Epilepsy & Behavior 49 (2015) 173–177

Contents lists available at ScienceDirect

Epilepsy & Behavior

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

Brief Communication

Outcome following postanoxic status epilepticus in patients with targeted temperature management after cardiac arrest

Irina Dragancea [a,*], Sofia Backman [b], Erik Westhall [b], Malin Rundgren [c], Hans Friberg [c], Tobias Cronberg [a]

[a] Department of Clinical Sciences, Division of Neurology, Lund University, Lund, Sweden
[b] Department of Clinical Sciences, Division of Clinical Neurophysiology, Lund University, Lund, Sweden
[c] Department of Clinical Sciences, Division of Anesthesiology and Intensive Care, Lund University, Lund, Sweden

ARTICLE INFO

Article history:
Accepted 19 April 2015
Available online 24 June 2015

Keywords:
Cardiac arrest
Seizure
Status epilepticus
Simplified continuous electroencephalogram
Therapeutic hypothermia

ABSTRACT

Background: Postanoxic electrographic status epilepticus (ESE) is considered a predictor of poor outcome in resuscitated patients after cardiac arrest (CA). Observational data suggest that a subgroup of patients may have a good outcome. This study aimed to describe the prevalence of ESE and potential clinical and electrographic prognostic markers.

Methods: In this retrospective single study, we analyzed consecutive patients who suffered from CA, and who received temperature management and were monitored with simplified continuous EEG (cEEG) during a five-year period. The patients' charts and cEEG data were initially screened to identify patients with clinical seizures or ESE. The cEEG diagnosis of ESE was retrospectively reanalyzed according to strict criteria by a neurophysiologist blinded to patient outcome. The EEG background patterns prior to the onset of ESE, duration of ESE, presence of clinical seizures, and use of antiepileptic drugs were analyzed. The results of somatosensory-evoked potentials (SSEPs) and neuron-specific enolase (NSE) at 48 h after CA were described in all patients with ESE. Antiepileptic treatment strategies were not protocolized. Outcome was evaluated using the Cerebral Performance Category (CPC) scale at 6 months, and good outcome was defined as CPC 1–2.

Results: Of 127 patients, 41 (32%) developed ESE. Twenty-five patients had a discontinuous EEG background prior to ESE, and all died without regaining consciousness. Sixteen patients developed a continuous EEG background prior to the start of ESE, four of whom survived, three with CPC 1–2 and one with CPC 3 at 6 months. Among survivors, ESE developed at a median of 46 h after CA. All had preserved N20 peaks on SSEP and NSE values of 18–37 μg/l.

Conclusion: Electrographic status epilepticus is common among comatose patients after cardiac arrest, with few survivors. A combination of a continuous EEG background prior to ESE, preserved N20 peaks on SSEPs, and low or moderately elevated NSE levels may indicate a good outcome.

This article is part of a Special Issue entitled "Status Epilepticus".

1. Introduction

Hypoxic–ischemic brain injury is the dominating cause of death for patients admitted to an intensive care unit (ICU) following cardiac arrest (CA) [1–3]. A subgroup of patients who suffered from CA develops postanoxic status epilepticus, which is associated with poor outcome [4–12]. Standard ICU management of comatose CA survivors includes temperature management, sedation, and muscle relaxants which may mask clinical seizures [12–14]. The use of continuous EEG monitoring (cEEG) after CA allows for early detection of electrographic epileptic activity, and an ESE prevalence of 12–31% has been reported [8,9,11,12,15–17]. Although the majority of patients with ESE after CA have a poor outcome, some studies suggest that a subgroup may recover well [7,9,13,18]. Development of a continuous EEG background, the presence of EEG reactivity to stimuli, and preserved brainstem reflexes have been associated with good outcome [7,8,19–22].

It is still unclear whether ESE is merely the electrographic expression of a widespread brain damage or if it represents a process that may inflict further injury through excitotoxicity and metabolic stress [23,24]. Diagnostic criteria for ESE [4,25–27] are controversial, and consensus regarding treatment is lacking [9,28].

We performed a retrospective cohort study to evaluate the prevalence of ESE and to identify possible clinical and electrographic prognostic markers of a favorable outcome.

* Corresponding author at: Department of Clinical Sciences, Division of Neurology, Skåne University Hospital, 22185 Lund, Sweden. Tel.: +46 46 171428.
E-mail address: irina.dragancea@med.lu.se (I. Dragancea).

http://dx.doi.org/10.1016/j.yebeh.2015.04.043
1525-5050/

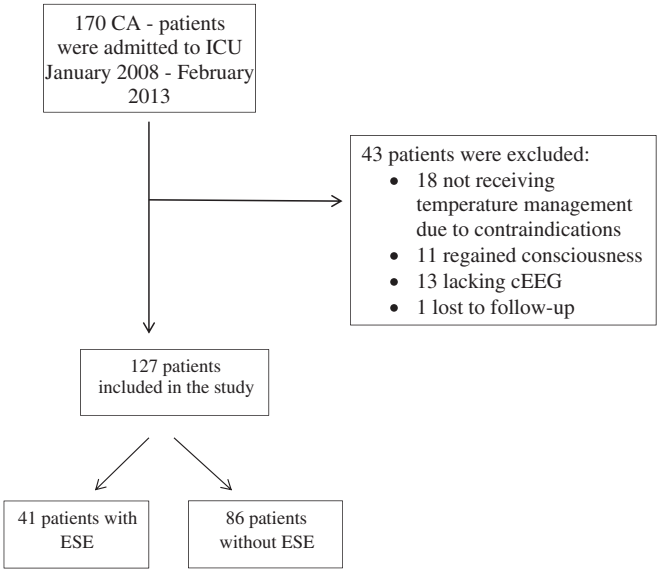

Fig. 1. Study flow chart.

2. Materials and methods

2.1. Patients

This retrospective study was performed at the ICU of Skane University Hospital in Lund, including patients who suffered from CA between January 1, 2008 and February 28, 2013. During this period, cEEG monitoring was routinely used, and temperature management was standard care after CA. Patients without cEEG monitoring or who did not receive temperature management, some of whom had recovered consciousness, were not included in the study.

Ethical permission was obtained from the Regional Ethical Review Board at Lund University (411/2004, 223/2008, 284/2013). Informed written consent was obtained from next-of-kin and retrospectively from patients who recovered. A subset of patients was included in the Target Temperature Management trial, clinicaltrials.gov NCT01020916.

2.2. Clinical procedures

Consecutive comatose survivors of cardiac arrest from 2008 to 2010 and January 2013–February 2013, regardless of initial rhythm and without contraindications for hypothermia, were cooled to 33 °C for 24 h. Patients included in the TTM trial were randomly assigned to 33 °C versus 36 °C from January 2011 to January 2013. The inclusion and exclusion criteria and the main and secondary outcomes of this trial have been published previously [29–31].

In all patients included in the present study, the intervention period including cooling, maintenance of core temperature, and rewarming lasted for 36 h. Sedation was maintained throughout the whole intervention period but was not protocolized.

Patients with clinical seizures or evidence of ESE were treated with combinations of propofol, midazolam, fosphenytoin, valproic acid, and levetiracetam at the discretion of the treating physician. The antiepileptic treatment was not protocolized. Throughout the study period, the neurological prognostication was standardized and scheduled for 72 h after rewarming. In patients still comatose at 72 h after rewarming, with a Glasgow Coma Scale motor score of 1–2 and a treatment refractory status epilepticus and/or bilateral lack of N20 peaks on somatosensory-evoked potentials (SSEPs), the prognosis was considered poor, and withdrawal of life-sustaining therapy (WLST) was allowed.

2.3. EEG recording and interpretation

All patients were monitored with cEEG from arrival at the ICU, using a two-channel bipolar montage (C3–P3, C4–P4 or F3–P3, F4–P4, according to the 10–20 system), displaying both the original EEG signal and trends of amplitude-integrated EEG. Patients' charts and cEEG statements were retrospectively screened to identify patients with detected or suspected ESE. In this subset of patients, the cEEG recordings were reviewed retrospectively by a neurophysiologist who was blinded to the patients' outcome. The EEG pattern at the start of cEEG monitoring, the best background pattern during 4 h prior to the onset of ESE, and the duration of ESE were described systematically. The EEG patterns were defined from the original EEG signal as flat (<10-μV peak-to-peak amplitude), burst suppression (50–99% suppression), discontinuous (10–49% suppression), nearly continuous (≤10% suppression), and continuous or ESE (continuous rhythmic polyspike-/spike-/sharp-and-wave or periodic discharges, with a typical frequency of ≥1 Hz for 30 min or unequivocal seizures, according to the EEG terminology of the American Clinical Neurophysiology Society [32], recurring for 30 min). The duration of ESE was calculated from the first 30-minute period with ESE to the end of the last 30-minute period of ESE or to the end of monitoring if ESE was still ongoing.

2.4. Data collection and outcome assessment

All medical records, including the results of neurological, radiological, and neurophysiological investigations (cEEG and SSEPs); level of neuron-specific enolase (NSE) at 48 h after CA; and prescribed medical

Table 1
Baseline characteristics.

	Patients with ESE N = 41	Patients without ESE N = 86	p-Value
Age	68 (60–72)	65 (56–73)	0.437
Male	28 (68%)	66 (77%)	0.387
Out of hospital	37 (90%)	71 (83%)	0.300
Initial rhythm			0.384
VF/VT	26 (63%)	55 (64%)	
Asystole	7 (17%)	17 (20%)	
PEA	7 (17%)	7 (8%)	
Unknown	1 (2%)	7 (8%)	
Time to ROSC (min)	28 (21–40)	20 (13–32)	0.001
Target temperature management			0.264
33 °C	38 (93%)	73 (85%)	
36 °C	3 (7%)	13 (15%)	
Presence of clinical seizures/myoclonus	35 (85%)	20 (23%)	≤0.001
ICU stay (h)	164 (98–272)	87 (61–173)	0.001
Hospital stay (days)	8 (5–14)	13 (6–18)	0.160
SSEP			≤0.001
Bilateral absent N20 peak	7 (17%)	9 (10%)	
Bilateral present N20 peak	26 (63%)	5 (6%)	
Not performed	8 (19%)	72 (84%)	
WLST			≤0.001
Yes	34 (83%)	28 (33%)	
No	7 (17%)	58 (67%)	
CPC at 6-month follow-up[a]			≤0.001
CPC1	1 (2%)	38 (44%)	
CPC2	2 (5%)	5 (6%)	
CPC3	1 (2%)	4 (5%)	
CPC4	0 (0%)	0 (0%)	
CPC5	37 (90%)	34 (39%)	

Data are presented as number of patients and percentages or medians and interquartile ranges. ESE = electrographic status epilepticus. VT/VF = ventricular fibrillation/ventricular tachycardia. PEA = pulseless electric activity. ROSC = return of spontaneous circulation. ICU = intensive care unit. SSEP = somatosensory-evoked potential. WLST = withdrawal of life-sustaining therapy. CPC = cerebral performance category score.

[a] 5 patients missing in the group without ESE.