
  - Maintain perfusion
  - Normalize BP
  - Maintain oxygenation
    - Normalize $\text{SpO}_2$
  - Maintain spinal alignment & stability
    - Restore, traction, Sx
PROMISING NEUROPROTECTIVE STRATEGIES

- Minocycline
- Cethrin® (Rho antagonist)
- Rolipram (PDE inhibitors)
- Polyethylene glycol (PEG-Mg²⁺)
- Riluzole (Na⁺ channel blocker)
- Modest Hypothermia

POTENTIAL BENEFITS OF SC MODEST HYPOTHERMIA

- ↓ volume of damaged tissue
- ↓ # of damaged neurons & axons
- ↓ edema
- ↓ hemorrhage
- ↓ metabolism & energy utilization
- ↓ hypoxic damage
- ↓ blood-brain barrier alterations

WHO TO COOL: INDICATIONS (ROSC)

- Cardiac arrest with ROSC
- Men & Women ≥ 18 yrs
  - Women of childbearing age must have a (-) uHCG
- Coma after ROSC
  - Coma is defined as: not following commands, no speech, no eye opening, no purposeful movements to noxious stimuli. Brainstem reflexes and pathological/posturing movements are permissible.
- ETI w/ mechanical ventilation
- SBP maintained at least 90 mm Hg
<table>
<thead>
<tr>
<th>Condition</th>
<th>Effective</th>
<th>Level of Evidence</th>
<th>Evidence for efficacy or lack of efficacy</th>
</tr>
</thead>
<tbody>
<tr>
<td>CPR for witnessed arrests &amp; ROSC &lt;60min</td>
<td>Yes</td>
<td>I</td>
<td>2 RCTs, 1 add RCT underpowered, much supporting evidence</td>
</tr>
<tr>
<td>Postanoxic encephalopathy in neonates</td>
<td>Yes</td>
<td>I</td>
<td>3 RCTs, 8 non-RCTs, much supporting evidence</td>
</tr>
<tr>
<td>Aortic aneurysm repair</td>
<td>Probably</td>
<td>III</td>
<td>1 small controlled study, 3 uncontrolled studies, persuasive data from animal experiments</td>
</tr>
<tr>
<td>Reducing ICP w/ cerebral edema</td>
<td>Yes</td>
<td>I</td>
<td>Numerous clinical trials</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>* &quot;Note: reduced ICP does not necessarily = improved outcome&quot;</td>
</tr>
</tbody>
</table>

Poulderman Lancet 2008; 371: 1955–69
HYPOTHERMIA FOR SCI HISTORY

- Techniques of local cooling
  - Practice of simple laminectomy ➔ access to cord
  - Irrigation w/ 4-5˚C saline
- Studies limited due to:
  - Limited # of patients
  - Shivering
  - Lacked randomized control
  - Concomitant interventions
    - SCI decompression, steroids, irrigation of SAS of blood

Beneficial Effects of Modest Systemic Hypothermia on Locomotor Outcome and Histopathological Damage Following Contusion Spinal Cord Injury in Rats


Beneficial effects of modest systemic hypothermia on locomotor outcome and histopathological damage following contusion spinal cord injury in rats.
Hypothermia in Experimental Spinal Cord Injury
W. Dalton Dietrich, III, PhD
Crit Care Med 2009 Vol. 37, No. 7 (Sept.)

LOCAL CORD COOLING IN HUMAN SCI

<table>
<thead>
<tr>
<th>FIRST AUTHOR/ YEAR</th>
<th>n, LEVEL</th>
<th>COOLING START</th>
<th>C°, DURATION</th>
<th>STEROIDS</th>
<th>APPROVED</th>
<th>MORTALITY</th>
</tr>
</thead>
<tbody>
<tr>
<td>Selker 1971</td>
<td>2, C, T</td>
<td>3 HRS</td>
<td>4.5 C, 3 HRS</td>
<td>-</td>
<td>50%</td>
<td>50%</td>
</tr>
<tr>
<td>Macnab 1972</td>
<td>3, C</td>
<td>4.0 HRS</td>
<td>4 C, 3 HRS</td>
<td>YES</td>
<td>70%</td>
<td>20%</td>
</tr>
<tr>
<td>Koons 1972</td>
<td>2, C, T</td>
<td>2.0 HRS</td>
<td>1.5 C, 30 MIN</td>
<td>YES</td>
<td>40%</td>
<td>0%</td>
</tr>
<tr>
<td>Negrin 1975</td>
<td>2, C, T</td>
<td>5 HRS, 1 YR</td>
<td>UNCERTAIN</td>
<td>-</td>
<td>0%</td>
<td>5%</td>
</tr>
<tr>
<td>Brooks 1976</td>
<td>4, C</td>
<td>7.24 HRS</td>
<td>5 C, 1.5 HRS</td>
<td>YES</td>
<td>50%</td>
<td>38%</td>
</tr>
<tr>
<td>Tator 1979</td>
<td>5, C, T</td>
<td>3.0 HRS</td>
<td>5 C or 36 C, 3 HRS</td>
<td>-</td>
<td>27%</td>
<td>38%</td>
</tr>
<tr>
<td>Hendriks 1984</td>
<td>6, C, T</td>
<td>6.0 HRS</td>
<td>6 C, 4 HRS</td>
<td>YES</td>
<td>43%</td>
<td>43%</td>
</tr>
</tbody>
</table>

HYPOTHERMIA HUMAN RESEARCH

- 14 Pts W/ CERVICAL SCI → MODEST HYPOTHERMIA
- Avg time to rewarm 9hrs
- Slow rewarming
- Evaluated complications
- No difference in complication rate w/ matched normothermic pt's
- No comment on clinical improvements

Complications – Acute Care / Rehab

AIS Outcome
14 patients
CLINICAL OUTCOMES USING MODEST INTRAVASCULAR HYPOTHERMIA AFTER ACUTE CERVICAL SCI - PHASE I

Phase I Study
- Levi et al.

Technique:
- Catheter via femoral vein
- Target T = 33°C
- <12 hrs after injury
- <48 hrs
- Retrospective safety study
- 1 yr median f/u

RESULTS
Overall 11 pt (39%) improved at latest follow up.

AIS Outcome (n=25 pts with initial ASIA A)

AIS Outcome (n=3 pts with initial ASIA >A)

Complications – n=28

Occurred 9mos post-hypothermia in a 62yo
OSBOURNE WAVE

SYSTEMIC RESEARCH CONCLUSIONS
- Effectively delivered systemic intravascular hypothermia (33°C) after acute cervical SCI
- \( T_{\text{Spine}} \) correlates with \( T_{\text{Spinal CSF}} \)
- Strong correlation between HR & Temp
- Systemic hypothermia appears safe
- Largest modern series (n=28) of hypothermia Tx of acute SCI
- Warrants larger, controlled prospective multi-center trials

SPINAL CORD MODEST HYPOTHERMIA
- What is modest hypothermia?
  - 33–36°C
- Best method of cooling?
  - Local?
  - Surface?
  - Systemic?
HYPOTHERMIA: LOCAL COOLING

- Eliminates systemic complications
- Invasive
- Difficult to maintain desired temp

HYPOTHERMIA: SURFACE COOLING

- Non-invasive
- Slower onset
- Difficulty reaching target temp
- Not feasible w/ trunk or extremities injuries
- Manipulation of patient to apply

ARCTIC SUN® 2002
- Pt temp is to a preset temp by water H₂O through Arctic Sun Energy Transfer Pads™
- Cools 2-3°C in 90 min
- Precise temp control minimizes overshoot
- Designed to mimic water immersion
- Uses cooled H₂O, but pads resistant to leaking unlike older H₂O blanket systems
HYPOTHERMIA: SYSTEMIC COOLING

- Non-invasive / minimally invasive
- Infection
- Coagulopathy
- Hypotension
- Electrolyte disturbance
- Arrhythmias
- Shaking chills

SPINAL CORD NEUROPROTECTION
PUBLIC ENEMY #1

Hyperthermia!!!

Yu et al. (Dietrich), Neurosurgery, 2001

Detrimental Effect of Hyperthermia on Locomotor function

Day Post-Trauma

Yu et al. (Dietrich), Neurosurgery, 2001
SPINAL CORD MODEST HYPOTHERMIA

- Indications for Neuroprotection
  - Acute Spinal Cord Injury
  - Intra-Operative
- Protocol
  - 33°C for 48 hours
  - Re-warming 1°C every 8 hours until normothermic (37°C)

SCI ACUTE MANAGEMENT

- Early cooling probably better
  - Role of EMS
  - Initiation of cooling protocol in the field
  - Transport to appropriate facility
  - At least prevent hyperthermia — Permissive Hypothermia!
- H&P
  - Evaluate for other trauma
  - Support spinal cord perfusion pressure \(\text{ISP ppt Taver} \)
    - Avoid SBP <90 mmHg
    - Maintain MAP 85-90 mmHg
  - Consider surgical decompression (Rabinowitz, Lax)
  - Other neuroprotective strategies?