Endovascular Selective Cerebral Hypothermia — First-in-Human Experience

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Introduction

Major limitations in acute ischemic stroke (AIS) therapies
• Time limitation for lytics excludes most patients
• Mech revascularization limited by small number of trained physicians
• Recanalization limited by reperfusion injury* — need neuroprotection

Therapeutic hypothermia (TH) — the most potent neuroprotectant in the laboratory
• Influences a variety of cell death mechanisms — “combinational protective strategy”

BUT, a failed therapy in AIS

Failures due to cooling techniques employed


Review of Literature — Stroke

“The efficacy of postischemic hypothermia is critically dependent on the duration and depth of hypothermia…”


“Efficacy was highest with cooling to lower temperatures (≤31 °C)…”

H Van der Worp, et al. Brain 2007; 130:3063-3074
Current Cooling Techniques

Total body cooling: Surface cooling and intravenous heat exchange

- Cool body
- Cooled blood flows to the brain
- Cool brain

Current Cooling Techniques

- Slow, unpredictable
- Detrimental systemic effects
  - Pharmacologic paralysis required to suppress shivering
  - Pulmonary infection
  - Electrolyte imbalance
  - Cardiac dysfunction – arrhythmias, arrest
- Limited to ≥32°C

TwinFlo Catheter — Novel endovascular selective cerebral hypothermia device and technique

- Proprietary perfusion catheter
  - Isolates, selectively perfuses CA
  - Single femoral insertion
- Used with std. extracorporeal circuit
1. Central aorta.
2. Warm blood removed, cooled blood returned.
3. Carotid artery perfusion.

Counter-current flow provides insulation.

TwinFlo Catheter — Novel endovascular selective cerebral hypothermia device and technique

In addition to providing hypothermia, the design allows selective delivery of drugs (e.g., lytics, Mg) and other devices (e.g., stent-retrievers and microcatheters), as well as control of perfusion pressure; recanalization be done in a cooled, protected brain to avoid reperfusion injury.
In Vivo Pig Studies
- Demonstrated cerebral cooling rates up to 2°C/min
- Brain temperatures as low 15°C
- Minimal systemic cooling
- No adverse events
- Normal heart rhythm, systemic arterial blood pressure, arterial blood values
- No rebound hyperthermia with passive rewarming

Porcine stroke model*
- 3 hours of ischemia followed by 3 hours of reperfusion
  - Pigs randomized to selective cooling or normothermia during reperfusion period. Analysis blinded.
- Blood pressure, heart rate, hemoglobin, glucose, and oxygenation levels did not differ between normothermic and hypothermic cohorts
- Statistically significant reduction in stroke volume by selective cooling with TwinFlo to mean 28°C for 1-3 hrs

Initial Human Experience (1)
Neurosurgical repair of giant aneurysm of MCA in a 59 year-old male; 2-hr occlusion time
- London (Canada) Health Sciences Center
- TwinFlo selectively cooled brain at 26°C with systemic normothermia (≥ 36.9°C)
- Full, rapid recovery with no neurological deficit
- Patient discharged home 4 days post-op
Initial Human Experience (2)

- Cardiac arrest, non-shockable PVT in a 38 year-old male; no flow >8 minutes*
  - No response after 44 min of CPR and 10 hours of 33°C ECMO, so TwinFlo tried as last resort
  - TwinFlo selectively cooled brain at 27°C nasal temperature (brain temp. estimated at ~22°C) for 12 hours
  - Full recovery with no neurological deficit, and patient back at work (urologist) after 2 months


Conclusion

This new endovascular system and technique may offer an improved method for neuroprotection in cardiac arrest, acute stroke and other conditions producing cerebral ischemia.
Conclusion: “The beneficial effect of mild therapeutic hypothermia increases with cumulative time of complete circulatory standstill in patients with witnessed out-of-hospital cardiac arrest.”

No difference in outcome when ‘no-flow’ time was ≤ 2 min.

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<tr>
<th>Hypothermia (°C)</th>
<th>Core Temp (°C)</th>
<th>No-Flow (min)</th>
<th>Heart Rate (bpm)</th>
<th>Ventilation</th>
<th>Systolic BP (mmHg)</th>
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Figure 1. Body temperature during the intervention period.