Clinical Investigations

Induced Hypothermia Following Out-of-Hospital Cardiac Arrest; Initial Experience in a Community Hospital

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Summary

Background: Successful resuscitation from sudden cardiac death is frequently accompanied by severe and often fatal neurologic injury. Induced hypothermia (IH) may attenuate the neurologic damage observed in patients after cardiac arrest.

Hypothesis: This study examined a population of non-selected patients presenting to a community hospital following successful resuscitation of sudden cardiac death. We sought to determine whether a program of induced hypothermia would improve the clinical outcome of these critically ill patients.

Methods: We initiated a protocol of IH at the Oklahoma Heart Hospital in August of 2003. Study patients were consecutive adults admitted following successful resuscitation of out-of-hospital cardiac arrest. Moderate hypothermia was induced by surface cooling and maintained for 24 to 36 h in the Intensive Care Unit with passive rewarming over 8 h.

Results: Forty-nine patients who were resuscitated and had the return of spontaneous circulation completed the hypothermia protocol. The cause of cardiac arrest was acute myocardial infarction in 24 patients and cardiac arrhythmias in 19 patients. Nineteen patients (39%) survived and were discharged. Sixteen of the patients

discharged had no or minimal residual neurologic dysfunction and 3 patients had clinically significant residual neurologic injury.

Conclusion: A program of induced hypothermia based in a community hospital is feasible, practical, and requires limited additional financial and nursing resources. Survival and neurologic recovery compare favorably with clinical trial outcomes.

Key words: sudden cardiac death, induced hypothermia, myocardial infarction, cardiac arrest, resuscitation

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Introduction

Advances in acute critical care coupled with the rapid initiation of interventional cardiovascular procedures have improved the physician's ability to restore hemodynamic stability following cardiac arrest. The early optimism of preventing a cardiac death is often replaced with feelings of disappointment when a stabilized patient survives, but is left with devastating neurologic damage.

Induction of hypothermia was utilized in the early days of cardiac surgery to prevent neurologic and cardiac sequelae associated with transient cardiac arrest.¹ Over the last 10 years, the medical community has witnessed a resurgence of interest in the use of moderate hypothermia (30–33 °C) to limit neurologic damage in patients suffering cardiopulmonary arrest.^{2–7} In the 1990s, a number of small trials of patients treated with hypothermia after neurologic injury were published. The early results suggested the possibility of attenuating some of the irreversible anoxic and postischemic damage observed in this patient population.

Subsequent series with more restrictive entry criteria demonstrated small but clinically significant improvement in survival and both short- and long-term neurologic function.^{2,3,5} This has led to a position paper

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by the International Liaison Committee on Resuscitation (ILCOR) in support of early-induced hypothermia.⁸ The current report describes the experience of a program of induced hypothermia (IH) following out-of-hospital cardiac arrest that was initiated at the Oklahoma Heart Hospital, a community-based cardiac specialty hospital.

Methods

Treatment Protocol

From August 2003 to September 2005, all patients who presented to the Oklahoma Heart Hospital after cardiac arrest, were successfully resuscitated, and had return of spontaneous circulation underwent the hypothermia protocol. All patients who entered into this treatment protocol were comatose, intubated, and receiving mechanical ventilation. Induced hypothermia was initiated as early as practical in the emergency department, cardiac catheterization laboratory, or intensive care unit.

Early in our experience, a combination of infused iced intravenous fluids and surface ice packs were used to obtain the desired target temperature. The temperature was monitored with an indwelling urinary catheter probe. The target temperature was 33°C. The final 22 patients were cooled using a currently available automated system manufactured by Arctic Sun Temperature Management System, Louisville, Colo. This device is a noninvasive thermoregulation system composed of a control module and water cooling pads that adhere to the patient.

Pancuronium was the paralytic of choice to prevent shivering and the accompanying increase in core temperature. Lorazepam was the sedative of choice, and narcotics were used at the discretion of the medical and nursing staff. Frequent chemistries, arterial blood gas analysis, and complete blood counts were obtained. The patients were monitored in the intensive care unit, receiving standard acute cardiovascular care. After 24 to 36 h of IH, the patients were passively rewarmed over 8 h.

The clinical status of the patient was determined by using medical records and telephone contact when required.

Results

Patient Characteristics and Clinical Course

The mean age of the 49 patients who underwent therapeutic hypothermia was 62 years (range 25–91 years); 28 were men. The cause of arrest was believed to be secondary to acute myocardial infarction (MI) in 25, primary cardiac arrhythmias in 19, pulmonary embolism in 1, and the cause of arrest could not be determined in the remaining 4 patients. Sixteen patients underwent emergent cardiac catheterization at the time of presentation and before induction of hypothermia. Twelve of these patients had emergent percutaneous coronary interventions (Table I). Three patients underwent coronary angiography after completion of the hypothermia protocol.

Of the initial cohort of 49 patients, 19 (39%—14 men, 5 women) survived, 11 died of progressive cardiogenic

TABLE 1 Patient characteristics

	Survivors	Nonsurvivors	Total patients
No. of patients (%)	19 (39)	30 (61)	49
Average age	58	65	62
Male sex (%)	14 (73)	14 (29)	28 (57)
Cause of arrest			
Acute myocardial infarction (%)	12 (63)	13 (43)	25 (51)
Cardiac arrhythmias (%)	7 (37)	12 (40)	19 (39)
Unknown/other (%)	0	5 (17)	5 (17)
Emergency angiography (%)	11 (58)	8 (26)	19 (39)
Percutaneous intervention (%)	7 (37)	4 (13)	11 (22)
Glasgow coma scale at admission	4.2	3.2	3.6
Race			
Caucasian (%)	17 (90)	23 (77)	40 (81)
African American (%)	1 (5)	4 (13)	5 (17)
Native American (%)	1 (5)	2 (7)	3 (6)
Hispanic (%)	0	1 (3)	1 (3)
Time to target temperature 33°C (Mean in min)	194	188	
Preexisting conditions			
Coronary artery disease (%)	9 (47)	10 (33)	19 (39)
Previous myocardial infarction (%)	6 (32)	6 (20)	12 (24)
Diabetes (%)	5 (26)	11 (36)	16 (33)

shock, and 19 developed signs of irreversible neurologic injury and were pronounced brain dead. Of the 30 patients who did not survive, 5 died before the completion of 24 h of hypothermia. The target temperature of 33° (32–34°) was obtained at a mean of 190 min (range 30–540 min) after the protocol was initiated. The mean cooling time to target temperature was essentially the same for both groups (194 min for survivors vs. 188 min for nonsurvivors).

The Glasgow Outcome Coma Scale (GOCS) was used to assess neurologic function.⁹ The average admitting GOCS of all patients was 3.7 (range 3–7). A total of 19 patients survived the initial event and were discharged from the hospital. Sixteen patients showed minimal or no evidence of significant residual neurologic defects (GOCS of 14 or 15). Three patients exhibited more severe neurologic injury at the time of hospital discharge (GOCS of 3, 6, and 9, respectively).

Correlation of Etiology and Outcome

Of the 19 patients who survived, 12 had acute MI as the initial cause of cardiopulmonary collapse. Seven patients were believed to have experienced a primary cardiac arrhythmia. The average age of the survivors was 58 years compared with 65 years in the nonsurvivors. No significant relationship between outcome and time between arrest and arrival at the emergency department, time to return of spontaneous circulation, or other clinical variables was found in the data.

More survivors than nonsurvivors underwent emergent angiography (58 vs. 26%). Similarly, more acute percutaneous coronary interventions were performed in the survivors. These findings are not surprising since 63% of the survivors had acute MI as a cause of arrest, compared with only 43% of the nonsurvivors experiencing acute infarction.

The patients who had a witnessed arrest were more likely to survive than those whose arrest was not witnessed. Sixteen patients experienced an unwitnessed arrest and only 3 (19%) survived. Patients with a witnessed arrest fared considerably better, with 16 of 33 (48%) surviving. Eight patients developed cardiogenic shock and all of them died. Two patients developed shock after the initial resuscitation, and six experienced cardiogenic shock after implementation of IH. Until further data are available, the ILCOR position paper advocates the use of IH, except for patients with severe cardiogenic shock.⁸ The ILCOR paper acknowledges that previous studies have specifically excluded these patient from enrollment; therefore, the effect of hypothermia therapy on this important patient population is unknown.

Long-Term Survival and Neurologic Outcomes

Using patient records and telephone contacts, the clinical status of the 16 survivors was determined. Fourteen

patients were alive at a mean of 12.5 months (range 4–30 months). The two patients with the most severe neurologic damage in the cohort of hospital survivors (GOCS of 3 and 6 at time of discharge) died at 2 and 4 weeks after discharge. The remaining fourteen survivors reported only mild short- and long-term memory deficits.

This clinical study was performed on consecutive patients experiencing out-of-hospital cardiac arrest and includes, by necessity, uncontrollable clinical variables, including the presence and severity of preexisting cerebrovascular and cardiovascular disease. The adequacy and timeliness of the initial attempts at obtaining and maintaining ventilatory and circulatory support cannot be controlled. Among the many patient characteristics that are potentially concerning are the preexisting use of medications that may influence neurologic or cardiovascular damage or recovery. In this relatively small clinical study, these confounding variables cannot be controlled and may have influenced the findings of this investigation.

Discussion

Sudden cardiac death is a major cause of premature mortality in patients who otherwise have stable, even minimally symptomatic cardiovascular disease, with an estimated annual incidence of 300,000 to 500,000 in the United States.¹⁰ Despite significant efforts examining the mechanisms of lethal cardiac arrhythmias over the past 30 years, survival from out-of-hospital cardiac arrest is virtually unchanged and estimated to be 5%. Clinical modeling suggests that the chance of survival after experiencing cardiac arrest declines by 10% for every minute a patient remains in ventricular fibrillation.¹¹ Neurologic disability is common in patients experiencing prolonged cardiovascular collapse, which contributes significantly to long-term morbidity in the few who survive. Therefore, employing traditional advanced cardiac life support protocols in patients who survive cardiac arrest long enough to receive in-hospital care is associated with discharge rates between 3 and 20%.^{12–15}

One technique applied to victims of out-of-hospital cardiac arrest that has shown promise to reduce mortality and morbidity is IH. Clinical trials involving highly selected populations found that IH for victims of cardiac arrest improved survival to hospital discharge rates to 20 and 50%.^{2–7} In addition to survival advantages, IH was associated with improved neurologic outcomes. The design of previous clinical trials, however, may limit application to daily practice because strict inclusion and exclusion criteria excluded over 90% of patients who survived to reach the hospital.^{2–6} Therefore, findings from the current study fills an important gap in the literature by reporting the impact of IH protocols in a series of consecutive, nonselected patients in a community hospital setting.

The current study demonstrates that IH for patients who experience out-of-hospital cardiac arrest can be used routinely in a community hospital setting, with outcomes similar to those in clinical trials. In addition, the patients in this study who survived their acute event had excellent long-term survival with minimal evidence of neurologic deficits. These important findings further support American Heart Association recommendations that adult patients with spontaneous circulation after out-of-hospital cardiac arrest should be cooled at 32° to 34° for 12 to 24 h when the initial rhythm was ventricular fibrillation. This approach is effective even in unselected consecutive patients and can be accomplished in community hospitals.

Potential Mechanisms in Induced Hypothermia

For successful outcome, the initial cardiac event must be rapidly treated with return of stable hemodynamics. A number of neuropathologic processes are involved following transient cerebral anoxia that leads to irreversible neurologic injury. The mechanism of such injury following ischemia and reperfusion appears to be multifactorial and related to a variety of biochemical reactions. Induced hypothermia seems to slow the rate of many of the chemical processes associated with postischemic neurologic injury.^{18–21} For each 1 °C decrease in body temperature, the cerebral metabolic rate decreases by 6 to 7%.²⁰ One of the primary mechanisms of anoxic injury relates to calcium entry into the cell which leads to mitochondrial damage and apoptosis.²¹ Postischemic reperfusion appears to produce oxygen-free radicals and further damage cellular organelles and cell membrane.^{17–21}

By virtue of these proposed mechanisms, then, hypothermia improves neurologic outcome in patients being supported after cardiac arrest and transient interruption in cerebral perfusion. Previous studies demonstrated that only 2 to 10% of normothermic-treated patients return to independent living following cardiac arrest.^{14–17} Many patients suffer significant neurologic injury with cardiac arrest, and anoxic brain injury leads to approximately 50% of deaths following admission.^{14–17} The current series demonstrates significant improvement in neurologic outcomes, with more than a third of admitted patients having no or minimal neurologic defects at the time of discharge.

Benefits of IH are further confirmed in a meta-analysis by Holzer *et al.* This study calculated that the number-needed-to-treat to save one life with favorable neurologic recovery was 6 (95% confidence interval 4–13).⁷ This compares favorably with many other routinely used procedural and pharmacologic interventions in patients with acute critical illness, suggesting that IH protocols for cardiac arrest survivors should be considered routine.

Technical Considerations

Current IH protocols typically aim for a target temperature of between 32 °C and 34 °C. The rate of cooling and rewarming and the time of each stage remain somewhat arbitrary. Animal studies suggest that the maximal benefit of hypothermia is realized when initiated immediately after the return of spontaneous circulation, and the delayed application of therapeutic hypothermia may decrease the effectiveness of the therapy. Clinical trials, however, suggest that benefit can still be obtained when the protocol is started several hours after cardiac arrest.^{22–24}

Early in the present study a combination of cooling methods, including placement of ice packs and rapid infusion of cooled intravenous fluids, were used. Subsequently the routine use of the Arctic Sun Cooling Blanket (Medivance, Louisville, Col., USA) was instituted in a formal protocol. This system has higher setup costs, but after initial application it requires significantly less nursing resources to maintain therapeutic hypothermia. The method tends to be more precise and reliable in attaining and maintaining the target temperature compared with cold packs and iced intravenous fluids. This device also can be used for the early application of hypothermia when patients are taken emergently to the cardiac catheterization laboratory from the emergency department. Instituting formal protocols are likely the best approach for establishing routine application of IH to deal with emergent care of cardiac arrest survivors in community hospitals.

Conclusions

Therapeutic hypothermia improves neurologic recovery and overall survival in patients following out-of-hospital cardiac arrest. To accomplish routine use of this approach, an institutional protocol requires limited financial resources, but strong support from the medical and nursing staff. This additional requirement of organizational assets appears justified by the significant improvement in clinical outcomes. This study confirms that IH improves patient survival and neurologic integrity and serves to demonstrate that this important component of emergent care for cardiac arrest survivors is feasible, effective, and economically justified as routine practice in community health care centers.

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