Status epilepticus treatment

61% of seizures that persist > 5 mins will continue > 1 hour [1)].

The treatment protocol is intensive and includes benzodiazepines, anticonvulsants, and eventually anesthetics to medically induce coma when polypharmacy is exhausted [2)].

Acute treatment of SE, and particularly refractory (RSE), and super-refractory status epilepticus (SRSE), is associated with high hospital costs and prolonged LOS. Patients with disabilities are at risk for an unfavorable course of SE, resulting in prolonged LOS. In general, mortality associated with SE is low in children and adolescents, however three or more treatment steps are associated with high treatment costs [3)].

General treatment measures for status epilepticus

Treatment success, like morbidity/mortality, may be time-dependent. One review showed that first-line AED therapy aborted SE in 60% of patients if initiated within the first 30 minutes, and efficacy decreased as seizure duration increased. As such, treatment should be initiated as soon as possible and should be directed at stabilizing the patient, stopping the seizure, identifying the cause (determining if there is an acute insult to the brain), and, if possible, also treating the underlying process. Treatment often must be initiated prior to the availability of test results to confirm the diagnosis and may even be initiated in the pre-hospital setting.

1. “ABC’s”

a) Airway: oral airway if feasible.Turn the patient on their side to avoid aspiration

b) Breathing: O2 by nasal cannula or bag-valve-mask.Consider intubation if respiration is compromised or if seizure persists > 30 min

c) Circulation: CPR if needed. Large bore proximal IV access (2 if possible: 1 for phenytoin (PHT) (Dilantin®), not necessary if fosphenytoin is available): start with NS KVO

2. Simultaneous with ABCs, AEDs should be prepared and/or given if SE suspected

3. neurologic exam

4. monitor: EKG & baseline vital signs. Pulse oximeter. Frequent blood pressure checks

5. bloodwork: STAT capillary blood (fingerstick) glucose (to R/O hypoglycemia), electrolytes (including glucose), CBC, LFTs, Mg + + , Ca + + , AED levels, ABG

6. head CT (usually without contrast)

7. correct any electrolyte imbalance (SE due to electrolyte imbalance responds more readily to correction than to AEDs) 8. if CNS infection is a major consideration, perform LP for CSF analysis (especially in febrile children) unless contraindicated. WBC pleocytosis up to 80 × 106/L can occur

following SE (benign postictal pleocytosis), and these patients should be treated with antibiotics until infection can be ruled out by negative cultures

9. general meds for unknown patient:

a) glucose:

● in patients with poor nutrition (e.g. alcoholics): giving glucose in thiamine deficiency can precipitate Wernicke's encephalopathy prior to glucose bolus give thiamine 50– 100 mg IV

● if fingerstick glucose can be obtained immediately and it shows hypoglycemia, or if no fin- gerstick glucose can be done: give 25–50 ml of D50 IV push for adults (2 ml/kg of 25% glu- cose for peds). If at all possible, draw blood for definitive serum glucose first

b) naloxone(Narcan®)0.4mgIVP(in case of narcotics)

c) ± bicarbonate to counter acidosis (1–2 amps depending on length of seizure)

d) forneonate<2years:considerpyridoxine100mgIVpush(pyridoxine-dependent seizures

constitute a rare autosomal recessive condition that generally presents in the early neonatal period

10. administer specific anticonvulsants for seizures lasting > 5-10 mins

11. EEG monitor if possible

12. if paralytics are used(e.g.to intubate), use short-acting agents and be aware that muscle paralysis alone may stop visible seizure manifestations, but does not stop the electrical seizure activity in the brain, which can lead to permanent neurologic damage if prolonged

Medications for generalized convulsive status epilepticus

General information

There are no randomized trials for refractory status epilepticus, although there is published data regarding specific treatment options. Numerous protocols exist.

"Peds dosing" refers to patients < 40 kg or approximately 12 yrs of age. Rapid treatment is indicated as delays are associated with neuronal injury and reduced response to medications.

Prehospital phase

1. impending SE: may be heralded by a crescendo in Sz. A 1–3 d course of lorazepam may preempt the development of SE 2. SE treatment may be initiated in the home setting with buccal midazolam or rectal diazepam

Hospital phase

Start IV drugs at half the maximal rate, and titrate up to maximal rate if VS stable.

1. First line drugs

a) benzodiazepine (main side effect: respiratory depression in ≈12%; be prepared to intubate). Onset of action is rapid (1–2 mins):

● lorazepam (Ativan®) 4 mg IV for adults, 2 mg IV for children @ < 2 mg/min

● OR midazolam (Versed®) 10 mg IM for adults, 5 mg IM for children > 13 kg. Repeat dose of benzodiazepine if necessary after 10 min.

● If no IV access or if midazolam injections not available, diazepam can be given rectally in Diastat® gel formulation (0.2–0.5 mg/kg)

2. If seizures persist after the first dose of benzodiazepine, initiate second-line agent in a different IV.

a) load with fosphenytoin (Cerebyx®) or phenytoin (Dilantin®).

Do not worry about acutely overdosing, but do follow dosing rates, monitor BP for hypotension and EKG for arrhythmias. After giving the following loading dose, start on maintenance. Fosphenytoin has the advantage of being less irritating and able to infuse at a faster rate, but phenytoin is less expensive and does not need to be metabolized.

● fosphenytoin: 15–20 mg PE/kg IV @ 150 mg PE/min

● OR phenytoin: 15–20 mg/kg IV @ 50 mg/min

- if no response to loading dose, an additional 10 mg/kg IV may be given after 20 min.

- if pt is on PHT and a recent level is known: a rule of thumb is giving 0.74 mg/kg to an adult raises the level by ≈ 1 mcg/ml

- if on PHT and level not known: adult: give 500 mg @ < 50 mg/min

b) There are several good alternatives to fosphenytoin/phenytoin as second-line AEDs:

● Sodium valproate: 20–30 mg/kg IV bolus (max rate: 100 mg/min)—has been shown to be equal or superior to phenytoin in a few small studies

● Phenobarbital: 20 mg/kg IV (start infusing @ 50–100 mg/min) – commonly used 2nd or 3rd line AED. A repeat dose of 25–30 mg/kg can be given 10 min after the first dose.

● Levetiracetam (Keppra®): 20 mg/kg IV bolus of over 15 minutes – evidence for Keppra as a first or second line drug is less clear

3. Traditionally, a third-line agent was given prior to continuous infusion therapy (CIT); however, it was successful in only 7%.42 As such, most new protocols proceed directly to anesthetic administration. If seizures are continuing after above therapies have been administered (15–30 min after initial presentation), begin CIT as follows:

● Midazolam: 0.2 mg/kg IV loading dose followed by 0.2–0.6 mg/kg/hr

● OR Propofol: 2 mg/kg IV loading dose followed by 2–10 mg/kg/hr

4. At this time, lab results and tests should be available. Ensure that all reversible etiologies have been addressed and that a CT head has been performed.

5. Pentobarbital is often reserved for SE that is refractory to all of the above interventions. If necessary, pentobarbital is administered as follows:

● Pentobarbital: 5 mg/kg IV followed by 1–5 mg/kg/hr

6. While some practitioners will try additional drugs (carbamazepine, oxcarbazepine, topiramate, levetiracetam, lamotrigine, gabapentin), these are likely to be of limited utility.

7. Experimental interventions include: lidocaine infusion, inhalational anesthesia, direct brain stimulation, transcranial magnetic stimulation, electroconvulsive therapy (shock therapy), surgical intervention if a seizure focus is identified

Remember: Paralytics stop the visible manifestations of the seizure and they may be useful for intubation and/or in order to obtain head imaging; however, they do not stop the abnormal electrical brain activity or the neurological damage that results.

Efficacy of drug therapy

Studies vary widely, but it appears that approximately 2/3 of patients will respond to initial therapy with the other 1/3 progressing to refractory SE.

Medications to avoid in status epilepticus

1. narcotics

2. phenothiazines: including promethazine (Phenergan®)

3. neuromuscular blocking agents in the absence of AED therapy: seizures may continue and cause neurologic injury but would not be clinically evident

Medications for non-convulsive status epilepticus

In non-convulsive status epilepticus, the first and second line AEDs should be utilized. However, many practitioners avoid escalating to the anesthetic options (CIT, pentobarbital), instead opting for trials of additional AEDs first (carbamazepine, oxcarbazepine, topiramate, lamotrigine, etc).

Miscellaneous status epilepticus

Myoclonic status

Treatment: valproic acid (drug of choice). Place NG, give 20 mg/kg per NG loading dose. Maintenance: 40 mg/kg/d divided.

Can add lorazepam (Ativan®) or clonazepam (Klonopin®) to help with acute control.

Absence status epilepticus

Almost always responds to diazepam.

Surgery

Status epilepticus surgery.

1)
Abend NS, Dlugos DJ. Treatment of refractory status epilepticus: literature review and a proposed proto- col. Pediatr Neurol. 2008; 38:377–390
2)
D. A. Greenberg, M. J. Aminof, and R. P. Simon, Clinical Neurology, McGraw-Hill Education, New York, NY, USA, 9th edition, 2015.
3)
Schubert-Bast S, Lenders C, Kieslich M, Rosenow F, Strzelczyk A. Costs and cost-driving factors of acute treatment of status epilepticus in children and adolescents: A cohort study from Germany. Seizure. 2022 Mar 19;97:63-72. doi: 10.1016/j.seizure.2022.03.014. Epub ahead of print. PMID: 35344919.