Status Epilepticus

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This chapter reviews common presentations of pediatric status epilepticus (SE) and discusses its management, evaluation, treatment, and prognosis. SE is a common neurologic emergency in children that signifies severe central nervous system (CNS) dysfunction. Initial management is directed at stabilization of vital functions and a quick but thorough investigation for an etiology. An organized treatment paradigm is essential and reduces associated morbidity and mortality.

Status epilepticus (SE) is a common pediatric emergency that is potentially life threatening. Of the 100,000 to 150,000 cases that occur each year in the United States, most take place in children. Additionally, close to 400,000 patients per year visit emergency departments for treatment of acute seizures.

Between the extremes of isolated seizure and SE lies the phenomenon of acute repetitive seizures (ARSs). ARSs are a severe form of epilepsy that differs from the patient’s normal pattern in seizure type, frequency, duration, or severity. ARSs may occur in any patient with epilepsy, despite chronic antiepileptic drug (AED) therapy, and require additional treatment. The cluster of seizures may be related to specific situations (eg, concurrent illnesses or sleep deprivation) or have no apparent precipitant.

The child who presents in generalized convulsive SE (GCSE) creates a frightening scenario for both the parents and the pediatrician or neurologist who is called to the emergency department. There is a perceived fear of permanent brain damage if the seizures are not quickly terminated. Most of these children have no prior history of epilepsy. In some children, SE is a response to an acute cerebral insult. In others, SE is the first manifestation of an ongoing seizure disorder. In 1981, the International League Against Epilepsy (ILAE) defined SE as “a seizure that persists for a sufficient length of time or is repeated frequently enough that recovery between attacks does not occur.” The core facet is that of a continuous seizure or of repeating seizures that occur so rapidly that the patient does not recover consciousness.

The ILAE definition did not include a specific duration. Recent literature has incorporated a 30-minute duration in the definition of SE, on the basis of research showing that deleterious effects in neurons occur after 30 minutes of continuous seizure activity in experimental animals. However, this specified duration is misleading as a guide to treatment decisions. The vast majority of self-limiting generalized convulsive seizures stop within 2 to 3 minutes of onset, with almost all ceasing within 5 minutes. As such, a more practical definition of SE has emerged as any seizure that lasts more than 5 to 10 minutes.

This rationale for earlier treatment is supported by evidence that the longer the seizures persist, the more difficult they are to stop and the higher the mortality. Less than 10% of the total cases are subsumed under the rubric of nonconvulsive SE (NCSE). Some forms of NCSE also may lead to neuronal injury, but others may not. Complex partial SE is more likely to result in neuronal injury similar to GCSE. Absence SE is much less likely to result in neuronal injury and complications, probably because it is mediated primarily through excess inhibition (not excess excitation). The comments below refer to GCSE, except where noted. Compared with adults with SE, children have unique differences (ie, etiology, intravenous [IV] access, drug side effects, treatment response, and mortality) that influence therapeutic decisions.
Background

Children younger than 3 years of age are most likely to develop SE. Febrile seizures are the most common seizure type. The initial febrile seizure is longer than 15 minutes in 9% of patients (9,000 children per year in the United States) and longer than 30 minutes in 5% (5,000 children per year in the United States). This is the most common cause of SE in children; however, it also has the most favorable prognosis. A subpopulation of children with epilepsy are prone to SE, and they can be identified early in the course of their epilepsy. Children without SE in the first 2 years after onset of epilepsy have very little risk of experiencing SE later. Twelve percent of patients with newly diagnosed epilepsy present with SE. Although seizure duration does not predict recurrence risk, if a second seizure does occur it is likely to be prolonged. This same trend is observed in afebrile and febrile seizures.

The common pediatric causes of SE are directly related to the child’s age. The child who develops seizures at < 1 year of age has a 70% chance of developing SE at some time. This age group also has the highest pediatric mortality due to SE. SE in a child younger than 3 years of age is more likely to occur in a neurologically normal child and be the result of an acute illness. Systemic infections and febrile illness are common precipitators. Other acute disorders include head trauma, meningitis, encephalitis, dehydration, and electrolyte disorders.

In children 3 to 16 years of age with symptomatic or cryptogenic partial seizures, 20% will develop SE within 5 years of their original epilepsy diagnosis. The 3- to 16-year-old child with SE is more likely to have a chronic encephalopathy and be neurologically abnormal. The chronic encephalopathy may be related to perinatal problems, a brain malformation, neurocutaneous syndrome, or a prior history of head trauma, meningitis, or stroke. In these patients, SE may be acutely precipitated by a febrile illness or subtherapeutic AED levels (often due to a medication change) in a child with a known seizure disorder. The outcome of SE is strongly influenced by the etiology. The worst prognosis occurs in children whose SE is precipitated by serious intracranial insults, such as encephalitis, cerebral hemorrhage, anoxia, stroke, or CNS toxins. Although children are at higher risk of SE than are adults, morbidity and mortality rates are lower in children (typically 3–15%) than in adults.

Key factors that influence the patient’s prognosis include (1) the patient’s age, (2) the etiology, and (3) the duration of SE (this is the only factor influenced by AED treatment). Long-term complications include epilepsy, encephalopathy, and focal neurologic deficits. Death after SE is usually secondary to the underlying cause, not to the prolonged seizure activity per se. Rapid intervention with safe, effective treatments will minimize the sequelae of SE.

The child in SE requires prompt intervention. This is a medical emergency. It is extremely important to have a treatment protocol in place and to work through it quickly. The goals of treating SE include stopping the seizure safely and in a timely manner and minimizing treatment-related morbidity. The systemic effects of SE must be understood and the side effects of the prescribed treatment (sedation and cardiovascular or respiratory compromise) anticipated.

Management of SE begins with the ABCs of life support (establishing an airway and supporting respiration, maintaining blood pressure, access to circulation) and, when possible, identifying and treating the cause (Tables 78-1 and 78-2). Vital signs, pulse oximetry, and the electrocardiogram (ECG) should be monitored closely. Skilled nursing care is crucial to the management of SE. Rapid determination of blood glucose level should be undertaken in all patients. If hypoglycemia is found or suspected, intravenous (IV) glucose is administered (in adolescents, IV thiamine 100 mg should be given first). Additional blood should be drawn for a complete blood count, serum chemistries, toxicology screening, and AED levels.

### TABLE 78-1. Guidelines for Treatment of Pediatric Generalized Convulsive Status Epilepticus (GCSE)

<table>
<thead>
<tr>
<th>I. Stabilization</th>
<th>Rectal Diazepam Gel Dose †</th>
</tr>
</thead>
<tbody>
<tr>
<td>Note time, diagnose status epilepticus</td>
<td>2–5 0.5 mg/kg</td>
</tr>
<tr>
<td>Check ABCs (airway, breathing, circulation), vital signs</td>
<td>6–11 0.3 mg/kg</td>
</tr>
<tr>
<td>ECG monitoring, frequent suctioning</td>
<td>&gt; 12 0.2 mg/kg</td>
</tr>
<tr>
<td>Nasal oxygen, give antipyretics as needed</td>
<td>Rectal Diazepam Gel Dose †</td>
</tr>
<tr>
<td>Obtain IV access, * pulse oximetry</td>
<td>25% glucose 2 mL/kg, AEDs, toxicology</td>
</tr>
<tr>
<td>Blood for laboratory tests (if hypoglycemic, 25% glucose 2 mL/kg)</td>
<td></td>
</tr>
</tbody>
</table>

#### I. Treatment

Lorazepam 0.1 mg/kg at 2 mg/min (or diazepam 0.3–0.5 mg/kg at 5 mg/min). If seizures stop, no other therapy may be required if cause is corrected.

Fosphenytoin 20 mg PE/kg at 3 mg/kg/min (maximum rate, 150 mg PE/min). If seizures continue, fosphenytoin 5–10 mg PE/kg; anticipate intubation.

If seizures continue, anesthesia. Midazolam 0.2 mg/kg, then 1–10 µg/kg/min (or pentobarbital 5–15 mg/kg, then 1–5 mg/kg/h) to produce a burst-suppression EEG pattern.

<table>
<thead>
<tr>
<th>Age (yr)</th>
<th>Rectal Diazepam Gel Dose †</th>
</tr>
</thead>
<tbody>
<tr>
<td>2–5</td>
<td>0.5 mg/kg</td>
</tr>
<tr>
<td>6–11</td>
<td>0.3 mg/kg</td>
</tr>
<tr>
<td>&gt; 12</td>
<td>0.2 mg/kg</td>
</tr>
</tbody>
</table>

AED = antiepileptic drug; ECG = electrocardiogram; EEG = electroencephalogram; IV = intravenous; PE = phenytoin equivalent.

*If unable to obtain immediate IV access, administer rectal diazepam gel, on the basis of the child’s age and weight, and continue to establish IV access.

†Supplied as 2.5, 5, 10, 15, or 20 mg syringes, to maximum 20 mg.
All patients in SE show an acidosis that usually resolves once seizure control is achieved. Treatment with sodium bicarbonate is indicated only in severe acidosis. Hyperthermia, which occurs in 28 to 79% of patients, is important to recognize. Prevention of significant hyperthermia is a top priority, as it may contribute to brain damage. Further evaluation, which should not delay the administration of AED therapy, includes a directed history and examination, with specific references to trauma, substance abuse, preexisting epilepsy, neurologic or medical disorders, and the presence of any focal neurologic signs. This initial stabilization phase should be accomplished within the first 5 to 10 minutes of the child’s arrival in the emergency department.

Treatment is then begun, with a clear plan, prompt administration of adequate doses of an effective drug, and attention to the possibility of hypoventilation or apnea. As far as possible, drugs should be given only intravenously. When an IV line cannot be established, diazepam may be administered rectally. If this is successful, and an IV line has still not been established, the loading dose of fosphenytoin can be given intramuscularly. This provides seizure protection while the evaluation is completed. The average time from onset of seizures to ambulance arrival can be 30 minutes. The development of a rectal diazepam gel may broaden treatment horizons as this allows treatment of the SE before the patient reaches the hospital (and IV access is established).

The ideal drug to treat SE does not exist (Table 78-3). Several effective drugs have led to numerous treatment protocols. More than one drug is often used to achieve all the goals of the ideal drug. The strategy is to combine the drugs necessary for each patient for appropriate treatment. The treatment protocol for GCSE (see Table 78-1) is designed to follow a logical sequence, assessing the patient for response at each interval between the steps and moving to the next step if the patient continues to be in SE. If the seizures stop, no further therapy may be needed, or decisions can be made about the choice of an AED for long-term therapy.

A benzodiazepine is administered as initial treatment. The onset of action is rapid, often within 1 to 2 minutes. Most patient’s seizures will stop. Too rapid IV administration of a benzodiazepine may produce cardiac or respiratory arrest. If diazepam is used, it may be necessary to administer a long-acting drug, preferably fosphenytoin, to prevent recurrent convulsions. If the seizures have not stopped, a loading dose of fosphenytoin should be administered. ECG and blood pressure monitoring are imperative. If hypotension develops, the infusion should be slowed or stopped. If the seizure ceases, the infusion rate should be slowed. Within 10 minutes of the end of the infusion, if not before, the seizures should stop. If the SE persists, an additional fosphenytoin dose can be given.

Historically, in the event of persistent seizures, phenobarbital was given next as a loading dose. However, although effective, this is slow in onset and places the patient at risk of cardiovascular collapse. Midazolam can be infused rapidly, is effective, and has fewer cardiovascular side effects. Monitoring the treatment of SE with simultaneous electroencephalogram (EEG), although ideal, is not possible in many emergency departments. Treatment should never be delayed while awaiting an EEG, unless there is diagnostic uncertainty (eg, an adolescent with suspected nonepileptic events). If the seizures stop but the coma persists, an EEG must be obtained to exclude NCSE.

### Table 78-2. Guidelines for Treatment of Pediatric Nonconvulsive Status Epilepticus (NCSE)

| I. Stabilization | Same as generalized convulsive status epilepticus |
| II. Treatment |
| --- | --- |
| Lorazepam 0.1 mg/kg at 2 mg/min (or diazepam 0.3–0.5 mg/kg at 5 mg/min). If seizures stop, slowly load with fosphenytoin or valproate. |
| Fosphenytoin 20 mg PE/kg at 3 mg/kg/min (maximum rate, 150 mg PE/min maximum). If seizures continue, fosphenytoin 5–10 PE/kg. |
| Valproate 25 mg/kg at 3–6 mg/kg/min. (Use this first or second in absence or atonic or myoclonic SE). (If partial SE, may use or go directly to next step.) |
| If seizures continue, anesthesia. Midazolam 0.2 mg/kg, then 1–10 µg/kg/min (or pentobarbital 15 mg/kg, then 1–5 mg/kg/h) to produce a burst-suppression EEG pattern. |

EEG = electroencephalogram; PE = phenytoin equivalent.

### Table 78-3. Status Epilepticus: Ideal Drug Characteristics*

<table>
<thead>
<tr>
<th></th>
<th>Diazepam</th>
<th>Lorazepam</th>
<th>Phenytoin</th>
<th>Fosphenytoin</th>
<th>Valproate</th>
</tr>
</thead>
<tbody>
<tr>
<td>Easy to administer</td>
<td>X</td>
<td>X</td>
<td>—</td>
<td>X</td>
<td>X</td>
</tr>
<tr>
<td>Rapid onset</td>
<td>X</td>
<td>X</td>
<td>—</td>
<td>X</td>
<td>X*</td>
</tr>
<tr>
<td>Long duration</td>
<td>—</td>
<td>X</td>
<td>X</td>
<td>X</td>
<td>X</td>
</tr>
<tr>
<td>Broad spectrum</td>
<td>—</td>
<td>X</td>
<td>X</td>
<td>—</td>
<td>X</td>
</tr>
<tr>
<td>Minimal morbidity</td>
<td>—</td>
<td>—</td>
<td>—</td>
<td>X</td>
<td>X</td>
</tr>
<tr>
<td>Useful as a chronic antiepileptic drug</td>
<td>—</td>
<td>—</td>
<td>—</td>
<td>X</td>
<td>X</td>
</tr>
</tbody>
</table>

*Based on animal studies and limited clinical observations.
In the 15 to 25% of patients who do not respond to treatment, the question of etiology must be revisited. One must consider whether the cause is toxic or metabolic, especially in young children who are not responding. Continuous EEG monitoring is necessary at this point if it has not been obtained previously.

The management of refractory SE has primarily used one of these three drugs: (1) midazolam 0.2 mg/kg, followed by 1 to 10 µg/kg/min, (2) pentobarbital 5 to 15 mg/kg, followed by 0.5 to 5 mg/kg/h, and (3) propofol 1 to 2 mg/kg, followed by 2 to 10 mg/kg/h. However, rare reports indicate that propofol may be associated with rhabdomyolysis, metabolic acidosis, and fatal myocardial failure in children. The U.S. Food and Drug Administration (FDA) has reviewed this, and, to date, no causal relation has been found. However, the author rarely uses this agent. If the child is treated with pentobarbital, then the author would administer a loading dose of phenobarbital prior to pentobarbital withdrawal. This should prevent potential barbiturate withdrawal seizures.

**Prehospital Treatment**

There is a long time period before the patient with SE arrives at the hospital. Treatments are needed for prolonged seizures that can be initiated by emergency medical technicians (EMTs) prior to the patient’s arrival in the emergency department. Currently, treatment decisions are often being made during this time.

The EMTs may administer diazepam intravenously. In young children (or other patients for whom IV administration is difficult), the options are increasing; diazepam rectal gel or an intramuscular loading dose of fosphenytoin can be administered. Prehospital treatment studies indicate that if treatment is given prior to hospital arrival, seizure duration should be shortened, recurrence prevented, and the risk of intubation and admittance to the intensive care unit minimized. Paramedic out-of-hospital acute seizure treatment improves outcome in SE, but is still short of the 5- to 10-minute response advocated by the Epilepsy Foundation of America. Acute treatment of seizures at home is a way to reach this treatment goal. The only acute seizure treatment FDA-approved for at-home use is diazepam rectal gel.

Children experiencing ARS also benefit from prehospital treatment. The physician and the parents should discuss in advance and carefully decide which episodes of ARS are appropriate to recommend home therapy. Many children have episodes of ARS that are predictable, and preplanning may alter the need for emergency department visits. The advantages of effective home treatment for ARS include reducing emergency department visits and lost school and work time, resulting in an improved quality of life for both the patients and their families. In addition, effective home treatment is cost effective and allows caregivers to have a sense of empowerment. They feel they have control over the situation and that there is something they can do to prevent a true medical emergency.

Preparations of rectal diazepam have been available in Europe for 30 years. Recently, diazepam rectal gel was approved in the United States. One reason for the effectiveness of rectal administration of diazepam is the rich venous plexus just inside the second anal sphincter. The medication comes in a predosed syringe that makes it easy to deliver medication to this area. Absorption is rapid, giving quick therapeutic blood levels that are often successful in interrupting seizure clusters. The benefits of this form of medication include its premeasurement, rapid absorption, and safety (without respiratory compromise). Sedation is the only common adverse effect, as might be expected from a benzodiazepine. This is effective in terminating ARS in more than 75% of episodes, and no drug tolerance develops with uses at intervals of 5 days or more. Even if the seizures are not stopped, the administration of rectal diazepam gel does not complicate subsequent medical management.

In addition to ARS, some patients are at high risk of recurrence of SE (Table 78-4). Ten to 20% of children experience recurrent SE. This is especially true in the neurologically abnormal child, and the risk of recurrence increases with the degree of neurologic impairment. Parents of these children should be instructed in the use of rectal diazepam gel and be given a prescription for an appropriate dose (see Table 78-1). Administration of the medicine at the onset of the next seizure that is over 5 minutes in duration may eliminate the need for hospitalization or reduce the length of stay. However, this does not replace the need for evaluation by the pediatrician or child neurologist (at a minimum, this may be a telephone consultation in an established patient).

**Evaluation**

SE is a medical emergency that requires therapy with IV medication as soon as an IV line is established. If a treat-

| TABLE 78-4. Risk Factors for Recurrent Status Epilepticus in Children |
|-------------------------|---------|
| Prior prolonged febrile seizure (>15 minutes) |         |
| Remote symptomatic* etiology as the cause of initial SE |         |
| Progressive neurologic disease |         |

*Remote symptomatic—a seizure occurring without acute cause in a child with a history of a prior brain insult known to be associated with an elevated risk of convulsions (eg, meningitis, cerebral palsy, head trauma, or mental retardation).
able cause is known or found (eg, hypoglycemia), then initial therapy is directed at treatment of this cause. However, in most cases, there is no obvious cause, and treatment is directed at stopping the seizures and then initiating appropriate laboratory studies (Table 78-5). This will usually include a magnetic resonance imaging (MRI) study of the brain. If acute trauma is causally related, an emergent computed tomography (CT) scan should be obtained.

Table 78-5. Second-Phase Studies*

<table>
<thead>
<tr>
<th>Study</th>
</tr>
</thead>
<tbody>
<tr>
<td>Liver function tests</td>
</tr>
<tr>
<td>Toxicology screen</td>
</tr>
<tr>
<td>EEG</td>
</tr>
<tr>
<td>Lumbar puncture</td>
</tr>
<tr>
<td>CT or MRI brain scan</td>
</tr>
<tr>
<td>Video-EEG monitoring</td>
</tr>
</tbody>
</table>

CT = computed tomography; EEG = electroencephalogram; MRI = magnetic resonance imaging.

*Studies vary depending on the clinic situation.

Other studies (eg, toxicology, urine drug screen, and lumbar puncture) may be necessary as clinically indicated. If the child is not beginning to awaken and show an improved mental status in the first 30 to 60 minutes after the seizure is stopped, an EEG should be obtained. If the child’s mental status is improving, an EEG may still be necessary but not urgent. The child may be maintained on AED therapy during the initial evaluation. Depending on the results of this evaluation, a decision will have to be made regarding the need for long-term AED therapy.

Conclusion

SE is a common neurologic emergency in children. It signifies severe CNS dysfunction. Initial management is directed at stabilization of vital functions and a quick but thorough investigation for an etiology. An organized treatment paradigm is essential and reduces the morbidity and mortality associated with SE. Inadequate treatment regimens and failure to recognize cardiorespiratory collapse are the common treatment errors. The treatment strategy for SE should accomplish four goals: (1) ensure adequate cardiorespiratory function, (2) stop seizure activity, (3) prevent recurrent of seizures, and (4) identify and, if possible, treat the etiology. Achieving these four goals will improve the outcome of SE in all children.

Suggested Readings


http://www.cene.com/Presentations/IV AEDSlideKit.ppt

Practitioner and Patient Resources


Epilepsy Foundation
4351 Garden City Drive, Suite 406
Landover, MD 20785-2267
Phone: (301) 459-3700 or 800-332-1000
E-mail: postmaster@efa.org
http://www.epilepsyfoundation.org
The Epilepsy Foundation will ensure that people with seizures are able to participate in all life experiences and will prevent, control and cure epilepsy through research, education, advocacy and services.

The Epilepsy Research Foundation
PO Box 3004
London, England W4 1XT
Phone: 020 8995 4781
E-mail: info@erf.org.uk
http://www.erf.org.uk
Devoted solely to sponsoring effective research for all who now suffer from epilepsy.

H.O.P.E. Mentoring Program
(a part of the Epilepsy Foundation)
Phone: 877-467-3496
http://www.epilepsyfoundation.org/programs/hope.cfm

H.O.P.E. was created to allow people who live with epilepsy to educate others and to share their experiences. H.O.P.E. trains people with epilepsy to be “patient educators” throughout the epilepsy and neurologic communities.

Epilepsy Information Service (EIS)
Department of Neurology
Wake Forest University School of Medicine
Medical Center Boulevard
Winston-Salem, NC 27137
Phone: 800-642-0500
http://www.bgsu.edu/neuro/disease/epilinfo.shtml

The EIS is a nonprofit resource center that offers a nationwide toll-free information line for people with epilepsy and their families, professionals, and the public. Free educational packets are available to all callers.

Epilepsy.com
11911 Freedom Drive #730
Reston, VA 20190
Phone: (703) 437-9720
http://www.epilepsy.com

Epilepsy.com is an online resource with information for children, parents, and professionals, provided by The Epilepsy Project, a nonprofit center that supports research.