Moderate Hypothermia In The Treatment of Acute Spinal Cord Injury and Review of Promising New Therapies

- Andrew Cappuccino BES, MD, FACS, FAAOS
- Director Buffalo Spine Surgery
- Assistant Team Orthopedist Buffalo Bills
  - Buffalo, NY
  - EATA Annual Meeting
  - Jan 5, 2013
DISCLOSURE

Nothing to disclose
C3-C4 BILATERAL FACET DISLOCATION IN AN NFL ATHLETE

Andy Cappuccino MD Asst. Team Orthopedist Buffalo Bills, John Marzo MD Team Orthopedist and Medical Director Buffalo Bills, Les Bisson MD Asst. Team Orthopedist Buffalo Bills, Tom White MD, Bud Carpenter AT-C Head Athletic Trainer Buffalo Bills, Greg McMillan AT-C, Chris Fischetti PT/AT-C, Shone Gipson AT-C
HISTORY K.E.

- 24 y.o. male Buffalo Bills tight end, helmet to shoulder pad collision during the opening kick-off second half on Sept. 9, 2007
- Falls to ground face down, no spontaneous movement below neck
ON FIELD ASSESSMENT

- Initial - Bud Carpenter, Les Bisson MD and John Marzo MD
  - Was conscious
  - Was prone
  - No voluntary movement or sensation below neck
  - Immediate in-line traction to stabilize C-spine

APPROX. 2:30 pm
SCI drill instituted
Six man roll technique to turn to supine
Airway assessed and found stable, Neuro Assessment C4 level motor and sensory quadriplegia (ASIA A)
Face mask removed
MANAGEMENT

- Stabilized with blocks and backboard while still in his helmet and shoulder pads
- Transferred into ambulance on field with paramedic and team orthopedist (AC)

Approx 2:45 pm
IN AMBULANCE

- Established 14 gauge IV access in both arms
- Establish continuous cardiac monitoring, pulse oximetry and dynamap (vitals BP138/74, HR=68 bpm, oximetry 98% on 4L NC). No sign of neurogenic shock
- Fluid resuscitation with cooled NS wide open to maintain BP and attempt to decrease core temp.
IN AMBULANCE

- Significant (Incomplete vs. Complete) SCI diagnosed Anterior Cord Syndrome?
- Bolus 3.5 gm MPSS per NASCIS II protocol (*#) 118kg x 30mg = 3,540 mg/kg
- Lowered ambient temp to 55 deg F on AC
- Removed wet clothing
- Ice packs in axillae and groins

Arrived at MFGH approx 3:10 pm

* NEJM May 1993
# Payer,M Acta Neurosurgical Vol 147 May 2005
IN AMBULANCE UPON ARRIVAL AT TRAUMA CENTER

- Contacted Spine Center for immediate needs in trauma room
- Repeat neuro assessment showed complete motor quadriplegia, normal rectal tone, + bulbocavernosus reflex, sensory sparing to deep pressure on upper trunk only (ASIA A/B). Not in spinal shock
- KE subjectively short of breath (dyspneic)

Arrival at MFGH approx. 3:10 PM
IN TRAUMA ROOM

- Maintained monitoring
- Placed KE between two cooling blankets
- Established MPSS 600 mg/hr for 23 hours per NASCIS II protocol
- Maintained traction and removed helmet and shoulder pads by protocol
- Philadelphia collar applied
- Maintained MAP >90
- Maintained O2 sats at 100%
IN TRAUMA ROOM

- Cross table lateral in collar
- Presumed Diagnosis bilateral facet fracture dislocation C3-C4
- Initial temperature in trauma room 98 deg
- Maintained resuscitation moved to CT

Approx 3:45 pm
CT SCAN
Leave CT approx 4:15 pm for MRI
Leave MRI approx 5:00 pm for pre-op holding
PRE-OP

- Discussed surgery and diagnosis
- Contacted family
- Discussed hypothermia and possible catheter utilization
- Consented
- Anesthesia evaluation
- Pre-op FVC1 = 600ml

To OR at 5:25 pm for closed reduction
- Initial temp in OR = 96 F
- Antibiotic given
- Gardner-Wells tongs applied under awake local anesthesia
- Manipulative closed reduction under fluoro with up to 35 # longitudinal traction
- Facets reduced with no change in neurological status
OR

- Awake fiber optic intubation and induction of general anesthesia, maintain MAP > 90 via fluids, volume expansion and pressors
- Commence anterior decompression and fusion at 6:30 pm
- Temperature at induction 95.2 F
- Complete anterior procedure 8:00 pm
- Temperature at flip for posterior decompression and fusion 95 F
OR

- Commence posterior surgery 8:20 pm
- Complete posterior decompression and fusion at 10:00 pm and transport to neuro ICU
SURGICAL STABILIZATION

- ACDF with partial corpectomy C3-C4 with peek cage, infuse BMP and plate/screw inst
- Posterior C3-C4 laminectomy and facet fusion with lateral mass screw/rod inst
ICU

- Intubated, sedated temp on admit to ICU is 94.8 F
- Continued with cooling blankets and rotating ice packs, continue MAP maintenance, insulin protocol for strict BS management, maintain SaO2 at 100%
- Repeat MRI CS at midnight
- CT at 2 AM 2/10/2007
POST-OP MRI

pre-op

Post-op
POST-OP CT
POST-OP DAY #1

- 6:00 am awakened neuro exam performed. Responsive to commands. Increased sensation in legs and feet. Voluntary movement in lower extremity adductors motor grade 2/5. Remains ASIA B (temp maintained at 94 deg)

- Serial exams by staff between 6:00 am and 8:00 am. Temp rises to 98.4 while alert despite external cooling
POST-OP DAY #1

- Placed cordis in left femoral vein at 6:45AM and Coolgard Catheter** into IVC at 7:00 AM. Catheter fully functional with active cooling by 7:27AM
- Resumed sedation at 8AM
- Cooled to 93 F by 11:00 AM maintained for next 24 hours to reassess
- NASCIS II protocol completed

** Alsius Corporation, Mountainside Ca.
POST-OP DAY #2

- Awakened at 6:00AM responsive to commands. Increased sensation globally.
- Voluntary movement of legs and arms. Motor 3/5 lower add, quad, hf, ehl, df/pf feet. Upper extremity 2+/5 left biceps, triceps and epl. 2/5 right triceps, biceps. 1/5 epl
- FVC1 1.4 L through ET tube
- Now ASIA C
- Commenced warming 1 degree every 6 hours over the next 30 hours
POST-OP DAY #3

- Warmed
- Extubated in early afternoon
- FVC1 1.7 L
- Drains out
- Plain x-rays active flex/ext
- Neuro increased movement legs and arms. Motors increase to 3/5
POST-OP DAYS 4-11

- NGT Feeds begin
- PT/OT commence
- Medical and Neurological status progress
- Plans for rehab at Memorial Hermann Hosp. TIRR arranged
- At discharge ASIA C/D
- Air ambulance to Texas 9/21/2007
POST-OP 5 MONTHS

- ASIA D with residual deficit fine motor hands, feet, sensory deficit stocking and glove bilateral.
  Global motor 4-4+/5

- Normal voluntary bladder, bowel and male sexual functioning
ONE YEAR POST INJURY

- KE returns to Ralph Wilson stadium opening day NFL season 2008 at halftime to receive NFL’s George Hallas “Man of Courage” Award.
- (Bills 38-Seattle Seahawks 14)
MODERATE HYPOTHERMIA IN THE TREATMENT OF ACUTE SPINAL CORD INJURY

- Andy Cappuccino MD, BES Asst. Team Orthopedic Surgeon Buffalo Bills, Bud Carpenter AT-C Head Trainer Buffalo Bills, Greg McMillan AT-C, Chris Fischetti PT AT-C, Shone Gipson AT-C Asst. Trainers Buffalo Bills, John Marzo MD Team Orthopedist and Medical Director Buffalo Bills
Update on Research Regarding Hypothermia and Spinal Cord Injuries

W. Dalton Dietrich, Ph.D.
Scientific Director
The Miami Project to Cure Paralysis
Department of Neurological Surgery, Neurology, Cell Biology & Anatomy
University of Miami Miller School of Medicine
Miami, FL USA
Demographics of SCI in U.S.

- Since 2000, about 78% of SCIs reported to the national database have occurred in males.
- Motor vehicle accidents followed by falls, acts of violence and recreational activities are the leading causes of SCI in the U.S.
- 12,000 new cases each year in the U.S.
- Approximately 250,000 Americans living with paralysis as a result of SCI.
Pathophysiology of Acute Spinal Cord Injury

- **Primary Injury mechanism** = mechanical insult (what we can’t control)
  - acute compression
  - impaction
  - laceration
  - Shear forces
  - missile injury
Pathophysiology of Acute Spinal Cord Injury

Secondary Injury Mechanisms (SIMs) (what we can and must control)

- Vascular changes (reduced blood flow, thrombosis, vasospasm, hemorrhage, loss of auto regulation)
- Electrolyte shifts ($Ca^{++}$, $K^+$, $Na^+$)
- Neurotransmitter accumulation (EAAs, glutamate)
- Free radicals (lipid peroxidation)
- Edema formation with Inflammation
- Loss of energy metabolism
- Hyperthermia
Spinal Cord Neuroprotection
Public Enemy

Hyperthermia!!!

Need to maintain normothermia!
Neuroprotection Following Spinal Cord Injury

- Steroids- Nascis II or III
- Gangliosides (sygen)
- Neurotrophic Factors
- Opiate Antagonists- naloxone
- Monoamine Antagonists
- Excitatory Amino Acid Antagonists
- Calcium Channel Antagonists
- Sodium channel blockers
Promising Treatments Targeting SCI

- Erythropoietin
- Minocycline
- Rolipram (phosphodiesterase 4 inhibitor) , anti-inflammation, neuro protection
- Polyethylene glycol (PEG)
- Cethrin® (Rho antagonist prevents activation of the Rho/Rho kinase activation) recombinant protein for neuronal regeneration promotion
- Riluzole (Na+ channel blocker, NMDA/glutamate receptor antagonism, glutamate transporter)
- Stem Cells
- Therapeutic Hypothermia
Erythropoietin

- Acute SCI produces local cell and tissue destruction causing lipid peroxidation exerting an extremely toxic effect on neuronal tissue
- Erythropoietin has shown in early clinical research to exhibit a cyto-protective benefit and inhibit the lipid peroxidation process

Kaptanoglu 2003
Minocycline

- Traumatic release of mitochondrial cytochrome c is a potent secondary injury mechanism leading to neuronal cell death
- Minocycline inhibits mitochondrial cytochrome release and mitigates functional deficits after acute SCI in experimental models, thus limiting reactive gliosis

Teng, Choi, Onario et al. 2004
Rolipram

- An inhibitor of phosphodiesterase 4 (PDE4) proteins that hydrolyze cAMP, increases axonal regeneration after acute SCI.
- Recent evidence indicates that Rolipram protects against multitude of apoptic signals which are implicated in secondary cell death post SCI, thus sparing functional neuronal tissue.

Whitaker, Beaumont, Wells et al. 2008
Polyethylene Glycol

- Is a hydrophilic polymer
- Shown to be effective in immediate “sealing of the cell membrane post SCI and prevents oxygen free radical formation, thus limiting cell death

Luo, Borgens, Jian et al. Journal of Neurochemistry 2002
Cethrin

- Orphan Drug 210A
- Rho antagonist, prevents activation of the Rho/Rho kinase pathway
- Recombinant protein
- Aggressively promotes neuronal regeneration. Applied directly to dura
Sodium Channel Blockers

- Persistent activation of voltage-sensitive Na+ channels is associated with cellular toxicity and contribute to neuronal destruction following traumatic SCI.
- Pharmacologic blockade of these channels can reduce destruction and lead to better behavioral and functional outcomes. Significant neuroprotection with sparing of gray and white matter was seen in experimental models. In particular utilizing Riluzole.

Fehlings, M and Schwartz, G
Stem Cells

- Pluripotential cells of lipid, marrow, and embryonic origin when used alone or in conjunction with a dacron scaffold
- Promising technology laden with many ethical issues
The History of Hypothermia for Spinal Cord Injury

- Clinical trials with SCI were begun in the 1960s following promising experimental reports.
- Techniques of local cooling were feasible for acute SCI because the practice of surgical decompression allowed exposure of the spinal cord.
- Evaluation of these studies was difficult due to:
  - limited number of patients
  - lack of randomized control groups
  - concomitant interventions, e.g. spinal cord decompression, steroid use (methylprednisone)
# Effects of Spinal Cord Cooling in Experimental Spinal Cord Trauma

<table>
<thead>
<tr>
<th>Study</th>
<th>Year</th>
<th>Species</th>
<th>Level</th>
<th>Method</th>
<th>Cooling Start</th>
<th>°C, Duration</th>
<th>Other</th>
<th>Outcome</th>
</tr>
</thead>
<tbody>
<tr>
<td>Albin et al.</td>
<td>1965</td>
<td>Dog</td>
<td>T10</td>
<td>WD</td>
<td>Immediate</td>
<td>12 SC, 2.5 h</td>
<td>DO</td>
<td>Positive</td>
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<tr>
<td>Albin et al.</td>
<td>1967</td>
<td>Dog</td>
<td>T10</td>
<td>WD</td>
<td>Immediate</td>
<td>5 SOL, 2.5 h</td>
<td>DO</td>
<td>Positive</td>
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<tr>
<td>Albin et al.</td>
<td>1968</td>
<td>Monkey</td>
<td>T10</td>
<td>WD</td>
<td>4 h post</td>
<td>10 SC, 3 h</td>
<td>DO</td>
<td>Positive</td>
</tr>
<tr>
<td>Ducker/Hamit</td>
<td>1969</td>
<td>Dog</td>
<td>T11</td>
<td>WD</td>
<td>3 h post</td>
<td>3 SOL, 3 h</td>
<td>DO</td>
<td>Positive</td>
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<tr>
<td>Kelly et al.</td>
<td>1970</td>
<td>Dog</td>
<td>T10</td>
<td>WD</td>
<td>Immediate</td>
<td>12 SC, 2.5 h</td>
<td>DO</td>
<td>Positive</td>
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<tr>
<td>Black/Markowitz</td>
<td>1971</td>
<td>Monkey</td>
<td>T10</td>
<td>WD</td>
<td>1 h post</td>
<td>4-8 SOL, 5 h</td>
<td>Some DO</td>
<td>Negative</td>
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<tr>
<td>Tator/Deecke</td>
<td>1973</td>
<td>Monkey</td>
<td>T9-10</td>
<td>ICD</td>
<td>3 h post</td>
<td>5, 3 h</td>
<td>Some DO</td>
<td>Positive</td>
</tr>
<tr>
<td>Campbell et al.</td>
<td>1973</td>
<td>Cat</td>
<td>T9</td>
<td>WD</td>
<td>3 h post</td>
<td>4 SOL, 3 h</td>
<td>DO</td>
<td>Positive</td>
</tr>
<tr>
<td>Hansebout et al.</td>
<td>1975</td>
<td>Dog</td>
<td>T13</td>
<td>ICD</td>
<td>Immediate</td>
<td>4 EP, 4 h</td>
<td>DO</td>
<td>Positive</td>
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<tr>
<td>Kuchner/Hansebout</td>
<td>1976</td>
<td>Dog</td>
<td>T13</td>
<td>ICD</td>
<td>15 m post</td>
<td>6 SOL, 4 h</td>
<td>DO</td>
<td>Positive</td>
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<tr>
<td>Eidelberg et al.</td>
<td>1976</td>
<td>Ferret</td>
<td>Mid-T</td>
<td>SWL</td>
<td>1 h post</td>
<td>10 EP, 3 h</td>
<td>DO</td>
<td>Positive</td>
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<tr>
<td>Wells/Hansebout</td>
<td>1978</td>
<td>Dog</td>
<td>T13</td>
<td>ICD</td>
<td>4 h post</td>
<td>6 EP, 1-18 h</td>
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<td>Positive</td>
</tr>
<tr>
<td>Green et al.</td>
<td>1973</td>
<td>Cat</td>
<td>T10</td>
<td>WD</td>
<td>1 &amp; 4 h post</td>
<td>6-18°C, 3 h</td>
<td>DO</td>
<td>Positive</td>
</tr>
<tr>
<td>Martinez/Green</td>
<td>1992</td>
<td>Rat</td>
<td>T8</td>
<td>WD</td>
<td>Pre &amp; post</td>
<td>31-32°C, 4 h</td>
<td>DI</td>
<td>Positive</td>
</tr>
<tr>
<td>Yu et al.</td>
<td>2000</td>
<td>Rat</td>
<td>T10</td>
<td>WD</td>
<td>Post</td>
<td>33°C, 4 h</td>
<td>DI</td>
<td>Positive</td>
</tr>
<tr>
<td>Chatzipanteli et al.</td>
<td>2000</td>
<td>Rat</td>
<td>T10</td>
<td>WD</td>
<td>Post</td>
<td>33°C, 4 h</td>
<td>DI</td>
<td>Positive</td>
</tr>
<tr>
<td>Dimar et al.</td>
<td>2000</td>
<td>Rat</td>
<td>T10</td>
<td>WD</td>
<td>Post</td>
<td>19°C, 2 h</td>
<td>DI</td>
<td>Positive</td>
</tr>
</tbody>
</table>

Guest and Dietrich, 2005
## Local Spinal 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>IMPROVED</th>
<th>MORTALITY</th>
</tr>
</thead>
<tbody>
<tr>
<td>Selker/1971</td>
<td>2, C 2, T</td>
<td>3 HRS</td>
<td>4-5 C, 3 HRS</td>
<td>-</td>
<td>50%</td>
<td>50%</td>
</tr>
<tr>
<td>Meacham/1973</td>
<td>12, C</td>
<td>4-8 HRS</td>
<td>4 C, 3 HRS</td>
<td>YES</td>
<td>70%</td>
<td>29%</td>
</tr>
<tr>
<td>Koons/1972</td>
<td>3, C 4, T</td>
<td>3-8 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>1, C 2, T</td>
<td>5 HRS; 1 YR</td>
<td>UNCERTAIN</td>
<td>-</td>
<td>0%</td>
<td>0%</td>
</tr>
<tr>
<td>Bricolo/1976</td>
<td>4, C</td>
<td>7-26 HRS</td>
<td>5 C, 1.5 HRS - 8 DYS</td>
<td>YES</td>
<td>50%</td>
<td>38%</td>
</tr>
<tr>
<td>Tator/1979</td>
<td>7, C 4, T</td>
<td>3-8 HRS</td>
<td>5 C or 36 C, 3 HRS</td>
<td>-</td>
<td>27%</td>
<td>38%</td>
</tr>
<tr>
<td>Hansebout/1984</td>
<td>4, C 6, T</td>
<td>8 HRS</td>
<td>6 C, 4 HRS</td>
<td>YES</td>
<td>43%</td>
<td>43%</td>
</tr>
</tbody>
</table>
Spinal Cord Modest Hypothermia

- **Temperature Levels**
  - **Mild**: 32-36°C
  - **Moderate**: 30-32°C
  - **Deep**: 10-20°C
  - **Profound**: 5-10°C
  - **Ultraprofound**: <5°C
Temperature Mechanisms in Ischemia and Trauma

1. Metabolism (1970)
2. pH (1992)
8. Cerebral blood flow (1954)
11. Calcium accumulation (1992)
12. Protein synthesis (1991)
13. Protein kinase-C activity (1991)
15. Platelet function (1987)
16. NMDA(N-methyl-D-aspartic acid) neurotoxicity (1991)
18. Growth factors (1994)
19. Calcium-dependent protein phosphorylation (1990)
22. NOS activity (1999)
“The first demonstration of cytoprotection translated from the laboratory to man”

Therapeutic Hypothermia

American Heart Association endorses therapeutic hypothermia for cardiac arrest patients 2005
Treatment of Comatose Survivors of Out-of-Hospital Cardiac Arrest with Induced Hypothermia (Australian Study) NEJM 346:557-563, 2002

- 77 out-of-hospital cardiac arrest patients
- Core temperature decreased from 34.9°C at 30 min after restoration of spontaneous circulation to 33.5°C at 120 min (maintained for 12 hr)
- Primary outcomes: Survival of hospital discharge and good neurological function
- Hypothermia associated with lower cardiac index, higher systemic vascular resistance, and hyperglycemia
- Moderate hypothermia appears to improve outcome
Is Modest Hypothermia Protective in Experimental and Clinical SCI?
Beneficial Effects of Modest Systemic Hypothermia on Locomotor Outcome and Histopathological Damage Following Contusion Spinal Cord Injury in Rats

Yu CG, Jimenez O, Marcillo AE, Weider B, Bangerter K, Dietrich WD, Castro S, Yezierski R

J Neurosurg 95:85-93, 2000
Hypothermia

One week after SCI

- 32% less tissue loss
- Improved behavior in cooled animals

Yu et al. (Dietrich), J Neurosurg, 2000

Normal Temperature
37°C

Hypothermia
32-33°C
Systemic _modest_ hypothermia improves outcome after cervical spinal cord contusion in rats

- Cervical SCI in adult female rats (moderate)
- Normothermia (37°C) vs. Hypothermia (34°C)
- Behavioral assessment
  - BBB  Basso-Brady-Bresnahan (open field locomotion)
  - Hang Test
  - Incline Plane
  - Grip Strength
- Histopathological outcome
- **Posttraumatic hypothermia effective in retarding tissue damage and reducing neurological deficits.**

Lo et al. (Dietrich, Pearse), 2007
Histological Improvement with Posttraumatic Hypothermia
Neuronal Survival with Hypothermia

*significantly different from normothermic animals
Forelimb Function

*significantly different from normothermia
Modest Hypothermia Systemic Cooling

- **Pro’s**
  - Non-invasive or minimally invasive

- **Con’s**
  - Infection (sepsis, pneumonia, wound)
  - Coagulopathy
  - Hypotension
  - Myocardial dysfunction
  - Shaking chills
  - Need for sedation
Ice Packs:
- Messy - Water spills
- Hard to transport patients
- Limited access to patients
- Poorly controlled cooling and rewarming overshoot

Forced Air or Water Circulation Blankets:
- Limited access to patients
- Cumbersome
- Hard to transport patients
- Probably slightly better controlled cooling and rewarming
- Patient temperature is to a preset temperature by water flowing through Arctic Sun Energy Transfer Pads™
- Cools 2-3°C in 90 minutes
- Precise temperature control minimizes overshoot
- Designed to mimic water immersion
- Uses cooled water, but pads resistant to leaking unlike older water blanket systems
Currently Available Systems

- Coolguard system by Alsius.
- Currently in use by Dept. of Neurosurgery at UM/JMH, MFGH SUNY Buffalo
- Cooled saline flows within balloons & venous blood is cooled as it passes in the vena cava
- Desired temperature & rate of achievement set in control panel.
- ICY catheter®
  - Placed in IVC
  - Multi-lumen
  - MRI compatible
COOLGARD 3000 CATHETER
RISKS OF SYSTEMIC MODERATE HYPOTHERMIA

- Cardiac arrhythmia
- Consumptive coagulopathy
- Hemorrhage
- Renal failure
- Pancreatitis
- Hepatic failure
- Pneumonia
Currently Available Systems

- **Celsius Control System™ (Innercool Therapies)**
  - Catheter incorporates a flexible temperature control element (TCE) that is cooled or warmed with saline solution circulated in closed-loop.
  - Placed in inferior vena cava & venous core blood is cooled/warmed as it flows past the TCE back to the heart.
  - Console receives feedback from intravascular sensor to achieve target temperature.
  - No fluid in infused into the patient.
Spinal Cord Neuroprotection

Public Enemy

Hyperthermia!!!

Need to maintain normothermia!
Football Spine Injuries

When Kevin Everett showed movement in his limbs late Sept. 11, his doctor called it “a minor miracle.” The Buffalo Bills defender had crumpled after a seemingly routine tackle during a Sunday game. Doctors quickly ran an ice-cold saline solution through his body—a relatively new treatment to prevent spinal swelling. That may have saved him from lifelong paralysis. These types of injuries are much rarer now since high schools and colleges prohibited head-first tackles in 1976.

Football injuries resulting in quadriplegia—
high school, college and professional

*Head-first tackling was banned at all levels in 1976*

- '76: 34
- '84: 5
- '91: 1 (Mike Utley, Detroit Lions)

Cervical vertebrae

Spinal cord

Disk pressing on spine

Spine crushed but not severed

C4

C3
Spinal Cord Injury Requires A Systems Approach

- Prevention
- Emergency Medical Services
- Trauma Center Protocols
- Critical Care Management
- Rehabilitation
- Post-Hospitalization programs
Clinical Protocols in Central Nervous System Trauma

- No clinical guidelines or protocols establishing efficacy for the use of therapeutic hypothermia after human spinal cord injury have been published in peer reviewed journals.
- Modest hypothermia treatment in SCI patients is therefore an experimental procedure.
- Unfortunately, media attention surrounding its recent use may have given the impression it should be a standard treatment.
Research Protocol at UMMSM/JMH

- The Department of Neurological Surgery/Miami Project at the UMMSM/JMH is currently conducting an IRB approved SCI research protocol.
- This protocol will evaluate the use of modest hypothermia in patients with acute SCI for risk factors and efficacy.
- Modest hypothermia (33° C/92° F) is induced via a cooling catheter that is placed in a large blood vessel.
- Cooling is maintained for a 48hr period followed by a slow re-warming of one degree every 8 hours.
Clinical Application of Modest Hypothermia after Spinal Cord Injury

Allan D. Levi, Barth A. Green, Michael Y. Wang, W. Dalton Dietrich, Ted Brindley, Steven Vanni, Gizelda Casella, Gina Elhammady, and Jonathan Jagid

Abstract

There is widespread interest in the use of hypothermia in the treatment of CNS injury. While there is considerable experience in the use of cooling for a variety of brain pathologies, limited data exist after spinal cord injury. In the past few years, technological advances in the induction and maintenance of cooling have been achieved and can potentially allow for a more accurate evaluation of this form of treatment. We report a series of 14 patients with an average age of 39.4 years (range, 16–62 years) with acute, complete (AIS A) cervical spinal cord injuries who underwent a protocol using an intravascular cooling catheter to achieve modest (33°C) systemic hypothermia. There was an excellent correlation between intravascular and intrathecal cerebrospinal fluid temperature. The average time between injury and induction of hypothermia was 9.17 ± 2.24 h (mean ± SEM); the time to target temperature was 2.72 ± 0.42 h; the duration of cooling at target temperature was 47.6 ± 3.1 h; the average total length of time of cooling was 93.6 ± 4 h. There was a positive correlation between temperature and heart rate. Most documented adverse events were respiratory in nature. We were able to effectively deliver systemic cooling using the cooling catheters with minimal variation in body temperature. The study represents the largest, modern series of hypothermia treatment of acute spinal cord injury with intravascular cooling techniques and provides needed baseline data for outcome studies to include larger multi-center, randomized trials.
Eligibility Criteria

**Inclusion:**
- Age: 18-65
- Nonpenetrating SCI
- Baseline neurologic exam of ASIA A
- Informed consent
- Protocol initiated within 6 hrs of injury

**Exclusion:**
- Penetrating SCI
- Severe systemic injury
- Severe bleeding
- Thrombocytopenia
- Coagulopathy
- Blood dyscrasias
- Known cardiac history
- Pregnancy
ASCI Hypothermia Study

- Perform baseline neurological exam (MUST be done PRIOR to intubation or sedation)
- Confirm presence of injury radiologically
- Institute hypothermia to target of 33˚ C within 6 hours
- Maintain MAP > 90 (volume expansion, vasopressors)
- Maintain hematocrit > or = 30 (blood transfusion)
- Obtain daily blood cultures from peripheral site and catheter.
- Obtain daily serum electrolytes, PT/PTT, CBC
- Doppler US (on day of catheter removal)
Systemic hypothermia for the treatment of acute cervical spinal cord injury in sports.

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Abstract

Spinal cord injury is a devastating condition that affects approximately 12,000 patients each year in the United States. Major causes for spinal cord injury include motor vehicle accidents, sports-related injuries, and direct trauma. Moderate hypothermia has gained attention as a potential therapy due to recent experimental and clinical studies and the use of modest systemic hypothermia (MSH) in high profile case of spinal cord injury in a National Football League (NFL) player. In experimental models of spinal cord injury, moderate hypothermia has been shown to improve functional recovery and reduce overall structural damage. In a recent Phase I clinical trial, systemic hypothermia has been shown to be safe and provide some encouraging results in terms of functional recovery. This review will summarize recent preclinical data, as well as clinical findings that support the continued investigations for the use of hypothermia in severe cervical spinal cord injury.
Hypothermic treatment for acute spinal cord injury.


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Abstract

Spinal cord injury (SCI) is a devastating condition that affects approximately 11,000 patients each year in the United States. Although a significant amount of research has been conducted to clarify the pathophysiology of SCI, there are limited therapeutic interventions that are currently available in the clinic. Moderate hypothermia has been used in a variety of experimental and clinical situations to target several neurological disorders, including traumatic brain and SCI. Recent studies using clinically relevant animal models of SCI have reported the efficacy of therapeutic hypothermia (TH) in terms of promoting long-term behavioral improvement and reducing histopathological damage. In addition, several clinical studies have demonstrated encouraging evidence for the use of TH in patients with a severe cervical spinal cord injury. Moderate hypothermia (33°C) introduced systemically by intravascular cooling strategies appears to be safe and provides some improvement of long-term recovery of function. TH remains an experimental clinical approach and randomized multicenter trials are needed to critically evaluate this potentially exciting therapeutic intervention targeting this patient population.
Systemic hypothermia in acute cervical spinal cord injury: a case-controlled study

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Introduction:

Systemic hypothermia remains a promising neuroprotective strategy. There has been recent interest in its use in patients with spinal cord injury (SCI). In this article, we describe our extended single center experience using intravascular hypothermia for the treatment of cervical SCI.
Methods:

Thirty-five acute cervical SCI patients received modest (33 °C) intravascular hypothermia for 48 h. Neurological outcome was assessed by the International Standards for Neurological Classification of Spinal Cord Injury scale (ISNCSCI) developed by the American Spinal Injury Association. Local and systemic complications were recorded.

Results:

All patients were complete ISNCSCI A on admission, but four converted to ISNCSCI B in <24 h post injury. Hypothermia was delivered in 5.76 (±0.45) hours from injury if we exclude four cases with delayed admission (>18 h). Fifteen of total 35 patients (43%) improved at least one ISNCSCI grade at latest follow up 10.07 (±1.03) months. Even excluding those patients who converted from ISNCSCI A within 24 h, 35.5% (11 out of 31) improved at least one ISNCSCI grade. Both retrospective (n=14) and prospective (n=21) groups revealed similar number of respiratory complications. The overall risk of any thromboembolic complication was 14.2%.
Conclusion:

The results are promising in terms of safety and improvement in neurological outcome. To date, the study represents the largest study cohort of cervical SCI patients treated by modest hypothermia. A multi-center, randomized study is needed to determine if systemic hypothermia should be a part of SCI patients’ treatment for whom few options exist.
Spinal Cord Injury
Trauma Center Priorities

- Physical and Neurological Assessment
- Systemic Assessment and Stabilization
- Neuroprotection / Modest Hypothermia/Drug
- Spinal Column and Spinal Cord Imaging
- Spinal Column Traction, Realignment and Immobilization
- Patient Triage for Definitive Management
Future Challenges
Modest Hypothermia for SCI

- Modest Hypothermia/Neuroprotection for Acute Injuries:
  - Pre-Hospital – Trauma Center – ICU – Operating room
  - Pediatrics/Adults/Gender?
  - Optimal time of initiating treatment?
  - Length of treatment?
  - Time for re-warming?
  - Patient sedation/intubation?
  - Combination Pharmacological/Hypothermic Therapy?
  - Prospective randomized clinical trials required!
MEDICAL RESEARCH

Clinical Trials

Clinical Investigations

Translational Studies

Basic Science Research

Treatment Guidelines & Recommendations
CONCLUSIONS

- Excellent outcome
- Potential variables responsible:
  - Well developed Buffalo Bills system to handle this situation
  - Timing to decompression and stabilization
  - Steroids
  - Modest hypothermia
CONCLUSION

- Early controlled studies show promising outcomes for the use of moderate systemic hypothermia in the treatment of ASCI.
- Would advocate further randomized double blind studies to assess the benefit of MH for possible future use in SCI.
- Would recommend standardizing protocols to treat such injuries, early decompression and stabilization if possible and steroids by protocol when appropriate.
THANK YOU