New Developments in Cardiopulmonary Arrest: Therapeutic Hypothermia in Resuscitation

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Case Presentation

• Oct 11, 2007, 3:25 PM
• Ohio State student, E.H. left calculus class.
• 3:34 – Collapsed on grass outside.
• Nurse walking by began aggressive chest compressions.
• 3:35 – 9-1-1 called.
• 3:36 – Ambulance dispatched.

Case Presentation

• 3:40 (+ 6:00 minutes) – Columbus EMS Medic 7 arrived at victim
• Initial rhythm: VF
• 3:42 (+ 8:00 minutes) – Shock once
• In coma
• Intubated & given amiodarone

Cooling

• Began therapeutic hypothermia
• Warmed 24 hours later
• Visited patient in hospital on post-arrest day 3...
Objectives

- Describe clinical efficacy for therapeutic hypothermia for comatose victims of cardiac arrest
- Detail the methods for inducing therapeutic hypothermia
- Review the political barriers to implementing a therapeutic hypothermia protocol
Hospital Care Matters

Saving the Brain

- Cerebral perfusion
- Sedation
- Control of seizures
- Glucose control
- Temperature control

Brain Temperature Control

- Prevention of hyperthermia
  - Hyperthermia common for 2-3 days
    - Takino M. Intensive Care Med 1991;17:419-20
  - Hyperthermia associated with poor outcome
    - Zeiner A. Arch Intern Med 2001;161:2007-12
    - Hickey RW. Crit Care Med 2003;31:531-5
- Therapeutic hypothermia

Hypothermia: Mechanism of action?
Hypothermia: Mechanism of action?

• Suppression of free radicals
• Blocking pathological protease cascades
• Suppression of apoptosis (48 h)
• Suppression of pro-inflammatory cytokines (5 days)

Number Needed to Treat

- Plavix for STEMI: NNT = 23 (composite endpoint)
- PCI vs tPA for STEMI: NNT = 100 (mortality)
- Statins for ASCVD: NNT between 163 – 639 (mortality per yr of therapy)
- Therapeutic hypothermia for comatose VF survivors: NNT = 6 (good neuro outcome)

HACA Study Cooling Technique

- External cooling (ED)
- 32-34°C for 24 hr
- Cooling tent +/- ice packs
- Passive rewarming over 8 hours
- Pancuronium
- Bladder temperature

The New England Journal of Medicine

Normothermia (n = 124)

Hypothermia (n = 124)

Cooling was Slow

The Hypothermia After Cardiac Arrest (HACA) Study Group

![Graph showing outcome comparison between Normothermia and Hypothermia](image1)

- Good Neurological outcome
- Death

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<thead>
<tr>
<th>Condition</th>
<th>P</th>
<th>NNT</th>
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<tbody>
<tr>
<td>Normothermia</td>
<td>0.009</td>
<td>6</td>
</tr>
<tr>
<td>Hypothermia</td>
<td>0.02</td>
<td>7</td>
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The Hypothermia After Cardiac Arrest (HACA) Study Group

Nolan J. Resuscitation 2003; 57:231-5

Therapeutic hypothermia after cardiac arrest

An Advisory Statement by the ALS Task Force of the International Liaison Committee on Resuscitation (ILCOR)

- Unconscious adult patients with spontaneous circulation after out of hospital cardiac arrest should be cooled to 32-34°C for 12-24 hours when the initial rhythm was VF
- For any other rhythm, or cardiac arrest in hospital, such cooling may also be beneficial

Exclusions (relative)

- Severe systemic infection
- Severe cardiogenic shock (SBP < 90 mmHg despite inotropes)?
- Established multiple organ failure
- Pre-existing medical coagulopathy

Early Cooling and Outcome

- 49 consecutive patients cooled with invasive cooling (Alsius system)
- 78% OHCA; 84% VF/VT
- 28/49 (57%) good outcome = CPC 1 or 2
- Multivariate analysis: time to target temperature = OR 0.69 (0.51 – 0.98) for good outcome per hour

Speed of Cooling May Matter

Fig. 1. Time course of MTH among patients with good and poor neurologic outcome. The curves indicate the course of mean body core T during MTH among patients with good and those with poor outcome as well as in the entire patient group.
Prehospital cooling versus emergency department cooling

- VF cardiac arrest (n = 234)
- 2 L cold saline prehospital vs. ED
- Temperature
  - Before saline = 35.8°C
  - On ED arrival = 34.4°C versus 35.9°C
- Survival to discharge 48% (EMS) versus 51% (ED)

Fig. 1. Time course of T°C on arrival in patients with poor outcome. The curves in each group represent patients who required
hypothermia.
Phases of Hypothermia

- Induction – get to < 34°C rapidly
- Maintenance phase – tight control (maximum fluctuation 0.2 – 0.5°C)
- Rewarming phase – slow 0.25°C h⁻¹
  ✓ Deranged cerebrovascular reactivity if > 37°C — Lavinio A. BJA 2007;99:237-44.

Polderman KH. Crit Care Med 2009;37:1101-20

Cooling Techniques

- External
  ✓ Ice packs, wet linen, fans
  ✓ Cooling blankets
    • Air, e.g. Polar Air
    • Water, e.g. Blanketrol
  ✓ Pre-refrigerated cooling pads
  ✓ Hydrogel-coated pads
  ✓ Cold water immersion

- Internal
  ✓ Cold IV saline
  ✓ Intravascular catheters
    • Intravascular balloons
    • Metal catheter
    • Helix system

Polderman KH. Crit Care Med 2009;37:1101-20

Induction of Cooling

- 2 liters of ice cold saline kept in refrigerator

External Cooling

Polderman KH. Crit Care Med 2009;37:1101-20
Laerdal MediCool

Water-circulating Surface Cooling Device (Arctic Sun)

Circulating cold water blankets

Arctic Sun vs Standard Cooling blankets & ice bags

- Multicenter, randomized trial with cooling blankets and ice (n=30) or the Arctic Sun (n=34)
- Subjects cooled <34°C target at 4 hours = 71% (Arctic Sun) vs 50% (standard cooling group, p=0.12).
- Median time to target was 54 minutes faster in the Arctic Sun group than the standard cooling group (p<0.01).
- Survival rates with good neurological outcome were similar: 46% of Arctic Sun patients and 38% of standard patients had a cerebral performance category of 1 or 2 at 30 days (P=0.6).

Heard K, et al., AHA Scientific Sessions 2007
**External techniques: Overcooling is frequent**

- Retrospective review of 32 cases
- Surface cooled to target of 32-34°C
  - 20/32 (63%) < 32°C
  - 9/32 (28%) < 31°C
  - 4/32 (13%) < 30°C
- Rebound hyperthermia (>38°C) at 12-18 h after rewarm in 7/32 (22%)

**Endovascular cooling after cardiac arrest**

\[\text{N} = 19\]

**Endovascular Cooling**

**Therapeutic Hypothermia: Physiological effects / complications**

- Shivering
- Vasoconstriction
- Bradycardia
- Infection, coagulopathy
- Diuresis - hypovolemia
- K⁺, Mg⁺, Ca²⁺
- Insulin sensitivity
- Impaired GI absorption

- Merchant RM. Crit Care Med 2006; 34: S490-4
- Sterz F. Curr Opin Crit Care 2003; 9: 205-10
- Polderman KH. Crit Care Med 2009;37:1101-20
### Prevent Shivering:

- NMBA may be used
  - Eliminates thermoregulatory defense mechanisms
  - If used:
    - Paralytic infusion may be discontinued when temp is 34 °C (93.2 °F)
    - If shivering occurs, then neuromuscular blockade should be resumed
    - No need to do Train of Four, it's not accurate in the hypothermic patient
- Sedation
  - Typically used, with or without NMBA
  - Given continuously

### Monitor Temperature

- Continuously Monitor Temperature with Core temp probes
  - Esophageal
  - Pulmonary artery
  - Bladder probe
  - Also use a secondary temperature to monitor
- Frequency
  - Every 30 minutes during cooling and rewarming
  - Every hour during maintenance

### Cardiovascular Effects

- Mild bradycardia and increase in BP
  - No treatment typically required
- CO decreased by 25-40%
  - Largely due to decreases in heart rate
  - Contractility typically increases
  - Supply-demand balance for O2 usually maintained or improved
- Peripheral vasoconstriction
  - Obtain good vascular access prior to cooling

### Prevent Shivering:

- Caution with maintenance dosing of sedatives and NMBA’s, as clearance decreases with hypothermia
- Lower doses needed in elderly due to blunted counter-regulatory response
### Cardiovascular Effects

- **“Cold diuresis”**
  - Due to vasoconstriction-induced shift of intravascular volume into central circulation
  - Can result in hypovolemia, particularly during induction phase
- Significant risk for severe arrhythmias occurs at temps below 28-30°C
  - Arrhythmias low risk until temp drops below 30°C
    - A-fib, then V-fib
    - Myocardium less responsive to treatment of defibrillation

### EKG Changes

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<td><img src="image1.png" alt="EKG Image" /></td>
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### Electrolyte Disorders

- Changes to cellular homeostasis
  - Related to dysfunction of electrolyte pumps causing intracellular shifts
  - Risk greatest in induction phase
- $\downarrow K^+$, $\downarrow Mg^+$, $\downarrow Ca^{2+}$
- $\downarrow$ Insulin sensitivity and production
- Careful monitoring

### Other Issues

- Bedsores
  - Prolonged exposure to ice packs and peripheral vasoconstriction increases risk
- Nutrition
  - Enteral feeding should be decreased or stopped

### Ventilatory Derangements

- Hypothermia affects ABG analysis
  - ABG machines warm sample to 37°C
  - Overestimates PaO2 and PaCO2
  - Underestimates pH
- Important to examine temperature-corrected values to avoid hypoxemia or significant alkalosis

### Rewarming

- Rewarming phase – slow $0.25^\circ C \; h^{-1}$
  - Deranged cerebrovascular reactivity if $> 37^\circ C$
- Concerns
  - Vasodilation
  - Rebound electrolytes
  - Cardiac arrhythmias
Inducing Hospitals to Give Hypothermia

Therapeutic Hypothermia Web Resources

Protocol is Essential

Local Expertise Helpful

- Physician who can provide phone or in person consultation to teach.
- Nurse with similar expertise is also desirable.
- After treating 2 patients, staff uniformly is impressed.
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<th>Therapeutic Hypothermia: Summary</th>
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<tbody>
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<td>• Mild hypothermia for VF OHCA supported by 2 RCTs</td>
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<td>• Lower level evidence for other groups</td>
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<td>• Target temp, cooling rate, duration??</td>
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<td>• Surface versus internal</td>
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<td>• Implementation has been slow</td>
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