Status Epilepticus in Adults: A Review of Diagnosis and Treatment

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Susan Yeager, RN, MS, CCRN, ACNP-BC

Status epilepticus is a medical emergency that requires rapid diagnosis and treatment. Nonconvulsive status epilepticus is frequently underdiagnosed and therefore undertreated, which can lead to permanent neuronal damage resulting in disability or death. Despite the frequent occurrence and morbidity associated with status epilepticus, this topic has received little attention within the literature. A systematic approach to treatment should start with management of airway, breathing, and circulation, followed by administration of benzodiazepines and intravenous antiepileptic drugs, and rapid escalation of therapy to prevent morbidity and mortality. Armed with the information in this article, nurses will have a higher-level understanding of what to do when encountering a patient in status epilepticus. (Critical Care Nurse. 2016;36[2]:62-73)

Minutes can seem like a lifetime when a nurse encounters a patient having a seizure. A seizure that continues into status epilepticus changes from a stressful situation into a life-threatening emergency. Guidelines for the evaluation and management of status epilepticus published by the Neurocritical Care Society1 in 2012 are used here to provide definitions and describe the pathophysiology, diagnostic evaluation, treatment options, and nursing considerations when caring for a patient in status epilepticus. With this information, nurses will be able to systematically provide treatment to support patients during this emergency.

Incidence and Definitions

The incidence of status epilepticus varies by region and age. Incidence ranges from 9.9 to 15.8 per 100,000 persons in Europe to 18.3 to 41 per 100,000 persons in the United States.2,3 The distribution is bimodal, with higher incidence in the first decade of life and then dramatically escalating incidence following the fifth decade.4,5 Risk of death from status epilepticus ranges from 1.9% to 40%, with the wide variation dependent on age, cause, and duration.3
Definition of status epilepticus has varied throughout the decades depending on the duration of seizure. Status epilepticus is currently defined as “5 minutes or more of continuous clinical and/or electrographic seizure activity or recurrent seizure activity without recovery (returning to baseline) between seizures.” The definition of status epilepticus has evolved through the 20th century from “the maximum expression of epilepsy” in 1904, to more than 30 minutes of continuous seizure activity from the 1960s to the early 2000s. The current definition’s more inclusive criteria reflect the need for urgent treatment. Although status epilepticus is defined as 5 minutes or more of clinical or electrographic seizure, refractory status epilepticus is defined as clinical or electrographic seizures after adequate dosing of an initial benzodiazepine and a secondary antiepileptic drug (AED). Others have used the term “super-refractory status epilepticus,” to describe continued status epilepticus 24 hours after administering anesthetic therapy or recurring status epilepticus after reduction in anesthetic dose. Convulsive status epilepticus involves jerking rhythmic movements of the arms and/or legs. Non-convulsive status epilepticus (NCSE) is electrographic, ongoing seizure activity without the motor findings of convulsive status. Table 1 lists signs of NCSE. Regardless of the exact definition, prompt recognition, diagnosis, and emergent treatment are key to minimizing neurologic sequelae. Recognition begins with a basic understanding of the pathophysiology that underlies status epilepticus.

Pathophysiology
Normal neuronal activity occurs through a balance of complex cellular-level mechanisms. The resting membrane potential is maintained across the cell wall of a neuron by the sodium-potassium pump. This mechanism pumps sodium and chloride to high concentrations into the interstitial space and potassium to high concentrations within the cell. When a sufficient stimulus is applied, an action potential is realized and the cell depolarizes. Neurotransmitters excite or inhibit other neurons. Normal brain function is a result of balance between inhibition and excitation. Glutamate is the most common excitatory neurotransmitter and γ-aminobutyric acid (GABA) is the most common inhibitory transmitter. During status epilepticus, failure of the inhibitory GABAergic mechanisms can cause the seizures to become self-sustaining and pharmacoresistant. Benzodiazepine resistance may develop after 10 to 45 minutes of status epilepticus, possibly because of changes in synaptic physiology that reduce the number of GABA receptors. GABA-enhancing drugs such as benzodiazepines, barbiturates, propofol, and some anesthetics are effective at stopping seizures by overwhelming the excitation with inhibitory stimulation, but withdrawal of these inhibitory medications may provoke rebound seizures.

Table 1

<table>
<thead>
<tr>
<th>Nonconvulsive</th>
<th>Convulsive</th>
</tr>
</thead>
<tbody>
<tr>
<td>Aggression</td>
<td>Convulsive syncope</td>
</tr>
<tr>
<td>Automatisms</td>
<td>Repetitive decerebrate or decorticate posturing</td>
</tr>
<tr>
<td>Blinking</td>
<td>Involuntary movement disorders</td>
</tr>
<tr>
<td>Crying</td>
<td>Psychogenic nonepileptic spells (pseudo-seizures)</td>
</tr>
<tr>
<td>Delirium</td>
<td></td>
</tr>
<tr>
<td>Delusions</td>
<td></td>
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<tr>
<td>Echolalia</td>
<td></td>
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<tr>
<td>Facial twitching</td>
<td></td>
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<tr>
<td>Laughter</td>
<td></td>
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<tr>
<td>Nausea/vomiting</td>
<td></td>
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<tr>
<td>Eye deviation contralateral to lesion</td>
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<tr>
<td>Perseveration</td>
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<tr>
<td>Psychosis</td>
<td></td>
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<tr>
<td>Tremulousness</td>
<td></td>
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<tr>
<td>Aphasia</td>
<td></td>
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<tr>
<td>Amnesia</td>
<td></td>
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<tr>
<td>Catatonia</td>
<td></td>
</tr>
<tr>
<td>Staring</td>
<td></td>
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</tbody>
</table>

*Based on information from Bazil and Pedley.*

Authors

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as the inhibitory/excitatory balance is tipped toward excitation.\textsuperscript{10} Seizure activity, whether nonconvulsive or convulsive, causes intense metabolic demands that require increased cerebral blood flow. This workload increases during the first seconds of a seizure.\textsuperscript{12} Even during the first few minutes of a seizure, the normally tight coupling of neuronal activity, energy demand, and cerebral blood flow is decoupled because of the very high energy demands of seizing neurons in the context of limited circulatory delivery of energy to cells that store essentially no energy.\textsuperscript{11,12}

When this increased cellular metabolic demand is not met, neuronal damage and cell death result.\textsuperscript{14,15} Unmet neuronal metabolic demand is not the only factor responsible for cell death. The massive depolarization of the neuronal action potential during seizures leads to excessive release of glutamate, which activates postsynaptic N-methyl-D-aspartate receptors, triggering an influx of calcium into the cell.\textsuperscript{16,17} Maintaining neuronal homeostasis requires large quantities of energy, but neurons do not generally use stored energy and are particularly susceptible to energetic stress.\textsuperscript{13,15} Thus during an event of status epilepticus, cellular homeostasis fails and high concentrations of intracellular calcium enter the mitochondria, which then lose their membrane potential, and mitochondrial respiration fails with a cascade ending in cell necrosis.\textsuperscript{16,17} The pathophysiologic changes and resulting neuronal injury resulting from status epilepticus demand urgent, aggressive diagnosis and treatment.

### Risk Factors for Seizure

Various factors can put a patient at higher risk of transitioning from seizure to status epilepticus. Specific factors can have a greater impact within different age groups, but seizure history alone increases a patient’s risk regardless of age. Following a single unprovoked seizure, risk of further seizure is 40% to 52%, and after 2 seizures, the risk is 73%.\textsuperscript{13} Age-related risk factors for status epilepticus are listed in Table 2. Additional causes that decrease seizure threshold can be broken down into structural, infectious, metabolic, and drug-related categories. Examples of structural factors include neoplasms, stroke, or traumatic brain injury. Infection, virus, fever, and metabolic derangements such as hyponatremia, hypoglycemia, hyperglycemia, hepatic encephalopathy, hypocalcemia, and hypomagnesemia also create environments that increase a patient’s risk of status epilepticus.

### Patient’s History

The initial encounter after stabilization should include an interview seeking details of the period surrounding the seizure. This interview should occur with the patient if coherent and with the bedside staff and a knowledgeable family member. Questions should clarify the patient’s seizure history. Of particular importance in regard to a seizure history is information regarding the patient’s AED regimen and adherence, and description of the event including duration, quantity, and character of the convulsions as well as any prodromal features (also known as an aura). Knowledge of what medications have controlled seizures before and what medications have failed may influence the selection of AEDs. Probing for social issues affecting medication adherence may reveal the

<table>
<thead>
<tr>
<th>Table 2</th>
<th>Risk factors for status epilepticus by age\textsuperscript{a}</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age, y</td>
<td>Contributing factors</td>
</tr>
<tr>
<td>≤35</td>
<td>Brain trauma, alcohol withdrawal, brain tumors, and illicit drug use</td>
</tr>
<tr>
<td>&gt;35</td>
<td>Cerebrovascular disease, brain tumors, alcohol withdrawal, metabolic disorders such as uremia and electrolyte imbalances, neurodegenerative diseases, and idiopathic causes</td>
</tr>
</tbody>
</table>

\textsuperscript{a}Based on information from Bazil and Pedley.\textsuperscript{8}

<table>
<thead>
<tr>
<th>Table 3</th>
<th>Drugs that can affect seizure threshold\textsuperscript{a}</th>
</tr>
</thead>
</table>
| Psychiatric medications | Tricyclic antidepressants  
Bupropion  
Venlafaxine  
Citalopram  
Quetiapine |
| Recreational drugs | Cocaine  
MDMA (ecstasy) |
| Antibiotics | \(\beta\)-Lactam antibiotics  
Carbenepams  
Isoniazid |
| Other medications | Carbamazepine/oxcarbazepine  
Diphenhydramine  
Flumazenil (in benzodiazepine-dependent patients) |

\textsuperscript{a}Based on information from Thundiyil et al.\textsuperscript{20}
necessity of choosing less expensive medications or counseling the patient or family on simple techniques for organizing medications for regular administration.

Assessment of Patients

Initial assessment should begin with a rapid evaluation of airway, breathing, and circulation. Examination of patients with suspected seizures should include a thorough yet rapid visual assessment of motor activity of the face and extremities. The tonic-clonic extremity movements are obvious and are easily identified by lay people. Patients with generalized NCSE may be critically ill and lethargic with or without subtle rhythmic movements. Subtle twitches may occur on any part of the body, may be unilateral or bilateral, and often involve the extracocular muscles or eyelids. NCSE patients with partial seizures may be less impaired: acting confused, aphasic, or staring, and they may show a lateral gaze preference contralateral to the focus of the seizure.\(^1\)

Electroencephalography

The bedside nurse caring for a patient in status epilepticus should have a basic knowledge of electroencephalographic (EEG) patterns in order to determine when to call the neurologist to request an official reading. Although it is clearly not the responsibility of the nurse to interpret an EEG, the nurse’s having a basic familiarity with typical EEG patterns and glancing at the bedside EEG monitor while caring for the patient may prompt additional attention by the neurologist and result in earlier identification of seizures. Figures 1 through 3 are examples of typical normal and abnormal EEG findings that may be encountered. A normal EEG shows lower amplitude and irregular frequencies (Figure 1). In NCSE, the amplitude is higher and the pattern is more regular with some similarities to the appearance of ventricular tachycardia on an electrocardiogram (Figure 2). During administration of anesthetic medications such as phenobarbital or propofol, a burst-suppressed pattern is found (Figure 3). Determining the desired frequency of the bursts (the sample EEG in Figure 3 shows 1 burst per page) is useful for anesthetic titration and communication with the prescriber.

Myoclonic muscle artifact reveals a disconcerting EEG pattern, and expert video EEG interpretation is required to discern between myoclonic artifact and
Figure 2 Electroencephalogram of a patient with nonconvulsive status epilepticus.

Figure 3 Electroencephalogram of patient during administration of anesthetic shows burst suppression.
status epilepticus. Use of a single dose of a paralytic agent to eliminate muscle artifact may be required. Timing of EEG application will be different from institution to institution and is likely to vary depending on the resources available from the EEG staff. If radiologic evaluation is also desired, special consideration should be given to the priority of these tests. Determination of the sequence of these diagnostic tests rests on both the clinical condition of the patient and the presumed underlying cause of the seizure. For example, for a patient with known brain cancer who had a witnessed onset of generalized convulsive status epilepticus and stopped convulsing after being given loading doses of lorazepam and fosphenytoin but has not returned to his baseline neurologic status, EEG most likely should be done before imaging as the patient is at high risk for NCSE. Another example is a patient with head trauma who had a seizure following an acute head injury but does not appear to have clinical seizure; in that case, a computed tomography scan of the head should be done to rule out bleeding that should be treated surgically.

In addition to electrographic monitoring, blood samples for laboratory tests should be collected soon after the patient arrives. All patients in status epilepticus should have blood glucose level measured, a complete blood cell count, and a comprehensive metabolic panel including measurement of calcium and magnesium levels. Patients being treated for epilepsy should have AED levels measured if applicable. Depending on the patient’s history and clinical findings, additional laboratory tests including a comprehensive toxicology panel, liver function tests, measurement of troponin levels, collection of blood samples to type and hold, arterial blood gas analysis, and lumbar puncture with measurement of protein and glucose levels, cell count, and culture should be considered.1

Except in cases with a clear cause, a radiologic workup to identify cranial abnormalities that may be causing an ictal focus should be undertaken. For example, a computed tomography scan may be obtained to rule out a traumatic hemorrhage and hemorrhagic stroke or magnetic resonance images may be obtained to rule out tumors or acute ischemic stroke.

Management of Patients

Seizures are a medical emergency; if they progress to status epilepticus and are not rapidly treated, permanent neuronal damage may occur within 24 hours.21,22 Both clinical and electrographic seizures should be emergently stopped.3 A prompt diagnosis should be followed by implementation of several therapies concurrently: critical care evaluation, emergency administration of an AED, and a search for the cause of the seizure. Initial management of status epilepticus is summarized in Table 4.

Airway, Breathing, and Circulation

As with all patient emergencies, all management begins with evaluation of airway, breathing, and circulation. Generalized seizure activity impairs mental status and the ability to protect the airway, so the airway should be assessed concurrently with initial AED administration and should be serially reevaluated as therapy is escalated. Initial airway management may involve just provision of airway protection and supplemental oxygen delivery. Initial airway protection maneuvers consist of placing a

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**Table 4** Initial management of status epilepticus

<table>
<thead>
<tr>
<th>Priorities for the first 0-5 min</th>
<th>Evaluation/treatment of airway with noninvasive management</th>
<th>Check initial vital signs and telemetry</th>
<th>Obtain intravenous access</th>
<th>Neurological examination</th>
<th>Finger-stick blood glucose</th>
<th>Administration of dextrose if hypoglycemic</th>
<th>Administration of benzodiazepine (first-line antiepileptic drug)</th>
<th>Fluid resuscitation if hypotensive</th>
</tr>
</thead>
<tbody>
<tr>
<td>Priorities for the first 15 min</td>
<td>Intubation if airway or gas exchange is compromised</td>
<td>Second-line intravenous antiepileptic drug</td>
<td>Vasopressor support if hypotensive</td>
<td>Collect blood samples for laboratory tests (complete blood cell count, Chem 7, calcium, magnesium, antiepileptic drug levels)</td>
<td>Electrocardiogram</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Priorities for the first 15-60 min</td>
<td>Third-line antiepileptic drug for refractory status epilepticus</td>
<td>Electroencephalography</td>
<td>Computed tomography of the head</td>
<td>Lumbar puncture</td>
<td>Additional laboratory tests (liver function tests, troponin levels, coagulation tests, arterial blood gases, comprehensive toxicology panel)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Within first 12-24 h</td>
<td>Magnetic resonance of the brain</td>
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</tr>
</tbody>
</table>

4 Adapted from the Neurocritical Care Society’s guidelines.1
Intravenous lorazepam is preferred; an initial dose of 4 mg of lorazepam is recommended for patients in status epilepticus.

Because of this, nurses caring for patients with status epilepticus should clarify with the prescriber how medication and ventilator weaning should be handled to avoid inadvertently causing a patient to go back into status epilepticus.

Most AEDs can induce hypotension, so frequent monitoring of blood pressure is required. Peripheral intravenous catheters should emergently be placed for administration of intravenous AEDs, fluid boluses for hypotension, and other emergency drugs if required. Insertion of a central venous catheter should be considered if status epilepticus is refractory and requires anesthetic EEG burst suppression or if blood pressure is low and vasopressor support is required.

Antiepileptic Drugs

The goal of treatment is to rapidly stop status epilepticus and prevent recurrence; thus, the most appropriate route of administration for AEDs is intravenous. Current guidelines for status epilepticus and the emergency neurologic life support protocol recommend parenteral benzodiazepines for emergent initial therapy. Intravenous lorazepam is preferred, but if intravenous access is not available, other benzodiazepines may be administered via alternative routes. Lorazepam has logistical issues in the prehospital setting (refrigeration requirements and shorter shelf-life), but intramuscular midazolam is at least as effective and is a safe alternative to intravenous lorazepam. An initial dose of 4 mg of lorazepam is recommended. Immediately following benzodiazepine administration, regardless of whether or not the patient has stopped convulsing, another AED should be administered to prevent rebound seizures as the benzodiazepine wears off. Therapeutic levels of a maintenance AED should be obtained urgently. Dosing of AEDs and special considerations are summarized in Table 5.

Several choices of medication are available for second-line AEDs. The most popular is fosphenytoin/phenytoin. Phenytoin is administered at a dose of 20 mg/kg at a rate not to exceed 50 mg/min. Fosphenytoin is a prodrug of phenytoin that has no pharmacological activity before its in vivo conversion to phenytoin. The half-life conversion to phenytoin is 8 to 15 minutes, and once converted, the phenytoin has 100% bioavailability. Fosphenytoin is dosed at 20-mg phenytoin equivalents per kilogram but can be administered at 150-mg phenytoin equivalents per minute, and because it is safe to administer 3 times faster and poses less risk of severe injury if extravasation occurs, fosphenytoin is typically preferred over phenytoin. Phenytoin and fosphenytoin may precipitate bradyarrhythmias and hypotension when infused rapidly, so caution should be exercised, particularly when administering a loading dose. Intravenous access, cardiac telemetry, and frequent monitoring of blood pressure are essential. Alternatives to fosphenytoin include valproate sodium 20 to 40 mg/kg intravenously, phenobarbital 20 mg/kg intravenously, levetiracetam 1 to 3 g intravenously, or continuous intravenous infusion of midazolam. Others have suggested lacosamide at doses of 200 to 400 mg intravenously as an alternative second-line agent with the caveat that no
<table>
<thead>
<tr>
<th>Drug/category/ mechanism</th>
<th>Dosing</th>
<th>Administration rate</th>
<th>Serious adverse effects</th>
<th>Considerations</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Intermittently dosed medications</strong></td>
<td></td>
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<td></td>
</tr>
<tr>
<td>Diazepam</td>
<td>0.15 mg/kg intravenously up to 10 mg, repeat in 5 min 0.2 mg/kg rectally up to maximum of 30 mg Alternate 0.2 mg/kg rectally</td>
<td>Up to 5 mg/min</td>
<td>Hypotension, respiratory depression</td>
<td>Short duration, active metabolite</td>
</tr>
<tr>
<td>Lorazepam</td>
<td>0.1 mg/kg intravenously up to 4 mg, repeat in 5-10 min</td>
<td>Up to 2 mg/min</td>
<td>Hypotension, respiratory depression</td>
<td></td>
</tr>
<tr>
<td>Midazolam</td>
<td>0.2 mg/kg intramuscularly up to 10 mg</td>
<td></td>
<td>Hypotension, respiratory depression</td>
<td>Short duration, active metabolite, renal elimination</td>
</tr>
<tr>
<td>Fosphenytoin</td>
<td>20-mg phenytoin equivalent/kg intravenously, may bolus with 5-mg phenytoin equivalent/kg 10 min after initial loading dose</td>
<td>Up to 150-mg phenytoin equivalent/min</td>
<td>Hypotension, arrhythmias</td>
<td>Cardiac monitoring for loading dose</td>
</tr>
<tr>
<td>Lacosamide</td>
<td>200-400 mg intravenously</td>
<td>200 mg per 15 min</td>
<td>PR prolongation, hypotension</td>
<td>Limited experience in status epilepticus</td>
</tr>
<tr>
<td>Levetiracetam</td>
<td>1000-3000 mg intravenously</td>
<td>2-5 mg/kg per min intravenously</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Phenobarbital</td>
<td>20 mg/kg, may give additional 5-10 mg/kg 10 min after initial loading dose</td>
<td>50-100 mg/min intravenously</td>
<td>Hypotension, respiratory depression</td>
<td></td>
</tr>
<tr>
<td>Phenytoin</td>
<td>20 mg/kg, may give additional 5-10 mg/kg 10 min after initial loading dose</td>
<td>Up to 50 mg/min intravenously</td>
<td>Arrhythmias, hypotension, purple glove syndrome with extravasation (rare)</td>
<td>Cardiac monitoring during loading dose</td>
</tr>
<tr>
<td>Topiramate</td>
<td>200-400 mg via nasogastric tube or by mouth, 300-1600 mg/d divided into 2-4 doses</td>
<td></td>
<td>Metabolic acidosis</td>
<td>No intravenous formulation available</td>
</tr>
<tr>
<td>Valproate sodium</td>
<td>20-40 mg/kg intravenously, may repeat</td>
<td>3-6 mg/kg per min</td>
<td>Hyperammonemia, pancreatitis, thrombocytopenia, hepatotoxicity</td>
<td>Caution in patients with traumatic brain injury Pregnancy category X</td>
</tr>
<tr>
<td><strong>Refractory/continuous medications</strong></td>
<td></td>
<td></td>
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</tr>
<tr>
<td>Midazolam</td>
<td>0.05-2 mg/kg per h, bolus 0.1-0.2 mg/kg and increase rate every 3-4 h</td>
<td>Respiratory depression, hypotension</td>
<td>Requires mechanical ventilation</td>
<td>Tachyphylaxis may occur Short duration9</td>
</tr>
<tr>
<td>Water-soluble benzodiazepine GABA&lt;sub&gt;a&lt;/sub&gt; enhancement</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Pentobarbital Barbiturate GABA&lt;sub&gt;a&lt;/sub&gt; enhancement</td>
<td>5-15 mg/kg loading dose followed by infusion at 0.5-5 mg/kg per h</td>
<td>Hypotension, respiratory depression, cardiac depression, paralytic ileus, loss of neuronal function at high doses</td>
<td>Requires mechanical ventilation</td>
<td>Half-life 15-60 h&lt;sup&gt;1,29&lt;/sup&gt; Lowers body temperature and theoretically is neuroprotective&lt;sup&gt;9&lt;/sup&gt;</td>
</tr>
<tr>
<td>Propofol</td>
<td>Start at 20 µg/kg per min, titrate up to 50 µg/kg per min</td>
<td>Hypotension, respiratory depression, cardiac failure, rhabdomyolysis, metabolic acidosis, propofol-related infusion syndrome&lt;sup&gt;5,30&lt;/sup&gt;</td>
<td>Requires mechanical ventilation</td>
<td></td>
</tr>
</tbody>
</table>

Abbreviations: GABA, γ-aminobutyric acid; NMDA, N-methyl-D-aspartate.

<sup>1</sup> Adapted from the Neurocritical Care Society’s guidelines.
data from randomized controlled trials are available to support this decision because the newer AEDs were not included in older trials.29,32

If the patient progresses to refractory status epilepticus, urgent escalation of therapy should be continued. At this point, options include administering another bolus of the same second-line agent that had been given or adding another agent from the ones just discussed. Limited evidence supports expanding the list of appropriate AEDs to include topiramate 200 to 400 mg via nasogastric tube or by mouth.33 If the status epilepticus remains refractory, induction of anesthesia with continuous intravenous medications is often required. Typical agents include propofol 20 to 200 µg/kg per minute, pentobarbital as a 5- to 15-mg bolus followed by 0.5 to 5 mg/kg per hour, and the aforementioned midazolam as a 0.2-mg/kg bolus followed by an infusion at 0.1 to 0.4 mg/kg per hour.1,34 Reevaluation after each of these steps must occur frequently, and subsequent escalation of treatment must be rapid and aggressive to avoid permanent neuronal damage. No data support use of one of these agents over the others.7

The most notorious side effect of pentobarbital, midazolam, and propofol infusions is hemodynamic suppression, which warrants close monitoring of vital signs.27 Before giving a patient a loading dose of phenytoin or fosphenytoin, telemetry should be applied because the drug may precipitate bradyarrhythmias, including high-grade atioventricular block, asystole, and death.31 Nurses should anticipate vasopressor use if an anesthetic medication is infusing continuously because anesthetics often cause hypotension. Vasopressor selection should be individualized to each patient’s hemodynamic profile and desired effect.

Although data indicate that intravenous anesthetic drugs such as propofol, midazolam, and high-dose barbiturates have a potent antiepileptic effect, these patients with super-refractory status epilepticus have high morbidity and mortality.35-38 In a recent study,38 researchers found higher rates of infection and death in patients receiving anesthetic agents, even when corrected for critical medical conditions and for the refractoriness of the status epilepticus. It remains unclear whether the anesthetic agents themselves or a selection bias led to this worsened mortality. These medications have considerable side effect profiles that require vigilance to avoid increased morbidity and mortality.29 Pentobarbital is known to cause immunosuppression and gastric paresis and is associated with elevated rates of ventilator-associated pneumonia, urinary tract infections, and ileus.37,39

Propofol has a rapid onset and short duration and is often considered a favorite first-line anesthetic for refractory status epilepticus because of its favorable properties of rapid onset and recovery and no serious drug-drug interactions.7,30 The most severe side effect is a rare condition known as propofol-related infusion syndrome (PRIS), typically associated with doses greater than 4 mg/kg per hour for longer than 48 hours, as is characteristic of the usage patterns in status epilepticus. Early findings include hyperlipidemia, acidosis, and elevated creatine kinase levels. Serial daily measurements of arterial blood gases, serum level of creatine kinase, and triglycerides can be used to screen for early signs of PRIS.30 If unrecognized and untreated, PRIS may result in rhabdomyolysis, renal failure, hypotension, metabolic acidosis, hyperthermia, cardiac dysfunction, and ultimately death.40

Midazolam has a strong antiepileptic action and a short duration, and like the others, it is a respiratory and cardiac depressant. The primary disadvantage is tachyphylaxis, which is a rapidly decreasing therapeutic effect following initial administration, which may allow breakthrough seizures as soon as 1 day after therapy is started.1,7,41

The barbiturate pentobarbital is the traditional anesthetic medication used for patients in status epilepticus. Some advantages of pentobarbital are its strong antiepileptic action as well as its tendency to lower core temperature.7 Mild hypothermia has a neuroprotective effect in status epilepticus.32 Pentobarbital causes more potent hypotension and cardiopulmonary depression, and pressors are typically required.41 Gastric paresis, immunosuppression, pneumonia, and splanchic hypoperfusion leading to gastric, pancreatic, and hepatic complications are more common with barbiturates.39,43,44 The pharmacokinetics of pentobarbital will typically cause a persistent anesthetic effect for several days following discontinuation.7 Duration of anesthesia before initial attempts to wean a patient off of any of these anesthetic agents is customarily 24 to 48 hours, but few data are available to support this. Maintenance AEDs should be continued during anesthesia and throughout weaning.1

Phenytoin and fosphenytoin often cause hypotension during the administration of loading doses.
Although multiple anesthetic medications exist, no randomized controlled trials with adequate power have been done to compare agents. In a meta-analysis45 of 121 studies including 1168 patients, the researchers were able to draw only broad conclusions and did not recommend one agent as better than another (it may vary from patient to patient). The Neurocritical Care Society’s guidelines1 do not recommend one anesthetic agent over another, citing limited evidence from less rigorous studies.

Dosing regimens must be adjusted on the basis of the patient and the EEG response. In refractory status epilepticus, the continuous EEG is the primary tool for determining anesthetic dose.46 Patients who are sedated to the point of burst suppression will often exhibit loss of all brainstem reflexes and appear to have palsy of cranial nerve III with dilated unresponsive pupils. Therefore the need for brain monitoring devices to continually assess patients at risk for herniation should be considered so that unnecessary imaging is not prompted by this examination, which would otherwise be very concerning.

**Nursing Considerations**

**Gastrointestinal**

The anesthetics, particularly barbiturates, can cause gastric paresis and ileus.39 Postpyloric nutrition in a patient with delayed gastric emptying and a suppressed cough reflex may be a logical approach. Additionally, the American Association of Critical-Care Nurses practice alert47 on prevention of aspiration recommends elevating the head of the bed to 30° to 45°. Should an ileus occur, a nasogastric tube may be required for gastric decompression to prevent aspiration. Tube feedings administered at a slow rate can promote the health of gastrointestinal membranes to prevent the translocation of organisms across the gastric cell membrane while also minimizing the potential of tube feeding intolerance.48

**Dermatologic**

During prolonged EEG monitoring, skin beneath the leads may break down. The scalp should be assessed carefully. A lead holiday in which the EEG monitoring is suspended after a stable medication regimen is established but before weaning off of pentobarbital may be appropriate in some cases. Alternative types of skin preparation and conductive paste may be requested to minimize breakdown, particularly if the patient has a skin allergy to a specific product.49 After extravasation of phenytoin, purple glove syndrome may develop; this syndrome may be treated with dry heat and elevation, but the patient should be monitored for tissue sloughing or compartment syndrome.29 Another dermatologic situation that may affect the patient is development of a rash. Certain medications such as phenytoin, carbamazepine, and lamotrigine may cause Stevens-Johnson syndrome or toxic epidermal necrolysis.50,51 Although rare, if one of those disorders is ignored and the medication continues to be administered, either Stevens-Johnson syndrome or toxic epidermal necrolysis can evolve into a life-threatening situation.

**Neurologic**

Daily interruption of sedation, although once a popular strategy to reduce oversedation and prolonged mechanical ventilation, does not reduce ventilator days or ICU length of stay,52 but in a Cochrane review,53 this practice was equivocal. The typical practice in patients with refractory status epilepticus is titrating anesthetics to burst suppression and maintaining this for 36 to 48 hours before weaning.54 It may be appropriate to perform abbreviated neurologic examinations during deep sedation or anesthesia. In situations where brain death is suspected, the brain death guidelines from the American Academy of Neurology suggest that sedative medications must be withheld for at least 5 half-lives, assuming normal hepatic and renal function, or until drug levels are undetectable before the brain death examination is performed.54

Patients with status epilepticus should be kept normothermic. Those receiving continuous anesthetic medications have a tendency to be hypothermic, especially those receiving pentobarbital. Warm air blankets can be used to gently rewarm or maintain normothermia. Intravascular techniques are not often necessary.

**Summary and Conclusions**

Status epilepticus is a medical emergency that requires emergent identification and treatment and urgent follow-up therapies to prevent neuronal death. Although convulsive status epilepticus is obvious, nonconvulsive status epilepticus is less apparent. Whether convulsive or nonconvulsive in nature, emergent treatment for status epilepticus should begin with management of airway, breathing, and circulation followed by...
benzodiazepines, urgent follow-up administration of intravenous AEDs, and rapid escalation of therapy, often to general anesthesia, to prevent morbidity and mortality. As with the evolving definition of status epilepticus over the years, ongoing rigorous research is needed to increase knowledge about the drug selection priorities and further development of our understanding of how the GABA-mediated inhibition fails in refractory status epilepticus.1,12 Knowing what to look for in this population of patients, nurses are uniquely positioned to assist with the identification and management of status epilepticus to minimize the untoward and intractable sequela of the natural course of the disease. CCN

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None reported.

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