EUROPEAN RESUSCITATION COUNCIL

Clinical paper

Efficacy of different cooling technologies for therapeutic temperature management: A prospective intervention study ☆

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ARTICLE INFO

ABSTRACT

Background: Mild therapeutic hypothermia (32–36 °C) is associated with improved outcomes in patients with brain injury after cardiac arrest (CA). Various devices are available to induce and maintain hypothermia, but few studies have compared the performance of these devices. We performed a prospective study to compare four frequently used cooling systems in inducing and maintaining hypothermia followed by controlled rewarming.

Methods: We performed a prospective multi-centered study in ten ICU's in three hospitals within the UPMC health system. Four different cooling technologies (seven cooling methods in total) were studied: two external water-circulating cooling blankets (Meditherm® and Blanketrol®), gel-coated adhesive cooling pads (Arctic Sun®), and endovascular cooling catheters with balloons circulating ice-cold saline (Thermogard®). For the latter system we studied three different types of catheter with two, three or four water-circulating balloons, respectively. In contrast to previous studies, we not only studied the cooling rate (i.e., time to target temperature) in the induction phase, but also the percentage of the time during the maintenance phase that temperature was on target ±0.5 °C, and the efficacy of devices to control rewarming. We believe that these are more important indicators of device performance than induction speed alone.

Results: 129 consecutive patients admitted after CA and treated with hypothermia were screened, and 120 were enrolled in the study. Two researchers dedicated fulltime to this study monitored TH treatment in all patients, including antishivering measures, additional cooling measures used (e.g. icepacks and cold fluid infusion), and all other issues related to temperature management. Baseline characteristics were similar for all groups. Cooling rates were 2.06 ± 1.12 °C/h for endovascular cooling, 1.49 ± 0.82 for Arctic sun, 0.61 ± 0.36 for Meditherm and 1.22 ± 1.12 for Blanketrol. Time within target range ±0.5 °C was 97.3 ± 6.0% for Thermogard, 81.8 ± 25.2% for Arctic Sun, 57.4 ± 29.3% for Meditherm, and 64.5 ± 20.1% for Blanketrol. The following differences were significant: Thermogard vs. Meditherm (p < 0.01), Thermogard vs. Blanketrol (p < 0.01), and Arctic Sun vs. Meditherm (p < 0.02). No major complications occurred with any device.

Conclusions: Endovascular cooling and gel-adhesive pads provide more rapid hypothermia induction and more effective temperature maintenance compared to water-circulating cooling blankets. This applied to induction speed, but (more importantly) also to time within target range during maintenance.

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Introduction

Therapeutic cooling is associated with improved recovery from post-hypoxic brain injuries in neonatal asphyxia and cardiac arrest (CA), and possibly other types of hypoxic injury [1].

Table 1
Brief description of cooling devices.

Cooling device	Cooling method	Manufacturer
Arctic Sun™	Hydrogel-coated water-circulating adhesive pads	Bard medical, Denver, Colorado, United States.
Medi-Therm II and III™	Disposable water-circulating blankets	Stryker/Gaymar, Kalamazoo, Michigan, United States.
Blanketrol II & III™	Re-usable (Blanketrol II) or disposable water-circulating blankets	Genthecm/Cincinnatti Sub Zero, Cincinnati, Ohio, United States.
Thermogard™	Catheters with two, three or four balloons circulating ice-cold saline (closed system)	Asahi Kasei/Zoll medical corporation, San Jose, California, United States.

Optimal target temperature is currently a matter of debate. Initial trials (2 RCT's followed by 45 non-randomized studies) targeted 32–34 °C [3–6]. A subsequent large RCT found that cooling to 36 °C resulted in similar outcomes as 33 °C [7]. The findings of this study have been criticized for various reasons [5,8–12], and data from a recent study suggest that target temperatures of 36 °C may be more difficult to maintain [13]. The optimal target temperature continues to be "hotly" debated; however, there is general consensus on the importance of temperature management after CA [2]. Current guidelines from the American Heart Association and European Resuscitation Council recommend targeting a core temperature between 32 and 36 °C for 24 h, followed by strict fever management [2].

Regardless of target, there is a need for accurate core temperature control. Around 8 mechanical surface- and invasive cooling technologies are currently commercially available [14–15]. Data on the efficacy of these systems is limited. We therefore performed a prospective study to compare the four most frequently used cooling systems, listed and briefly described in Table 1.

Methods

Study population

The study was performed at in 3 Emergency Departments and 10 ICU's in three large hospitals in Pittsburgh, PA (Presbyterian-Montefiore, Mercy, and Shadyside hospital). Consecutive patients who remained comatose after OHCA or IHCA were screened for the study. The only exclusion criterion was a decision not to use TH, based on pre-existing conditions (e.g. terminal disease). All hospitals used the same protocol for treating post-CA patients, including 24-h cooling to 32 or 33 °C followed by slow rewarming. Patients with (high risk for) active bleeding were cooled to 35 °C; data for these patients were collected, but not included in the comparative analyses because hypovolemic shock can affect temperature. The University of Pittsburgh IRB approved the study and waived the need for informed consent because no changes were made in clinical treatment.

The target temperature was determined by the attending physician before screening; according to our protocol target temperature could be 32, 33 or 34 °C (35 °C if active bleeding was present). Choice of cooling method was random or based on availability of cooling devices, unless contraindications for specific cooling methods (e.g. recent history of deep venous thrombosis, skin disease) were present.

Cooling efficacy was measured as follows. In the *induction phase* the aim was to reduce core temperature to target as rapidly as possible; in the *maintenance phase,* to maintain temperature close to target for 24 h; and in the *re-warming* phase, to achieve slow and controlled re-warming (maximum 0.25 °C/h) [14–15].

Intervention

The cooling devices compared in this study were: Meditherm disposable water-circulating blankets (Stryker/Gaymar, Michigan, United States); Blanketrol water-circulating blankets (Gentherm/CSZ, Cincinnati, United States); Arctic Sun gel-coated adhesive pads (Bard Medical, Colorado, United States); and Coolgard/Thermogard endovascular cooling using catheters with two, three or four balloons (Zoll, Sunnyvale, United States). Details of these cooling technologies have been reported elsewhere [14–15], and our cooling protocol has been described previously [16–17]. Management included EEG monitoring, MAP target ≥80 mmHg, and target PaCO2 40–45 mmHg (alpha-stat blood gas management). Treatment in all ICU's was overseen by members of the post-cardiac arrest team, who are consulted on all CA patients [16–17]. If patients were enrolled in the trial, one of the investigators (PS, GJ or KP) would monitor the hypothermia treatment and shivering management, and collect all data pertinent to temperature management (temperature, clinical data, monitoring method, hemodynamic data, shivering, medications, accessory cooling methods, etc.).

Cold fluid infusion was permitted, and often used, during the induction phase; volumes and infusion speeds were recorded. Rewarming was done at a maximum speed of 0.25 °C/h, or slower at the discretion of the attending physician.

Primary outcomes were:

1. Speed of cooling to target;
2. Temperature fluctuations during maintenance, defined as percentage of time with temperature ≥0.5 °C above or below target. Fluctuations were divided into moderate (0.5 °C–1.0 °C) and severe (1.0 °C–1.5 °C) deviations from target. Temperature >1.5 °C out of range was regarded as absence of effective temperature control.
3. Too rapid re-warming, defined as time during which target re-warming speed was exceeded by 0.01–0.05 °C/h (moderate) or 0.06–0.1 °C/h (severe).

Failure to reach target within 12 h despite intensive shivering management was considered failure of the cooling device.

Secondary endpoints were:

1. 6-month survival with good neurologic outcome (Cerebral Performance Category 1 or 2).
2. Incidence of adverse events such as infections;
3. Any complications directly linked to cooling method (skin lesions, catheter-associated thrombosis, etc.).

Survival with good neurologic outcome (CPC 1–2) was assessed by phone (patients or family members were called). If we were unable to verify neurologic outcome this was recorded as CPC 5.

Shivering management

Shivering was managed aggressively according to protocol. Antishivering measures included skin counterwarming, infusion of magnesium, fentanyl, propofol and/or midazolam, and/or buspirone 15–60 mg by mouth. Short-term paralysis was used only as option of last resort for refractory shivering. Continuous paralysis was reserved for ARDS with persistent hypoxemia.