Therapeutic Hypothermia

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Nothing to disclose

Overview

- Hypothermia as a neuroprotectant
- Proven indications:
  - Adult out-of-hospital cardiac arrest
  - Pediatric hypoxic ischemic encephalopathy
- Other indications:
  - Traumatic brain injury, Spinal cord injury
- Practical issues: Induction, rewarming, shivering control

Mechanisms for neuroprotection

- Energy depletion
- Disruption of the blood-brain barrier
- Free radical formation
- Excitotoxicity
- Inflammation

Olsen et al Lancet Neurol 2003

Post-arrest global cerebral ischemia

Treatment:
- Old way
  - Wait 3 days and prognosticate
  - “Levy criteria” JAMA, 1985
- New way
  - Mild hypothermia (neuroprotection)

“Save the hearts and brains of those too young to die.”
Peter Safar

The New England Journal of Medicine

Hypothermia – clinical trials

- European study – NEJM 2002; 346:549-56
  - V fib arrest; still comatose after resuscitation
  - 24 hours of external cooling (special mattress) – 33° C
  - 6-month outcome (NNT=number needed to treat=6)
    - Hypothermia 55%
    - Normothermia 39% (OR 1.4 (1.08-1.81))
- Australian study – NEJM 2002; 346:557-63
  - V fib arrest; still comatose after resuscitation – 12 hours of surface cooling; often started prehospital
  - Outcome at hospital discharge (NNT=4)
    - Hypothermia 49%
    - Normothermia 26% (P=0.046)

American Heart Association Guidelines

Cardiopulmonary Resuscitation and Emergency Cardiovascular Care

- Unconscious adult patients with return of spontaneous circulation after out-of-hospital cardiac arrest should be cooled to 32°C to 34°C (89.6°F to 93.2°F) for 12 to 24 hours when the initial rhythm was ventricular fibrillation (Class IIa).
- Similar therapy may be beneficial for patients with non-VF arrest out of hospital or for in-hospital arrest (Class IIb).

Circulation 2010

Lost in Translation?


Current opinion

- Barriers
  - Better data needed
  - Lack of awareness
  - Poor prognosis
  - Implementation
  - MD, RN cooperation
  - Technically difficult
- Benefits
  - Unselected population benefits similar to trial subjects
  - Improved neurological outcomes (50-60%)
  - Decreased mortality


Breakdown of multidisciplinary system, with patient caught in the middle. Everyone is responsible.

Controversies

- Meta-analyses with differing interpretations
- Optimal cooling method
- Duration and onset (therapeutic window)
- In-hospital and non-VF arrest
- Rewarming rate
- Fever control
- Children
- Targeted temperature trial needed?
- Intra-arrest cooling?
- With PCI, bypass?
- RINSE trial pre-hospital
- Cold-PACK Post Arrest Cooling in Kids study

Sunde K and Soreide E. Curr Op Crit Care 2011
Abidi et al. Anesth Analg 2010
Nielsen et al. Anesth Analg 2010
Pediatric hypoxic ischemic encephalopathy

- Infants with moderate or severe hypoxic-ischemic encephalopathy could benefit from therapeutic hypothermia.
- Several clinical trials and prospective observational studies reported improvement in neurological outcomes or were inconclusive.
- A systematic review published by the Cochrane Library in 2007 concluded that 72 hours of moderate hypothermia started within 6 hours of birth reduces the rate of death and disability at 18 months of age.

Other indications

- Peri-operative vascular neurosurgery
- Traumatic brain injury
- Spinal cord injury

Traumatic brain injury

- Use of hypothermia in TBI remains controversial.
- Strong pre-clinical data to support reduction in neurological damage and improved outcomes.
- Multicenter trials showed no improvement in both adults and children with TBI.
- Meta-analyses did show favorable outcome in adults.
Interpretation of studies difficult due to:

- Wrap garments
- Initiate VAP bundle
- Continuous EEG
- Interpretation

Learning from the Hypothermia TBI trials

- Speed of induction of hypothermia--animal studies show better outcomes when cooling is initiated rapidly
- Duration of cooling--this is dependent on the severity of injury and time taken to reach target temperature
- Speed of re-warming--should be slow to prevent any secondary injury, i.e. exacerbation of intracranial pressure
- Proper management and prevention of side effects
- Ongoing European trial - www.eurotherm3235trial.eu

Hypothermia for Spinal Cord Injury

- Clinical trials with SCI were begun in the 1960s
- Local cooling feasible for acute SCI with surgical decompression and exposure of the spinal cord
- Interpretation of studies difficult due to:
  - Limited number of patients
  - Lack of randomized control groups
  - Concomitant interventions, e.g. spinal cord decompression
  - Concomitant use of steroids (methylprednisone)

Spinal Cord Injury - Need for a trial?

- No clinical guidelines or protocols establishing efficacy for the use of therapeutic hypothermia after human spinal cord injury
- Modest hypothermia treatment in SCI patients has been used with some success, but remains experimental
- Hypothermia is not currently standard practice
- Ongoing trials of hypothermia for SCI started

Practical issues for cooling

- Many methods
  - Surface blankets
  - Cold saline
  - Wrap garments
  - Endovascular
- You need a protocol and it can be simple
  - Initiate IV bolus of chilled saline (30-40 ml/kg (4ºC) isotonic fluids)
  - Place ice packs under the armpits, next to the neck, on the torso and the limbs.
- Two cooling blankets should be used, one under and one over the patient. Alternatively, may use vest/thigh wrap around surface cooling device if available.

Hypothermia induction monitoring

- Neurological assessment (Glasgow Coma Score):
  - Level of consciousness
  - Pupils and cranial nerves
  - Motor function
- Head of bed at 30 degrees
- Head CT
- Monitor for seizures
  - Continuous EEG
- Vital signs:
  - GCS-min, GCS-48, HR/Min, HR/Beat
  - Arterial line for BP monitoring
  - MAP + I & O monitoring
- Core Temp:
  - Esophageal
  - Axillary
- Respiration
  - ABG, O2 sat, PEEP
- Glucose
  - O2 set点 of oxygen
  - Initiate VAP bundle
  - CAB
  - Mouth care
  - Antibiotics if indicated
  - GI prophylaxis
  - Volume status
  - Electrolytes
  - Glucose control

Cochrane Relative benefit (95% confidence interval [CI]) on neurological outcome (Glasgow Outcome Scale [GOS] 4 or 5) for hypothermia therapy versus normothermia in trials of adults with traumatic brain injury.
Shivering

- Shivering can be harmful to the patient
- Predictors of shivering
  - Male gender
  - Low magnesium level
  - Altered hypothalamic set point (can be associated with severity of injury)
- Activates autonomic response:
  - Cardiovascular/sympathetic stress
  - Systemic metabolic stress
- Increases BP; HR; RR; ICP
- Hinders the cooling process
- Painful and uncomfortable

Rewarming

- Begin rewarming 24 hours after the beginning of cooling (not 24 hours after target temperature is reached)
- Patient should be slowly rewarmed to 37.0°C over 18-24 hours:
  - Allow slow passive rewarming.
  - If cooling catheter or surface/feedback device is in place, then use console to control rewarming (0.2°C/hr).
- Turn room thermostat up to normal.
- Turn off cooling blanket.
- May use regular blankets, but not warming blankets.

Rewarming management

- Monitor for post-resuscitation syndrome
  - Increased cytokine activation
- Controlled rewarming avoids hemodynamic fluctuations
- Cerebral edema
  - Increased ICP/low CPP
- Hypotension
- Vasodilation
- Electrolyte shifts
- Glucose levels

Conclusions

- Therapeutic hypothermia is an effective neuroprotectant
- Best benefit reported in global ischemia from out-of-hospital Vfib cardiac arrest and in newborn hypoxic ischemic encephalopathy
- Implementation of hypothermia post-arrest has improved in Europe, yet many barriers still exist in North America
- Need leaders to champion the cause and implement protocols and teams
- Majority of evidence is from observational studies; need for clinical trial level data for other indications
- Future challenge is to incorporate emerging evidence and new technologies to improve our understanding and refine current management strategies