Review Article

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Status Epilepticus in Children, both Refractory and Super-Refractory

Abstract

Purpose

Focusing on the epidemiology, etiologies, therapeutic approaches, and clinical outcomes of pediatric Refractory Status Epilepticus (RSE) and Super-Refractory Status Epilepticus (SRSE). Methods: Utilizing the MEDLINE database, narrative review of the medical literature.

Results

Status Epilepticus (SE) that does not respond appropriately to first- and second-line antiepileptic medications is referred to as RSE. When SE persists for at least 24 hours following anesthesia administration or recurs after its withdrawal, this condition is known as SRSE. Complex neurological emergencies like RSE and SRSE are associated with high mortality, long-term neurological dysfunction, and the lack of prompt identification of the underlying etiology presents management challenges, and prolonged seizures limit therapeutic options. The majority of treatment decisions are based on case series or the opinions of experts. Large prospective series or randomized clinical trials have not evaluated the comparative efficacy of various treatment approaches. The most common treatment for RSE and SRSE is continuous infusion of anesthetics, but many questions about the best dose and rate of administration remain unanswered. The utilization of non-pharmacological treatments is recorded in the event that series or reports with low level of proof. Children with RSE/SRSE frequently experience systemic complications as a result of poly pharmacy and a prolonged hospital stay, in addition to neurological complications brought on by prolonged seizures.

Conclusion

Neurological emergencies like RSE and SRSE have few treatment options. Evaluations of the current RSE/SRSE therapies' safety and efficacy, as well as their potential impact on patient outcomes, would benefit from international collaboration.

Keywords: Epilepsy • Refractory status epilepticus •Super-refractory status epilepticus • Neurocritical care unit

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Introduction

A life threatening neurological emergency known as Refractory Status Epilepticus (RSE) is associated with significant morbidity and mortality. Seizures that persist after taking a first-line Benzodiazepine (BZD) and a Second-Line Antiseizure Drug (ASD) are considered to be RSE. RSE patients typically receive additional boluses of second-line ASDs (such as fosphenytoin, levetiracetam, and valproate) or are placed in a medically induced coma with Intravenous (IV) Continuous Infusions (CI) of an anesthetic (such as midazolam, propofol, or barbiturates) for seizure control. These patients are typically seen and treated in the Intensive Care Unit (ICU). However, after general anesthesia has been administered, continuous or intermittent seizures may recur or last for up to 24 hours. Super-Refractory Status Epilepticus (SRSE) is the ensuing condition. It can be hard to figure out what causes RSE and SRSE in the first place. The majority of treatment decisions are based on case series or the opinions of experts. Large prospective series or randomized clinical trials have not consistently evaluated the comparative efficacy of diverse treatment approaches [1-3].

Etiology

Pediatric RSE and SRSE have diverse reported etiologies in the literature. The following are the most frequently cited causes:intense suggestive causes (for example assumed irresistible or insusceptible intervened encephalitis, focal sensory system (CNS) contaminations, awful mind injury (TBI), cerebrum ischemia), far off side effect with intense precipitant causes (for example CNS lymphoproliferative illness, human immunodeficiency infection (HIV) contamination, hypoxic-ischemic encephalopathy, formative deferral, epilepsy), far off indicative and moderate encephalopathies (for example Alpers illness, metabolic infections like medium chain acyl-CoA dehydrogenase lack, epileptic encephalopathies), febrile SE (barring CNS contaminations), and obscure etiologies (for example cryptogenic). However, previous research demonstrates that etiology varies by age group and location. Acute symptomatic (28.5 percent) in neonates and infants was the most common etiology in a study of 151 refractory convulsive SE (RCSE) episodes; prolonged febrile convulsions in children aged 1 to 5 (33.8 percent); and remote symptoms in 40% of patients between the ages of 5 and 10 and 368.8% of patients between the ages of 10 and 16 . In contrast, acute brain injury (such as cerebrovascular disease, CNS infections, brain tumor, and traumatic brain injury), intoxication/withdrawal syndromes, low levels of antiepileptic drugs, metabolic disturbances, and systemic infections are the causes of RSE and SRSE in adults. Acute symptomatic etiologies continue to be the most common etiology for children in developing nations, followed by remote symptomatic and unknown etiologies [4,5].

CNS infections like Herpes Simplex Virus (HSV), HIV, neuro cysticercoids, malaria, and tuberculosis, as well as viral/autoimmune encephalitis and meningitis, are common etiologies of acute symptoms. New Beginning RSE (NORSE), then again, is a clinical show portrayed in patients without epilepsy or an important prior neurological confusion, who present with RSE without a recognizable intense reason or dynamic underlying, poisonous or metabolic cause[6-8].

Pathophysiology

In RSE and especially SRSE, components liable for seizure end fall flat and extra pathophysiologic processes foster prompting perseverance of SE. SE intensifies the internalization of synaptic G-Amino Butyric Acid type A (GABA-A) receptors at the cellular level while preserving the function of additional synaptic receptors. Synaptic "receptor trafficking" plays a crucial role in the development of pharma coresistance by reducing GABA's inhibitory activity overall. Changes in the concentrations of ions in the cellular environment, such as chloride, may also contribute to the perpetuation of seizures through an increased number of glutaminergic receptors at the neuronal surface. Sensitivity to NMDA-mediated neuronal stimulation mitochondrial failure, damage to the blood-brain barrier, and neuro inflammation (i.e. pro-inflammatory cytokines, autoantibodies to neural elements) may also account for the persistence of seizures and the development of SRSE. Excitotoxicity, the direct cause of neuronal injury, cell loss, and ultimately poor clinical outcomes, is the result of all of these factors. Finally, previous research demonstrates that the amount of time between the onset of a seizure and the start of treatment has a significant impact on the duration of the seizure[9,10].

Treatment

Ketogenic Diet (KD) is a diet high in fat, low in carbs, and high in protein that can be used as an alternative treatment for people with drug-resistant epilepsy. Due to its anti-inflammatory and anti-seizure properties, it has received significant attention in recent years for the treatment of SE as an adjunctive therapy. Small series report a collective efficacy rate of approximately 54 percent in the pediatric population. Between days 4 and 55 of the onset of a seizure, KD was administered to nine children with FIRES in a series at a 4:1 fat to combined protein and carbohydrate ratio. Within two to four days of ketonuria, seven of eight (87.5 percent) patients reached ketosis and stopped having seizures. Six of the seven patients remained on the diet, resuming mild seizures (two per week) after a few months. After KD was stopped, the remaining patient went back to RSE and died 10 days later. Clinical outcomes, the time to ketosis, and the timing of KD implementation are all highly variable. In addition, the full understanding of the impact of KD efficacy in RSE/SRSE as well as the optimal administration parameters is challenged by the simultaneous use of pharmacologic and non-pharmacologic therapies. The inclusion of a dietitian on the multidisciplinary team is a crucial consideration because they will be essential for achieving and maintaining ketosis

in these patients. Implementing KD can be difficult for children who are unable to consume enteral nutrition. As a result, these patients may benefit from IV KD as a temporary treatment. Carnitine deficiency, beta-oxidation metabolic defects, pyruvate carboxylase deficiency, and porphyria are all contraindications to the use of KD. KD could be considered in the early stages of RSE and SRSE management if there is no contraindication.

Conclusion

The diverse etiologies and numerous factors involved in the progression from SE to RSE and SRSE pose a challenge to current clinical practice. In addition, the inherent risks of treatment and their impact on clinical outcomes must be taken into consideration when determining how aggressively RSE/SRSE patients should be treated initially. In order to provide more definitive evidence for their efficacy and safety in RSE and SRSE, a multicenter and multinational collaborative effort to evaluate epidemiological data on pediatric RSE/SRSE, prevention strategies, and available therapeutic options is desirable.

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