Convulsive status epilepticus in adults

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Definition of GCSE

- ≥5 minutes of continuous seizures, or
- ≥2 discrete seizures between which there is incomplete recovery of consciousness

Epidemiology of status epilepticus

- U-shaped distribution, with relatively high incidence rates in children<1 yr and then rising again in older adults>60yrs

- Over a lifetime, up to 10 percent of adults with epilepsy and 20 percent of children with epilepsy will have one or more episodes of status epilepticus

Etiology

- Most cases of status epilepticus :symptomatic of an underlying structural brain lesion or a toxic or metabolic disturbance.

- Many episodes: combination of an earlier lesion and a superimposed new metabolic, infectious, or pharmacologic stressor such as uremia or a medication change.

- Status epilepticus also commonly arises in patients with an established diagnosis of focal or generalized idiopathic epilepsy and occasionally the presenting manifestation of epilepsy.

Etiology

✓In adults, the most common etiologies :

- 1) Acute symptomatic:50% (stroke, head trauma, SAH, cerebral anoxia or hypoxia, infection or brain tumor)

- 2) Remote symptomatic (prior head injury or neurosurgery, perinatal cerebral ischemia, cortical malformations, AVM and benign brain tumors)

- 3) low antiseizure drug levels in a patient with known epilepsy·

Etiology

- Withdrawal syndromes associated with the discontinuation of alcohol, barbiturates, or benzodiazepines.

- Metabolic abnormalities (eg, hypoglycemia, hepatic encephalopathy, uremia,hyponatremia, hyperglycemia, hypocalcemia hypomagnesemia) or sepsis.

Etiology

- Use of, or overdose with, drugs that lower the seizure threshold (eg, theophylline,imipenem, high-dose penicillin G, cefepime, quinolone antibiotics, metronidazole,isoniazid, tricyclic antidepressants, bupropion, lithium, clozapine, flumazenil, cyclosporine, lidocaine, bupivacaine, metrizamide, dalfampridine, and, to a lesser extent, phenothiazines, especially at higher doses).

- ✓ Patients with convulsive status epilepticus present with characteristic motor manifestations that vary according to the seizure type.

- ✓ patients with generalized convulsive status epilepticus (GCSE) have obvious bilateral tonic and clonic motor activity and loss of consciousness.

- ✓ patients with focal motor status epilepticus may have jerking movements restricted to one area of the body, usually with preserved consciousness.

- Myoclonic status epilepticus typically involves much more rapid, but lower amplitude, jerking muscle activity, but with marked variability.

- Tonic status epilepticus includes slower, more sustained maintenance of a posture, or slow movement

Generalized convulsive status epilepticus

- ✓ potential for serious complications, morbidity and even mortality. GCSE includes both primary generalized and secondarily generalized convulsive seizures.

- ✓ There is always impaired consciousness and bilateral tonic stiffening, followed by rhythmic jerking of the limbs (clonus) that is usually symmetric

Focal motor status epilepticus

- Focal status epilepticus has many clinical manifestations, largely depending on the location of the epileptogenic brain area. Focal motor status epilepticus is the most easily recognized

Myoclonic status epilepticus

- Rhythmic or arrhythmic
- Myoclonic seizures are often generalized, but some are focal.
- Divided into epilepsy syndrome-related causes and symptomatic causes
- The most ominous cause is anoxia, but MSE may also be caused by a metabolic disturbance such as uremic or hepatic encephalopathy, or an encephalopathy caused by sepsis or multiple medical problems, such as a combination of uremia and sepsis (a typical cause)

- *Nonconvulsive status epilepticus*

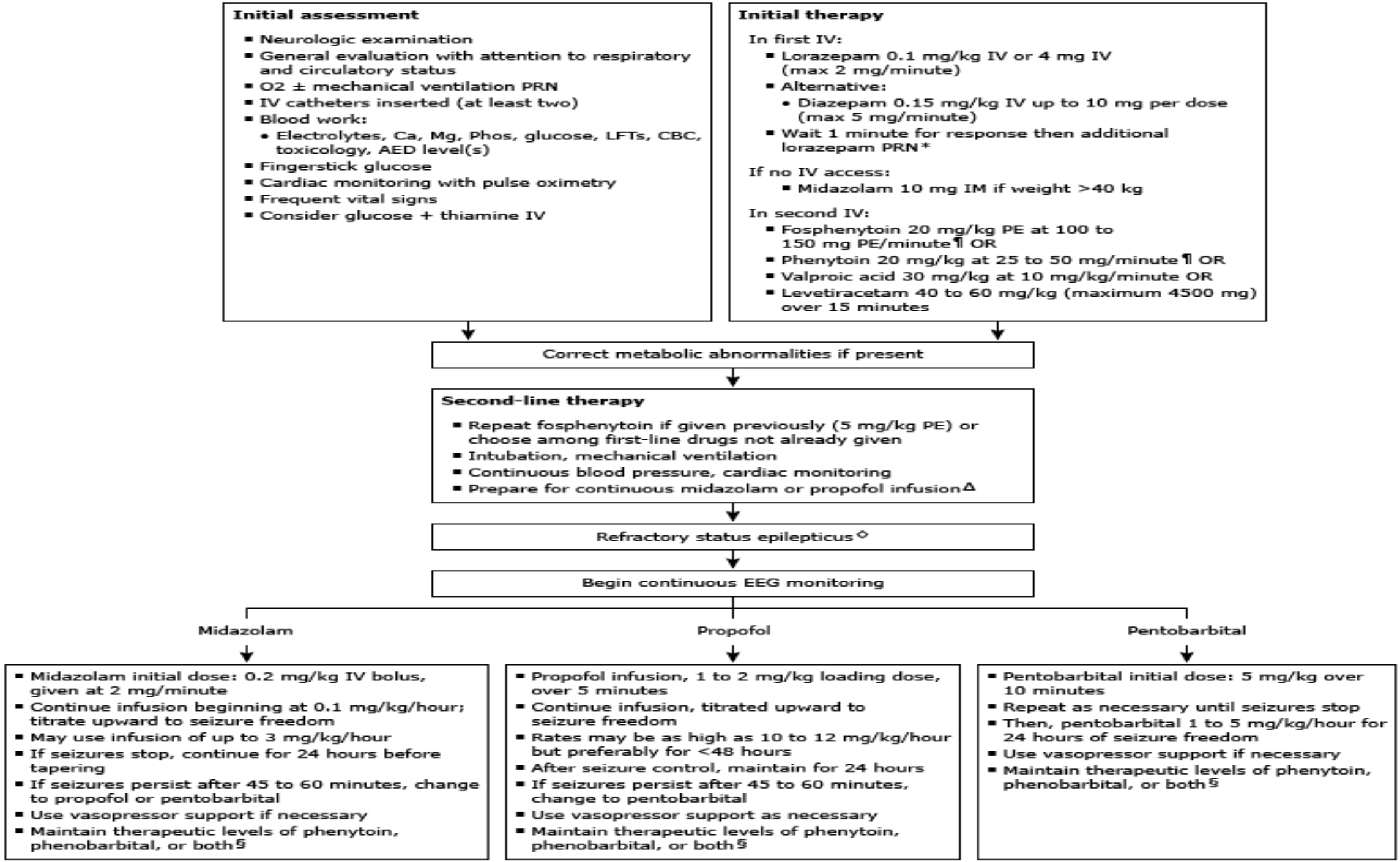
DIAGNOSIS

- Is a clinical diagnosis
- confirmed in most cases by the presence on examination of sustained and rhythmic generalized tonic and clonic motor activity lasting for longer than five minutes or repetitive convulsive seizures without a return to baseline consciousness between seizures.
- Although the diagnosis of GCSE is usually obvious, a detailed neurologic examination is important in making the diagnosis of more subtle or focal forms of status epilepticus

- Clinically obvious status epilepticus should be treated immediately; there is no need to wait for an EEG.
- EEG is critical in the diagnosis of more subtle forms of status epilepticus, for distinguishing myoclonic status epilepticus from nonepileptic myoclonus, and in the aftermath of generalized convulsive status epilepticus to exclude ongoing nonconvulsive seizures.

Treatment

- Initial management is divided into three phases:
- Assessment and supportive treatment
- Initial pharmacologic therapy with a benzodiazepine
- Urgent therapy that achieves long-term control using a nonbenzodiazepine antiseizure drug such as fosphenytoin


Initial assessment
Neurologic examination
General evaluation with attention to respiratory and circulatory status
O2 ± mechanical ventilation PRN
IV catheters inserted (at least two)
Blood work:
Electrolytes, Ca, Mg, Phos, glucose, LFTs, CBC, toxicology, AED level(s)
Fingerstick glucose
Cardiac monitoring with pulse oximetry
Frequent vital signs
Consider glucose + thiamine IV
Initial therapy
In first IV:
Lorazepam 0.1 mg/kg IV or 4 mg IV (max 2 mg/minute)
Alternative:
Diazepam 0.15 mg/kg IV up to 10 mg per dose (max 5 mg/minute)
Wait 1 minute for response then additional lorazepam PRN*
If no IV access:
Midazolam 10 mg IM if weight >40 kg
In second IV:
Fosphenytoin 20 mg/kg PE at 100 to 150 mg PE/minute¶ OR
Phenytoin 20 mg/kg at 25 to 50 mg/minute¶ OR
Valproic acid 30 mg/kg at 10 mg/kg/minute OR
Levetiracetam 40 to 60 mg/kg (maximum 4500 mg) over 15 minutes
Correct metabolic abnormalities if present
Second-line therapy
Repeat fosphenytoin if given previously (5 mg/kg PE) or choose among first-line drugs not already given
Intubation, mechanical ventilation
Continuous blood pressure, cardiac monitoring
Prepare for continuous midazolam or propofol infusionΔ
Refractory status epilepticus◇
Begin continuous EEG monitoring
Midazolam
Midazolam initial dose: 0.2 mg/kg IV bolus, given at 2 mg/minute
Continue infusion beginning at 0.1 mg/kg/hour; titrate upward to seizure freedom
May use infusion of up to 3 mg/kg/hour
If seizures stop, continue for 24 hours before tapering
If seizures persist after 45 to 60 minutes, change to propofol or pentobarbital
Use vasopressor support if necessary
Maintain therapeutic levels of phenytoin, phenobarbital, or both§
Propofol
Propofol infusion, 1 to 2 mg/kg loading dose, over 5 minutes
Continue infusion, titrated upward to seizure freedom
Rates may be as high as 10 to 12 mg/kg/hour but preferably for <48 hours
After seizure control, maintain for 24 hours
If seizures persist after 45 to 60 minutes, change to pentobarbital
Use vasopressor support as necessary
Maintain therapeutic levels of phenytoin, phenobarbital, or both§
Pentobarbital
Pentobarbital initial dose: 5 mg/kg over 10 minutes
Repeat as necessary until seizures stop
Then, pentobarbital 1 to 5 mg/kg/hour for 24 hours of seizure freedom
Use vasopressor support if necessary
Maintain therapeutic levels of phenytoin, phenobarbital, or both§

Rapid assessment and support

- Attention to airway, breathing, and circulation is urgent
- Supportive therapy (eg, oxygen, mechanical ventilation
- Cardiac monitoring, frequent measurement of blood pressure, and pulse oximetry
- Check BS with Glucometer
- Check CBC, BUN,ABG, Cr, Ca, P, Mg, serum glucose, liver function tests, toxicology studies, and antiseizure drug levels

- Neuromuscular blocking agents are often used to facilitate rapid intubation, but they can abolish the motor manifestations of seizures and thus mask ongoing status epilepticus. They are not a treatment for status epilepticus.
- Alternative agents, such as midazolam or thiopental, are therefore preferred to facilitate rapid intubation.
- When neuromuscular blocking agents are used, EEG monitoring is mandatory in order to know whether status epilepticus has resolved or is continuing and needs further treatment.

Initial pharmacologic therapy

- **When IV access is available**
- Benzodiazepines are the first-line treatment for GCSE· nonbenzodiazepine antiseizure drug is recommended to prevent recurrence, even if convulsions have ceased following benzodiazepine treatment ·

- Among the antiseizure drugs that can be loaded IV, fosphenytoin or valproate have been preferred for most patients ·
- Small randomized trials also support the use of intravenous levetiracetam,

- Diazepam - high lipid soluble→rapidly cross the BBB.
- Highly effective in terminating seizure
- Dose: 0.1 to 0.3 mg/kg IV
- Effect starts early as 10 to 20 seconds after administration, and CSF concentrations reach half of their maximum value in three minutes.
- Duration is typically <20 minutes
- Initial termination of seizure activity with IV diazepam is seen in 50 to 80% of patients.

- if no other medication is provided, there is a 50 percent chance of seizure recurrence within the next two hours

Bnz

- For IV therapy, lorazepam is preferred in adults
- Midazolam is preferred for intramuscular (IM) intranasal or buccal therapy
- Diazepam is preferred for rectal administration.

Phenytoin

✓ Fosphenytoin dose: 20 mg/kg ---- 100 to 150 mg/min

✓ **Phenytoin:20 mg/kg----25 to 50 mg/minute**

- An additional dose (5 mg PE/kg fosphenytoin or 5 mg/kg phenytoin) can be given 10 minutes after the loading infusion if seizures persist.

✓ Valproic acid 20 to 40 mg/kg and

✓ levetiracetam 40 to 60 mg/kg (maximum 4500 mg) are reasonable alternatives to fosphenytoin as initial nonbenzodiazepine therapy in patients with hypersensitivities.

Phenytoin

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A common error is giving a "standard" dose of 1 gram, which is inadequate dosing for most patients weighing more than 50 kg.

Cardiac monitoring during the initial infusion is mandatory because cardiac arrhythmias may occur.

modify the infusion rate if hypotension or other adverse cardiovascular events occur.

the risks of local pain and injury (including venous thrombosis and the rare purple glove syndrome) increase with more rapid infusions.

- Optimally, this phase of treatment is completed within 10 to 20 minutes.
- In patients who are actively seizing despite two initial doses of lorazepam or other BNZ, preparation for a continuous midazolam or propofol infusion should occur simultaneously with administration of fosphenytoin, valproic acid, or levetiracetam, since the primary role of the nonbenzodiazepine antiseizure drug is to prevent recurrence rather than break the seizures.

Levetiracetam

- Dose: 1000 to 3000 mg IV in adults and the other suggests 60 mg/kg up to a maximum of 4500 mg

- Doses are typically infused over 15 minutes [58].

Phenobarbital

- Not used as a firstine treatment in adults because administration is slow, it causes prolonged sedation, and it may involve a higher risk of hypoventilation and hypotension than either benzodiazepines, phenytoin, valproate, or levetiracetam.

- Initial doses of 20 mg/kg infused at a rate of 30 to 50 mg/minute are generally used; slower infusion rates should be used in older adult patients, although phenobarbital may have fewer cardiac side effects than phenytoin in these patients.

- The primary drugs used for refractory status epilepticus are midazolam, propofol, and pentobarbital (or thiopental in some countries).

- Continuous EEG monitoring should be instituted as soon as possible, along with continuous pulse oximetry and blood pressure monitoring, often with an arterial catheter.
- Vasopressors should be available at the bedside.

Refractory status Epilepticus(Barbiturates or Midazolam)

- Treatment with high-dose pentobarbital
- Many experts prefer to start with midazolam or propofol-> quick resolution of the status epilepticus and shorter duration of sedation.

- This can be particularly advantageous for patients who are at risk for ventilator dependence with prolonged therapy (eg, those with severe pulmonary disease, severe debilitation, or malignancy).
- On the other hand, longer infusions and higher doses of propofol may precipitate the propofol infusion syndrome

- Both barbiturates and propofol may exacerbate hemodynamic problems in unstable patients; the primary alternative, midazolam infusion, is usually well-tolerated in this setting.

- In addition to drugs administered by continuous intravenous infusion, one or more longeracting antiseizure drugs are typically administered in an effort to achieve and maintain seizure control and increase the likelihood of eventual tapering of the continuously infused drug.

Take Home Messages

- Nonbenzodiazepine antiseizure drug is recommended to prevent recurrence, even if convulsions have ceased following benzodiazepine treatment .

- A common error is giving a "standard" dose of 1 gram, which is inadequate dosing for most patients weighing more than 50 kg.

- Do Not forget NCSE.

- Time is important

Thank you