Absence and reappearance of N20 response after thiopental withdrawal in postanoxic coma

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Practical Implications

Absence of N20 response in postanoxic coma should be interpreted with caution if high-dose thiopental is used for refractory status epilepticus.

Supplemental Data

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A 42-year-old woman with witnessed out-of-hospital cardiac arrest (CA) reached the emergency department after 38 minutes of cardiopulmonary resuscitation. Since the return of spontaneous circulation did not occur, extracorporeal membrane oxygenation (ECMO) was applied. The ECMO circuit was connected to a heat exchanger to induce therapeutic hypothermia (34°C). Continuous EEG monitoring with a simplified 4-channel montage (EEG Infinity POD, Dräger, Lübeck, Germany) was started. After 24 hours of hypothermia, the patient was gradually rewarmed, according to the local protocol. At the withdrawal of sedation, she remained comatose, and standard reduced-montage (8-channel) EEG showed nonconvulsive status epilepticus (NCSE, figure e-1 at Neurology.org/cp), which was initially treated with propofol and valproate infusion (20 mg/kg followed by 1 mg/kg/hr). She was weaned from ECMO 48 hours after CA. She remained in a coma, all brainstem reflexes were present, neuron-specific enolase was 21 ng/mL, and brain CT scan was normal, with no evidence of traumatic brain injury or other brain lesions. Standard EEG was repeated and showed refractory NCSE. Levetiracetam was added (2,000 mg bolus followed by 2,000 mg/24 hours), and propofol-induced coma was initiated to obtain a burst-suppression pattern for 24 hours, guided by EEG monitor. Propofol was gradually stopped 72 hours after CA, and EEG still showed refractory NCSE. High-dose barbiturate coma was induced (thiopental 10 mg/kg/hr). At this time point, EEG was isoelectric and the patient was hemodynamically stable. Median nerve somatosensory evoked potentials (SSEP, see figure 1 for technical details) were recorded 72 hours after CA, and N20 cortical responses were bilaterally absent, while potentials at Erb point (N9), cervical spine (N13), and lower brainstem (P14) were present (figure 1A). Barbiturate coma was maintained for 24 hours. After barbiturate withdrawal, EEG showed diffuse slow wave activity with superimposed irregular beta activity. SSEP recording was repeated 10 days after the first recording (9 days after thiopental withdrawal) and showed bilateral reappearance of the N20 response (figure 1B). The patient showed a gradual improvement in both consciousness and

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Figure 1 EEG monitoring and somatosensory evoked potential (SSEP) recordings during and after thiopental infusion

(A) EEG tracing obtained with a 4-channel EEG monitor (left) and bilateral median nerve SSEP recordings (right) during thiopental infusion. (B) EEG tracing obtained with a 4-channel EEG monitor (left) and bilateral median nerve SSEP recordings (right) after 48 hours of thiopental withdrawal. SSEP stimulation parameters: single pulse, duration 0.2 msec, frequency 5 Hz, intensity approximately 2 times that necessary to evoke a visible thumb twitch, maximum 100 mA. SSEP recording parameters: low-pass filter 10 Hz, high-pass filter 2,000 Hz, amplifier gain 2.0 μ V/division, SSEP is the averaged result of 500 stimulus presentations, 2 SSEPs for each limb were superimposed for waveform reproducibility.

neurologic examination and was discharged from the intensive care unit 4 weeks after CA. At 3-month follow-up she was independent in activities of daily living (Cerebral Performance Category 2).

The absence of cortical N20 response of the median nerve SSEP has been established as one of the strongest indicators of poor neurologic outcome in comatose survivors of CA, whether they are treated with hypothermia or not.¹⁻³ A negative prognostic value has also been associated with refractory status epilepticus after CA,⁴ although the evidence on this issue has been limited by controversies about diagnostic criteria (particularly regarding periodic patterns) and treatment of this common condition. Recent studies showed that at least a subset of patients with postanoxic NCSE might have a favorable outcome if treated aggressively,⁵ although the exact cliniconeurophysiologic profile of these patients remains to be identified.

The decision to treat the patient's refractory NCSE aggressively was based on the predominance of positive prognostic indexes (presence of brainstem reflexes, low levels of neuron-specific enolase, and normal neuroimaging), despite the initial absence of N20 response.

The present case showed that aggressive treatment of refractory status epilepticus after CA with high doses of antiepileptic drugs and barbiturate coma can be associated with a reversible disappearance of N20 response. This is an unexpected finding, since previous studies showed that thiopental did not abolish N20 responses in humans but rather caused a variable increase in latency and a decrease in amplitude.⁶

Notably, these early reports did not include patients with postanoxic coma. Our report prompts further experimental and clinical studies on the susceptibility of the N20 response to barbiturate/antiepileptic drugs in postanoxic encephalopathy, which may display a distinct pattern compared to nonanoxic brains. Clinicians should be especially vigilant when using thiopental after CA during SSEP recording in order to avoid the risk of self-fulfilling prophecies and

to be in accordance with the current guidelines, which recommend a multimodal approach to prognostication after CA.⁷

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