Induced hypothermia after out-of-hospital cardiac arrest: one hospital's experience

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ABSTRACT

Objective: Induced mild hypothermia has been shown to reduce in-hospital mortality and to improve neurological outcome in patients who remain comatose after out-of-hospital cardiac arrest (OHCA). We conducted a retrospective audit to assess whether induced hypothermia had been successfully incorporated into routine care at our hospital, and whether this improved patient outcomes.

Design and setting: Retrospective audit of patients admitted to a Level III intensive care unit, Melbourne, Victoria, between 2001 and 2007. Patients treated with therapeutic hypothermia (introduced in 2004) were compared with those who did not receive this therapy.

Participants: Patients admitted to the ICU comatose after OHCA with a presumed cardiac cause.

Interventions: Induction of mild hypothermia by rapid infusion of cold intravenous fluids.

Main outcome measures: Hospital survival and neurological outcome at hospital discharge; time taken for core temperature to reach the target range (33° ±0.5° C) and time temperature was maintained, determined from patient ICU records.

Results: 123 patients were admitted comatose after OHCA with a presumed cardiac cause: 75 were admitted after induced hypothermia was introduced into routine care and received this treatment; and 48 admitted earlier did not receive the treatment. For patients with the initial rhythm of ventricular fibrillation (VF) or unstable ventricular tachycardia (uVT), treatment with induced hypothermia was associated with a higher hospital survival rate ($P = 0.03$; odds ratio [OR], 2.51; 95% CI, 1.06–5.95) and better neurological outcome ($P = 0.02$; OR, 2.85; 95% CI, 1.19–6.86). In 90% of patients treated with induced hypothermia, core temperature reached the target range within 6 hours of hospital presentation; mean duration of in-hospital cooling was 25.5 hours (SD, 2.9 hours).

Conclusions: We found that induced hypothermia can be incorporated into routine care of patients admitted to an ICU after OHCA. For patients with an initial rhythm of VF or uVT, this seems to have significantly improved hospital survival and neurological outcome. We also found that rapid infusion of cold intravenous fluids was effective for inducing hypothermia.

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In 2002, it was reported that the induction of mild hypothermia for 12–24 hours reduced in-hospital mortality and improved neurological outcome in patients who remain comatose after out-of-hospital cardiac arrest.[1,2] The Advanced Life Support Task Force of the International Liaison Committee on Resuscitation subsequently recommended that "unconscious adult patients with spontaneous circulation after out-of-hospital cardiac arrest should be cooled to 32° C to 34° C for 12 to 24 hours when the initial rhythm [is] ventricular fibrillation. Such cooling may also be beneficial for other rhythms or in-hospital cardiac arrest".[3] This recommendation was implemented as standard practice at our hospital in March 2004, following the development of guidelines for induction and maintenance of mild hypothermia (core temperature, 33° ± 0.5° C) and for patient care during the period of hypothermia.

We undertook a retrospective audit to determine whether the implementation of this new practice in our hospital was successful, whether it improved patient outcomes, and whether the cooling process used was effective in our hands.

Methods

Box Hill Hospital is a 340-bed teaching hospital in the eastern metropolitan area of Melbourne, Victoria. The ICU is a closed nine-bed Level III[4] unit that cares for both medical and surgical patients. Data on patient demographics, clinical variables and outcome are prospectively collected for all patients admitted to the ICU.

Patients admitted to the ICU after an out-of-hospital cardiac arrest between 1 January 2001 and 31 December 2007 were identified. Patients in whom the arrest was due to a primary respiratory arrest or neurological event were excluded from further analysis. The remaining patients were divided into two groups according to the initial rhythm: one group with ventricular fibrillation or unstable ventricular tachycardia (VF/uVT), and the other with pulseless electrical activity or asystole (PEA/A).

A comparison was then made between patients who were treated with induced hypothermia (core temperature, 33° ± 0.5° C) and those who were not so treated for each group. Hospital discharge destination was used as a surrogate marker of neurological outcome: a good neurological outcome was defined as discharge home or to a rehabilitation

Table 1. Characteristics and outcomes of patients admitted to the ICU after OHCA with a presumed primary cardiac cause and ventricular fibrillation or unstable ventricular tachycardia as the initial rhythm, by hypothermia treatment

	No hypothermia ($n = 35$)	Hypothermia ($n = 60$)	P
Age in years, median (IQR)	70 (59–80)	69 (55–79)	0.93
Time in minutes to ROSC, median (IQR)	20 (11–34)	20 (14–30)	1.00
APACHE II score, median (IQR)	29 (23–35)	31 (27–36)	0.29
Required inotropes, no. (%)	26 (74%)	39 (65%)	0.37
ICU LOS in hours, median (IQR)	69 (45–120)	113 (71–188)	0.01
Hospital LOS in hours, median (IQR)	146 (50–333)	242 (106–414)	0.05
Survived ICU, no. (%)	23 (66%)	38 (63%)	1.00
Survived hospital, no. (%)	11 (31%)	34 (57%)	0.03
Good neurological outcome, no. (%)*	11(31%)	34 (57%)	0.02

OHCA = out-of-hospital cardiac arrest. IQR = interquartile range. ROSC = return of spontaneous circulation. LOS = length of stay.
* Good neurological outcome was defined as discharge home or to a rehabilitation hospital or another acute care hospital. Patients transferred to other acute care hospitals were noted to be for full active treatment at ICU discharge and to have promising signs for good neurological recovery.

hospital or another acute care hospital; and a bad neurological outcome was defined as death in hospital or discharge to a nursing home. For patients who were transferred to another acute care hospital, an additional cross-check of ICU records was performed to determine neurological status at ICU discharge.

To determine the time taken for temperature to reach the target range and the duration of induced hypothermia, we reviewed the ICU observation charts for a subgroup of 50 patients treated with induced hypothermia. The subgroup included patients distributed throughout each year of the post-hypothermia implementation period.

The method used to induce hypothermia throughout the study period was rapid intravenous infusion of cold fluid (4° C Hartmann's solution).[5] This was initiated by the ambulance service, in the emergency department, in the ICU or in another hospital. Core temperature was monitored using bladder catheter temperature probes, and hypothermia was maintained by surface cooling with ice-packs. Continuous intravenous sedation was administered throughout the period of hypothermia, together with intermittent boluses of muscle relaxants for observed shivering. Additional boluses of cold intravenous fluids were administered if required. The planned duration of cooling was 24 hours from time of hospital presentation, with rewarming to occur over 12 hours.

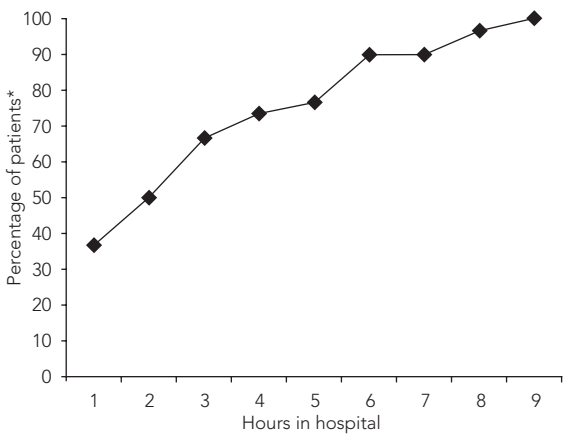
Statistical analysis

Numerical data are presented with medians and interquartile ranges, and categorical data with absolute frequencies and percentages. Data for continuous variables were compared by Student's t test or Mann–Whitney U test, and data for categorical variables by Fisher's exact test, with one-tailed tests used for hospital survival and neurological outcome. P values less than 0.05 were considered significant. Analysis was by GraphPad Prism, version 5.01 for Windows (Graph Pad Software, San Diego, Calif, USA).

Results

Between 2001 and 2007, 142 patients were admitted to the ICU after out-of-hospital cardiac arrest. Of these, 19 patients were excluded from further analysis because of a primary respiratory arrest or neurological event. In 123 patients, the cause of the arrest was presumed to be a primary cardiac event: 75 presented after March 2004 and were treated with induced hypothermia, and 48 presented before March 2004, none of whom received this therapy.

Figure 1. Time taken to reach target temperature range (33° ± 0.5° C) ($n = 30$)



* Cumulative percentage of patients whose temperature was in the target range.

In the 123 patients in whom the presumed cause of arrest was a primary cardiac event, the initial rhythm was VF/uVT in 95 and PEA/A in 28.

Patients with VF/uVT as initial rhythm

In the group with VF/uVT as the initial rhythm, patients treated with hypothermia are compared with those who did not receive this treatment in Table 1. No significant differences were found in age, severity of illness, time to return of spontaneous circulation, or need for inotropic support. However, patients treated with hypothermia had significantly longer ICU length of stay (LOS) and a trend to longer hospital LOS. They were also significantly more likely to survive hospital ($P=0.03$; odds ratio [OR], 2.51; 95% CI, 1.06–5.95) and to have a good neurological outcome ($P=0.02$; OR, 2.85; 95% CI, 1.19–6.86).

Patients with PEA/A as initial rhythm

Of the 28 patients with an initial rhythm of PEA/A, 15 were treated with induced hypothermia. There were no significant differences in patient characteristics or outcomes between the hypothermia and non-hypothermia groups.

The cooling process

The records of 50 patients treated with induced hypothermia were examined to determine the effectiveness of the cooling process. Six patients were excluded because of incomplete records, and a further 14 patients because cooling was initiated by the ambulance service or another hospital. Of the 30 patients in whom cooling was confirmed as having commenced in our hospital, core temperature reached the target range within 6 hours of hospital presentation in 27 (90%) (Figure 1).

The mean duration of in-hospital hypothermia (defined from hospital arrival to the commencement of rewarming) was 25.5 hours (SD, 2.9 hours). Individual patients showed varying core temperature patterns during the cooled phase, with most having minor deviations from the target temperature of 33° C (± 0.5–1.0° C), but six patients had marked fluctuations (±2.0° C). These patients were distributed throughout all years after 2004 (post-hypothermia). Rewarming data from the same 30 patients also showed considerable variability. The median time taken to re-warm to 36.5°C was 6.5 hours (range, 1–13 hours).

Discussion

This retrospective audit found that incorporating induced hypothermia into routine treatment of patients after out-of-hospital cardiac arrest was both feasible and significantly increased rates of hospital survival and good neurological outcome in those with VF/uVT as the initial rhythm. Further, we found that the cooling technique used was effective, with the core temperature of most patients reaching the target range within 6 hours of hospital presentation, and remaining in that range for the intended 24 hours.

Our study shows that induced hypothermia can be successfully incorporated into routine care. There has been a worldwide reluctance to use this treatment in patients who present to hospital after out-of-hospital cardiac arrest, despite two randomised controlled trials and a meta-analysis that reported favourable outcomes with its use.[1,2,6] This reluctance has been demonstrated in a number of recent studies. In 2007, the report of the European Resuscitation Council Hypothermia After Cardiac Arrest Registry Study Group showed that 22% of eligible patients did not undergo induced hypothermia,[7] and an analysis of a Finnish national database showed that 72% of post-out-of-hospital-arrest patients did not undergo induced hypothermia.[8] The previous year, an international survey of doctors practising in critical care found that only 26% of United States respondents and 36% of non-US respondents (including 42% of Australian respondents) had used induced hypothermia following resuscitation,[9] and a survey of United Kingdom ICUs found that only 39% had treated patients after out-of-hospital arrest with induced hypothermia.[10] Common reasons given for not using this treatment included "not enough data" and "too technically difficult to use".[9,10]

Our favourable outcome results are similar to those found in previous randomised controlled trials. The Hypothermia after Cardiac Arrest Study Group in Europe assessed outcomes at 6 months, with the significant findings of an absolute reduction of 14% in mortality, and an increase of 16% in the proportion with good neurological outcome.[2] In Australia, Bernard et al reported a 23% increase in the proportion with good neurological outcome and a trend to better hospital outcome.[1]

Our study included all patients who were comatose at presentation to our hospital after out-of-hospital arrest. This contrasts with the European study, which included only 8% of screened patients (exclusions included unwitnessed collapse, age >75 years, emergency response time <15 minutes, and hypotension following return of spontaneous circulation), and the study of Bernard et al, which excluded patients with cardiogenic shock, those aged <50 years if female, and cases where no ICU bed was available at the institution. The favourable outcomes we observed for patients with an initial rhythm of VF/uVT in our unselected population (lower hospital mortality and better neurological outcome) have also been reported in other studies.[7,11,12]

As well as differences in outcome, we found differences in ICU length of stay between our patients who were treated with hypothermia and those who were not. This is consistent with the reported pharmacokinetics of drugs used for sedation during the cooling phase, which can prolong the sedating

effect.[13-15] Clinically, this can mean that assessment for neurological recovery is unreliable for more than 72 hours after ICU admission.[16] The use of induced hypothermia can thus increase ICU LOS, as found in our audit and as reported previously.[11]

For patients with an initial rhythm of PEA/A, we found no significant differences between those who were treated with hypothermia and those who were not. This may reflect the small numbers available for analysis, or it may indicate that induced hypothermia is not beneficial in these patients. This therapy has not been studied in a randomised controlled trial in this group of patients, and findings from other studies are inconclusive.[7,11]

Similarly to previous investigators, we found in-hospital administration of cold intravenous fluids and surface cooling to be effective for inducing and maintaining hypothermia.[5,17,18] In 95% of our patients, core temperature reached the target range within 6 hours of hospital arrival. This is comparable to published findings: 75% of patients with temperature in the target range within 16 hours of the restoration of spontaneous circulation,[2] within 6 hours of the time of collapse[7] or within 6 hours of hospital presentation.[11] We found that the ease with which temperature could be kept in the target range varied between patients, with a small number displaying marked fluctuations in core temperature. Similar difficulties in maintaining temperature control during hypothermia have been reported previously.[19] Rewarming was faster than was intended, despite an early change in our guidelines from the recommendation of active rewarming to passive.

Our study is limited by its retrospective nature. The use of hospital discharge destination as a surrogate marker for neurological outcome may be unreliable, given the possibility that some patients discharged to rehabilitation or other acute care hospitals may have had considerable disability and been unable to return home after the illness. In addition, we cannot discount the possibility that the change in outcome for patients admitted after out-of-hospital arrest reflects other changes within the ICU or hospital during the audit period.

In conclusion, we found that induced hypothermia can be incorporated into routine care of patients admitted to an ICU after out-of-hospital arrest and that, for patients with the initial rhythm of VF/uVT, this seems to have resulted in a significant improvement in hospital survival and neurological outcome. We also found that the simple technique of rapidly infusing cold intravenous fluids was effective for inducing hypothermia. Our experiences should encourage others to introduce this potentially useful therapy into institutions in which it is not currently part of routine care.

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