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The Specialist

Status Epilepticus

Margaret C. McBride*

Status epilepticus has been defined as continuous seizure activity or intermittent seizure activity without recovery of consciousness between seizures that lasts for more than 30 minutes. However, if a seizure has continued unabated for 5 minutes, status epilepticus should be presumed and therapy initiated. Status epilepticus is a medical emergency, and all primary care physicians should know how to initiate its treatment.

Usually status epilepticus consists of generalized or asymmetric clonic activity with unconsciousness. However, prolonged absence or partial seizures comprise 10% of episodes. Absence status epilepticus usually occurs in children who have severe primary generalized epilepsy or Lennox-Gastaut syndrome. Partial status epilepticus occurs in children who have focal brain pathology. The initial treatment of both is like that for generalized status epilepticus, with only slightly less urgency. The remainder of this review concerns generalized status epilepticus.

Etiology

It is important to obtain both remote and recent histories from the child's family or attendant as soon as possible so that an appropriate differential diagnosis may be developed. In 25% of cases, status is idiopathic. In another 25% it is provoked only by fever (febrile status). In the 20% of children who have a static encephalopathy, the condition is termed remote symptomatic status epilepticus.

In another 20%, status is termed acute symptomatic and is an expression of an acute encephalopathy or brain injury. Causes in this group include infection (either central nervous system [CNS] infection or systemic infection associated with parainfectious phenomena); hypoxia, hypoglycemia, or another metabolic abnormality such as low sodium, calcium, or magnesium; subarachnoid bleeding; stroke; or overdoses of drugs, including anticholinergics, sympathomimetics, cholinergics, and narcotics. Toxic or even high therapeutic levels of theophylline in children who are prone to seizures may provoke status, especially when levels rise abruptly. Rarely, status results from a degenerative disease. Status epilepticus is an extremely rare presenting sign of malignant brain tumors.

Twenty-five percent of children who present in status epilepticus had previous seizures (most are in the remote symptomatic group). Acute illness or falling levels of anticonvulsant medication may be the provocative factor in these children.

Management

INITIAL STABILIZATION

The management of status epilepticus begins with assessing the patient's airway, breathing, and circulation; initiating oxygen therapy; measuring serum glucose by finger stick; and checking body temperature. When a child in status is positioned supinely with limbs extended, the head should be turned to one side and the limbs of the opposite side should be free so that the patient can be pulled quickly

over onto his or her side if pharyngeal secretions build up or vomiting ensues. Suction equipment with large-diameter tubing through which small chunks of food can pass should be available to clear the airway. Venous access should be established as quickly as possible and blood drawn for immediate complete blood count and measurement of electrolytes, glucose, calcium and magnesium concentrations, and levels of anticonvulsant medications if the child already is receiving therapy for seizures. Extra serum should be obtained for further studies that might be indicated as the history and course of treatment unfold.

The importance of lowering body temperature in a patient who has febrile status has been underemphasized in textbooks and review articles. Experimental data indicate that higher body temperatures increase the neuronal discharges and the tissue damage associated with induced status epilepticus (see Liu et al and Lundgren et al). A few children who have prolonged febrile status (and no CNS infection) will have long-term sequelae (see Hauser). Fever and status epilepticus both increase the metabolic demands of the brain markedly. The combination of the two may create such a large increase in metabolic demand that the usual compensatory increase in blood flow cannot keep up with substrate supply. Additionally, the work of status epilepticus can increase body temperature further, making it more difficult to lower the temperature into the normal range. Therefore, therapy should include early and repeated measurements of body temperature and prompt initiation of therapy if the

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temperature is elevated. Therapy for fever should include maximum doses of rectal antipyretics. If the temperature is higher than 103°F (39.4°C) and the status has not stopped after administration of a benzodiazepine, then physical cooling with cold water, cold wet towels, ice, or ice blankets in addition to the antipyretics may help. Generation of heat from shivering following cold applications to the skin is of no concern in a patient who already is generating tremendous heat from the muscle work of status epilepticus.

DRUG THERAPY

As the patient is being positioned and stabilized and treatment is initiated as indicated for hypoglycemia (1 to 2 mL/kg of 50% dextrose if finger stick sample indicates <50 mg%) and fever, the physician should begin anticonvulsant treatment as summarized in the Table. A benzodiazepine is the first drug used because of its rapid onset of action; lorazepam is the benzodiazepine of choice because of its longer half-life. Because the half-life of diazepam is very short, it must be followed immediately by phenytoin if it is used as the first drug. However, if the patient is known to be receiving phenytoin, 5 mg/kg of phenytoin should be given first because phenytoin withdrawal is the mostly likely cause of status in such patients. For seizures related to withdrawal of other anticonvulsants, a benzodiazepine should be given first.

Veins can be difficult to access in infants and toddlers who are having seizures. The intravenous (IV) preparations of lorazepam and diazepam are absorbed readily through the rectum, although the time to peak level is longer and the height of the peak is lower than with IV administration. If an IV line is not available by the time initial stabilization steps have been taken and the dose of lorazepam or diazepam appropriate for the child's estimated weight has been drawn up, the needle should be removed from the syringe, and the syringe should be lubricated and inserted into the rectum so that its tip is beyond the internal sphincter. The dose then is injected and the buttocks held together for 2 to 3 minutes to

keep it from being expelled. When venous access is obtained, IV therapy can be initiated and repeated as per the Table.

IV access is mandatory for phenytoin, the next step in anticonvulsant therapy of status. Phenytoin solution is very irritating and cannot be given rectally or intramuscularly. A child who still is having seizures 5 to 6 minutes after three doses of a benzodiazepine should be given a loading dose of phenytoin over 15 to 20 minutes. If seizure activity continues for another 5 to 6 minutes, 0.25 mEq/kg of sodium bicarbonate is indicated to treat metabolic acidosis that will have developed after continuous seizure activity of this duration. If status does not stop within 10 minutes of the total dose of phenytoin being given, phenobarbital is the next drug. The combination of loading doses of phenobarbital and full doses of the benzodiazepines may cause respiratory depression after the cessation of the seizure; the clinician should be ready to support respiration at this point and, indeed, at any point during the treatment of status.

Endotracheal intubation in children who have status epilepticus has become increasingly popular in the past 12 years. In some instances, this trend represents improved medical care and effective management. However, in some instances, this trend toward intubation early in the treatment of status represents a misunderstanding of: 1) the rapidly changing blood gases during the course of status, 2) the natural course of respiration after generalized seizures, or 3) the fact that it rarely is necessary to obtain a computed tomographic scan on an urgent basis (and, therefore, to intubate the patient as a part of stabilizing him or her for the period he or she is in the scanner and less accessible).

If indicated, a CT scan may be obtained after the status has stopped and regular respirations are established. Blood gases obtained during status are obsolete within seconds of the end of the seizures. During status, gas exchange is limited by the low volume of air in the lungs when the chest and abdominal muscles are contracted. As soon as the seizure has ended and muscles relax, the chest involuntarily expands to a neu-

tral position and takes in a volume of air (or, hopefully, oxygen); hypoxia and hypercarbia begin correcting immediately. Often a patient is hypopneic in the first 1 to 3 minutes following status just as occurs following a brief generalized seizure. If this hypopnea is prominent or the patient's color remains poor, a few breaths per minute of oxygen may be administered by bag. Postictal patients usually are flaccid, especially after receiving benzodiazepines; it is easy to open their airways and inflate their lungs by mask and bag unless the airway is obstructed internally by food or vomitus.

Thus, the threat of respiratory depression should not deter the treating physician from aggressive therapy for status. In general, it is better for the child to have respiratory depression requiring ventilatory support by mask (or endotracheal tube) than to be in continued status.

If status is not responsive to a benzodiazepine followed first by phenytoin and then by phenobarbital, the patient will require further therapy. This is done best after endotracheal intubation and with intensive monitoring of vital signs and, if possible, electroencephalographic (EEG) monitoring. Intermittent recordings using a regular EEG machine can be helpful if continuous EEG monitoring is not available. In either situation, a person who is knowledgeable about EEGs must be available. The EEG is essential if the patient requires paralysis to allow effective respiration because it will be the only way to tell if the patient is still in status.

POSTICTAL MANAGEMENT

Once status has been controlled and underlying causes have been identified or excluded, it is important to communicate with the parents, who often are distressed from having witnessed the seizure and who usually have been neglected as treatment is initiated. Parents who have no previous experience with seizures usually think that their child is dying. Once the seizure has stopped and the child is deeply sedated and unresponsive, they may fear that he or she never will be the same. They should be warned that their child will be sleepy, irritable, and often ataxic for several

TABLE. Anticonvulsant Therapy for Status Epilepticus

ANTI-CONVULSANT	DOSE	SIDE EFFECTS	COMMENTS
Lorazepam	0.1 mg/kg IV/PR up to 4 mg over 1–2 min. May repeat after 5 to 6 min for total of three doses.	Respiratory depression Muscle flaccidity (including pharyngeal muscles)	Rapid acting (1–3 min). Half-life is 10 to 12 h, giving time for observation and evaluation; preferable to diazepam.
OR Diazepam	0.2 mg/kg IV up to 6 mg over 1–2 min. May repeat after 5 to 6 min for total of three doses. 0.5 mg/kg PR.	Same as for lorazepam	Rapid acting, but duration of action is only 20 min because it is redistributed rapidly into fat. Must be followed by another anticonvulsant, usually phenytoin.
Phenytoin	20 mg/kg IV up to 1000 mg (may <i>not</i> be given IM). Give 1/3 of dose over 1–2 min and remaining as 1 mg/kg/min or slower if bradycardia or hypotension occurs.	Cardiac depression Bradycardia Hypotension	Fairly rapid acting (brain concentrations in 4 min). Half-life is 12 to 24 h. If seizure continues after 5–6 min, give 0.25 mEq/kg of sodium bicarbonate.
Phenobarbital	20 mg/kg IV up to 800 mg over 10 min.	Respiratory depression Hypotension	Slow acting (brain concentrations in 15 to 30 min). Must be ready to intubate a patient who has received a benzodiazepine and phenobarbital.
Status epilepticus that continues despite the above treatment will require further treatment in a setting of intensive monitoring and support. Often the patient will require intubation. One of the following drugs should be tried next.			
Diazepam	0.5 mL/kg/h IV up to 40 mL/h of solution of 100 mg diazepam in 500 mL 5% dextrose.	Respiratory arrest Cardiac depression	Aim for serum levels of 0.2 to 0.8 mcg/mL.
OR Midazolam	0.15 mg/kg IV bolus, then 1 mcg/kg/min increased q 15 min as needed to control.	Respiratory depression Hypotension	Mean time to consciousness postinfusion is 4.2 h.

days. If the child has required intubation, they feel anxious about taking the child home where they cannot provide emergency support in case of another seizure. The issues relating to intubation should be explained. Parents may become reluctant to let the child out of their sight, even in sleep, and will need support and reassurance to resume a pattern of regular living. The prognosis for recurrent seizures and for morbidity should be discussed.

Prognosis

Mortality and morbidity from status epilepticus has declined in the past 25 years, probably because of the availability of benzodiazepines and better access to medical care. Morbidity and mortality depend primarily

on the cause and the underlying condition of the child. Mortality from status epilepticus is rare in children who have idiopathic or febrile status. However, mortality within 3 months among those who have acute symptomatic status or status related to a progressive encephalopathy is 10% to 15%. Likewise, morbidity in the form of new neurologic dysfunction occurs in fewer than 5% of children who have idiopathic or febrile status, but it occurs in 20% of survivors in the acute symptomatic group.

Subsequent seizures are more likely than residual neurologic dysfunction in a child who presents with status epilepticus. Of children who had not had previous seizures, 70% in the remote symptomatic group, 50% in the idiopathic (afebrile) group, and 20% in the acute symp-

tomatic group developed seizures within 2 years or less of follow-up in the series by Maytal and Shinnar. In the febrile status group, 8% generally will develop subsequent afebrile seizures by 20 years of age. This group has the same 30% risk for subsequent febrile seizures as any child presenting with a febrile seizure.

The risk for recurrence of status is considerably lower than the risk for recurrence of seizures. Children who have abnormal neurologic findings have a 27% risk of recurrent status in the first year and a 58% risk of recurrent status in the subsequent 3 years. However, children who have normal neurologic findings and who present in status have a less than 5% risk of recurrence of status.

The afebrile child who presents in status and has not had a previous

TABLE. Continued

ANTI-CONVULSANT	DOSE	SIDE EFFECTS	COMMENTS
Phenobarbital	5–10 mg/kg IV increments to total serum levels of 70–300 mcg/mL.	Respiratory arrest Prolonged sedation	Must be intubated initially and have cardiac monitoring.
OR			
Pentobarbital	10–15 mg/kg IV loading dose over 1 h, then 0.5–1.5 mg/kg/h adjusted to status control or burst suppression on EEG.	Respiratory arrest Cardiovascular depression	Half-life up to 10 h. May need drugs to control hypotension. Levels should not exceed 40 mcg/mL.
OR			
Sodium thiopental	3–4 mg/kg IV bolus over 2 min, followed by 0.2 mg/kg/min (0.1 mL/kg/min of 1000 mg in 500 ml saline). Increase dose q 3–5 min by 0.1 mg/kg/min until status is controlled or the EEG is isoelectric.	Same as for pentobarbital	May need drugs to control hypotension. Very short acting (20–30 min).
Lidocaine	1–2 mg/kg IV up to 50–100 mg bolus over 2–4 min followed, if effective, by 3–5 mg/kg/h as solution of 100–1000 mg in 250 mL 5% dextrose.	Respiratory arrest Cardiac conduction abnormalities	High doses of lidocaine can cause seizures.
Halothane anesthesia	Given by anesthesiologist, titrated to suppression of discharges on EEG		
When using an intravenous infusion or a general anesthetic, withdraw medication cautiously after 24 to 48 h and monitor patient and EEG for seizures. Medication may need to be restarted if seizures recur. Other possible drugs are:			
Paraldehyde	0.3 mL/kg PR mixed with equal amount mineral oil. IV no longer available in USA.	Respiratory depression Sedation Coughing Pulmonary edema Renal and hepatotoxicity Acidosis	Partially excreted through the lungs and can irritate them. Cannot have long contact with plastic (tubing or syringes). Light-sensitive and must be stored protected from light. Do not use discolored solution (brownish) or solution that has strong acetic (vinegar) odor.
Valproic acid	40–60 mg/kg/d PR diluted 1:1 with tap water		Irritative; cannot be given for more than a few doses.

seizure should be started on anticonvulsant therapy just as if he or she had presented with a second seizure. If evidence of primary generalized epilepsy is clear and the child is more than 2 years of age, valproate usually would be used. If there were any focal features during status on examination or in the EEG, carbamazepine is the drug of choice. In the past, children who presented in febrile status were treated long-term with anticonvulsants. Recently available data indicate that they have a

low risk of recurrence of seizures and status. Therefore, the current trend is to treat these children for 2 weeks to 3 months or to give them no ongoing therapy.

SUGGESTED READING

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