Status Epilepticus

defined as continuous seizure activity or recurrent seizure activity without regaining of consciousness lasting for more than 5 min.

Status Epilepticus

In the past, the cutoff time was 30 min, but this has been reduced to emphasize the risks involved with the longer durations.

Types of SE

The most common type is **convulsive** status epilepticus (generalized tonic, clonic, or tonic–clonic)

Types of SE

nonconvulsive status (complex partial, absence), myoclonic status, epilepsia partialis continua, and neonatal status epilepticus.

incidence

- ranges between 10 and 60 per 100,000 population

- Status epilepticus is most common in children younger than 5 yr of age.

incidence

- Approximately 30% of patients presenting with **SE**

are having their first seizure

- approximately 40% of these later develop epilepsy..

incidence

Febrile **SE** is the most common type of **SE** in children..

incidence

In the 1950s and **1960s**, mortality rates of **6-18%** were reported after **SE**

currently

lower mortality rate of **4-5%** is observed, most of it secondary to the underlying etiology rather than to the seizures

Refractory SE

is **SE** that has failed to respond to therapy, usually with at least **2** (such as a benzodiazepine and another medication).

Refractory SE

- often of unknown etiology

- presumed to be **encephalitic or postencephalitic**

- can last but not always, has a poor prognosis

ETIOLOGY

- new-onset epilepsy of any type

- drug intoxication (e.g., tricyclic antidepressants) in children

- drug and alcohol abuse in adolescents

ETIOLOGY

- drug withdrawal or overdose in patients on AEDs
- Hypoglycemia
- Hypocalcemia
- Hyponatremia
- hypomagnesemia;.

ETIOLOGY

- acute head trauma
- encephalitis
- Meningitis
- autoimmune encephalitis

ETIOLOGY

- Acute complex syndromes
- ischemic (arterial or venous) stroke
- intracranial hemorrhage

ETIOLOGY

- **folinic acid and pyridoxine** and pyridoxal

phosphate dependency (these usually present in infancy but childhood onset is also possible)

- inborn errors of metabolism.

ETIOLOGY

- hypertensive encephalopathy
- renal or hepatic encephalopathy

ETIOLOGY

- brain tumors
- brain malformations
- neurodegenerative disorders
- different types of progressive myoclonic epilepsy
- storage diseases

infections likely to cause encephalitis with SE

- **Herpes simplex** (complex partial and convulsive status)
- ***Bartonella*** *(particularly nonconvulsive status)*
- ***Epstein-*** **Barr virus**, and mycoplasma postinfectious encephalomyelitis

ETIOLOGY

Postinfectious encephalitis and acute disseminated encephalomyelitis are common causes of SE including refractory SE

RISK

increased cerebral metabolic rate and a compensatory **increase in cerebral blood flow** that, after approximately 30 min, is not able to keep up with the increases in cerebral metabolic rate

THERAPY

- SE is a medical emergency requires initial and continuous attention to securing airway, breathing, and circulation

THERAPY

- continuous monitoring of vital signs including ECG

- determination and management of the underlying etiology (e.g., hypoglycemia).

Laboratory studies

including glucose, sodium, calcium, magnesium, complete blood count, basic metabolic panel, CT scan, and continuous EEG, are needed for **all patients**

.

Laboratory studies

Blood and spinal fluid cultures

toxic screens

tests for inborn errors of metabolism are

often needed.

EEG is helpful in ruling out

pseudo–status epilepticus (psychologic conversion reaction mimicking SE

or other movement disorders (chorea, tics), rigors, clonus with stimulation

decerebrate/decorticate posturing..

THERAPY

The initial emergent therapy usually involves intravenous **diazepam, lorazepam**, or **midazolam**

If intravenous access is not available

- Buccal midazolam
- intranasal midazolam
- intranasal lorazepam
- rectal diazepam

- Intramuscular midazolam is equally effective as intravenous lorazepam..

respiratory depression

With all options, is a potential side effect for which the patient should be monitored and managed as needed

In some infants

a trial of **pyridoxine** may be warranted

THERAPY

The strongest evidence for initial and emergent therapy is for

diazepam or **lorazepam**

followed by **phenytoin/ fosphenytoin** and **phenobarbital**

then **valproate** and **levetiracetam**

THERAPY

After the emergent therapy usually with a **benzodiazepine**, the subsequent urgent therapy medication is usually **fosphenytoin**

Benzodiazepines

are the first-line treatment for SE because they can rapidly control seizures

Benzodiazepines

The three most commonly used benzodiazepines to treat SE are diazepam , lorazepam , and midazolam

Management of SE

Timeline

0 to 5 minutes

Assessment

- Obtain initial vital signs, including temperature
- identify airway obstruction and hypoxemia
- identify impaired oxygenation or ventilation

Management of SE

Timeline

0 to 5 minutes

Supportive care

- Open airway
- Suction secretions
- Administer 100 percent O2
- Place continuous cardiorespiratory monitors and pulse oximetry

0 to 5 minutes

Supportive care

Perform bag-valve-mask ventilation, as needed

Prepare for **RSI**

Establish **IV** **or** **IO** access

Treat hypoglycemia (**IV dextrose** 0.25 to 0.5 gram/kg)

treat fever (**acetaminophen** 15 mg/kg rectally)

0 to 5 minutes

Seizure therapy

Benzodiazepine (first line):

Lorazepam 0.05 to 0.1 mg/kg IV or IO, maximum 4 mg

IV or IO access not achieved within 3 minutes:

Rectal diazepam (Diastat® gel or injection solution given rectally) 0.5 mg/kg, maximum 20 mg

0 to 5 minutes

Seizure therapy

OR

Buccal midazolam 0.2 mg/kg, maximum 10 mg

OR

IM midazolam 0.1-0.2 mg/kg, maximum 10 mg

5 to 10 minutes

Assessment

Reevaluate vital signs, airway, breathing, and circulation

Evaluate for signs of trauma, sepsis, meningitis, or encephalitis

5 to 10 minutes

Supportive care

Maintain monitoring, ventilatory support, and vascular access

Place second IV

RSI potentially indicated*

5 to 10 minutes

Seizure therapy

Fosphenytoin (second line):

20 mg PE per kg IV or IO ◊

OR

Phenobarbital:

20 mg/kg IV or IO, maximum 1 gram, if toxin-induced seizure (expect respiratory depression with apnea) §

15 to 30 minutes

Assessment

Reevaluate vital signs, airway, breathing, and circulation

Obtain continuous EEG monitoring, if available

15 to 30 minutes

Supportive care

Maintain monitoring, ventilatory support, and vascular access

15 to 30 minutes

Seizure therapy

Phenobarbital (third line):

20 mg/kg IV or IO, maximum 1 gram, (10 mg/kg if phenobarbital given as second line) §

OR

Valproic acid 20 to 40 mg/kg IV or IO

AND

15 to 30 minutes

Seizure therapy

AND

Pyridoxine 100 mg IV or IO in infants <1 year of age

Pyridoxine 70 mg/kg IV or IO, maximum 5 grams, if INH poisoning suspected

Obtain pediatric neurology consultation (see Refractory status epilepticus algorithm)

RSI: rapid sequence endotracheal intubation

- should be performed if airway, ventilation, or oxygenation cannot be maintained and if the seizure becomes prolonged

Diazepams

- has high lipid solubility
- rapidly crosses the blood-brain barrier
- highly effective in terminating seizures

Diazepams

- An effect upon seizure activity can be seen as early as 10 to 20 seconds after administ

- duration of anticonvulsant effect is typically <20 minutes

Diazepams

because it is stable in liquid form for long periods at room temp

Therefore, diazepam is available in resuscitation kits in premixed form

whereas Lorazepam , midazolam , phenytoin are not.

Diazepams

However, in controlled trials, diazepam is less effective and causes more respiratory depression than **lorazepam**

Diazepams

A rectal gel formulation of diazepam (Diastat®) provides rapid delivery when intravenous access is problematic

Lorazepam

appears to be more effective than diazepam in the treatment of acute SE and causes less respiratory depression

Lorazepam

- Respiratory depression occurred in fewer patients treated with lorazepam (3 versus 15 percent)

- As with diazepam, **rectal** administration of lorazepam can be **effective** when intravenous access cannot be achieved.

Lorazepam

An **intranasal** formulation of lorazepam is another probably effective treatment option

Lorazepam

- The effective duration of action, as long as four to six hours, is longer than diazepam

Midazolam

- very effective in acutely terminating seizures, frequently in less than one minute

- but it has a short half-life in the central nervous system.

Midazolam

In addition to intravenous administration, it can be given by the intramuscular , intranasal , buccal , or rectal routes

Midazolam

On arrival to the emergency department, seizure remission was more likely in patients treated with **IM midazolam** compared with **IV lorazepam**

Midazolam

The need for endotracheal intubation, recurrence of seizures, and other adverse event rates were similar in the treatment groups.

Midazolam

can be given as a continuous infusion for refractory SE and is associated with minimal cardiovascular side effects

Phenytoin

- is a long-acting drug that has been widely used to treat acute and chronic seizures in children

- Its principal advantage is in preventing recurrence of SE for extended periods of time.

Phenytoin

However, because its onset of action may be delayed for 10 to 30 minutes, a rapidly acting agent, such as lorazepam , usually must be given first.

Phenytoin and fosphenytoin

may be **less effective** for the treatment of seizures due to toxins or drugs and may intensify seizures caused by cocaine, other local anesthetics, theophylline , or lindane

phenytoin's side effects

- hypotension and cardiac arrhythmias

- Thus, heart rate and blood pressure should be monitored during the initial infusion

phenytoin's side effects

- these complications are less common in children than adults

- can be minimized by an infusion rate that does not exceed 50 mg per minute

WARNING

Phenytoin must not be infused along with a **dextrose** containing IV fluid, as it may form a **precipitat**

Phenytoin and fosphenytoin

risks of local pain and injury, including venous thrombosis and the purple glove syndrome, also increase with more rapid rates of infusion.

The purple glove syndrome

is characterized by **edema**, **discoloration**, and **pain** in the extremity distal to the site of phenytoin infusion.

The purple glove syndrome

Severe cases can lead to skin necrosis and **limb ischemia**, sometimes requiring amputation.

More common in **older adults**, a few cases have been reported in children, usually late in the first decade, and adolescents

The purple glove syndrome

Venous extravasation must be avoided because the high pH and osmolality of this drug cause **tissue** inflammation and **necrosis**

Fosphenytoin

is a **pro-drug** of phenytoin that is hydrolyzed into phenytoin by serum phosphatases

Fosphenytoin is highly water soluble at neutral pH and therefore **unlikely to precipitate** during intravenous administration..

Fosphenytoin

Compared with phenytoin, the drug has fewer side effects, including a reduced risk of local irritation at the site of infusion; therefore, fosphenytoin can be infused much more rapidly

Fosphenytoin

Hypotension and cardiac arrhythmias remain a risk, so cardiac monitoring is still required.

Barbiturates

Phenobarbital and pentobarbital are the most commonly used barbiturates in the treatment of SE.

a **long-acting** antiepileptic drug (AED)

Phenobarbitals

Side effects of intravenous administration include **sedation** and **respiratory depression**, especially when it is preceded by a benzodiazepine. .

Phenobarbital

As a result, phenobarbital is considered a **second-line** long-acting agent after fosphenytoin or phenytoin and usually is used only when benzodiazepines and fosphenytoin are not effective.

Phenobarbital

Respiratory and cardiac monitoring should be performed, because endotracheal intubation and mechanical ventilation may be needed

Phenobarbital

The risk of **prolonged sedation** with phenobarbital is greater than with the other anticonvulsants because its half-life is 87 to 100 hours, and often longer in newborns

Pentobarbital

a **short-acting barbiturate** with a rapid onset of action

most commonly used as a continuous **intravenous infusion** to treat **refractory SE** and is effective in stopping seizures

Pentobarbital

significant side effects include

- respiratory depression
- Hypotension
- myocardial depression
- reduced cardiac output..

Pentobarbital

Other complications include

- pulmonary edema
- ileus
- prolonged sedation..

Pentobarbital

intubation and mechanical ventilation and intravascular monitoring are required prior to treatment, and inotropic agents frequently are needed..

Thiopental

Some centers use thiopental instead of pentobarbital for refractory SE. However, animal studies suggest that thiopental carries a higher incidence of adverse cardiovascular effects than pentobarbital.

Propofol

an intravenous anesthetic with rapid onset and short duration of action that is often used for elective procedures in children

Valproic acid

The intravenous preparation of valproic acid (VPA) can be used for short-term replacement in patients maintained on this drug when oral medication cannot be given or to rapidly attain therapeutic levels in patients with inadequate seizure control


THANK YOU