UniversitätsKlinikum Heidelberg

HAiS-SE

Hypothermia in Acute Ischemic Stroke: Surface versus Endovascular cooling

S. Poli[1], H. Amiri[1], A. Rocco[1], J. Diedler[1], M. Sykora[1], J. Bösel[1], E. Popp[2], P. Ringleb[1], W. Hacke[1], T. Steiner[1]
[1]Dept. of Neurology, Heidelberg University, [2]Dept. of Anesthesiology, Heidelberg University

Background: Mild therapeutic hypothermia improves clinical outcome in patients with global cerebral ischemia after cardiac arrest.[1] Via animal models hypothermia has been identified as the most promising neuroprotective therapy in focal cerebral ischemia as well.[2]

But the prove of clinical benefit in patients with acute ischemic stroke is still missing: Most likely due to the prolonged time window until hypothermia-induction (14h) in previous studies.[3]

In addition, practicability of the method through which hypothermia is applied is crucial for a broad implementation of hypothermia in stroke therapy. Feasibility, tolerability and safety of surface versus endovascular cooling have never been studied in a prospective controlled trial in awake stroke patients.

Our question is: Is surface cooling equally effective but safer than endovascular cooling?

Methods:

Study design: Prospective, controlled, randomized trial: Comparison of feasibility, tolerability and safety of surface cooling (CSZ Blanketrol III) versus endovascular cooling (Zoll Thermogard XP) versus standard stroke treatment (ESO guidelines).

Inclusion criteria: Acute ischemic stroke, intravenous rt-PA within 3h after symptom onset, age 18-80, NIHSS 2-20, item 1a on NIHSS ≤ 1, written informed consent.

Main exclusion criteria: Contraindications to hypothermia, e.g. vasospastic disorders or coagulopathies; medical conditions likely to complicate therapy, e.g. uncompensated arrhythmia, heart failure NYHA III/IV, severe liver or renal insufficiency.

Primary endpoint: Time to 35°C body core temperature after hypothermia-induction.

Primary safety endpoint: Number of (severe) adverse events ≥ 35°C .

Hypothermia-induction (cold infusions) starts simultaneously with rt-PA. Surface cooling starts as soon as possible, catheter placement for endovascular cooling is performed 30min after the end of rt-PA-infusion. The intended body core temperature is 34°C. Hypothermia will be maintained for 12h, 18h or 24h depending on detectable vessel occlusion (CTA or TCD) at 0h, 6h or 12h, followed by controlled re-warming (0,2°C/h).

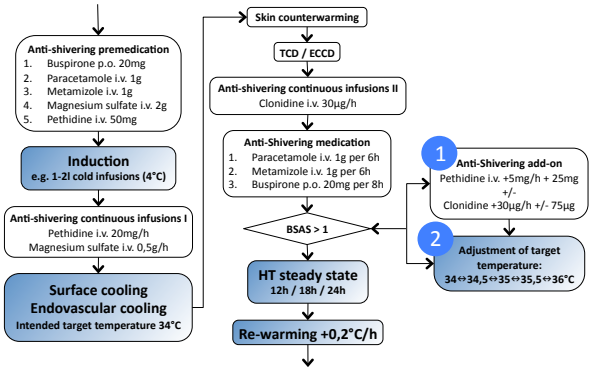

Fig 1.: Hypothermia treatment flowchart, BSAS: Bedside Shivering Assessment Scale[8]

Discussion:

Time window: Strong animal data only for treatment delays < 3h, probable greater effect with shorter delay.[2,4]

Target temperature: Significant depth-response relationship, but rising side-effects. Substantial reduction in infarct volume still observed with cooling to 35°C.[2]

Duration: In models of temporary ischemia, the effect of cooling was largest if continued during both ischemia and reperfusion.[2] But higher incidence of side-effects with longer duration.[5]

Benefit-risk: Benefit: Possible neuroprotection. Risk: Higher incidence of infections, bleeding complications, co-medication associated side-effects.

Cold infusions: Benefit: Fast and easily applicable method for hypothermia-induction. Risk: Volume overload.

Surface cooling: Benefit: Non-invasive. Risk: More shivering?[6] Lower cooling rate?[5,7]

Endovascular cooling: Benefit: Less shivering?[6] Higher cooling rate?, Risk: Invasive.[5,7]

Trial status:

Start of recruiting: March 2010. Until now 4 patients have been included, see Table.

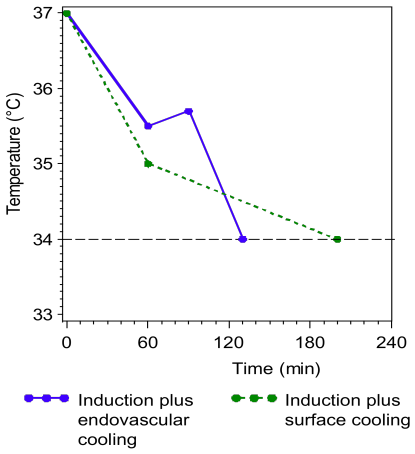

Fig 2.: Assumed cooling rates of surface and endovascular cooling

[1]Arrich, J., et al., Cochrane Database Syst Rev, 2009
[2]van der Worp, H. B., et al., Brain, 2007
[3]den Hertog, H. M., et al., Cochrane Database Syst Rev, 2009
[4]Lees, K. R., et al., Lancet, 2010
[5]Poldermann, K. H., Crit Care Med, 2009
[6]Frank, S. M., et al., J Appl Physiol, 1999
[7]Hoedemaekers, C. W., et al., Critical care, 2007
[8]Badjatia, N., et al., Stroke, 2008