Original Contributions

Indications and limitations of induced hypothermic therapy for out-of-hospital cardiopulmonary arrest

Youichi Yanagawa MD, PhD*, Akira Takasu MD, PhD, Toshihisa Sakamoto MD, PhD, Yoshiaki Okada MD, PhD

Department of Traumatology and Critical Care Medicine, National Defense Medical College, Saitama 359-8513, Japan

Received 15 August 2005; accepted 30 September 2005

Abstract

Purpose: To identify candidates indicated to undergo induced hypothermic therapy (IHT) among comatose survivors of out-of-hospital cardiopulmonary arrest (CPA) based on a retrospective review of medical charts.

Methods: Between 1995 and 2004, 49 patients who recovered from CPA and treated by IHT were analyzed. The subjects were divided into 2 groups. The first group (GR, n = 16) consisted of patients with a recovery of consciousness and the second group (VD, n = 33) consisted of patients who either remained unconscious or who died.

Results: Using a multiple logistic regression analysis, out-of-hospital return of spontaneous circulation was the only factor independently associated with the outcome (odds ratio, 0.03; 95% confidence interval, 0.00-0.23; \( P = .001 \)).

Conclusion: IHT may be beneficial for CPA patients with out-of-hospital return of spontaneous circulation. Because of the small sample size, further large human studies are warranted.

© 2006 Elsevier Inc. All rights reserved.

1. Introduction

The use of induced hypothermic therapy (IHT) has been proven to be useful for the treatment of cerebral ischemia after out-of-hospital cardiopulmonary arrest (CPA) [1,2], because IHT may attenuate the postresuscitation syndrome induced by perfusion failure, reoxygenation, extracerebral causes, and/or blood derangement during stasis in cardiac arrest [3]. However, not all comatose survivors from CPA are always able to regain consciousness after IHT. Holzer et al [2] applied IHT for comatose survivors with witnessed cardiac arrest and ventricular fibrillation at the scene and thus obtained a significantly successful outcome after IHT. Bernard et al [1] applied IHT for comatose survivors with ventricular fibrillation at the scene and a successful return of spontaneous circulation and also obtained a significantly good outcome after IHT. Hachimi-Idrissi et al [4] applied IHT using a helmet device for comatose survivors with asystole or pulseless electrical activity at the scene and a successful return of spontaneous circulation, and some cases of these cases showed a good outcome after IHT. Because the indications for IHT in comatose survivors with cardiac arrest were different in each study, and no one has yet investigated the indications of IHT for survivors of CPA, we retrospectively analyzed the
2. Material and methods

Between November 1995, when the institutional protocol of IHT Blinded Manuscript was established, and December 2004, 1488 patients with CPA arrived at this department. Among them, 1047 patients were not admitted to the hospital because they were not able to obtain either return of spontaneous circulation (ROSC) or a stabilized circulation by resuscitation. After excluding them, none of the patients who satisfied the following criteria underwent IHT: (a) a systolic blood pressure was maintained at less than 90 mm Hg in 10 minutes after the ROSC with less than 0.3 μg/kg per minute of epinephrine administration (n = 189 in total); (b) their age was older than 70 years (n = 150 in total); (c) patients with trauma (n = 27 in total), central nervous system disease (n = 75 in total), or terminal illness (n = 50 in total) as the cause of CPA; or (d) the physicians on duty judged that patients were not suitable to undergo IHT because of their general medical condition (ominous signs such as convulsion or hypoxic encephalopathy on a postresuscitated computed tomogram and so on). After eliminating them, the subjects of this study included 49 consecutive patients, who showed a persistent comatose state (sum of the Glasgow Coma Scale <7) in the emergency room, and were treated with IHT. All subjects had no disability before CPA. The protocol for IHT and ICU in our institute has been described in detail before [5]. To be brief, the core temperature was maintained at between 33°C and 34°C for 48 hours. Intravenous pancuronium (0.01-0.02 mg/kg per hour) and midazolam (0.2-0.5 mg/kg per hour) were continuously administered to prevent shivering with the support of mechanical ventilation. After 48 hours, the patients were rewarmed to 37°C, at a rate of no greater than 0.1°C/h and no greater than 1°C/d.

The subjects were divided into 2 groups. The first group consisted of patients with a recovery of consciousness (cerebral performance category [6] 1-3; GR group, n = 16), whereas the second group consisted of patients who were either unconscious or who died (cerebral performance category 4-5; VD group, n = 33). The cerebral performance category was determined at the time of hospital discharge. The following variables were analyzed as background information: age, sex, cause of arrest, witnessed collapse, bystander cardiopulmonary resuscitation (CPR), electrocardiogram (ECG) at the scene, and the number of out-of-hospital returns of spontaneous circulation (oh-ROSC).

The χ² and Student t test were used for statistical analyses. A P value less than .05 was considered to be significant. A multivariate analysis using a logistic regression analysis was used to evaluate the independent factors regarding the outcome. The variables included in the multivariate analysis were those with significance levels of P < .01 in a univariate analysis. The odds ratio and corresponding 95% confidence intervals were also calculated.

3. Results

Table 1 shows the results of our analysis. There were no significant differences between the 2 groups regarding age, sex, the cause of arrest, and the number of witnessed collapses. The number of bystander CPR and the number of oh-ROSC in the GR group were significantly greater than those in the VD group. On the other hand, the number of asystole at the scene in the VD group was significantly greater than that in the GR group. In addition, all 5 subjects with a witnessed collapse, ventricular fibrillation at the scene, and oh-ROSC attained full recovery; however, all 10 subjects with nonwitnessed nonbystander CPR who were asystole at the scene and non-oh-ROSC did not regain consciousness after IHT.

Using a multiple logistic regression analysis, oh-ROSC was the only factor independently associated with the outcome (odds ratio, 0.03; 95% confidence interval, 0.00-0.23; P = .001).

Among the VD group, 22 patients died (2-166 hospital days; average, 12.2 days; SE, 2.0), and 2 of them died during IHT. After eliminating these subjects (because the consciousness level was not judged during IHT), the statistical trends did not change.

4. Discussion

In this study, the cases of CPA who received bystander CPR and showed oh-ROSC tended to regain consciousness
after IHT similar to the reports of Holzer [2] and Bernard et al [1]. Such cases tend to have a shorter duration of no cerebral flow and thus are considered to have a good prognosis [7]. On the other hand, there were no recoveries of consciousness after IHT among the cases without a witnessed collapse, bystander CPR, and oh-ROSC and with standstill of ECG findings at the scene. Such cases are considered to have a longer duration of no cerebral flow and a poor prognosis [7]. Because IHT is not considered to be beneficial to such cases, other strategies such as a combination of neuroprotective agents [8] or the introduction of prehospital hypothermic therapy [9] may be required to obtain a good outcome.

In this study, some cases with oh-ROSC but without a witnessed collapse, bystander CPR, or ventricular fibrillation of ECG at the scene, which are thus considered to have relatively poor prognosis, also regained consciousness after IHT. Because asystole usually follows ventricular fibrillation, being asystole at the scene means a longer duration of no cerebral flow from collapse in comparison to those undergoing ventricular fibrillation. Hypothermia has neuroprotection [3], and this effect may thus be beneficial to even CPA cases who are considered to have a relatively poor prognosis. Hachimi-Idrissi et al [4] also reported 2 cases with both nonventricular fibrillation of ECG at the scene and oh-ROSC who regained full recovery after IHT, but none of these cases were able to attain full recovery without hypothermic therapy. We therefore believe that the CPA cases with oh-ROSC who did not have either a witnessed collapse, bystander CPR, or ventricular fibrillation at the scene nevertheless benefit from IHT.

Several problems exist in our study. First, because of the small sample size, it may be difficult to conclude that the outcomes were primarily attributed to IHT. Second, this study lacked controls, which were not administered IHT, to compare the neurological outcome. Further large human studies are thus warranted to determine the indications for IHT among the survivors of CPA.

5. Conclusion

Our results suggested that IHT may be beneficial for CPA patients with oh-ROSC.

References