Case Report

Successful Use of Ketamine for Burst Suppression in Super Refractory Status Epilepticus Following Substance Abuse

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Abstract

Status epilepticus is frequently encountered in neuro Intensive Care Units. It is a medical emergency and if not treated promptly can lead to severe brain damage and even death. Here, we present the case of a 18-year-old male with uncontrolled and unrelenting seizures with a rare etiology requiring ketamine infusion for burst suppression as it was resistant to thiopentone and midazolam infusions. The management of this case is presented in detail.

Keywords: Burst suppression, ketamine, status epilepticus

Introduction

It is not uncommon to treat seizures in Intensive Care Units (ICUs) due to various causes and also status epilepticus (SE) with burst suppression. Seizures persisting or recurring after adequate doses of benzodiazepine followed by a second acceptable anti-epileptic drug (AED) are considered to be refractory. When the bolus intermittent therapy of AED fails, continuous infusion of anesthetic agents is recommended.[1] Super refractory status epilepticus (SRSE) is defined as SE that continues or recurs 24 h or more after the onset of anesthetic therapy, including those cases where SE recurs on reduction or withdrawal of anesthesia.[2] Around 10%–15% of patients admitted to hospital become super refractory. The reported mortality is 35% and the incidence of severe neurological deficit in such cases is 13%.[3] The common causes are very well documented in the literature along with uncommon causes such as drug intoxications [Table 1].[4] We present a rare case of SRSE following marijuana intoxication requiring burst suppression with ketamine infusion for almost 7 days. The gold standard for achieving burst suppression in SE is thiopentone and midazolam which were found inefficient requiring ketamine for the same.

Case Report

An 18-year-old college student came with intractable seizures, received midazolam and levetiracetam, and then shifted to ICU after a computed tomography (CT) brain. In the ICU, lumbar puncture was performed immediately for cerebrospinal fluid (CSF) analyses as the CT scan of brain was normal and there was a history of febrile illness of 4 days. The patient was intubated and ventilated on the same day for repeated seizures which continued to occur in spite of higher doses of multiple antiepileptic agents such as midazolam, levetiracetam, lacosamide, and later phenytoin, clobazam, and valproate. Even though phenobarbitone and topiramate were also tried later as the intermittent seizure, vertical nystagmus and epileptiform discharges on electroencephalogram did not disappear. Hence, on day 3 of admission, thiopentone 4 mg/kg intravenous (IV) bolus followed by up to 4 mg/kg/h infusion was added with midazolam infusion to achieve burst suppression. But when this was ineffective, the burst suppression was finally achieved with IV ketamine 1 mg/kg bolus followed by 2 mg/kg/h infusion which was continued for 48 h and then tapered off slowly over the next 5 days. As the parents of the patient did not reveal history of substance abuse initially, he was extensively investigated. Meanwhile, all the investigations

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Table 1: Etiologies of refractory status epilepticus

S No.	Etiology	Percentage
1	Infection	19
2	Preexisting epilepsy	18
3	Metabolic	13
4	Acute stroke	11
5	Tumor related	10
6	Alcohol or another drug withdrawal	9
7	Drug intoxication	6
8	Acute hypoxemic ischemic encephalopathy	6
9	Acute trauma	6
10	Miscellaneous or undetermined	2

such as CSF for viral, bacterial, and fungal infections, magnetic resonance imaging with contrast, blood cultures, and serology for any common and rare bacterial, tropical, viral, or parasitic infections along with antinuclear antibodies profile, and autoimmune encephalitis panel were followed. But when all the test results were negative, the patient's brother revealed that the patient was habituated to smoking weed (synthetic marijuana). As it was the 5th day of admission, the urine toxicology report was also negative for marijuana. But when we searched the literature, we found that the synthetic marijuana is available in different forms and its ingredients are too toxic and can cause refractory status epilepticus (RSE) as in this case. He developed ventilator-associated pneumonia on the 8th day of ICU stay which was treated with meropenem and colistin and then he was tracheostomized on the 10th day and subsequently weaned off ventilator over a period of another 7 days as all the sedatives and most of the antiepileptics were tapered off. Then, he was decannulated on the 20th day and shifted out of the ICU the next day. The patient was discharged on the 25th day without any sensory motor deficit to follow-up after 7 days.

Discussion

SE is an acute and severe illness of the central nervous system and prolonged SE can lead to brain damage and even death. Ketamine is a noncompetitive antagonist of glutamatergic N-methyl-D-aspartate (NMDA) receptors. During prolonged seizures, the number and activity of the gamma-aminobutyric acid receptors gradually decrease, making it resistant to the first- and second-line AEDs. Simultaneously, the numbers and activity of the glutamatergic NMDA receptors increase often causing RSE, providing the rationale for using ketamine.[5] Studies have demonstrated the efficacy and safety of ketamine for the treatment of RSE.[6,7] RSE carries a mortality rate as high as 23%–61% depending on the underlying cause and the time taken to start the treatment.[1] Although drug intoxication accounts for about 6% of all the causes of RSE, marijuana is a rare cause. According to a recent review, synthetic marijuana compounds (K2/spice) are falsely marketed to adolescents as a safe alternative to marijuana and are widely known to avoid detection in standard drug screens as they lack structural similarity to tetrahydrocannabinol, the active ingredient in marijuana.[8] The exact mechanism of toxicity is unknown, but it is stated that these synthetic cannabinoids act through CB1 and CB2 cannabinoid receptors which are present all over the brain and are linked to a number of serious side effects, including seizures, psychosis, and even death, although it has been suggested that cannabidiol might reduce seizure and might have an adequate safety profile in children and young adults with highly treatment-resistant epilepsy.[9] This case reiterates the usefulness of ketamine for SRSE and emphasizes on detailed and repeated history taking with a high index of suspicion about substance abuse.

Declaration of patient consent

The authors certify that they have obtained all appropriate patient consent forms. In the form, the patient has given his consent for his images and other clinical information to be reported in the journal. The patient understand that his name and initials will not be published and due efforts will be made to conceal identity, but anonymity cannot be guaranteed.

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Conflicts of interest

There are no conflicts of interest.

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