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Status Epilepticus

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Continuing Education Activity

Status epilepticus is a neurological emergency requiring immediate evaluation and management to prevent significant morbidity or mortality. Previously, status epilepticus was defined as a seizure with a duration equal to or greater than 30 minutes or a series of seizures in which the patient does not regain normal mental status between seizures. The Neurocritical Care Society guidelines from 2012 revised the definition to a seizure with 5 minutes or more of continuous clinical and/or electrographic seizure activity or recurrent seizure activity without recovery between seizures. This activity reviews the evaluation and management of status epilepticus and highlights the role of the interprofessional team in the care of affected patients.

Objectives:

- Summarize the etiology of status epileptics.
- Describe the typical presentation of status epilepticus.
- Identify the treatment and management options available for status epilepticus.
- Explain interprofessional team strategies for improving coordination and communication to advance the treatment of status epilepticus and improve patient outcomes.

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Introduction

Status epilepticus is a neurological emergency requiring immediate evaluation and management to prevent significant morbidity or mortality. Previously, status epilepticus was defined as a seizure with a duration equal to or greater than 30 minutes or a series of seizures in which the patient does not regain normal mental status between seizures. The Neurocritical Care Society guidelines from 2012 revised the definition to a seizure with 5 minutes or more of continuous clinical and/or electrographic seizure activity or recurrent seizure activity without recovery between seizures.[1][2][3][4]

Status epilepticus may be convulsive, non-convulsive, focal motor, myoclonic, and any can become refractory. Convulsive status epilepticus consists of generalized tonic-clonic movements and mental status impairment. Non-convulsive status epilepticus is defined as seizure activity identified on an electroencephalogram (EEG) with no accompanying tonic-clonic movements. Focal motor status epilepticus involves the refractory motor activity of a limb or a group of muscles on one side of the body with or without loss of consciousness is myoclonic status epilepticus. Refractory status epilepticus refers to continuing seizures (convulsive or non-convulsive) despite appropriate antiepileptic drugs.

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Status epilepticus is the most common pediatric neurological emergency.[5][6]

Etiology

There are multiple etiologies for status epilepticus.[7] Potential acute processes include:

- Central nervous system (CNS) infections (meningitis, encephalitis, and intracranial abscess)
- Metabolic abnormalities (hypoglycemia, hyponatremia, hypocalcemia, hepatic encephalopathy, and inborn errors of metabolism in children)
- Cerebrovascular accidents
- Head trauma (with or without intracranial bleed)
- Drug toxicity
- Drug withdrawal syndromes (e.g., alcohol, benzodiazepines, and barbiturates)
- Hypoxia
- Hypertensive emergency
- Autoimmune disorders

Chronic processes that may result in status epilepticus include pre-existing epilepsy with breakthrough seizures or non-compliance with anti-epileptic drugs, ethanol withdrawal, CNS tumors, and remote CNS pathology (e.g., traumatic brain injury, stroke).

Acute processes account for most cases of status epilepticus in adults. Febrile status epilepticus is the most common cause in pediatric patients. CNS infections and inborn errors of metabolism are also common etiologies in children. The majority of pediatric patients with the first presentation of status epilepticus have no previous history of seizures.

Epidemiology

The incidence of status epilepticus has a bimodal age distribution with peaks during infancy and in the elderly. The incidence rate ranges between approximately 7 to 40 cases per 100,000 persons/year. Status epilepticus seems to be more common in males. A significant proportion of both children (16 to 38%) and adults (42 to 50%) with status epilepticus have a history of epilepsy. The short-term mortality (within 30 days) of status epilepticus ranges from 7.6 to 22% across all age groups and is highest amongst the elderly.[8]

Pathophysiology

A seizure is a paroxysmal electrical discharge of neurons in the brain resulting in a change of function or behavior. It is important to understand that a seizure is a CNS event and may present as convulsive or non-convulsive. There are both excitatory neurotransmitters (glutamate, aspartate, and acetylcholine) and inhibitory neurotransmitters (gamma-aminobutyric acid) and mechanisms (calcium ion-dependent potassium ion current and magnesium blockade of N-methyl-d-aspartate (NMDA)) in the brain that play a role in the genesis and inhibition of isolated seizures. Excessive excitation and/or inadequate inhibition results in status epilepticus.

Status epilepticus is classified into different types based on the following axes:[9]

1. Semiology
2. Etiology
3. EEG correlates

4. Age

History and Physical

Status epilepticus is defined as a seizure with 5 minutes or more of continuous clinical and/or electrographic seizure activity or recurrent seizure activity without recovery between seizures. The findings of convulsive status epilepticus include generalized tonic-clonic movements of the extremities and impaired mental status. Temporary focal neurological deficits (e.g., Todd paralysis) may be present in the postictal period. Non-convulsive status epilepticus presents with impaired mental status and may or may not have subtle motor signs such as tonic eye deviation. In non-convulsive status epilepticus, seizure activity is seen on the electroencephalography (EEG) despite the absence or paucity of overt clinical signs.

Evaluation

The diagnosis of convulsive status epilepticus is made clinically but requires emergent neuroimaging and laboratory studies to identify a potential etiology. A head computed tomography (CT) scan is appropriate in most situations and most easily obtained. Magnetic resonance imaging (MRI) of the brain is more sensitive for identifying malformations in pediatric patients but may be difficult to obtain and may require sedation. Laboratory studies should include bedside blood glucose level, serum electrolytes (sodium, potassium, calcium, and magnesium), BUN, creatinine, serum bicarbonate, a complete blood count, and a lumbar puncture with cerebrospinal fluid (CSF) evaluation. If the patient has a known seizure disorder, anti-epileptic drug levels should be obtained. Suspicion of toxic ingestion mandates toxicology studies (e.g., urine toxicology screen, serum levels of specific toxins such as theophylline or lithium). Other studies may be considered based on the presentation (liver function tests, inborn errors of metabolism, and coagulation studies). A pregnancy test should be obtained in all women of child-bearing age. An EEG should be obtained. Non-convulsive status epilepticus requires all of the previously mentioned imaging and laboratory studies for the identification of an underlying etiology but also requires EEG monitoring for diagnosis.[10][11][12]

Treatment / Management

Status epilepticus must be addressed quickly and in an organized manner, with simultaneous assessment/management of the airway, breathing, and circulation, while also administering antiepileptic drug (AED) treatment. The primary goal of management is to definitively abort seizure activity as rapidly as possible while supporting the patient's cardiovascular and respiratory status.[12][13]

- Position the head to maintain an open airway (rapid sequence intubation may be necessary at any point during management if oxygenation or ventilation is impaired).
- Provide supplemental oxygen.
- Initiate monitoring of the heart rate, respiratory rate, blood pressure, and oxygen saturation.
- Obtain vascular access.
- Check a bedside blood glucose and treat hypoglycemia if present. If thiamine deficiency is a possibility, administer thiamine before dextrose.
- Benzodiazepines are the antiepileptic drug of choice for emergent control. Lorazepam is preferred because of its rapid onset of action and is dosed at 0.1 mg/kg IV. No more than 2 mg should be administered per minute. If lorazepam is not available, then diazepam can be used at 0.15 mg/kg IV up to a maximum of 5 mg per minute. A repeat dose may be administered after 3 to 5 minutes if seizures do not resolve following the first dose. Intravenous administration is preferred, but benzodiazepines can be administered via the intramuscular, rectal, nasal, or buccal route if vascular access is not available.

- Antiepileptic drugs should be administered concurrently with benzodiazepines. Choices include fosphenytoin (20 mg/kg phenytoin equivalents [PE] up to 100 to 150 PE/minute, phenytoin (20 mg/kg up to 25 to 50 mg/minute), levetiracetam (40 to 60 mg/kg up to a total of 4500 mg over 15 minutes) and valproic acid (30mg/kg at up to 10 mg/kg/minute) (concern for hepatotoxicity with valproic acid use in children younger than two years).
- If the second dose of benzodiazepines does not abort seizures, then treat as refractory status epilepticus.
- Refractory status epilepticus should be treated with a continuous infusion of an antiepileptic drug. Choices include an intravenous (IV) infusion of midazolam, pentobarbital, thiopental, or propofol (propofol infusion should not be used in children due to the risk of propofol infusion syndrome).
- Magnesium sulfate is indicated for pregnant women with eclampsia.
- A neurologist should be consulted early in the management, simultaneously with the administration of first-line therapy.

All patients with status epilepticus require hospital admission, preferably to the intensive care unit.

Differential Diagnosis

Differential diagnoses of status epilepticus include:

- Acute intoxication
- Early catastrophic brain hypoxia
- Encephalopathy of toxic and metabolic origin
- Ischemic stroke
- Non-epileptic seizures
- Trauma

Prognosis

The mortality rate for patients with the first episode of generalized convulsive status epilepticus is between 16 to 20 percent.[13][14] Mortality is dependent on the etiology of status epilepticus, with anoxic status epilepticus approaching 80 percent.[15] Refractory status epilepticus has mortality rates between 35 to 60 percent, with patients needing prolonged courses of barbiturates or benzodiazepines worst affected. Young patients who have cryptogenic refractory status epilepticus fare somewhat better than older patients who have etiology identified.[16][17]. Some in vitro models show that permanent neurological damage can set in after 30 minutes of status epilepticus. About 40 percent of patients with the first episode of status epilepticus develop subsequent epilepsy, and there is a 25 to 30 percent risk of recurrent status epilepticus after the first episode.[18]

Complications

Complications of status epilepticus can be separated into medical and neurological complications and also immediate and delayed complications.

Medical complications include cardiac arrhythmia, cardiac damage because of catecholamine surge, respiratory failure, hypoventilation, hypoxia, aspiration pneumonia, pulmonary edema, fever, and leukocytosis are some of the common and serious complications seen in patients with status epilepticus[19].

Neurological complications include progression to chronic epilepsy and recurrent status epilepticus. In cases of prolonged refractory status epilepticus, there can be permanent neurological damage induced by the hyper-metabolic

activity in regions of the brain undergoing prolonged and abnormal electrical activity.

Consultations

Neurology

Neurocritical care

Pearls and Other Issues

There are known risks of congenital disabilities due to exposure to some antiepileptic drugs (phenytoin, valproate sodium, and phenobarbital) during the first trimester of pregnancy. In the setting of status epilepticus, fetal well-being is dependent on the immediate, successful management of seizure activity in the mother. Lorazepam is recommended for emergency control treatment if status epilepticus occurs during the first trimester. Levetiracetam should be considered for urgent control therapy in this setting as evidence suggests a lower risk of associated congenital disabilities in comparison to some other antiepileptic drugs (phenytoin, valproate sodium, and phenobarbital). If eclampsia is suspected, intravenous magnesium sulfate is the antiepileptic drug of choice. Delivery of the fetus is the definitive treatment of eclampsia.

Enhancing Healthcare Team Outcomes

Status epilepticus is best managed by an interprofessional team that includes emergency and neurology nurses. Pharmacists are responsible for making sure medications are readily available. To improve outcomes, clinicians should avoid unnecessary imaging studies or laboratory workup when the patient is having a seizure. Status epilepticus must be addressed quickly and in an organized manner, with simultaneous assessment/management of the airway, breathing, and circulation, while also administering antiepileptic drug (AED) treatment. The primary goal of management is to definitively abort seizure activity as rapidly as possible while supporting the patient's cardiovascular and respiratory status.

Once the patient is stable, investigations can begin.

Review Questions

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