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Review Article

Super-Refractory Status Epilepticus Treatment in a Critical Care Unit – Deep Thiopental Sedation with Bispectral Index (BIS) Monitoring

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Abstract

Status epilepticus can lead to multi-organ failure through the damage to the central nervous system. Its most severe forms require treatment at an intensive care unit with deep sedation and electroencephalograph (EEG) monitoring. Deep sedation is associated with the need for mechanical ventilation, invasive monitoring of vital functions, artificial nutrition and other intensive care procedures. This type of therapy is associated with numerous complications that may be an independent risk factor for death, such as: sepsis, pneumonia, hemodynamic and metabolic instability, altered level of consciousness when recovering. We report a case of refractory status epilepticus which developed likely as a delayed consequence of carbon monoxide poisoning and which was treated with deep thiopental sedation monitored by bispectral index (BIS).

ABBREVIATIONS

BIS: Bispectral Index; EEG: Electroencephalograph; MRI: Magnetic Resonance Imaging; CSF: Cerebrospinal Fluid; ICU: Intensive Care Unit; SE: Status Epilepticus; RSE: Refractory Status Epilepticus; SRSE: Super Refractory Status Epilepticus

INTRODUCTION

Deep sedation in an intensive care unit is of limited use due to the lack of clear specific indications and high probability of complications. In certain situations, such as: intracranial hypertension, severe respiratory insufficiency or status epilepticus, deep sedation may be helpful to obtain specific intermediate points: normalization of intracranial pressure, improvement of ventilation, achieving a specific pattern in the EEG [1]. In this last case, untreated status epilepticus may lead to severe and irreversible brain damage. On the other hand, therapy based on a continuous infusion of intravenous anesthetics until obtaining deep sedation (even an isoelectric line in EEG) may have adverse consequences, including metabolic, hemodynamic, infectious and, while recovering from deep sedation, delirium and other cognitive disturbances.

CASE PRESENTATION

A 31-old male presented to an emergency room with headaches, dysphasia, drooping of the left mouth, and a weakness of his left extremities. The symptoms had begun on awaking several hour earlier. His mother reported similar presentation on several occasions during the previous 6 months, but symptoms had always subsided promptly and without treatment. Tonic-clonic seizures led to admission year earlier, but details were not available. Three years prior to current admission patient had suffered carbon monoxide poisoning, resulting in the neurological sequelae of spinocerebellar syndrome. He had no other significant past medical history and was not taking any medication. His vital signs on admission were: BP 226/110, HR 97/min, SpO2 97%, RR 16/min, temperature 39.0 centigrade.

The patient's motor symptoms subsided before a full neurological examination was performed, leaving only elevated tendon reflexes in the left upper extremity, whereas some confusion, a headache and fever persisted. A computer tomography (CT) and magnetic resonance imaging (MRI) ruled out intracranial bleeding and an ischemic stroke. A lumbar puncture was performed, with the only abnormality being

a markedly elevated protein level (104 mg/dl). Due to the suspicion of viral encephalitis, acyclovir was administered intravenously (750 mg q8h), and persistent epileptic activity prompted treatment with intravenous sodium valproate (a loading dose of 800 mg, followed by an infusion 1600 mg/24h) and levetiracetam 500 mg q12h. On the second day ceftriaxone 1g q12h was added. Patient's condition did not improve and on the second day another prolonged generalized tonic-clonic seizure occurred necessitating intensive care unit (ICU) admission, The patient was sedated, intubated, and administered a continuous infusion of sodium thiopental (titrated up to 4mg/kg/h until the motor seizures stopped appearing). Blood, CSF and tracheal aspirate were cultured, but they came back negative. Repeated cerebrospinal fluid (CSF) analysis revealed no abnormalities, except for elevated protein levels (69 mg/dl). Sedation with thiopental was stopped after 24 hours with two episodes of tonic-clonic seizures within few hours. We reintroduced therapeutic coma while recording EEG activity. We increased thiopental dose until the suppression of electroencephalographic activity, up to 7mg/kg/h. Because of the unavailability of continuous EEG monitoring, a bispectral index (BIS) monitor was used as a surrogate, with the index fixed at 0 (usually the level of 40-60 on a scale from 0-100 is associated with general anesthesia). The infusion was continued for 24 hours with the follow-up EEG showing an isoelectric line. Four days after the end of the thiopental infusion, the patient began to regain consciousness with temporary agitation and delirium. The seizures did not recur. Throughout that time observed complications included: hypokalemia, thrombocytopenia, hypotension and elevated liver enzymes. After his condition stabilized, he was transferred back to the neurology department. After a follow-up contrast MRI scan, a diagnosis of Posterior Reversible Encephalopathy Syndrome was made. His stay at the neurology department was uneventful, no further seizure episodes occurred until his discharge to the neurorehabilitation facility.

DISCUSSION

Status epilepticus (SE) is a well-recognized neurological emergency. Treatment protocols are well established, and in most cases, first- and second-line therapies are effective when timely administered [2-7, 19]. However, the most severe forms, known as refractory status epilepticus (RSE) and super refractory status epilepticus (SRSE) are associated with significant morbidity, mortality, complications and greatly increased resource utilization [7-13,19, 21, 24, 29, 32,33]. In the event of a failure to control seizures with conventional anti-epileptic drugs (AEDs), a therapeutic coma with intravenous anesthetics (IVADs) is sometimes the recommended option [3,5-7,19]. Unfortunately, the evidence supporting either the induction of the coma itself or the use of any particular drug over another is lacking [3,5,6,14-19,29]. Such treatment requires ICU admission, mechanical ventilation and usually vasoactive support. It is not devoid of severe and potentially fatal complications [5, 9,14-16,20, 22-24,26], therefore, it is not surprising that its value has been questioned. [14,25,27,28]. There is even less clarity regarding the management of seizures recurring within 24 hours from withdrawal of intravenous anesthetics (i.e. SRSE) [4,12,19,20,31], although reports have been published describing various treatments including ketamine, surgery, electrotherapy [19,20, 30,32,34-41]. Re-initiation of implanted venous access device (IVAD) infusion in higher doses has also been advocated [19]. There is no evidence-based recommendation regarding the depth and duration of a coma for the treatment of SRSE [6,19,20]. The prolonged recovery of consciousness after thiopental withdrawal is also noteworthy, as it has raised concerns among members of our ICU team about possible permanent neurological damage, which could have led to the de-escalation of supportive treatment.

The use of BIS in this particular clinical case might appear controversial, but throughout the therapeutic process we were well aware of its design and limitations. The purpose of this technology is to monitor the depth of sedation using intravenous anesthetics. 4-lead EEG can undergo rapid Fourier analysis in order to deliver quantitative, real-time estimates of the depth of sedation [42]. It does not enable a comprehensive analysis of EEG, hence it is useless in detecting specific EEG patterns or monitoring epileptiform activity. During the second barbiturate coma, the therapeutic goal was not a specific EEG pattern (such as burst-suppression), but a certain level of sedation characterized by an absence of cortical electrographic activity. In order to counter the risk of an under-detection of epileptoiform activity resulting from the BIS electrode placement (one-sided frontoparietal), a complete EEG was performed on a daily basis. The authors would like to underline that, regarding epilepsy management, BIS cannot be considered an alternative to EEG, but in certain clinical scenarios it might be used complimentary to repeated EEG, especially when 24-hour EEG monitoring is unavailable.

Not only does this report describe the successful treatment of SRSE, but to the authors' knowledge it is the first one describing SRSE as a possible remote sequela of carbon monoxide poisoning, although the presence of seizures in the setting of acute poisoning is a well-established fact.

DISCLOSURE

The work was performed at Medical University in Poznań, Poland, without any financial support.

CONFLICTS OF INTEREST

There are no conflicts of interest by any of the authors.

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