Prehospital Resuscitated Cardiac Arrest Patients: Role for Induced Hypothermia

Resource Paper for the NAEMSP Position Paper on Induced Therapeutic Hypothermia in Resuscitated Cardiac Arrest Patients

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Abstract

This article is a support paper for the National Association of EMS Physicians' position paper on induced therapeutic hypothermia in resuscitated cardiac arrest patients. Induced hypothermia is one of the newest treatments aimed at increasing the dismal neurologically intact survival rate for out-of-hospital cardiac arrest patients. Two landmark studies published in 2002 by the *New England Journal of Medicine* led to the American Heart Association (AHA) Guidelines for Cardiopulmonary Resuscitation and Emergency Cardiovascular Care IIa recommendation of cooling unconscious adult patients with return of spontaneous circulation after out-of-hospital cardiac arrest due to ventricular fibrillation to 32°C to 34°C for 12 to 24 hours. Despite many limitations of those studies, the AHA also suggests that this therapy may be beneficial for patients with non–ventricular fibrillation arrests. However, the literature is lacking in answers with regard to the best methods to utilize in cooling patients. While avoiding delay in the initiation of cooling seems logical, the literature is also lacking evidence indicating the ideal time at which to implement cooling. Furthermore, it remains unclear as to which patients may benefit from induced hypothermia. Finally, the literature provides no evidence to support mandating induced hypothermia in the prehospital setting. Given limited prehospital resources, sometimes consisting of only two providers, attention first needs to be given to providing the basic care with the utmost skill. Once the basics are being delivered expertly, consideration can be given to the use of prehospital cooling for the resuscitated cardiac arrest patient in the setting of continued cooling in the hospital.
Key words: induced hypothermia; hypothermia; cardiac arrest; emergency medical services

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Introduction

Survival rates from out-of-hospital cardiac arrest (OOHCA) are dismal.[1] Witnessed cardiac arrest, bystander cardiopulmonary resuscitation (CPR), rapid defibrillation, and minimally interrupted chest compressions[2] have all been associated with improved outcomes.[3] Despite these facts, overall survival is still poor and the search continues for interventions to improve outcomes. One such intervention that holds promise is the induction of hypothermia in the postresuscitation phase of care.

Background

Induced hypothermia protects the brain from postischemic injury. Hypothermia decreases brain metabolism by 6% for each 1 degree Celsius of cooling.[4,5] Additional benefit likely comes from a complex synergistic compilation of effects including decreasing intracranial pressure, decreasing excitatory amino acid levels, and decreasing lactate level, as well as yet-to-be-understood effects.[6,7]

History

Induced hypothermia was first used in the 1940s to treat cancer patients.[8] Case reports showed that the induction of hypothermia was feasible and safe, although its benefit was not established. During the 1950s, human case reports of induced hypothermia were published.[9,10] There was evidence to suggest that hypothermia benefited intact survival from cardiac arrest as well as being protective during cardiac surgery, and this work led to the induction of intraoperative hypothermia during cardiac surgery as a standard.[11] Its use in cardiac arrest, however, had seemed to have disappeared.

While most papers do not recognize a resurgence of interest until the 1980s, one individual, Dr. Robert White, was a firm believer in the benefit of induced hypothermia for cardiac arrest patients. He presented work in the 1960s evaluating methods to cool the brain.[12] More widespread research did not start again until the 1980s. Many animal studies have demonstrated the benefit of induced hypothermia in cardiac arrest models.[13–17] Several small human studies have been published as well,[18–21] but showed only statistically insignificant trends toward improved outcomes with hypothermia. It was not until 2002 that randomized controlled trial–level evidence supported the use of induced hypothermia in postresuscitative care for a small group of patients.[22,23]

CURRENT EVIDENCE

In 2002, two prospective trials were published in the *New England Journal of Medicine*.[20,21] The first study was a European multicenter randomized controlled trial that enrolled 275 subjects resuscitated from OOHCA between 1996 and 2001.[20] A total of 3,551 subjects were assessed for eligibility, but only 275 met the inclusion criteria. Some exclusion criteria included pregnancy, toxin-mediated cardiac arrest, hemodynamic instability, and advanced age. Enrolled subjects had witnessed cardiac arrests with an initial rhythm of ventricular fibrillation (VF) or pulseless ventricular tachycardia, with no more than 15 minutes of downtime before emergency medical services (EMS) care. All remained comatose with no significant hypotension or hypoxia after return of spontaneous circulation (ROSC). All subjects were sedated and paralyzed. Subjects were randomly assigned to standard normothermia or to 24 hours of therapeutic hypothermia induced with an external cooling mattress/blanket that delivered cold air augmented as needed with ice packs to maintain a temperature of 32°C to 34°C. Endpoints included blinded evaluation of six-month neurologic outcome, six-month mortality, and complications during the first seven days after resuscitation. Of those randomized to the hypothermia treatment, 55% had a favorable neurologic outcome (defined as a Pittsburgh cerebral performance category of 1 or 2) at six months, compared with 39% in the control group (risk ratio 1.40, 95% confidence interval [CI] 1.08–1.81). The death rate at six months was 41% for the hypothermia group, as compared with 55% (risk ratio 0.74, 95% CI 0.58–0.95). The complication rates did not differ significantly.

The second study encompassed four sites in Australia between 1996 and 1999.[21] Seventy-seven subjects were enrolled with similar inclusion criteria: initial rhythm of VF, persistent coma after ROSC, and age greater than 18 years. Cooling was assigned to subjects presenting on odd-numbered days and was initiated in the prehospital setting by removing clothing and applying cold packs. In the hospital, cooling was continued with ice packs until a patient's temperature reached 33°C and was maintained for 12 hours. Four subjects assigned to hypothermia did not receive this treatment. The primary outcome measure was survival to hospital discharge with good neurologic function as defined by discharge to home or a rehabilitation facility. Secondary outcomes included potential complications of hypothermia as identified by monitoring hemodynamic, biochemical, and hematologic effects. The initial study planned to enroll 62 subjects, but when these subjects were enrolled there was only "a strong trend toward improved outcome,"[21] so the study was continued for an additional 12 months. Forty-nine percent of those receiving hypothermia survived to discharge with good function, as compared with 26% in the control group (odds ratio 2.65, 95% CI 1.02–6.88; $p = 0.046$). There was no difference in the frequency of adverse events.

Based on these studies, the 2005 AHA Guidelines for Cardiopulmonary Resuscitation and Emergency Cardiovascular Care recommend that "Unconscious adult patients with ROSC after out-of-hospital cardiac arrest should be cooled to 32°C to 34°C (89.6°F to 93.2°F) for 12 to 24 hours when the initial rhythm was VF (Class IIa). Similar therapy may be beneficial for patients with non-VF arrest out of hospital or for in-hospital arrest (Class IIb)."[24] A few additional retrospective studies have provided further evidence demonstrating benefit from induced hypothermia after cardiac arrest from VF.[25,26] Others have demonstrated benefit from hypothermia in all-cause cardiac arrest[27] and those who are hemodynamically unstable.[28]

PREHOSPITAL CONSIDERATIONS

Emergency medical services will care for many cardiac arrest victims in the prehospital setting. It is here that improved resuscitative techniques may provide the most impact in improving outcomes.

Delay in the institution of hypothermia is a perceived limitation of these studies. Kuboyama et al. had shown that any benefit from induction of hypothermia was lost 15 minutes after cardiac arrest in his dog model.[29] Another animal study[30] suggest benefit from quick induction of hypothermia, but no human data exist. In fact, the 15 minutes referred to by Kuboyama et al.[29] has been refuted in the AHA guidelines[24] and in several studies,[16] including the two described in this paper.[20,21] Intuitively, the sooner therapeutic hypothermia is initiated, the better. Thus, prehospital induction should be considered; however, the ideal time frame has yet to be established.[31]

The best method to cool patients is unknown. Several studies have looked at cooling methods. Some methods by which to induce hypothermia include simple ice packs, infusion of cold intravenous fluids,[32–35] cooling blankets and mattresses,[18] a cooling helmet,[36] wet clothes,[24] ice-water-soaked towels,[37] a cooling catheter,[38] hemofiltration,[19] peritoneal lavage,[39] and cardiopulmonary bypass.[40] Obviously, any prehospital use would necessitate a method usable in the field by prehospital providers. Ice packs and the infusion of cold fluids have been shown to be feasible and to appropriately decrease patient temperature in the prehospital setting,[16,30] with the infusion of cold fluids showing much promise;[31,32] the ideal method is still unknown. Many patients are already mildly hypothermic after resuscitation.[41,42] It may be more realistic for EMS agencies to avoid postresuscitation rewarming rather than inducing hypothermia in the prehospital setting.

It is unclear as to which patients derive the most benefit from induced hypothermia. Victims of VF and pulseless ventricular tachycardia likely experience the most benefit. Data from 2003 suggest that others may benefit.[43] Characteristics of those most likely to benefit have not been defined.[44]

STANDARD OF CARE

Many argue and support the concept of induced hypothermia as a standard of care.[22,45] However, several surveys demonstrate that this therapy has yet to be widely accepted and implemented.[46–48] A survey of EMS medical directors indicates that current prehospital cooling is also infrequent.[49] Given that all evidence of benefit is for patients who are kept mildly hypothermic for at least 12–24 hours in the hospital and that early rewarming may be harmful, prehospital hypothermia should be initiated only in cooperation with a hospital program that will provide for continued in-hospital hypothermia treatment.

CONCLUSION

While there is excellent evidence that induced hypothermia in the postresuscitative period can increase neurologically intact survival in select patients who have had cardiac arrest from VF, many questions still need to be answered. There is evidence to suggest that the sooner cooling is initiated, the better, but no current evidence exists to support a mandate for cooling in the prehospital setting. Furthermore, while there are several methods of cooling that may be feasible in a prehospital setting, the best method remains unknown, as do the parameters regarding a target temperature. Given limited prehospital resources, sometimes consisting of only two providers, attention first needs to be given to providing the basic care with the utmost skill. Once the basics are being delivered expertly, consideration can be given to the use of prehospital cooling for the resuscitated cardiac arrest patient in the setting of continued cooling in the hospital.

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