Resuscitation 82 (2011) 1162–1167

Contents lists available at ScienceDirect

Resuscitation

journal homepage: www.elsevier.com/locate/resuscitation

Clinical paper

Mild therapeutic hypothermia is associated with favourable outcome in patients after cardiac arrest with non-shockable rhythms☆

Christoph Testori, Fritz Sterz*, Wilhelm Behringer, Moritz Haugk, Thomas Uray, Andrea Zeiner, Andreas Janata, Jasmin Arrich, Michael Holzer, Heidrun Losert

Department of Emergency Medicine, Medical University of Vienna, Austria

ARTICLE INFO

Article history:
Received 10 March 2011
Received in revised form 5 May 2011
Accepted 14 May 2011

Keywords:
Cardiopulmonary resuscitation
Heart arrest
Induced hypothermia
Prognosis
Resuscitation
Survival

ABSTRACT

Aim: Mild therapeutic hypothermia (32–34 °C) improves neurological recovery and reduces the risk of death in comatose survivors of cardiac arrest when the initial rhythm is ventricular fibrillation or pulseless ventricular tachycardia. The aim of the presented study was to investigate the effect of mild therapeutic hypothermia (32–34 °C for 24 h) on neurological outcome and mortality in patients who had been successfully resuscitated from non-ventricular fibrillation cardiac arrest.
Methods: In this retrospective cohort study we included cardiac arrest survivors of 18 years of age or older suffering a witnessed out-of-hospital cardiac arrest with asystole or pulseless electric activity as the first documented rhythm. Data were collected from 1992 to 2009. Main outcome measures were neurological outcome within six month and mortality after six months.
Results: Three hundred and seventy-four patients were analysed. Hypothermia was induced in 135 patients. Patients who were treated with mild therapeutic hypothermia were more likely to have good neurological outcomes in comparison to patients who were not treated with hypothermia with an odds ratio of 1.84 (95% confidence interval: 1.08–3.13). In addition, the rate of mortality was significantly lower in the hypothermia group (odds ratio: 0.56; 95% confidence interval: 0.34–0.93).
Conclusion: Treatment with mild therapeutic hypothermia at a temperature of 32–34 °C for 24 h is associated with improved neurological outcome and a reduced risk of death following out-of-hospital cardiac arrest with non-shockable rhythms.

1. Introduction

The incidence of out-of-hospital cardiac arrest ranges from 37 to 46 per 100,000 events per year.[1] Approximately 25% of all cardiac arrest patients are younger than 65 years of age.[2] The favourable outcomes of patients who are admitted to the hospital range from 11% to 48%, indicating that a large number of patients die after successful resuscitation during their hospital stay or develop severe permanent neurological impairment.[3,4] The only therapy that has been shown to improve survival and neurological outcome after successful resuscitation from sudden cardiac arrest is the induction of mild therapeutic hypothermia for 12–24 h.[5,6]Two large randomised clinical trials investigating the effect of mild hypothermia in cardiac arrest survivors only included patients with primary shockable cardiac rhythms.[5,6] There is a lack of data concerning the effect of mild therapeutic hypothermia in survivors after cardiac arrest with asystole or pulseless electrical activity as the first documented rhythms. Approximately 60–80% of patients who have suffered from an out-of-hospital cardiac arrest present with an initial non-shockable rhythm.[4,7–9] Some preliminary analyses have reported a non-significant reduction in unfavourable outcomes in patients who present with pulseless electrical activity or asystole and who were treated with mild hypothermia.[10–12]

The aim of this retrospective cohort study was to investigate the effect of mild therapeutic hypothermia on neurological outcome and mortality in patients who had been successfully resuscitated from non-ventricular fibrillation cardiac arrest.

2. Methods

This cohort study is based on a cardiac arrest registry that consists of all adult patients who were admitted to the department of emergency medicine of a tertiary-care hospital with cardiac arrest between January 1992 and October 2009. The institutional ethical review board has approved this registry. The data of all patients

☆ A Spanish translated version of the abstract of this article appears as Appendix in the final online version at doi:10.1016/j.resuscitation.2011.05.022.

* Corresponding author at: Universitätsklinik für Notfallmedizin, Medizinische Universität Wien, Allgemeines Krankenhaus der Stadt Wien, Währinger Gürtel 18-20/6D, 1090 Wien, Austria. Tel.: +43 1 40 400 1964; fax: +43 1 40 400 1965.
E-mail address: fritz.sterz@meduniwien.ac.at (F. Sterz).

0300-9572/$ – see front matter © 2011 Elsevier Ireland Ltd. All rights reserved.
doi:10.1016/j.resuscitation.2011.05.022

Table 1
Baseline characteristics of the patients.

	Non-hypothermia (*N* = 239)	Hypothermia (*N* = 135)	*p*
Age (years)			
Median	60	58	0.239
Interquartile range	48–70	43–68	
Female sex; no./total no. (%)	97/239 (41)	38/135 (28)	0.019
Medical history; no./total no. (%)			
Diabetes	51/239 (21)	25/135 (19)	0.593
Coronary heart disease	56/239 (23)	29/135 (22)	0.702
Cerebrovascular disease	10/239 (4)	6/135 (4)	1.000
Chronic obstructive lung disease	41/239 (17)	20/135 (15)	0.544
Presumed origin of arrest; no./total no. (%)			
Presumed cardiac origin	113/239 (47)	61/135 (45)	0.746
Presumed pulmonary origin	56/239 (23)	39/135 (29)	0.267
Unknown origin	26/239 (11)	17/135 (13)	0.617
Other	44/239 (18)	18/135 (13)	0.247
Pulseless electrical activity; no./total no. (%)	110/239 (46)	71/135 (53)	0.237
Basic life support provided by bystander; no./total no. (%)	55/239 (23)	31/135 (23)	1.000
No flow time (interval between collapse and start of life support) (min)			
Median	2	3	0.048
Interquartile range	0–8	0–9	0.376
Low-flow time (interval between start of life support until ROSC[a]) (min)			
Median	9	9	0.061
Interquartile range	15–22	17–29	
Total epinephrine dose (mg)			
Median	3	3	0.189
Interquartile range	2–5	1–4	
Shockable rhythm[b] during life support; no./total no. (%)	67/239 (28)	47/135 (35)	0.198
GCS[c] on admission			
Median	3	3	0.144
Interquartile	3–3	3–3	
pH on admission to ED[d]			
Median	7.12	7.12	0.276
Interquartile range	6.97–7.27	6.98–7.22	
Lactate on admission ED[d] (mmol/l)			
Median	10.9	10.3	0.232
Interquartile range	7.9–14.8	7.5–13.8	

[a] Return of spontaneous circulation.
[b] Ventricular fibrillation or pulseless ventricular tachycardia.
[c] Glasgow Coma Scale.
[d] Emergency department.

were prospectively documented according to the 'Utstein Style Criteria', which are the recommended guidelines for cardiac arrest and cardiopulmonary resuscitation outcome reporting.[13]

2.1. Patient selection criteria

We included patients with 18 years of age or older, with a witnessed out of hospital cardiac arrest of non-traumatic origin, with a non-shockable initial cardiac rhythm (asystole or pulseless electric activity) and a restoration of spontaneous circulation. Patients who died during the first 24 h after restoration of spontaneous circulation were excluded. Patients with a Glasgow coma scale of greater than 8 after restoration of spontaneous circulation as well as patients with limited neurological and overall functionality [cerebral performance categories (CPC) and overall performance categories (OPC) >2] before cardiac arrest were not included. A performance score of 1 (good function) or 2 (moderate disability) on a 5-category scale was considered as a good functionality; the other categories were 3 (severe disability), 4 (a vegetative state), and 5 (death).[14–16] Furthermore, patients with a known cerebrovascular origin of cardiac arrest and patients with a core temperature of <30 °C upon emergency department admission were also excluded.

2.2. Endpoints

The primary endpoint was the best neurological outcome within a six-month observational period. Patients with good recovery or moderate disability had sufficient cerebral function to live independently and work at least part-time. The secondary end point was overall mortality at six months.

2.3. Treatment

All patients received standard intensive care. Patients were sedated by the administration of Midazolam (0.125 mg/kg of body weight per hour) and Fentanyl (0.002 mg/kg/h). Paralysis was induced by the intravenous administration of pancuronium (0.1 mg/kg every 2 h) or rocuronium (0.5 mg/kg/h). Each patient's temperature upon admission was measured with an infrared tympanic thermometer, an oesophageal probe, or a Foley catheter. Patients treated with hypothermia were cooled to a target temperature of 33 °C ± 1 °C by the use of surface, invasive, or combined cooling techniques. The temperature was maintained at 32–34 °C for 24 h.

2.4. Statistical analysis

Continuous variables are reported as the median and interquartile range. Categorical variables are presented as absolute and relative frequencies. Primary and secondary outcomes were binary, and the chi-square test was used to compare the outcomes between experimental groups. For normally distributed continuous variables, the Student's *T*-Test was performed. To test non-normally distributed variables, we used the Kruskal–Wallis Test. A multivariate logistic regression model was used to determine whether the association between the intervention and the primary and