Clinical Neurophysiology 128 (2017) 681–688

Contents lists available at ScienceDirect

Clinical Neurophysiology

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

Electroencephalographic characteristics of status epilepticus after cardiac arrest

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

[a] Lund University, Skane University Hospital, Department of Clinical Sciences Lund, Clinical Neurophysiology, Lund, Sweden
[b] Lund University, Skane University Hospital, Department of Clinical Sciences Lund, Neurology, Lund, Sweden
[c] Lund University, Skane University Hospital, Department of Clinical Sciences Lund, Intensive and Perioperative Care, Lund, Sweden
[d] Clinical Studies Sweden – Forum South, Skane University Hospital, Lund, Sweden

See Editorial, page 660

ARTICLE INFO

Article history:
Accepted 14 January 2017
Available online 21 January 2017

Keywords:
EEG
Continuous EEG monitoring
Cardiac arrest
Coma
Electrographic status epilepticus
Hypoxic-ischemic encephalopathy
Therapeutic hypothermia
Outcome prediction

HIGHLIGHTS

- Patterns along the ictal-interictal continuum are commonly encountered after cardiac arrest.
- Unequivocal and possible electrographic status epilepticus (ESE) patients have similar clinical features.
- Since ESE patterns appear as a continuum they should not be used in isolation for prognostication.

ABSTRACT

Objective: To describe the electrophysiological characteristics and pathophysiological significance of electrographic status epilepticus (ESE) after cardiac arrest and specifically compare patients with unequivocal ESE to patients with rhythmic or periodic borderline patterns defined as possible ESE.
Methods: Retrospective cohort study of consecutive patients treated with targeted temperature management and monitored with simplified continuous EEG. Patients with ESE were identified and electrographically characterised until 72 h after ESE start using the standardised terminology of the American Clinical Neurophysiology Society.
Results: ESE occurred in 41 of 127 patients and 22 fulfilled the criteria for unequivocal ESE, which typically appeared early and transiently. Three of the four survivors had unequivocal ESE, starting after rewarming from a continuous background. There were no differences between the groups of unequivocal ESE and possible ESE regarding outcome, neuron-specific enolase levels or prevalence of reported clinical convulsions.
Conclusion: ESE is common after cardiac arrest. The distinction between unequivocal and possible ESE patterns was not reflected by differences in clinical features or survival.
Significance: A favourable outcome is seen infrequently in patients with ESE, regardless of using strict or liberal ESE definitions.

1. Introduction

Hypoxic-ischaemic brain injury is the major cause of death among resuscitated cardiac arrest (CA) patients treated at an intensive care unit (ICU). Electrographic status epilepticus (ESE) is common during the first days of post-arrest care (Rundgren et al., 2006; Rossetti et al., 2007). ESE is recognised as a predictor of poor

Abbreviations: CA, cardiac arrest; cEEG, continuous EEG monitoring; CPC, Cerebral Performance Category; EEG, electroencephalogram; ESE, electrographic status epilepticus; ICU, intensive care unit; IQR, interquartile range; NSE, neuron-specific enolase; ROSC, return of spontaneous circulation; SSEP, somatosensory evoked potentials; WLST, withdrawal of life-sustaining therapy.

* Corresponding author at: Department of Clinical neurophysiology, Skane University Hospital, 221 85 Lund, Sweden. Fax: +46 46 146528.
E-mail address: sofia.backman@med.lu.se (S. Backman).

http://dx.doi.org/10.1016/j.clinph.2017.01.002
1388-2457/

neurological outcome in recent guidelines, recommending the use of repeated routine EEG or continuous monitoring to detect and treat electrographic seizures (Cronberg et al., 2013; Nolan et al., 2015). Considering the grave consequences of a statement of poor neurological prognosis, often leading to withdrawal of life-sustaining therapy (WLST), it is striking that no agreement exists on the definition of status epilepticus in this setting. Without clear EEG definitions it is a challenging task to decide which patients have a potential for good long-term outcome and for whom prolonged active antiepileptic treatment may be beneficial.

The reported prevalence of ESE varies considerably between studies (Rundgren et al., 2010; Legriel et al., 2013; Ruijter et al., 2015), partly due to the usage of diverse definitions, especially regarding criteria for discharge frequency. Several EEG criteria have been proposed (Young et al., 1996; Chong and Hirsch, 2005; Kaplan, 2007; Beniczky et al., 2013; Hirsch et al., 2013) and there is still no international consensus.

Gradual changes in electrographic seizure patterns during status epilepticus were described in experimental models and in humans (Treiman et al., 1990; Pender and Losey, 2012). Continuous EEG monitoring (cEEG) may be used to follow these fluctuations along a continuum of rhythmic or periodic patterns ranging from interictal to clearly ictal. The American Clinical Neurophysiology Society (ACNS) has published a standardised terminology for critical care EEG patterns (Hirsch et al., 2013). This terminology includes definitions of periodic and rhythmic patterns that may represent seizure activity, and strict criteria for unequivocal electrographic seizure activity.

We have previously described the clinical features, prognostic implications and prevalence of ESE in a well-characterised cohort of CA patients monitored with simplified cEEG (Dragancea et al., 2015). In the present study we used the ACNS terminology to further describe ESE, focusing on the electrophysiological characteristics and development over time. Our main objective was to investigate whether the patients with strictly defined unequivocal ESE differ from patients with possible ESE patterns along the ictal-interictal continuum.

2. Methods

2.1. Patient population and clinical characteristics

Retrospective cohort study including consecutive adult CA patients treated with targeted temperature management at the general ICU at Skane University Hospital in Lund between January 2008 and March 2013. Patients were excluded if they had contraindications to temperature management, regained consciousness before start of temperature management, lacked cEEG or follow-up at six months.

Patients were intubated, sedated with propofol or midazolam and treated with targeted temperature management at 33 °C or 36 °C for 24 h. Rewarming was completed approximately at 36 h after CA. Sedation was stopped as soon as possible after rewarming. According to local routine, clinical and electrographic seizures were treated by the attending physician with combinations of sedatives and antiepileptic drugs. ESE was actively treated at least until the time-point of prognostication, but without a systematic treatment protocol. The ICU staff noted clinical convulsions including myoclonus on a chart.

The study was approved by the Regional Ethical Review Board at Lund University (411/2004, 233/2008, 284/2013). Informed written consent was obtained from next-of-kin and retrospectively from patients who survived.

The clinical data and patient characteristics of this cohort were previously published (Dragancea et al., 2015).

2.2. Data acquisition and electrophysiological characteristics

Patients were monitored with Nicolet One monitors (Viasys Health care, WI, USA) with a simplified cEEG-montage displaying two bipolar channels according to the 10–20 system (F3-P3 and F4-P4 or C3-P3 and C4-P4). Filter settings of 1–70 Hz were used. All EEG characterisation was performed by reviewing the original EEG-signal. Amplitude-integrated EEG trend curves were available during analysis, but were not included in the EEG characterisation.

All clinical cEEG reports were screened for the presence of epileptiform activity. The cEEG recordings were then retrospectively reviewed by a senior consultant in clinical neurophysiology (SB), blinded to outcome and other clinical parameters. Patients fulfilling the criteria for possible or unequivocal ESE were identified and their cEEG-data was further characterised, from the start of ESE and during the following 72 h.

The criteria for unequivocal ESE were based on the ACNS terminology (Hirsch et al., 2013) and considered fulfilled if one of the following patterns occurred:

- Bilateral spike/sharp-and-waves at a rate of $\geqslant$3 Hz and constituting at least 50% of a 30 min period (Fig. 1a).
- Repeating sequences of at least 10 s with discharges of any type clearly evolving in frequency, reaching >4 Hz and constituting at least 50% of a 30 min period (Fig. 1b).

If the criteria for unequivocal ESE were not fulfilled and rhythmic spike/sharp-and-waves or periodic discharges at a rate of $\geqslant$1 Hz were present for at least 30 min, the pattern was defined as possible ESE (Fig. 1c).

The best background pattern was identified during four hours preceding ESE start. The amount of interictal epileptiform discharges during a 30 min period at 12 h and 6 h before ESE start was assessed. Presence of highly epileptiform bursts were noted and defined as bursts with multiple epileptiform discharges with a frequency of $\geqslant$1 Hz in >50% of the bursts (Hirsch et al., 2013).

Three consecutive 24-h periods after ESE start were analysed for unequivocal and possible ESE periods. The discharge frequency was assessed and categorised within 0.5 Hz intervals. The dominating and the best background patterns were evaluated for each 24-h period and also for the ESE free periods. Background was assessed for continuity and reported as suppressed (<10 μV peak-peak amplitude), burst-suppression (50–99% suppression), discontinuous (10–49% suppression), nearly continuous (<10% suppression) or continuous according to the ACNS terminology. Only patterns persistent for a minimum of 30 min were reported.

According to local practice a routine EEG, recorded with 22 electrodes (10–20 system), was performed before neurological prognostication. The first available routine EEG after ESE start was reviewed retrospectively for background pattern, reactivity and further characterisation of discharges. Reactivity was tested according to a standardised protocol including at least two sound stimulations and at least two pain stimulations (central and peripheral).

Bilateral median nerve somatosensory evoked potentials (SSEP) were performed on clinical indication in patients still comatose the day preceding prognostication, typically corresponding to 48–72 h after rewarming.

2.3. Laboratory characteristics

Serum levels of neuron-specific enolase (NSE) were analysed at 48 h after CA using NSE Cobas e601 (Roche Diagnostics, Mannheim, Germany).