Commentary

New indications for the use of therapeutic hypothermia

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Related to *Research* by Hartemink *et al*., see Issue 8.5, page 395

Abstract

Randomised, controlled trials of therapeutic hypothermia have demonstrated improved outcomes after out-of-hospital cardiac arrest, where the initial cardiac rhythm was ventricular fibrillation. This therapy is now endorsed by the International Liaison Committee on Resuscitation. The role of therapeutic hypothermia in patients with anoxic neurological injury due to stroke, spinal cord injury or asphyxial cardiac arrest is uncertain. However, given the strong theoretical benefit and the minimal adverse side-effects, it is reasonable for clinicians to consider the use of therapeutic hypothermia in such cases.

Keywords cerebral, hypothermia, induced, injury, spinal

During the 1950s therapeutic hypothermia (TH) became widely used for neurological protection during cardiac surgery, and there were numerous anecdotal reports of the use of TH in the treatment of neurological injury following head injury, stroke and anoxic brain injury [1]. For reasons that are unclear, there were few reports of the use of TH between 1960 and 1992 [2]. Interestingly, at the same time that intensive care units were developing, the use of TH was becoming rare. Presumably, intensive care physicians became sceptical that the unproven benefit of TH was outweighed by the possibility of adverse effects with this treatment.

In 1991, in a pivotal study conducted in a dog model, Stertz and coworkers [3] demonstrated that mild TH applied immediately after resuscitation from prolonged cardiac arrest significantly improved outcomes. These findings were confirmed in numerous other animal studies [2]. Given the poor prognosis with standard treatment of anoxic brain injury after prolonged out-of-hospital cardiac arrest in adults, it seemed reasonable to undertake clinical trials of TH in this condition. However, at that time, most intensive care physicians regarded hypothermia as quite hazardous, leading inevitably to cardiac arrhythmias, sepsis, coagulopathy and electrolyte abnormalities. Therefore, few centres appeared to be interested in this novel treatment.

In contrast, our intensive care unit was using TH in selected patients with severe traumatic brain injury, and we found this treatment to be associated with minimal adverse effects [4]. Largely because of this experience, our ethics committee approved preliminary clinical studies of TH in adults who were comatose after resuscitation from out-of-hospital cardiac arrest. Subsequently, we cooled 22 patients to 33°C for 12 hours and compared their outcomes with those of the previous 22 cardiac arrest patients who had been maintained at normothermia [5]. Our results were sufficiently supportive that we proceeded to conduct a randomized, controlled trial. Both our study [6] and a European study [7] found that TH improved outcomes after out-of-hospital cardiac arrest, where the initial cardiac rhythm was ventricular fibrillation. In 2003, the International Liaison Committee on Resuscitation [8] recommended treatment with TH in such patients.

Should TH be used in patients with neurological injury outside this indication? In a recent issue of *Critical Care*, Hartemink and coworkers [9] described three case reports in which TH was used as part of the treatment for unusual neurological injuries, including focal brain injury due to vascular disruption, spinal cord injury and global anoxic injury following asphyxial cardiac arrest. In these conditions, any

TH = therapeutic hypothermia.

benefit from TH is unproven. Is it therefore reasonable to use TH in such patients outside the context of a clinical trial?

To answer this question, both the theoretical benefits and possible adverse effects of TH must be carefully considered. Clearly, there are considerable theoretical benefits from TH in the three conditions described. In particular, laboratory data for the use of TH in stroke, spinal cord injury and asphyxial cardiac arrest is very supportive of benefit of TH in animal models of these injuries [10,11].

Fortunately, there is now also extensive clinical data that suggest that TH carries a very low risk for adverse side effects in adults in a modern intensive care unit. For example, in our studies of patients with severe head injury and anoxic brain injury after out-of-hospital cardiac arrest, we have rarely seen complications such as cardiac arrhythmias, sepsis or coagulopathy [4,5,12]. In addition, there are minimal logistic and cost issues.

Finally, it is highly unlikely that randomized controlled trials could be conducted in patients with the types of injuries described in the report by Hartemink and coworkers [9]. Such injuries in any one city are very rare, and controlled trials would need to enrol large numbers of patients to have sufficient power to demonstrate benefit.

Therefore, given that there is a sound scientific basis and likelihood of benefit, a proven low incidence of adverse events and a high morbidity or mortality rate with the injury, the use of TH seems well justified in the types of cases presented. Intensive care physicians are therefore encouraged to consider the use of TH in similar cases in the future.

Competing interests

The author(s) declare that they have no competing interests.

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