BRIEF ORIGINAL

Results of using a therapeutic hypothermia protocol after cardiac arrest: design and application by an emergency medical service and a hospital emergency department

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Received:
17-5-2011

Accepted:
20-7-2011

Conflict of interest:
None

Objective: To describe a multidisciplinary team's use of therapeutic hypothermia to improve neurologic outcome after cardiac arrest.

Methods: Retrospective, descriptive study of consecutive patients treated over a period of 16 months in the area served by the emergency department of Hospital de Cruces in Barakaldo, Bizkaia, Spain, and the emergency response services in the hospital's referral area. Clinical and sociodemographic data were analyzed for patients in whom spontaneous circulation returned after out-of-hospital cardiac arrest.

Results: We included 34 patients: 10 (29.4%) were treated with hypothermia, in 7 (20.5%) hypothermia was induced but then interrupted, and in 17 (50%) use of hypothermia was ruled out. In 4 patients in the last group, heart rhythm recovered in situ and consciousness returned on early pre-hospital defibrillation. Survival with good neurologic recovery was achieved in 60% of the hypothermia-treated patients and in 15% of those who were excluded from hypothermia ($P<.05$). However, the patients who received hypothermia were younger ($P<.001$) and did not have a relevant medical history ($P<.05$).

Conclusions: The use of therapeutic hypothermia requires effective coordination between emergency services (staff of pre-hospital and hospital services and critical care units) in order to achieve optimal results. With strategic coordination, it is possible to use this approach in nearly 30% of pre-hospital cardiopulmonary resuscitations. [Emergencias 2012;24:39-43]

Key words: Hypothermia. Emergency health services. Cardiac arrest.

Introduction

Anoxic encephalopathy after heart arrest is one of the most severe complications in those who survive cardiorespiratory arrest (CRA). It is a serious neurological condition which in most cases has a significant negative impact on patient quality of life, with great emotional distress for families and a significant economic cost to the health system. In the U.S. the cost of caring for patients with severe neurological damage during the first 6 months post-CRA is around $300,000[1]. The term "cardio-cerebral resuscitation" has been used in recent years to refer to treatments in this regard[2]. It is based on rapid action and application of a protocol during cardiopulmonary resuscitation (CPR) to maintain neurological integrity in survivors. It is in this context of attempts to define, prevent and treat anoxic encephalopathy that the practice of post-CPR therapeutic hypothermia (TH) has developed. Lowering core temperature to 32-34°C in CPR survivors has been applied for many years[3,4]. The mechanisms by which this prevents brain damage are not clearly known, but may be due to inhibition of destructive enzyme cascades, and of cellular oxidative mechanisms, and, ultimately, neuronal death[5].

Studies by Holzer[6] in Europe and Bernard[7] in Australia, published in 2002, were instrumental in recovering TH to protect against post-CPR neurological damage. Because of these two publications, in 2003 the International Liaison Committee on Resuscitation made a recommendation to include TH in post-CPR care[8]. In Spain, Castrejón 2009 published an excellent study involving a series of 69 patients during an 8-year study period[9]. In Euskadi, in 2009, our emergency medical services (EMS) working in the reference area of Hospital de Cruces in critical care designed an TH protocol for application as part of post-CPA care. This protocol starts from EMS arrival on the scene and continues in the emergency department (ED) until definitive treatment in the intensive care unit or coronary care unit. The process required specific training and multidisciplinary consensus, but since the beginning the need for consensual treatment by the EMS and the emergency department (ED) was evident[10]. The present study describes the results of implementing this protocol.

Method

From September 24, 2009 to February 1, 2011, we included all CRA survivors transferred to the ED, Hospital de Cruces (Barakaldo, Bizkaia) by advanced life support (ALS) units of Emergentziak-Osakidetza and medicalized ambulances in other communities. We also included patients who experienced CRA in the ED itself. Patients were classified into three groups: the group where TH was applied (TH group), a second group where TH was applied initially but later discontinued (TH interrupted) and a third group receiving standard care without TH (No TH). Both the TH interrupted and the No TH groups had exclusion criteria for the application of TH (Figure 1).

Neurological status of patients was assessed using the Glasgow-Pittsburgh Cerebral Performance Categories (CPC), which classifies no sequelae or only mild neurological deficits as CPC1, moderate neurological deficit as CPC2 (independent daily activities, does not require institutionalization), and severe neurological impairment (severe disability disallowing independent daily activities and requiring institutionalization), persistent vegetative state as CPC4 and brain death as CPC5. For the purposes of the present study and following the recommendations of earlier publications in this field, we considered that patients classified as CPC1 and 2 had good prognosis, while those classified as CPC3 or higher had poor prognosis, and this was assessed at the end of the study (February 2011).

TH protocol was applied in both the pre-hospital and hospital setting. We followed the protocols currently used in centers with experience in TH. Core body temperature was measured at baseline and then every 15 minutes until transfer of the patient to the critical care unit (by tympanic thermometer in the hospital and urethral catheter during EMS care). The pre-hospital cooling method consisted of intravenous infusion of saline at 4°C, 30 ml / kg to a maximum of 2 liters infused during 30 minutes, supplemented by applying Dispoice® chemical ice to the armpits, groin and neck. Other treatment was performed according to the specific needs of the patient and we alerted the hospital before arrival there. In the hospital, TH measures were maintained and optimized, or initiated if not already applied (some patients were not transferred in Osakidetza ALS ambulances), using the same technique applied in the pre-hospital setting, and using Artic-Sun® cooling method. The ED alerted other departments involved in the process, and performed echocardiography. The results are expressed as means ± standard deviation for quantitative variables and as absolute values and percentages for qualitative variables. Comparisons were performed using the non-parametric Mann Whitney test for quantitative variables, and Fisher's exact test for qualitative variables, after grouping by categories. Differences with a p value less than 0.05 were considered statistically significant.

Results

We initially included 34 patients: 10 in the TH group, 7 in the TH interrupted and 17 in NO TH. The interruption of TH in the TH interrupted group was due to non-compliance with the inclusion criteria, specifically, suspected prolonged CRA (> 30 minutes) or severe chronic disease. In the NO TH group we excluded 4 of the 17 patients since they had ventricular fibrillation (VF) attended by emergency teams with successful early defibrillation and recovery of consciousness in situ, so the protocol was not applied. Finally the NO TH group comprised 13 patients (Table 1). On comparing the TH group with the remaining patients (Table 2), we observed increased survival with good neurological outcome (60% versus 15%, $P < 0.05$), but there were also significant dif-

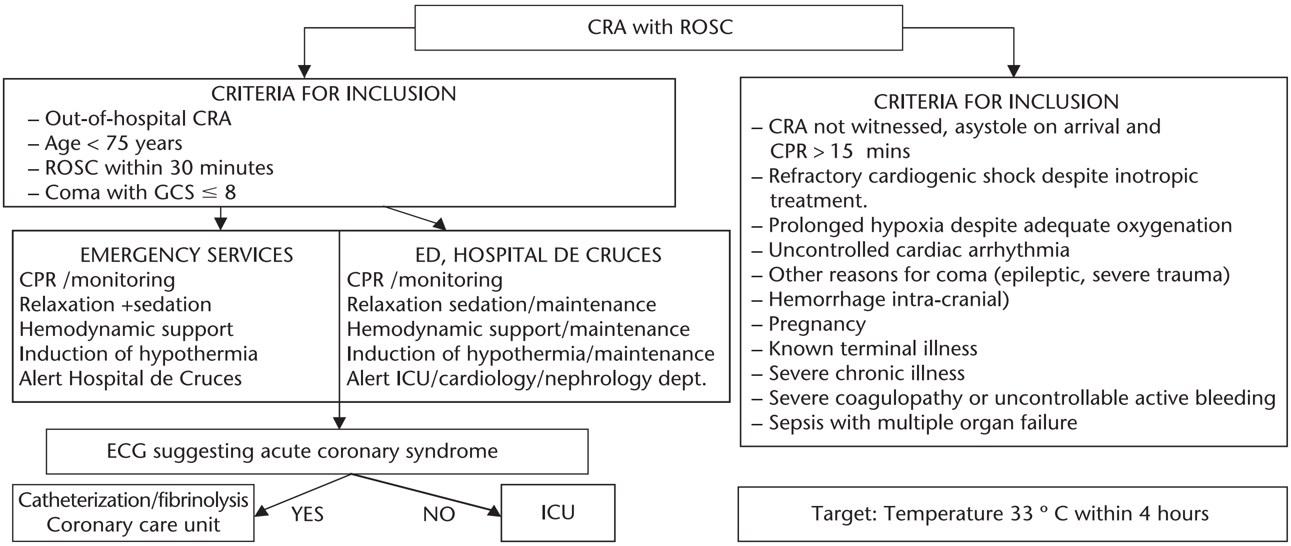

Figure 1. Hypothermia protocol. CRA: cardio-respiratory arrest, ROSC: return of spontaneous circulation, ED: Emergency department, ECG: electrocardiograph, ICU: intensive care unit.

ferences in other characteristics: younger age (52.7 ± 11.2 years versus 71.8 ± 10.1; p <0.001), and a higher number of cases with VF as initial rhythm, although in this case the differences were not significant (70% versus 40%, P = 0.43). Time from the cardiac arrest to EMS arrival on the scene was higher in the TH group compared to the rest of the patients (7.6 ± 2.8 minutes versus 6.1 ± 4.9, p = 0.25).

Regarding post-CPA outcome and neurological status, 4 patients (40%) in the TH group died and 2 (20%) were classified as CPC2, which had significantly improved 6 months later after rehabilitation treatment. The remaining 4 (40%) showed complete neurological recovery (CPC1). In the TH interrupted group, 6 patients (85.7%) died and 1 patient had neurological status CPC 2. Finally, in the NO TH group, a total of 10 patients were excluded from treatment with TH due to age >75 years, 2 due to the presence of severe disease and 1 for CRA secondary to multiple trauma. In summary, 11 patients died and 2 were

Table 1. General characteristics of the series by groups

	Hypothermia N = 10	Hypothermia interrupted N = 7	No hypothermia N = 13	Total N = 30
Age (years) (mean ± SD)	52.7 ± 11.2	65.0 ± 11.8	75.5 ± 8.6	65.4 ± 14.1
Male gender [n (%)]	7 (70%)	6 (85.7%)	10 (76.9%)	23 (76.6%)
Initial rhythm [n (%)]				
VF/VT	6 (60%)	1 (14.3%)	7 (53.9%)	14 (46.7%)
Asystole	4 (40%)	5 (71.4%)	5 (38.4%)	14 (46.7%)
EMD	0 (0%)	1 (14.3%)	1(7.7%)	2 (6.6%)
Witnessed CRA [n (%)]	9 (90%)	6 (85.7%)	11 (84.6%)	26 (86.7%)
CPR performed [n (%)]	8 (80.0%)	5 (71.4%)	5 (38.5%)	18 (60%)
Arrival time (min) (mean ± SD)	7.7 ± 2.8	6.7 ± 6.7	5.7 ± 4.1	6.8 ± 4.1
Arrival time (min) (perc 25-50-75)	5.5-6.0-10.0	1.2-5.5-13.5	3.0-5.0-10.0	4.2-6.0-10.0
ROSC Time (min) (mean ± SD)	23.8 ± 8.01	35.0 ± 19.7	19.5 ± 10.8	24.3 ± 13.1
ROSC Time (min) (perc 25-50-75)	14.0-25.0-30.0	15.0-40.0-52.5	11.7-17.5-22.5	13.5-20.0-30.0
AMI [n (%)]	4 (40%)	3 (42.9%)	2 (15.4)	9 (26.5%)
Medical History [n (%)]				
Not relevant	7 (70.0%)	3 (42.8%)	2 (15.4%)	12 (40%)
Diabetes mellitus	0	2	1	3
Ischemic cardiopathy	1	1	6	8
Lung disease	1	3	2	6
Kidney Disease				
Neurological disease	0	2	5	7
Tumors	0	1	2	3
HT	1	0	4	5

SD: standard deviation. VF: Ventricular fibrillation, VT ventricular tachycardia; EMD: electromechanical dissociation. CRA: cardiopulmonary arrest, CPR: cardiopulmonary resuscitation. ROSC: recovery of spontaneous circulation. AMI: acute myocardial infarction. HT: hypertension.

Table 2. Comparison of the group receiving therapeutic hypothermia versus the rest

	Hypothermia (N = 10)	No hypothermia (N = 20)	p Value
Age [n (%)]	52.7 ± 11.2	71.8 ± 10.8	< 0.001
Male gender [n (%)]	7 (70%)	16 (80%)	0.43
Initial rhythm VF/VT [n (%)]	6 (60.0%)	8 (40%)	0.26
Witnessed CRA [n (%)]	9 (90%)	17 (85%)	0.59
CPR performed [n (%)]	8 (80.0%)	10 (50%)	0.12
Arrival time (min) (mean ± SD)	7.7 ± 2.8	6.1 ± 4.9	0.26
ROSC Time (min) (mean ± SD)	23.8 ± 8.1	24.7 ± 15.6	0.64
Acute myocardial infarction [n (%)]	4 (40%)	5 (25%)	0.33
No relevant history [n (%)]	7 (70.0%)	5 (25%)	< 0.05
Good neurological recovery (CPC1 or CPC2)	6 (60%)	3 (15%)	< 0.05

CRA: cardiorespiratory arrest, VF: Ventricular fibrillation, VT: ventricular tachycardia; CPR: cardiopulmonary resuscitation, ROSC: recovery of spontaneous circulation, SD: standard deviation.

neurologically classified as CPC1; one of these suffered CRA in a rehabilitation center and was attended immediately.

Discusión

Moderate cooling in CRA survivors is a consensus recommendation in the current guidelines of the American Heart Association. It is a type I recommendation for patients who remain comatose after CRA secondary to FV and type IIb for other rhythms[11,12]. Thus the objective of this work was not to corroborate the usefulness of TH, but to present the results of a multidisciplinary protocol where TH is started in the pre-hospital setting or in the ED, both actively participating in the induction phase of TH. In this context, TH was initiated in 10 patients and 40% of them presented excellent neurological outcome (CPC1). The 2 patients with moderate neurological impairment (CPC2) received initial rehabilitation treatment in hospital and are currently treated on an outpatient basis. During this time there has been substantial and progressive improvement. We therefore conclude that the percentage of neurological survival in the TH group was 60%.

Our results are similar to those of other authors[13-19], even taking into account that TH was limited to patients with VF-induced CRA in most previous work published. Our survival figures in the TH group are similar to those of Oddo et al.[14] (60%), Belliard et al.[20] (56%), Castrejon et al.[9] (56%) and Bernard et al.[7] (55%), and our survival rate in patients not treated with TH is very close to those reported by Sunde et al.[15] (31%) and Bernard et al.[7] (32%). We would highlight the fact that in our study the initial heart rhythm of CRA was also a determinant of prognosis, since only 1 patient who presented asystole as the initial rhythm survived. This patient had a prolonged delay before recovery of spontaneous circulation (CPR after 30 minutes), was treated with TH and is currently classified as CPC2 with moderate neurological impairment.

In the work presented, treatment with TH was limited to those who fulfilled the inclusion criteria of our protocol. These criteria were extracted from the scientific literature available at the time. Today we are debating the utility of post-CRA TH for patients who would have been excluded before, such as who received CPR and other invasive procedures (eg. people over 75 years, pregnant women, prolonged CPR maneuvers, etc.). The low number of patients included relates to the study period and the reference population of our hospital (16 months, 400,000 inhabitants). Also, we were unable to collect all relevant data on some patients or the time taken to reach the target temperature. These factors limit the quality of the study and its conclusions. Furthermore, comparisons should be made with caution, given the non-experimental method of the study, which did not include randomized assignment to a particular group of treatment. However, knowing that TH is recommended by international guidelines on CPR, it seems logical to apply it in the same way we apply CPR after cardiac arrest, and that TH will contribute to the well-being of survivors.

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Resultados de la puesta en marcha de un protocolo de hipotermia terapéutica en la parada cardiaca consensuado entre un sistema de emergencias médicas y un servicio de urgencias hospitalario

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Objetivos: Exponer la experiencia en el uso de la hipotermia terapéutica (HT) como tratamiento del daño neurológico secundario a la parada cardiaca por parte de un equipo multidisciplinar.
Método: Estudio de cohortes, sin intervención, con inclusión consecutiva durante 16 meses en el área de referencia de Urgencias y Emergencias del Hospital de Cruces (Barakaldo, Bizkaia). Se trataba de pacientes con parada cardiaca extrahospitalaria, y en ellos se revisaron los datos clínicos y demográficos. Se compararon los resultados neurológicos a largo plazo en función de si se aplicó HT.
Resultados: Se incluyeron 30 pacientes: 10 fueron tratados mediante HT, en 7 (20,5%) casos se inició HT y posteriormente se interrumpió y 13 pacientes fueron excluidos para ese tratamiento. La supervivencia con buena recuperación neurológica fue del 60% en los 10 pacientes en que se aplicó HT y de 15% en los 20 pacientes que no ($p < 0,05$), si bien ésta se aplicó con mayor frecuencia a pacientes mas jóvenes ($p < 0,001$) y sin antecedentes relevantes ($p < 0,05$).
Conclusiones: La aplicación de HT requiere una coordinación eficaz entre los servicios implicados (urgencias extra e intrahospitalarias, unidades de pacientes críticos) para alcanzar los mejores resultados, y con esta estrategia es posible aplicar esta técnica en cerca del 30% de las paradas cardiorrespiratorias acontecidas en el medio extrahospitalario. [Emergencias 2012;24:39-43]

Palabras clave: Hipotermia. Medicina de Urgencias y Emergencias. Parada cardiaca. Encefalopatía anóxica.