Should we be cooling patients after out of hospital cardiac arrest?

The incidence of out-of-hospital cardiac arrest is 0.05–0.19% per year (Arrich et al, 2012). Guidelines exist for management of these patients during cardiac arrest, but post-arrest management following return of spontaneous circulation is more controversial. Therapeutic hypothermia involves cooling the resuscitated patient to 32–34°C for 24–36 hours, although the exact temperature and the best method of cooling is unclear. Therapeutic hypothermia is believed to work by multiple mechanisms to reduce cerebral damage, but discussion of these mechanisms is beyond the scope of this article.

National Institute for Health and Care Excellence (NICE) (2011) guidance suggests that therapeutic hypothermia is indicated following cardiac arrest (including out-of-hospital cardiac arrest), stating: 'Current evidence on the safety and efficacy of therapeutic hypothermia following cardiac arrest is adequate to support the use of this procedure...'. The guidance was issued for cardiac arrest following ventricular fibrillation arrest with ongoing reduction in conscious state, not all forms of cardiac arrest. However, subsequent studies raise the question: should patients be cooled at all?

The case for therapeutic hypothermia

Wang et al (2012) studied 175 patients who had return of spontaneous circulation following out-of-hospital cardiac arrest – 51 received therapeutic hypothermia and 124 did not. Good neurological outcome was the primary outcome measured, defined as a cerebral performance category 1 or 2. The authors found that 7.9% of the therapeutic hypothermia group had good neurological outcome *vs* 1.7% of patients who did not receive therapeutic hypothermia ($P<0.05$). However, the study was small and only just achieved significance.

Hörburger et al (2012) conducted a retrospective chart review on 632 patients who had suffered out-of-hospital cardiac arrest, comparing cerebral performance category and 180-day mortality. Patients whose baseline temperatures exceeded 37.5°C were excluded. Patients in the therapeutic hypothermia group were significantly more likely to survive to 180 days with a good neurological outcome (cerebral performance category of 1 or 2).

NICE (2011) guidelines on therapeutic hypothermia considered a systematic review of 481 patients and two randomized controlled trials to assess the efficacy of therapeutic hypothermia, all of which found significantly better neurological outcomes in the therapeutic hypothermia groups.

Most recently, the Cochrane Anaesthesia Group published a review of therapeutic hypothermia after cardiopulmonary arrest (Arrich et al, 2012). This found moderate grade evidence in favour of therapeutic hypothermia in survival to discharge (relative risk reduction 1.35, range 1.1–1.65) and neurological outcome (relative risk reduction 1.55, range 1.22–1.96) defined as cerebral performance category 1–2.

The case against therapeutic hypothermia

Rebound hyperthermia is a side effect of therapeutic hypothermia which is believed to worsen neurological outcome and survival. Winters et al (2013) retrospectively analysed 141 patients who had undergone therapeutic hypothermia: 40.3% of patients without rebound hyperthermia died during admission *vs* 60.4% of patients who developed rebound hyperthermia (odds ratio 2.66, 95% confidence interval = 1.26–5.61, $P=0.011$). Neurological outcome was significantly worse in patients who developed rebound hyperthermia ($P=0.01$). The study did not have a control group.

Patients undergoing therapeutic hypothermia are cooled to 32–34°C. Nielsen et al (2013) randomly assigned 950 adults who were unconscious following return of spontaneous circulation after out-of-hospital cardiac arrest to be cooled at either 33°C or 36°C. This is the largest, most robust and only truly randomized trial comparing therapeutic hypothermia with standard best care and found no significant benefit to cooling to 33°C compared to 36°C.

Conclusions

Historically, it has appeared that therapeutic hypothermia following out-of-hospital cardiac arrest confers benefit and most guidelines reflect this, but the risk of rebound hypothermia must be considered. Large, randomized and well-conducted studies are needed to decide whether patients should be cooled or not. Before these take place, the authors believe that NICE should consider revising their guidelines on therapeutic hypothermia. **BJHM**

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