Emergency Neurological Life Support

Status Epilepticus Protocol

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Status Epilepticus

Diagnosis

Emergent Initial Treatment

Urgent Control Therapy

Status Epilepticus Terminated?

Yes

Anticonvulsant Dosing

No

Treatment of Refractory SE

Checklist & Communication
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Checklist

☐ Fingerstick glucose
☐ Obtain IV access
☐ Monitor pulse oximetry, BP, cardiac; supplemental O₂, fluid as needed, cardiac monitor
☐ Order labs: Complete Blood Count, Basic Metabolic Profile, Calcium, Magnesium, anticonvulsant drug levels
☐ Head CT (appropriate for most cases)
☐ Continuous EEG monitoring - Notify EEG tech (as soon as available unless patient returns to pre-status epilepticus baseline)

Communication

☐ Clinical presentation
☐ Duration of status epilepticus
☐ Relevant Past Medical History and Past Surgical History
☐ Prior medications, medication given so far, anticonvulsant drug levels if drawn
☐ Neurological examination
☐ Brain imaging/LP results (if available)
Diagnosis

The diagnosis of status epilepticus

The clinical definition of status epilepticus is five minutes or more of convulsions or 2 or more convulsions in a 5-minute interval without return to preconvulsive neurological baseline. However, a patient may be seen to seize, then, when brought into the hospital may not regain consciousness quickly. This too may be status epilepticus and usually requires EEG monitoring to diagnose.

Traditional definition of status epilepticus required 30 minutes of intermittent on continuous seizure activity. Do not wait for 30 minutes to pass before starting antiepileptic medications since permanent brain injury may occur before 30 minutes have elapsed and most seizures that do not progress to status will be shorter than 5 minutes.
Emergent Initial Treatment of Status Epilepticus

Treatments administered before hospital admission

Seizures are most frequently diagnosed outside of the hospital and EMTs and paramedics are the often the first responders to the patient. Do the following:

- ABCs, including supportive care if needed (O₂, airway, blood pressure)
- Obtain IV access if possible
- Diagnose hypoglycemia: if hypoglycemic give D₅₀W 50 ml IV and thiamine 100 mg IV (may be given empirically if suspected in the absence of a definitive diagnosis)
- For adult patient give lorazepam 4 mg over 2 min IV or diazepam 5 mg IV or midazolam 10 mg IM
- Adult alternatives include: diazepam 20 mg PR (may use diastat or IV solution of diazepam)

In children with IV access, give:

- Lorazepam 0.1 mg/kg IV, maximum dose 4 mg
- For children 13-40 kg, an alternative is midazolam 5 mg given IM
- For children 40 kg or larger, an alternative is midazolam 10 mg IM

Comments:

- Time is control. The most important factor in predicting ease of seizure control is the time elapsed prior to initiating anticonvulsants. If the medical professional is unable to get intravenous access for IV benzodiazepine, give benzodiazepines via an alternate route. IM administration of midazolam 10 mg has been proven to be effective.
- Respiratory decompensation is more commonly encountered in untreated status epilepticus than in status epilepticus treated with benzodiazepines.
- Weight based benzodiazepine administration may be appropriate in certain circumstances but is an off-label use, more prone to dose calculation error, and there are no data showing that it is superior
- Lorazepam needs to be refrigerated or restocked every 60 days. For this reason, it is usually impractical for EMS use and diazepam or midazolam are used as alternatives.
Seizures Have Stopped

And the patient is following commands

The half-life of benzodiazepines is brief and therefore a longer-lasting anticonvulsant needs to be administered to prevent recurrent seizures.

For Adult patients, give:
- Fosphenytoin: load 20 mg/kg IV at up to 150 mg/min
  - OR –
  - Phenytoin 20 mg/kg IV at up to 50 mg/min
  - OR -
  - Valproic acid: load: 40 mg/kg IV over 10 min

For children, give:
- Fosphenytoin: load 20 mg/kg IV at up to 150 mg/min

If possible connect to EEG unless the patient wakes up or returns to pre-convulsive baseline. Determine the cause of the seizure (prior history of seizures and medication non-compliance, new onset seizure, etc.) Serum levels of anticonvulsants are useful to determine what threshold the patient with epilepsy has for developing seizures. Urine toxicology screen may be helpful for recreational drug-associated seizures.

In children CNS infections or underlying genetic or metabolic disorders are more frequently the cause of status epilepticus.
Status Epilepticus

Unremitting seizures

Status Epilepticus: Ongoing seizure activity is injurious to the brain and can cause other organ system problems like pneumonia and sudden death. Making an accurate diagnosis is essential as is the orderly institution of anticonvulsant drugs to terminate the seizure activity. This protocol gives a practical, step-by-step guide to how status epilepticus can be terminated.

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Status Epilepticus Terminated?

Have the seizures stopped or the patient began following commands?

Status epilepticus is terminated when the patient returns to his/her pre-status responsiveness or there is EEG evidence of seizure cessation. Even if the convulsions have stopped the patient may still be seizing. If the patient does not rapidly awaken following the administration of the first line anticonvulsants, one should consider the patient still may be seizing.

Seizures have not stopped, or they stopped but the patient will not awaken

Start second line anticonvulsant.

For adults, choose one of the following:

- Fosphenytoin: load 20 mg/kg IV at up to 150 mg/min  
  - OR -
- Phenytoin 20 mg/kg IV at up to 50 mg/min  
  - OR -
- Valproic acid: load: 40 mg/kg IV over 10 min (may give additional 20 mg/kg over 5 min if still seizing)

For children, give:

- Fosphenytoin: load 20 mg/kg IV at up to 150 mg/min

Arrange EEG monitoring .

If status epilepticus persists despite starting second line anticonvulsants:

For adults, intubate the patient, then choose one of the following:

- Continuous infusions of midazolam: load: 0.2 mg/kg IV over 2-5 min; repeat 0.2-0.4 mg/kg boluses every 5 minutes until seizures stop, up to a maximum loading dose of 2 mg/kg. Initial rate: 0.1 mg/kg/hour. Bolus and increase rate until seizure control; maintenance: 0.05-2.0 mg/kg/hour
- Continuous infusions of propofol: Load: 1-2 mg/kg IV over 3-5 min; repeat boluses every 3-5 minutes until seizures stop, up to maximum total loading dose of 10 mg/kg. Initial rate: 33 mcg/kg/min (2 mg/kg/hour). Bolus and increase rate until seizure control; maintenance: 17 – 250 mcg/kg/min (1-15 mg/kg/hour)
- Valproic acid (if not chosen already as second line agent): 40 mg/kg IV over 10 min (may give additional 20 mg/kg over 5 min if still seizing)
- Phenobarbital: Load: 20 mg/kg IV up to 60 mg/min; maintenance: 1-3 mg/kg/day in 2-3 divided doses
For children:

- Proceed to recommendation under Treatment of Refractory Status Epilepticus
- Propofol is not recommended

Comments:

- Titrate anticonvulsants to therapeutic levels. When checking post-load drug levels, wait at least 2 hours post infusion for fosphenytoin and phenytoin, or immediately post infusion of valproate
- Continue second line antiepileptic medication when starting treatment of refractory status epilepticus
- Phenobarbital has been used traditionally for status epilepticus refractory to first and second line therapy, but recently experts recommend more rapid advancement to continuous IV antiepileptic medications
- Definition of refractory status epilepticus is unclear. Some controversy regarding duration of time and number of agents that patients have to have failed exists.
Treatment of Refractory Status Epilepticus

If status epilepticus has still not halted

For adult patients: If the patient is still having seizures despite benzodiazepines, phenytoin or valproate loading transfer the patient to the ICU, intubate them, establish good blood pressure monitoring, and start propofol or midazolam infusions. If all these steps have been done so far and seizures continue, the patient will need more aggressive intervention. Give:

- Start continuous EEG if not done already
- Pentobarbital: Load: 5 mg/kg IV up to 50 mg/min; repeat 5 mg/kg boluses until seizures stop; Initial rate: 1 mg/kg/hour; maintenance: 0.5-10 mg/kg/hour traditionally titrated to suppression-burst on EEG but titrating to seizure suppression is reasonable as well

For children, give:

- Phenobarbital: Load: 20 mg/kg IV at 1 mg/kg min, no faster than 30-60 mg/min
- OR -
- Midazolam 0.2 mg/kg, maximum dose 10 mg. If seizures persist after 5 more minutes, repeat midazolam 0.2 mg/kg (max 10 mg) and start midazolam infusion at 0.1 mg/kg/hour.
- If seizures persist, start pentobarbital 5 mg/kg, followed by pentobarbital 1 mg/kg/hour infusion, increase as needed to maximum 3 mg/kg/hour
- Continuous EEG monitoring is essential; if not available in your center consider transfer to a regional center with this capability.
- Administer vitamin B6 IV, especially if isoniazid poisoning is present

Comments:

- Hypotension is frequently encountered as a side effects of pentobarbital and pressors should be readily available. Other side effects include gastric stasis, myocardial suppression, thrombocytopenia, metabolic acidosis (several IV anticonvulsants contain polyethylene glycol).
- Often this step will be done in ICU setting but at times with patients that are highly refractory, pentobarbital infusions may need to be started while in the ER and within the first hour of status epilepticus onset.
- The recommended duration of continuous IV antiepileptic medications is unclear. Once seizures are controlled, many physicians continue treatment for at least 24 hours prior to consideration of weaning medications. The rapidity of weaning is also controversial but should not be done too abruptly.
- Other methods to control refractory status epilepticus are controversial. Choices include, but are not limited to, ketamine (which should be used in combination with a
benzodiazepine), lacosamide, levetiracetam, and hypothermia to 33 degrees Celsius.
Urgent Control Therapy

If not already done pre-hospital

Once the patient has arrived to the hospital, determine what treatments if any have been given to the patient and quickly assess their ability to follow commands. If they are currently seizing or have not awakened yet, do the following:

- ABCs, including supportive care if needed (O₂, airway, BP)
- Place on continuous EEG
- Monitors: ECG, BP, O₂Sat
- Obtain IV access
- Draw labs: CBC, BMP, CA, Mg, anticonvulsant levels. Additional orders for specific circumstances: Labs: PO₄, LFTS, Troponin, Toxicology screen (urine and blood), ABG, type and hold, coagulation studies
- Diagnose hypoglycemia: if hypoglycemic give D₅₀W 50 ml IV and thiamine 100 mg IV (may be given empirically if suspected in the absence of a definitive diagnosis)
- Give lorazepam 4 mg/2 min IV or diazepam 5 mg IV or midazolam 10 mg IM
- Alternatives include: diazepam 20 mg PR (may use diastat or IV solution of diazepam)

In children with IV access, give:
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Comments:
- First line benzodiazepines are frequently under dosed.
- Initiate a complete workup of the underlying etiology for status epilepticus. Seizures will be difficult to control with antiepileptic medications if they are caused by an underlying uncorrected metabolic problem.
- Blood sugar testing is widely available and reliable. Therefore, administration of D₅₀W to all patients is not warranted and may worsen outcome in a number of acute brain injuries. However, hypoglycemia needs to be treated promptly if this is the underlying cause of status epilepticus.
- ECG, Chest X-ray
- Consider toxins that can cause seizures: INH (treat with lorazepam followed by pyridoxine 70 mg/kg; max dose 5 gm); tricyclics (look for QRS widening on the EKG, treat with sodium bicarbonate); theophylline; cocaine / sympathomimetic; alcohol withdrawal (rarely causes SE, treat with accelerating doses of a benzodiazepine); Organophosphates (treat with atropine, midazolam, and pralidoxime)
Almost any agent in overdose may cause a seizure indirectly if they cause hypoxia, hypotension, or electrolyte (including hypoglycemia) abnormalities.