Magnesium Treatment for Patient with Refractory Partial Status Epilepticus

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Abstract

Refractory status epilepticus defined as continuous clinical and/or electrical seizure after second line antiepileptic drug treatment is one of main cause for neurological mortality and morbidity. The therapeutic options of refractory status epilepticus were limited in the lack of evidence and serious side effects. Intravenous ketamine, high dose combination of 2-3 antiepileptic drugs, high dose steroid, and intravenous immunoglobulin are alternative therapeutic options. Intravenous magnesium is also known as treatment option of RSE. We report a case of refractory status epilepticus treated successfully by intravenous magnesium.

Keywords: Status Epilepticus; Magnesium; Anticonvulsants

Abbreviations

SE: Status Epilepticus; RSE: Refractory Status Epilepticus; IV: Intravenous; ER: Emergency Room; SRSE: Super-Refractory Status Epilepticus

Introduction

Refractory status epilepticus (RSE) defined as continuous clinical and/or electrical seizure after second line antiepileptic drug treatment is one of main cause for neurological mortality and morbidity [1]. The therapeutic options of RSE were limited in the lack of evidence and serious side effects. Intravenous ketamine, high dose combination of 2-3 antiepileptic drugs, high dose steroid, IV immunoglobulin are alternative therapeutic options [2]. IV magnesium is first choice agent in treating seizures in eclampsia, and may be effective in seizure of other origin, although reports on this topic are sparse [3]. We report a case of RSE due to post-stroke epilepsy, which was treated successfully with IV magnesium.

Case

A 68-year-old woman was admitted to the emergency room (ER) for the uncontrolled seizures. Suddenly developed headache continued for two hours, and since then intermixed regular and irregular clonic seizures in the right face, arm and legs followed and persisted more than 20 minutes. She was unresponsiveness and taken to our ER by emergency medical technician. 9 years ago, she had taken warfarin because of atrial fibrillation and heart valve surgery. 3 years ago, after discontinuation of anticoagulation to be taken dental treatment, she suffered from left hemispheric cerebral infarction. Thereafter mild sensory aphasia remained. 1st seizure occurred three months ago. Seizure was brief right facial spasm and paresthesia in right upper extremity. Scalp EEG showed occasional spikes and sharp waves in the left parietal cerebral cortex. She was prescribed levetiracetam 500 mg twice a day to prevent seizure. When she arrived at ER, her vital signs were blood pressure of 150/80 mmHg, pulse rate of 82/min, respiration rate of 20/min and no fever. Serum glucose level was 117

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mg/dL. Initially, IV lorazepam was administered. After IV lorazepam 4 mg injection, the frequency and amplitude of clonic jerks became diminished and discontinued. 5 minutes later, partial seizure recurred, so IV lorazepam 4 mg was re-injected, but repeated clonic jerks of face, arm and leg relapsed 2 times per hour. Brain MRI performed 1 hr after seizure onset. There was no evidence of newly developed cerebral lesions except past left parietal region (Figure 1). Examination findings showed sedative mental state, forced eyeball deviation to the right side, the right eyelid twitching, clonic seizures in right extremities. Inspite of IV lorazepam 8mg, partial seizure continued with somewhat impaired mental state. So we decided to give fosphenytoin 1500 mg. After loading of fosphenytoin, seizures stopped. Blood pressure was 140/90 mmHg, heart rate is 130/min, respiration rate 30/min, body temperature was 38.0°C. On ICU admission, EEG monitoring began. The EEG revealed continuous wax and waning periodic lateralized epileptiform discharges (PLEDs) and electrical seizures in left T3, C3, P3 electrodes (Figure 2). Valproic acid 1000 mg/day and oxcarbazepine 1200 mg/day added to levetiracetam 1000 mg/day. On admission day 1 intermittent seizure lasted, recovery of consciousness was not fully achieved, so we applied to tracheal intubation and ventilator, started midazolam continuous infusion (civ midazolam). Although we increased midazolam up to maximal dosage, unilateral EEG seizures and following clinical seizures continued. Given IV ketamine (0.5 – 2 mg/kg/hr), Phenobarbital (20 mg/kg at 50 – 100 mg/min), Propofol (45 mg loading, civ 2 mg/kg/hr) could not abolish electrical and clinical seizure completely. On day 4, clinical seizures lasting 2 - 5 minutes have been observed for more than 20 times a day. We gave a pentotal coma therapy (5 mg/kg infusion; civ 3 - 6 mg/kg/hr). After increased to 6 mg/kg/hr there were no longer clinically observed seizures. EEG showed burst-suppression patterns. Although there were no seizures during 2 days pentotal coma therapy maintenance, hypotension and pneumonia developed. *Acinetobacter baumannii* was detected in blood and sputum cultures. Because sepsis occurred, so we decreased dosage of pentotal to 3 mg/kg/hr and then seizure of the same pattern began again. Infection proceeded to septic shock, we administered IV immunoglobulin. Failure of 3rd line drug treatment for SE leaded to administer IV magnesium. According to 4g intravenous over the initial 30 minutes and was then intravenously administered to 2g/hr. Pretreatment serum magnesium level was 2.1 mg/dL and, after administration of 7.2 mg/dL. While increased up magnesium, clinical seizures and EEG seizure disappeared (Figure 3). During keeping for 3 days, seizure was not observed anymore and she had other adverse effects. We tapered dosage of magnesium and kept only oral anticonvulsant. Her mental state improved to lethargic state and cooperation was possible partly. General condition including breathing altered for the better, so she was transferred to general ward. During 1 month keeping oral anticonvulsants, seizure didn't recur.

Figure 1: Brain MRI at ER. FLAIR images show an old infarction at the left parietal area.
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**Discussion**

Status epilepticus (SE) usually manifest as generalized form in more than two thirds although it starts as partial seizures. As shown in this case, it is uncommon that SE remained as partial status epilepticus. This case was classified as complex partial status epilepticus because the patient showed partial seizure involved right side of body without regaining consciousness and EEG showed continued focal epileptiform discharges in left posterior quadrants [4]. Prognosis of SE depends on proper diagnosis and treatment of underlying disease

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as well as rapid seizure control and prevention of cerebral damage. RSE is defined as continued seizure despite 1st and 2nd line antiepileptic (eq. benzodiazepine, phenytoin) drug treatment. 3rd line antiepileptic drug such as midazolam, propofol, pentobarbital or phenobarbital are injected by intravenous route in case of uncontrolled seizure within 30 minutes. During this 3rd line drug treatment, cautious observation for suppressed respiration, low blood pressure is needed. Super-refractory status epilepticus (SRSE) is defined as SE that continues or recurs 24hr or more after the onset of anesthetic therapy, including those cases that recur on the reduction or withdrawal of anesthesia. SRSE is devastating neurological condition with limited treatment options including inhaled anesthetics, ketamine, magnesium, hypothermia, ketogenic diet, IV immunoglobulin (IVIG), IV steroids and resective neurosurgery. The choice of treatment options for given patient is based on clinical presentation by single or combination therapy [5,6]. IV magnesium has a unique place in the treatment of seizures. In a large well-conducted randomized controlled study, magnesium was shown to be the drug of choice in controlling seizures in eclampsia and superior to phenytoin and benzodiazepine. In addition, it is used to control seizure in very rare congenital magnesium deficiencies, seizure due to acquired hypomagnesaemia, and SE in porphyria. Blocking of NMDA receptor may be the basis of anti-seizure mechanism. Magnesium also acts as a voltage-dependent calcium channel antagonist and prevents membrane depolarization, which could be an additional mechanism of anti-epileptic action [7].

Magnesium appears to act as vasodilator (particularly on the small diameter vessels), which may reduce cerebral ischemia and to increase concentration of prostacyclin, which prevent endothelial injury [8]. In previously reported cases, target level of serum magnesium varied between 4.2 mg/dL to 17.2 mg/dL empirically, and so appropriate standards for target concentration is needed [9,10]. Although no serious side effects are known in most cases, careful attention is needed for it causes cardiac dysfunction including heart block by high concentration of 8.0 mEq/L. During SE and RSE, the NMDA receptor plays a key role in pharmaco-resistance and epileptogeneity. As seizures remain uncontrolled, there is an up-regulation of NMDA receptor, leading to a glutamate mediated excitotoxity and seizure potentiation [11].

Based on review article, it is not recommended for all the non-eclamptic RSE patients even though half of the patients were controlled by IV magnesium successfully for its low evidence [9].

In our opinion, the low evidence of IV magnesium is attributable to small number of cases. As RSE was controlled dramatically by IV magnesium in our case, it would be considered as another therapeutic option of RSE if failure or serious side effect of other therapeutic options occurred. Further prospective and large well controlled study is required to determine the efficacy of seizure control and additive neuroprotective effects.

Conclusion

We report a case of RSE treated successfully by IV magnesium.

Bibliography


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