Status Epilepticus
What's New?

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KEYWORDS

• Status epilepticus • Seizures • Epilepsy

KEY POINTS

- Status epilepticus (SE) is diagnosed at 5 minutes of continuous seizure activity, and has the potential for high morbidity and mortality if not diagnosed promptly and treated accurately and effectively
- Devising specific protocols for management of SE improves outcomes.
- The first line for management of SE is benzodiazepines, followed by phenytoin, fosphenytoin, or valproic acid.
- Second line adjuncts for management of SE are levetiracetam, lacosamide, phenobarbital and ketamine, followed by intravenous anesthetics.
- Subtle SE occurs frequently after convulsive SE and should be treated in the same manner
- Underlying causes leading to provoked seizures should be considered early on in the disease, especially in patients not responding to first line agents

INTRODUCTION

Seizures are commonly encountered in the emergency department (ED) because approximately 5% to 10% of people who live to the age of 80 years experience a seizure.[1] The spectrum of disease, from a partial complex seizure to refractory status epilepticus (SE), can present a daunting treatment task to emergency physicians. Epilepsy is defined as 2 or more unprovoked seizures occurring at least 24 hours apart, a heightened tendency toward unprovoked seizures (as shown by electroencephalographic or neuroimaging testing), or an epilepsy syndrome.[2] The determination of a provoked versus an unprovoked seizure is paramount because the underlying treatment options can be very different. At the far end of the spectrum of disease, generalized convulsive SE (GCSE) can be defined in a variety of ways, but

Disclosures: None.
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Emerg Med Clin N Am ■ (2016) ■–■
http://dx.doi.org/10.1016/j.emc.2016.06.012 **emed.theclinics.com**

the most common is an active seizure lasting greater than 5 minutes or 2 seizures without return to baseline. There are also subclassifications of subclinical or nonconvulsive, refractory, and super-refractory SE as well. SE is associated with increased morbidity and mortality, with the reported mortality after the first episode of GCSE approaching 20%.[3] The mortality is partly a function of the underlying cause, refractoriness of the seizure, age, and medical comorbidities, with the last 2 factors playing the greatest role. Reported mortality is from 4% to 40%, depending on the definition of SE used in the study and the underlying cause, with hypoxic ischemic brain injury producing the worst outcomes.[4–6]

The patient's hospital course from the prehospital setting, continuing through the ED, and ultimately the time spent in an intensive care unit (ICU) can be greatly affected by the choices the emergency physician makes. This article reviews the current diagnosis and treatment recommendations for GCSE, including refractory and other forms of SE.

PATHOPHYSIOLOGY

The common pathway for all seizures is an abnormal electrical discharge of cortical neurons, in which a hyperexcitable neuron group fires in a coordinated manner, recruiting adjacent neurons in a synchronized manner. The most common excitatory neurotransmitter is glutamate, which works via the *N*-methyl-D-aspartate (NMDA) receptor. In contrast, the most common inhibitory neurotransmitter is gamma-aminobutyric acid (GABA), which works via the $GABA_A$ receptors. In normal circumstances, the neuronal membrane only allows a single action potential to pass from one neuron to another in a given time interval. Seizures can occur once this stability is altered, which could either be caused by sensitized inhibitory $GABA_A$ receptors (eg, in the setting of alcohol or benzodiazepine withdrawal), an altered ion concentration (eg, hyponatremia), or altered cellular metabolism (eg, hypoglycemia). If these mechanisms are involved, these seizures are considered provoked (**Box 1**).

Unprovoked seizures, which by definition are epileptic, are mostly caused by abnormalities of sodium channels, but other mechanisms can be involved, such as self-excitation, abnormal calcium channel stimulation, or a mutation in acetylcholine receptors.[7]

The imbalance of excess excitation and decreased inhibition is what ultimately manifests as a seizure. Many abortive medications, such as benzodiazepines, barbiturates, propofol, and some anesthetics, work via enhancing GABA inhibition. There are many endogenous seizure-terminating processes, which is why most seizures last for only 1 or 2 minutes before spontaneously aborting, but, when they fail, a single seizure is transformed into SE. A seizure that has lasted 30 minutes or more will not spontaneously stop, because at this point the seizure has become self-sustaining even if the inciting factor was removed.[8]

Physiologic Changes in Generalized Convulsive Status Epilepticus

Multiple systemic physiologic changes accompany GCSE, mostly caused by the catecholamine surge. These changes can include hyperthermia, leukocytosis, cerebrospinal fluid (CSF) pleocytosis, increased blood pressure, pupillary dilatation, and other cardiovascular and respiratory abnormalities. Attributing hyperthermia, leukocytosis, and CSF pleocytosis to the seizure is a diagnosis of exclusion, because a true infectious cause needs to be excluded first. As the seizure progresses there can also be resultant lactic acidosis caused by the conversion to anaerobic metabolism as the