



Soonu Udani

A 13-year-old boy with no known seizure disorder was brought to the emergency department with generalized tonic–clonic seizures for the past 30 min. He was unresponsive with a temperature of 99 °F, heart rate 140/min, systolic blood pressure 100 mmHg, respiratory rate 30 breaths/min, and SpO₂ 94% on room air. Both pupils were equal and reactive.

Step 1: Identify Status Epilepticus and Resuscitate

- Status epilepticus may be defined as follows:
 - *A child having a seizure lasting for more than 5 min*
 - A child brought to hospital with a seizure
 - A child having a series of seizures without return to baseline mental status between episodes
- For purposes of quick identification and timely treatment to prevent brain damage, the other definitions used as the working one in practice.
- The initial priority in an ongoing seizure is airway protection. This can be achieved by proper positioning, oral suctioning, and an oral airway device. If necessary, the patient should be intubated.
- Urgent peripheral intravenous access (preferably two) should be established.

S. Udani (✉)

Department of Critical Care and Emergency Services, Narayana Health, SRCC Children's Hospital, Mumbai, India

Step 2: Terminate Seizures

- While monitoring heart rate, blood pressure, and respiratory rate, give a benzodiazepine.
- Give lorazepam 0.1 mg/kg, maximum 2 mg, slow IV. The same dose can be given via the intraosseous, per rectal or buccal route.
Or
- Diazepam or midazolam (MDZ) 0.2 mg/kg can be given, slow IV. The same dose can be given by intraosseous route. Rectal dose is 0.3–0.5 mg/kg.
- Respiratory depression or hypotension can occur, and this needs to be monitored closely.
- Out-of-hospital intranasal or buccal MDZ is an easily available option. The intranasal easy calculation is 1 puff for every 2 kg weight of the current available medication MIDAZIP
- If the seizures do not stop in another 10 min, go to the next step.

Step 3: Treat Resistant Seizure

- Give phenytoin 20 mg/kg IV by slow push over 20 min.
Or
- Fosphenytoin (20 mg/kg of phenytoin equivalents (PE)) IV by slow push over 5–10 min. This dose can also be given by the intraosseous route.
- If seizures do not stop within 5 min after dose completion, go to next step
- This is also to be used if diazepam is the first benzodiazepine used but not needed if lorazepam is used.
- Phenobarbitone should be given 20 mg/kg IV. It can cause respiratory depression and hypotension, particularly if given with benzodiazepines. If required, secure the airway with endotracheal intubation. This could be the first choice in neonates and infants.
- If seizures continue, then go to step 4—the patient is now in refractory status epilepticus (RSE). One of the discussed drugs could be given depending on the patient's evaluation and availability of resources.
- A general caveat is that it is best to optimize the levels of one drug before adding another, and hence a repeated dose of these may be given.

Step 4: Manage Refractory Status Epilepticus (RSE) 30–45 min Have Passed

- An accelerated protocol can be used here where the step of an additional drug in step 3 is now not advocated as it is deemed a waste of precious time and the drugs in step 4 are given together. i.e. VPA or LEV + MDZ infusion started simultaneously

Step 4.

- IV valproic acid (VPA) 30–35 mg/kg diluted with normal saline is administered over 20 min as profound hypotension can occur.
- Levetiracetam (LEV) at a dose of 30–35 mg/kg loading infusion and then 10 mg/kg 12-hourly can also be tried where intubation and ventilation need to be deferred for transport.

However, by now an hour may have passed and the clock is ticking, so if seizures are not aborted, coma-producing therapies need to be started.

Transfer to a center capable of long-term life support is needed as the respiratory depression and hemodynamic instability is unpredictable and varies from patient to patient.

- *Midazolam (MDZ) infusion*
 - A loading dose of 0.2 mg/kg is followed by infusion of 2–6 mcg/kg/min. MDZ 3 mg/kg added to 50 mL normal saline when given 1 mL/kg will deliver 1 mcg/kg/min.
 - Start at low dose and increase by 1–2 mcg/kg/min every 15 min until control is achieved.
 - Maximum rate, 20–22 mcg/kg/min, is recommended or till hemodynamic instability is a problem to manage.
 - Once control is achieved, maintain the same dose for 24 h and then wean by 1 mcg/kg/min every 2–3 h.

If in 24 h the seizures have not stopped, the child is now in super refractory status epilepticus (SRSE) and needs advanced medication as well as advanced neuromonitoring and hemodynamic monitoring and support.

- Propofol: Start with 2–4 mg/kg bolus and then 1–5 mg/kg/h. This is not recommended for children younger than 12 years. Approval for this drug is for usage for 12 h only, so informed consent before usage is advised. (Vigilance for the propofol infusion syndrome is required).
- Thiopentone infusion (cautionary warning for non-intensivists)
 - This general anesthesia drug is reserved for super refractory status epilepticus (SRSE).
 - The patient should be intubated and ventilated prior to starting the infusion, and inotropes should be put on standby.
 - Invasive BP monitoring and real-time EEG monitoring will be needed, at least intermittently if not continuously.
 - A separate IV line is needed. The loading dose is 3–5 mg/kg slowly immediately, followed by an infusion of 1–5 mg/kg/min.

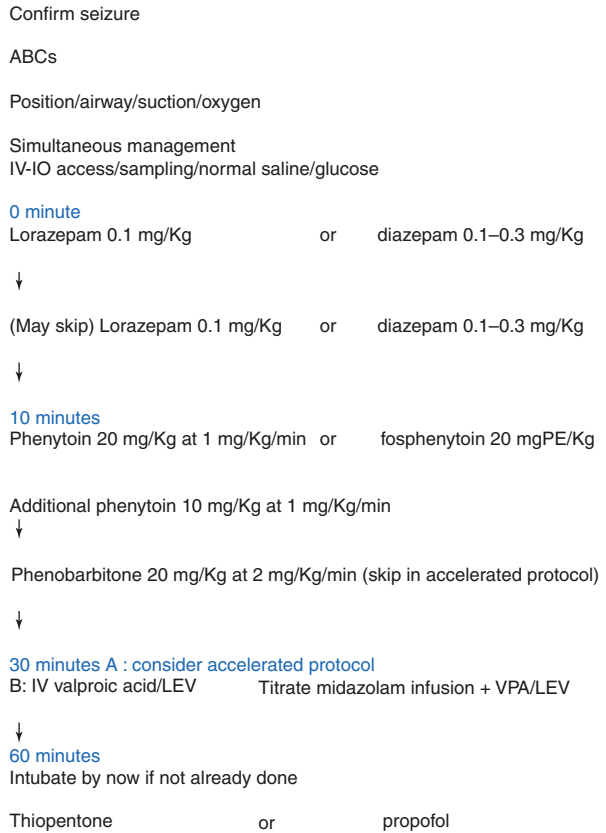
- Hemodynamic support in terms of extra fluids, vasopressors, and inotropes may be required. Hence, this needs to be done within a fully equipped PICU.
- Burst suppression with 6–8 bursts/min is the target, and hence it should be done with EEG monitoring.

Step 5: Anesthetic Agents

- Once this stage is reached, the mortality and morbidity of refractory status epilepticus is more than 50%.
- These agents need to be delivered through a proper circuit and monitoring done by an anesthetist who understands the drug.
- Aborting the seizures is usually easy, but maintenance and survival are a universal issue.
- In addition to these drugs, oral drugs like topiramate can be started. Other drugs that have been tried with success are as follows:
 - Give lidocaine 1.5–2 mg/kg IV over 2 min and then give a drip at 3–4 mg/min—same class of drugs as phenytoin and an excellent membrane stabilizer. Neonatal studies have shown this drug to be effective.
 - MDZ infusion as in older children can also be used in neonates because the same principles of quick resolution apply.
 - Pyridoxine (vitamin B6) should be given to all neonates and infants with resistant seizures (B6-responsive seizures). Dose is 100 mg IV.
 - Steroids for autoimmune encephalitis, ketogenic diet as an adjunct need to be considered

Step 6: Tapering of Infusion

- Tapering of any infusion should only be done after complete electrical seizure freedom for at least more than 24 h.
- Very gradual tapering should be done as seizures will return and will often be nonconvulsive and only be detected by EEG monitoring.
- The most toxic drug or last introduced should be removed first.
- Hence, long-term agents should be on board and all levels are well maintained before new drugs are added or tapering is begun
- An algorithm for control of seizure is described in Fig. 35.1

Fig. 35.1 Algorithm for seizure control

Suggested Reading

- Boylan GB, Rennie JM, Chorley G, Pressler RM, Fox GF, Farrer K, Morton M, Binnie CD. Second-line anticonvulsant treatment of neonatal seizures: a video-EEG monitoring study. *Neurology*. 2004;62(3):486–8.
- Castro Conde JR, Hernandez Borges AA, Domenech Martinez E, Gonzalez Campo C, Perera Soler R. Midazolam in neonatal seizures with no response to phenobarbital. *Neurology*. 2005;64(5):876–9. *Nonresponders to phenobarbital/phenytoin had a significantly worse outcome than responders. This study shows that midazolam effectively controls seizures in nonresponders to phenobarbital/phenytoin and improves long-term neurodevelopment.*
- Lowenstein DH, Bleck T, Macdonald RL. It's time to revise the definition of status epilepticus. *Epilepsia*. 1999;40:120–2.
- Painter MJ, Scher MS, Stein AD, Armatti S, Wang Z, Gardiner JC, Paneth N, Minnigh B, Alvin J. Phenobarbital compared with phenytoin for the treatment of neonatal seizures. *N Engl J Med*. 2009;341(7):485–9. *Phenobarbital and phenytoin are equally but incompletely effective as anticonvulsants in neonates. With either drug given alone, the seizures were controlled in fewer than half of the neonates in this study.*
- Stecker MM, Kramer TH, Raps EC, O'Meeghan R, Dulaney E, Skaar DJ. Treatment of refractory status epilepticus with propofol: clinical and pharmacokinetic findings. *Epilepsia*. 1998;39(1):18–26. *Propofol infusions can effectively and quickly terminate many but not all episodes of refractory status epilepticus. More studies are required to determine its true value in comparison with other agents.*