Consultation with the Specialist: Management of Status Epilepticus in Children
Tonia Sabo-Graham and Alan R. Seay
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Consultation with
the Specialist

Management of Status Epilepticus in Children
Tonia Sabo-Graham, MD* and Alan R. Seay, MD†

The definition of status epilepticus (SE) is a simple, prolonged seizure or recurrent seizures associated with impaired consciousness for 30 minutes or longer. There are two types of SE: convulsive and nonconvulsive. The latter consists of prolonged absence or complex partial seizures.

Etiology
SE occurs most frequently in patients younger than 1 year of age and those between 60 and 80 years. Determining the underlying cause of SE is of utmost importance and is directed by the clinical presentation. The differential diagnosis is similar in all age groups, although the frequencies change in the various diagnostic categories. Table 1 delineates some of the leading causes of SE in various age groups.

The differential diagnosis in any age group should include both systemic and central nervous system (CNS) infections; trauma; hypoxia; CNS malformations; ischemic events, including stroke or hemorrhage; and toxic or metabolic causes, including electrolyte imbalance, alcohol use, illicit drug use, and inborn errors of metabolism. External and internal antiepileptic drug withdrawal also is a significant factor.

The incidence of SE due to infection and congenital anomalies is higher in the pediatric age group. If a child is younger than 3 years of age, infection, hypoxia, or metabolic disturbances are the most likely causes. In the child older than 3 years, idiopathic epilepsy, congenital anomalies, or chronic encephalopathies are the more likely precipitants. Although usually benign, febrile seizures can progress to SE.

Neonatal SE is challenging to diagnose and treat because seizures in neonates are usually subtle and not dramatic in appearance. Clinical manifestations include rhythmic eye movements, rowing or pedaling motions of the legs, tonic posture, or less commonly focal or multifocal generalized tonic, clonic, or tonic-clonic seizures. It often is difficult to correlate clinical seizures with electrocerebral epileptiform activity on electroencephalography (EEG). The decision to treat needs to be based on the underlying etiology of the seizures, background and ictal activity of the EEG, and consideration of the consequences of chronic antiepileptic drug administration.

SE is associated with a poorer prognosis in adults than in children. Average mortality rates in one study were 25% for adults versus 2.5% in children. Alcohol and drug abuse account for a large percentage of cases of SE.

Nonconvulsive SE
Table 2 lists a classification scheme for SE. Convulsive, either generalized or partial, is the most easily recognizable form of SE. Nonconvulsive often is difficult to identify and to differentiate from confusional migraine and psychiatric fugue states. Cascino reported that 25% of persons experiencing SE have absence or complex partial SE.

Important differential diagnoses in patients who have nonconvulsive SE (absence or complex partial), depending in part upon their age, include confusional states or unre sponsiveness associated with transient ischemic attacks, transient global amnesia, stroke, or migraine. Toxic and metabolic causes should be sought early in the evaluation. One must always consider psychiatric disorders, such as various forms of psychosis, fugue states, and “nonepileptic pseudoseizures” in the differential.

Absence SE
Patients who have absence SE usually have a generalized or secondarily generalized seizure disorder. It rarely is the first manifestation of a seizure disorder and infrequently

| TABLE 1. Common Etiologies of Status Epilepticus in Various Age Groups |
|-----------------------------|----------------------------------|
| Neonate | Hypoxic-ischemic encephalopathy |
| | Infection |
| | Inborn errors of metabolism (eg, nonketotic hyperglycemia) |
| | Stroke or intraventricular hemorrhage |
| | Congenital malformation |
| | Pyridoxine deficiency and dependency |
| Child | Infection |
| | “Simple febrile seizure” |
| | Metabolic disturbance |
| | Congenital malformation |
| | Presentation of epilepsy |
| Adult | Stroke |
| | Inadequate anticonvulsant concentrations |
| | Trauma |
| | Tumor |
| | Unknown or undefined |

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occurs before the age of 10 years. Approximately 10% of adults and 3% of children who have absence epilepsy eventually experience at least one episode of SE. Symptoms may be as subtle as mild incoordination or paucity of speech. The patient usually appears drowsy and confused. The EEG is diagnostic and shows bilateral, synchronous 3-Hz spike and slow wave complexes.

**COMPLEX PARTIAL SE**

The true incidence of complex partial SE is uncertain. A patient who has this form of disease often exhibits bizarre behavior or localizing neurologic signs. The patient also may exhibit typical (automatistic) motor phenomenon. An EEG will help determine if the patient is in continuous or frequently recurring complex partial seizures.

**Treatment (Tables 3 and 4)**

**0 TO 5 MINUTES**

During the first few minutes in the management of SE, the highest priority is ensuring airway patency. Monitoring vital signs, maintaining perfusion, supplying oxygen, and monitoring cardiac rhythm are essential. Once the patient is stable, the physician should obtain a detailed history and perform a rapid, thorough general and neurologic examination, looking for signs of trauma, focality of the neurologic examination, or clues suggesting an infection.

**5 TO 10 MINUTES**

When seizures extend beyond 5 minutes, the next level of care involves establishing intravenous access and drawing blood for a complete panel of electrolytes, including Ca, P, and magnesium; glucose; complete blood count (CBC); blood urea nitrogen (BUN); and if appropriate, levels of anticonvulsants. SENDING a urine sample for toxicologic drug screening may be appropriate. The first line of treatment for either a convulsive or nonconvulsive seizure is a benzodiazepine or barbiturate. Lorazepam (0.05 to 0.1 mg/kg) is preferable to diazepam (0.2 to 0.5 mg/kg) because it has a longer half-life and is less sedating than diazepam. Doses can be readministered after 10 to 15 minutes if the seizure continues. Midazolam is another alternative that can be administered at 0.05 to 0.1 mg/kg per dose intravenously (an intramuscular preparation is available).

If the patient is hypoglycemic, 2 mL/kg of 50% glucose can be given. In adults, 100 mg of thiamine can be administered.

**10 TO 15 MINUTES**

After 10 minutes of continual or intermittent convulsive seizures, a longer-acting anticonvulsant such as phenobarbital or phenytoin is given. Phenobarbital (20 mg/kg per dose) usually is administered as the initial antiepileptic drug to the neonatal group; fosphenytoin (20 mg/kg per dose) is administered to children and adults. Fosphenytoin (which has fewer side effects than phenytoin) is now available, but it must be requested specifically on some formularies. This phenytoin prodrug is converted to phenytoin rapidly by blood phosphates. It is much less caustic than parenteral phenytoin. It can be administered intramuscularly or intravenously; the standard intravenous dose is 150 mg/min (children, 3 mg/kg per min). In comparison, phenytoin can be administered at only 50 mg/min. Fosphenytoin can be given intramuscularly and does not produce muscle necrosis; intravenous admin-

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**TABLE 2. Classification Scheme for Status Epilepticus**

<table>
<thead>
<tr>
<th>Nonconvulsive SE</th>
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</tr>
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<tbody>
<tr>
<td>• Absence</td>
<td>• Partial (focal motor)</td>
</tr>
<tr>
<td>• Complex partial</td>
<td>• Generalized tonic/tonic</td>
</tr>
</tbody>
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**TABLE 3. Management of Convulsive Status Epilepticus**

<table>
<thead>
<tr>
<th>DURATION OF SEIZURE</th>
<th>PROCEDURES</th>
</tr>
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<tbody>
<tr>
<td>0 to 5 minutes</td>
<td>Ensure safety of patient Monitor cardiopulmonary function and vital signs Give oxygen Obtain history and perform complete physical examination Note time</td>
</tr>
<tr>
<td>5 to 10 minutes</td>
<td>Obtain intravenous access Draw blood for laboratory tests Give 2 mL/kg of glucose and B vitamins Give lorazepam: 0.05 to 0.1 mg/kg (Maximum dose, 4 mg) or diazepam: Pediatric, 0.2 to 0.5 mg/kg Adult, 5 to 10 mg/dose</td>
</tr>
<tr>
<td>&gt;10 minutes</td>
<td>Convulsive status Neonatal patient: Phenobarbital 20 mg/kg Pediatric and adult patients: Phenytoin 20 mg/kg (Prescribe as: fosphenytoin at 20 mg phenytoin equivalents/kg)</td>
</tr>
<tr>
<td>&gt;30 minutes</td>
<td>Load with second long-acting agent Phenobarbital 10 mg/kg. May give additional 5- to 10-mg doses until 40 mg/kg or maximum dose of 1 g is reached Anticipate intubation</td>
</tr>
<tr>
<td>45 to 60 minutes</td>
<td>Transfer to intensive care unit Institute general anesthesia Monitor continuously via electroencephalography</td>
</tr>
</tbody>
</table>
administration does not cause respiratory depression or arrhythmias. Common side effects are pruritus and paresthesias in the groin area. (Diphenhydramine hydrochloride is often helpful for treatment if this should occur.)

It is best to administer the full 20 mg/kg loading dose of phenytoin or phenobarbital to control seizures for a prolonged time. In one study, average phenytoin blood levels 24 hours after a loading dose of 20 mg/kg were 17 mcg/mL (normal, 10 mcg/mL to 20 mcg/mL). In contrast, a bolus of 12 mg/kg of phenytoin resulted in a peak blood level of only 12 mcg/mL within several hours after the initial loading dose and a blood level of only 8 mcg/mL at 24 hours. Lack of seizure control after the phenytoin dose suggests that a possible severe insult to the CNS has occurred.

While the longer-acting anticonvulsant is being administered, intermittent seizure activity can be treated with additional doses of lorazepam or diazepam.

### 30 TO 45 MINUTES

For seizures that persist beyond 30 to 45 minutes, it is advisable to administer a loading dose of another long-acting anticonvulsant (phenobarbital or fosphenytoin), adding whichever of the two was not used as first-line therapy. At times, fosphenytoin or phenobarbital dosages are increased to 30 mg/kg.

<table>
<thead>
<tr>
<th>Lorazepam:</th>
<th>Phenobarbital:</th>
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<tr>
<td><strong>Route:</strong> Intravenous, IO</td>
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<td><strong>Dose:</strong> 0.05 to 0.1 mg/kg up to 4 mg/dose</td>
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</tr>
<tr>
<td><strong>Rate:</strong> Can give IV push over 2 minutes; can be given 5 to 10 minutes apart</td>
<td><strong>Maximum dose:</strong> Additional 5 to 10 mg/g dose every 20 minutes until maximum dose of 40 mg/kg or total dose of 1 g</td>
</tr>
<tr>
<td><strong>Maximum dose:</strong> 4.0 mg</td>
<td><strong>Rate:</strong> &lt;100 mg/min</td>
</tr>
<tr>
<td><strong>Onset of action:</strong> 2 to 3 minutes</td>
<td><strong>Onset of action:</strong> 10 to 20 minutes; intramuscular may take up to 2 to 4 hours</td>
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<tr>
<td><strong>Duration:</strong> Usually 12 to 24 hours</td>
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### Diazepam:

**Route:** Intravenous, IO, PR

**Dose:** Pediatric: 0.2 to 0.5 mg/kg

- **Adult:** 0.2 mg/kg (10 mg average adult dose)

**Rate:** May repeat every 15 to 30 minutes

**Maximum dose:** Usually not more than three doses given at 5 mg/min

**Onset of action:** 1 to 3 minutes; PR doses take 1 to 2 hours

**Duration of action:** 5 to 15 minutes

**Side effects:** Somnolence, confusion, hypotension, ataxia, bradycardia, respiratory depression

### Phenytoin:

**Route:** Intravenous, IO

**Dose:** 20 mg/kg

**Maximum dose:** 1,000 mg

**Rate:** <0.5 mg to 1.0 mg/kg per min to a maximum rate of 50 mg/min

**Onset of action:** 10 to 30 minutes after infusion

**Duration of action:** 12 to 24 hours

**Side effects:** Hypotension, respiratory depression, risk of cardiac arrhythmia

### Fosphenytoin:

**Route:** Intravenous, intramuscular

**Dose:** 20 mg/kg phenytoin equivalents

- **Children:** 3 mg/kg per min phenytoin equivalents
- **Adult:** 150 mg/min phenytoin equivalents

**Onset of action:** Within 2 to 3 minutes after loading dose

**Duration:** 12 to 24 hours

**Side effects:** Pruritus, paresthesia in groin area

### Valproate:

**Route:** Oral, PR

**Dose:** NG: 67 mg/kg; RP: 200 mg suppositories; enema: 60 mg/kg

**Side effects:** Gastrointestinal irritation, tremor, ataxia, liver failure, pancreatitis

### Midazolam:

**Route:** IV (oral, intravenous available)

**Dose:** 0.05 to 0.1 mg/kg IV

**Rate:** Load with 0.2 mcg/min and titrate continuous infusion to 0.4 to 0.6 mcg/kg per min

**Onset of action:** IV within 5 to 10 minutes

**Duration:** 1 to 6 hours

**Side effects:** Hypotension, bradycardia, central nervous system and respiratory depression

### TABLE 4. Drugs Used Commonly in the Treatment of Status Epilepticus

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**Maximum dose:** Usually not more than three doses given at 5 mg/min

**Onset of action:** 1 to 3 minutes; PR doses take 1 to 2 hours

**Duration of action:** 5 to 15 minutes

**Side effects:** Somnolence, confusion, hypotension, ataxia, bradycardia, respiratory depression

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**Rate:** <0.5 mg to 1.0 mg/kg per min to a maximum rate of 50 mg/min

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**Route:** Intravenous, intramuscular

**Dose:** 20 mg/kg phenytoin equivalents

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- **Adult:** 150 mg/min phenytoin equivalents

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**Route:** Oral, PR

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**Onset of action:** IV within 5 to 10 minutes

**Duration:** 1 to 6 hours

**Side effects:** Hypotension, bradycardia, central nervous system and respiratory depression
loading dose. By this point, results of laboratory studies should be available to identify abnormalities that can be corrected immediately and guide additional evaluation and management. If the patient is stable, imaging tests can be considered, such as a cranial computed tomography.

**45 TO 60 MINUTES**

For seizures persisting more than 45 minutes, general anesthesia in the form of high-dose barbiturates or inhalation anesthesia is recommended. The patient is intubated electively and paralyzed. Pentobarbital, a short-acting barbiturate, can be given at 5 to 8 mg/kg by intravenous bolus. This is followed by a continuous infusion of phenobarbital at 3 to 5 mg/kg per hour for several hours. Pentobarbital administration is adjusted to produce a burst suppression on continuous EEG monitoring.

**New Drugs**

Occasionally, lidocaine is used in the treatment of refractory SE. It has been shown to be useful in some trials among adults for whom monitoring the level of consciousness is paramount, such as patients who have head injury or chronic pulmonary disease.

Several new anticonvulsants, including gabapentin, vigabatrin, and lamotrigine, do not yet have an established place in the treatment of SE. Further experience with these drugs will help to standardize their role in seizure management.

Intravenous preparations of valproate recently have become available. It is recommended that the drug be administered to a valproate-naïve patient at a dose of 15 to 20 mg/kg every 6 hours. However, the use of this drug has not been studied for the treatment of SE.

Another medication used in selected cases of intractable focal seizures is intravenous immunoglobulin. Although there is no formal proof of efficacy in the treatment of focal motor status associated with Rasmussen encephalitis and other forms of epilepsy, there have been promising results in a few pilot studies. It was found to be effective in 15 children who had intractable West or Lennox-Gastaut syndrome in whom dramatic reductions of seizure frequency and improvements in EEG patterns occurred in response to therapy.

Another less commonly used method to control SE consists of continuous infusion of midazolam at a rate of 0.4 to 6 mcg/kg per minute.

**Morbidity and Mortality**

The primary complications associated with SE are the side effects of therapy and systemic effects caused by the prolonged seizure. Complications of SE include hypoxia, lactic acidosis, hyperkalemia, hypoglycemia, shock, hyperpyrexia, renal failure, and pulmonary failure. Experimental studies suggest that seizures must persist longer than 1 hour before permanent neuro-pathologic changes develop. The duration of SE has been correlated directly with increased mortality when the SE episode lasts longer than 1 hour. Mortality relates more to the underlying etiology than to the duration of the seizure.

Cognitive or motor deficits following an episode of SE usually are related to the underlying cause of the SE rather than the actual seizure. Movement disorders were observed more frequently in one study of children who had suffered an episode of SE lasting at least 30 minutes.

Therapies for treatment of SE are associated with potentially serious risks. The barbiturates and benzodi-azepines are associated with the highest risk for respiratory depression and need to be avoided or used with caution. Seizures must persist longer than 15 minutes, phenobarbital 20 mg/kg per dose or phenytoin 20 mg/kg per dose should be administered with strict adherence to the proper rate of administration. Further seizure activity during drug administration can be treated with additional doses of lorazepam or diazepam.

If a seizure lasts longer than 10 minutes, phenobarbital 20 mg/kg per dose or phenytoin 20 mg/kg per dose should be administered with strict adherence to the proper rate of administration. Further seizure activity during drug administration can be treated with additional doses of lorazepam or diazepam.

**Summary**

Treatment of SE is based on the age of the patient and the possible underlying etiology. Initial treatment should include a benzodiazepine (lorazepam 0.1 mg/kg or diazepam 0.5 mg/kg). Specimens for laboratory tests should be drawn early in the event of a prolonged seizure and geared toward the clinical presentation and age of the patient.

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If a seizure lasts longer than 10 minutes, a second long-acting anticonvulsant should be administered, followed by induction of general anesthesia.

**SUGGESTED READING**

Cascino G. Nonconvulsive status epilepticus in adults and children. Epilepsia. 1993;34 (suppl 1):21–27


In the immediate neonatal period, the least likely cause of status epilepticus is:
A. Hemorrhage into the central nervous system.
B. Hypoxic-ischemic encephalopathy.
C. Inborn errors of metabolism.
D. Infection.
E. Unsuspected parental abuse.

In early childhood, the most likely cause of status epilepticus is:
A. Chromosomal disease with central nervous system abnormalities.
B. Drug overdose.
C. Febrile seizure lasting longer than 30 minutes.
D. Metabolic disease with lactic acidosis.
E. Unsuspected head trauma.

The most correct statement regarding absence status epilepticus is that:
A. Abnormalities in the electroencephalogram require hyperventilation for detection.
B. It occurs frequently in those younger than 6 years of age.
C. It often is the first sign or symptom of an intracranial neoplasm.
D. It typically manifests as a drowsy, confused state in a patient who has had prior seizures.

The recommended initial pharmacologic approach to the treatment of status epilepticus is:
A. Lorazepam 0.05 to 0.1 mg/kg intravenously.
B. Nitrous oxide by inhalation.
C. Pentobarbital 3 to 5 mg/kg intravenously.
D. Phenytoin 15 to 20 mg/kg intravenously.
E. Sodium valproate syrup 20 mg/kg in water rectally.

The most urgent laboratory test(s) to perform in a patient who has status epilepticus is:
A. Blood glucose by Dextrostix®.
B. Blood pH and lactic acid levels.
C. Complete blood count.
D. Serum calcium and magnesium levels.
E. Urine toxicology screen.
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