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Postanoxic alpha, theta or alpha-theta coma: Clinical setting and neurological outcome[☆,☆☆]

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ABSTRACT

Aim: The aim of this study was to determine the prognosis of 26 consecutive adults with alpha coma (AC), theta coma (TC) or alpha-theta coma (ATC) following CRA and to describe the clinical setting and EEG features of these patients.
Methods: We retrospective analyzed a prospectively collected cohort of adult patients diagnosed as having AC, TC or ATC after CRA between January 2008 and June 2016. None of patients included in this analysis underwent therapeutic hypothermia (TH). Neurological outcome was expressed as the best score 6 months after CRA using the five-point Glasgow-Pisttsburgh Cerebral Performance Categories (CPC)
Results: Twenty-six patients were identified with a diagnosis of postanoxic AC, TC or ATC coma. There were 20 (77%) men and 6 (23%) women. The mean age was 63 ± 16 years. The most frequent EEG pattern was TC (21 patients, 80%), followed by AC (3 patients, 12%) and ATC (2 patients, 8%). The cardiac rhythm as primary origin of the CRA was ventricular fibrillation (VF) in 16 patients (61.5%), asystole in 8 patients (34.6%) and ventricular tachycardia (VT) in one patient (3.8%). The presence of EEG reactivity was present in 8 patients (30%). The mortality rate was 85%. Of the 4 surviving patients, two (3.8%) had moderate disability (CPC 2), one (3.8%) had severe disability (CPC 3) and one (3.8%) reached a good recovery. The age was significantly lower in survivors 46.2 ± 10.8 versus nonsurvivors 63.3 ± 15.5 ($p = 0.04$). There was increased association of EEG reactivity with survival ($p = 0.07$).
Conclusion: Hypoxic-ischemic AC, TC and ATC are associated with a poor prognosis and a high rate of mortality. In younger patients with AC, TC and ATC and incomplete forms showing reactivity on the EEG, there is a greater probability of clinical recovery.

Introduction

Cardiorespiratory arrest (CRA) is a severe clinical condition that is a frequent cause of coma and admission to the intensive care unit (ICU). Supportive care imposes a high economic burden and this effort is balanced against the chance and quality of neurological recovery and the expectations of the patient's family [1].

It is now widely accepted that accurate prognostication in comatose patients after CRA is on a multimodal assessment that includes clinical, electrophysiological, laboratory and neuroimaging data is warranted [2]. The utility of electroencephalography (EEG) in determining outcome in hypoxic-ischemic encephalopathy (HIE) has been the subject of extensive investigation over the

Abbreviations: AC, Alpha coma; ATC, Alpha-theta coma; CRA, Cardiorespiratory arrest; EEG, Electroencephalogram; HIE, Hypoxic-ischemic encephalopathy; TH, Therapeutic hypothermia; TC, Theta coma.

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past dozen years [3–21]. Hence, much effort has been directed at determining those EEG patterns or specific EEG alterations that carry prognostic significance. It has been reported that a uniform, continuous, diffuse, unreactive pattern with alpha and theta frequencies (complete alpha coma (AC), theta coma (TC) or alpha-theta coma (ATC)), with frontal predominance, has been associated with poor outcome [22–26]. Incomplete or atypical variants of these patterns are not rare and, in these cases, neurological recovery may be possible [26,27]. The interpretation of the EEG changes in AC, TC and ATC may not be straightforward and there is a spectrum of variants to these patterns that may have different prognostic significance.

The aim of this study was to determine the prognosis of 26 consecutive adults with AC, TC or ATC following CRA and to describe the clinical setting and EEG features of these patients.

Methods

Data collection and patients

This investigation is a retrospective analysis of a prospectively collected series. The Department of Clinical Neurophysiology at Marqués de Valdecilla University Hospital provides adult neurophysiologic service to 591,886 inhabitants in an urban and rural area of the region of Cantabria, located in the north of Spain. It is the only neurophysiology department in the area. Between January 2008 and June 2016, we prospectively identified all those patients older than 18 years with a diagnosis of AC, TC or ATC after CRA. Other patients with coma from toxic or metabolic causes, and de-efferented states resulting from brainstem lesions were excluded. None of patients included in this analysis underwent therapeutic hypothermia (TH) since this technique was not routinely used in our hospital.

All clinical data were gathered from chart review, EEG reports and protocols, discharge summaries, and resident sign-out notes. Baseline demographic data (age, gender), past medical history, focusing our attention on cardiovascular antecedents including the shockable cardiac rhythm as primary origin of the CRA were recorded. When we had 26 consecutive patients, we retrospectively analyzed all our data.

EEG inclusion criteria

Electroencephalography was performed with 21 needle or surface electrodes placed according to the International 10–20 System at the ICU. Routine video-EEG was obtained for at least 30 min including manual eye opening, photic, auditory, tactile and noxious stimuli. All tracings were reviewed by one board-certified clinical neurophysiologist (JLF-T), and the frequency of the cerebral rhythms, distribution and reactivity were analyzed. Reactivity was defined as any reproducible change in amplitude or frequency in the cerebral EEG activity, excluding stimulus-induced rhythmic, periodic or ictal discharges (SIRPIDs) and muscle artifacts, related to patient sensory stimulation [28]. In the majority of subjects follow-up EEGs were done.

All EEGs recordings carried out in CRA comatose patients showing continuous widespread rhythms of alpha (8–13 Hz), theta (4–7 Hz) or both frequencies, in comatose patients following CRA were selected. This pattern was present throughout the full recording. We used the term ATC when AC and TC patterns were observed in the same recording. All patients were without sedation at the moment of the EEG. Although AC, TC and ATC are classically characterized by the lack of reactivity, in our study, the presence of EEG reactivity was not an exclusion criterion since partially reactive EEG recordings have been observed in subjects with incomplete forms of AC and TC [24,26,27].

Outcome assessment

Neurological outcome was expressed as the best score 6 months after CRA using the five-point Glasgow-Pistsburgh Cerebral Performance Categories (CPC) (1 = good recovery, 2 = moderate disability, 3 = severe disability with dependency for daily life activity, 4 = comatose or vegetative state, and 5 = death) [29]. Neurological state was collected from the clinical visits, medical records and EEG charts.

Outcome was dichotomized between “good” and “poor”. Good outcome was defined as a CPC score of 1 or 2 and poor outcome as a CPC score of 3, 4 or 5. CPC scores were determined after 6 months of CRA.

Statistical analysis

All data were coded and entered into a database in SPSS 20.0 for statistical purposes. Quantitative variables were expressed as mean and standard deviation (SD), or median and interquartile range. Qualitative variables were presented as total number of events and percentages. The comparison of qualitative variables was done by Chi-square test or 2×2 tables. Quantitative variables were compared by Student *t*-test or non-parametric Mann–Whitney *U* test, as appropriate, verified by Kolmogorov–Smirnov test.

Results

Twenty-six patients were identified with a diagnosis of postanoxic AC, TC or ATC coma. All demographic, clinical, EEG and neuroimaging features are summarized in Table 1.

There were 20 (77%) men and 6 (23%) women. The mean age was 63 ± 16 years (range 30–82 years). The median duration of the presumed time of CRA was 20.2 min (IQR, 10–30 min). In 5 patients the duration of the CRA could not be reliably determined. The median time from admission to the first EEG was 48.0 h (IQ 24–72 h). The median time of hospitalization was 10 days (IQR, 7-16 days). The most frequent EEG pattern was TC (21 patients, 80.7%), followed by AC (3 patients, 11.5%) and ATC (2 patients, 7.6%) (Fig. 1). EEG features included widespread predominantly monotonous, more frequently nonreactive (70%), alpha or theta frequencies with or without frontal predominance. Occasionally, delta waves or brief episodes of generalized electrodecremental events were also observed (Fig. 2). The median number of EEGs was 2 (IQR 1–3). Eighteen patients (69%) had a second EEG. In 9 (50%) the EEG remained invariable, in 2 patients (11%) EEG evolved in to a burst-suppression pattern and in 7 (39%) a moderate or severe encephalopathy was present. Seven subjects had a third EEG, 5 had a fourth EEG and in 2 cases we carried out 5 EEGs. Thirteen patients (50%) had arterial hypertension, 8 (31%) coronary heart disease, 5 (19%) had diabetes mellitus, 4 (15%) had alcoholism and 3 (12%) had dyslipidemia. The cardiac rhythm as primary origin of the CRA was ventricular fibrillation (VF) in 16 patients (61.5%), asystole in 8 patients (34.6%) and ventricular tachycardia (VT) in one patient (3.8%) (Fig. 1). The presence of EEG reactivity was present in 8 patients (30%). Five (63%) of these patients died and 3 (38%) survived (Fig. 3). In one subject (patient 7) that survived with a favorable evolution with moderate disability (CPC 2), the EEG was unreactive. Neuromaging was obtained in only 16 patients (61%). Brain computed tomography (CT) scan was done in 15 of these patients, and only two had a brain magnetic resonance imaging (MRI). In all cases neuroimaging was unremarkable. The mortality rate was 85% (22/26) including 19 TC (90%), 2 ATC (100%) and 1 AC (33%). Four subjects (15%) survived counting 2 TC and 2 AC. Two

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