
ICU Volume 7 - Issue 3 - Autumn 2007 - Special Focus on Hypothermia

Hypothermia in Acute Ischaemic Stroke

Author

Gene Sung, M.D., M.P.H.

Director: Neurocritical Care and Stroke Division,

University of Southern California

Los Angeles, California, US

gsung@usc.edu

The use of hypothermia has been an area of interest for scientists for many decades. Scientific rationale seemed obvious, cold temperatures stopped many of the destructive processes of cell injury and death. Observations of the mammalian diving reflex in humans, with often, full recovery of victims submerged in freezing water for extended periods of time, was certainly one of the many scenarios that have stimulated this research. There has been investigation in all areas of acute neurological injury, including stroke, brain and spine trauma, post-cardiac arrest and even in multiple sclerosis exacerbation.

Two highly studied randomised clinical studies, one from Australia and the other from Europe, involve patients treated after cardiac arrest. The hypothermia protocol in the Australian study (Bernard et al. 2002) began immediate cooling in the ambulance of comatose patients randomly assigned to the hypothermia arm after return of spontaneous circulation from ventricular fibrillation arrest. The temperature goal was 33°C for 18 hours. Of the hypothermia assigned patients, 49% had a good outcome, compared to 26% of those in the normothermia group.

In the European study, there was a similar random selection of arrest patients and early cooling, but with a target temperature of 32° to 34°C, with maintenance for 24 hours. Here again, a statistically significant better outcome was seen, 55% in the hypothermia group versus 39% in the normothermia group.

The largest randomised study to date in traumatic brain injury did not find a significant benefit in outcome or mortality (Clifton et al. 2001). However, the hypothermia group did have lower intracranial pressure readings and there was a benefit seen in the subgroup that was younger than 45 years of age and arrived at hospital already hypothermic.

Unfortunately, the evidence in for hypothermia in the treatment of acute ischaemic stroke is incomplete. There are animal studies that show, in very controlled settings, infarct size is minimised and functional outcome is improved with hypothermia. In a meta-analysis of the literature, 101 publications were reviewed reporting on 3353 animals treated (Van Der Worp et al. 2007). Overall, infarct size was reduced by 44% and neurobehavioral scores were improved by 46%.

Studies in humans have been limited to small studies, often non-randomised. Examples are the COOL-AID (Cooling for Acute Ischaemic Brain Damage) studies. In the first, 10 patients were treated with an external cooling blanket to reach a goal temperature of 32°C and in the second, forty patients were treated within 12 hours of symptom onset using an endovascular cooling device (Fig.1) for a goal temperature of 33°C (Krieger et al. 2001). The range of times after symptom onset that hypothermia was initiated averaged 6 hours and the duration ranged from 23.5 to 96 hours in the first study. In the latter study, the range of times averaged 9 hours and the duration goal was 24 hours (De Georgia et al. 2004). These studies showed that it was feasible and safe to cool acute ischaemic stroke patients, though they were too small to demonstrate any definitive benefit.

The Intravascular Cooling in the Treatment of Stroke-Longer tPA Window (ICTuS-L) study is currently under way and is testing the combination of intravenous tissue plasminogen activator (tPA) and hypothermia. ICTuS-L is a phase I safety study and is building on the initial ICT-uS study (Lyden et al. 2005) which examined the feasibility and safety of an endovascular cooling device in awake acute ischaemic stroke patients.

In another study done in Copenhagen, 17 patients were treated using a cool air blanket and body temperature decreased on average from 36.8°C to 35.5°C (Kammersgaard et al. 2000). This led to a multi-centre randomised trial called the Nordic Cooling Stroke Study, which was unfortunately terminated because of slow recruitment. A multi-centre study that the author has organised, (CHILI) Controlled Hypothermia in Large

© For personal and private use only. Reproduction must be permitted by the copyright holder. Email to copyright@mindbyte.eu.

Infarction) has a temperature goal of 35°C for 48 hours in subjects with large hemispheric strokes prior to significant mass effect and controlled re-warming over 72 hours using a super-conductive gel pad cooling device (Fig. 2).

While the majority of investigators believe that hypothermia, as a concept should work in the treatment of acute ischaemic stroke, proving it has been difficult. None of the parameters integral to hypothermia have been definitively determined. The timing after stroke onset, the speed of induction, the best temperature, the duration of hypothermia, nor the delivery of hypothermia.

Certainly, hypothermia can lead to medical complications. The potential complications are almost unlimited, with the effects of hypothermia stopping harmful cellular injury processes, but also blunting useful processes such as the immune response. Complications noted included pneumonia, sepsis, hypotension, bradycardia, arrhythmias and coagulopathies. Another direct response to hypothermia is shivering, which is the body's attempt to combat the abnormally cool temperature and must be controlled.

A novel device that is being examined in an attempt to limit cooling to the brain and perhaps avoid some of the complications of systemic hypothermia is the BeneChill device (Fig. 3). This device uses the nasal cavity for heat transfer, taking advantage of its highly vascularised environment and its proximity to the brain. An inert cooling agent is delivered directly to the nasal cavity and circulates in gaseous form. A study is underway examining its cooling capabilities to the brain.

Hypothermia in acute ischaemic stroke is an extremely promising treatment undergoing continued investigation to find the best therapeutic parameters and delivery methods for the best results.

Published on : Thu, 15 Aug 2013