Emergency Department Management of Pediatric Status Epilepticus

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Preface

Status epilepticus in children is often an anxiety-provoking condition to treat for most emergency department physicians. It requires prompt treatment and evaluation to prevent complications[1] and often requires transfer to a higher level of care. This guideline is designed to provide assistance in the initial management, evaluation, and seizure termination of pediatric status epilepticus. Drug dosing has been compiled from multiple sources including LexiComp™[2], published research articles, and standard practice at Arkansas Children's Hospital.[2]

Definition, Etiologies, and Complications of Status Epilepticus

Definition of status epilepticus (SE)

- Classic definitions[3]
  - Continuous seizure activity >30 minutes
  - ≥2 seizure within 30 minutes without gaining consciousness between them
- New definitions[1]
  - Early SE 5-30 minutes
  - Established SE >30 minutes
  - Refractory SE not terminated by 2 medications
  - Malignant SE not terminated with anesthetics

Etiologies of Pediatric SE

- Remote symptomatic (34%)
    - Traumatic brain injury (TBI), chromosomal disorder, static encephalopathy, migrational defect, etc.
    - One percent (1%) of all SE patients has an underlying remote etiology but also has an acute precipitant such as fever, metabolic, toxic ingestion.
- Acute symptomatic (26%)
    - Meningoencephalitis or other infection
    - Hypoxia
    - Trauma
    - Metabolic (i.e. hypoglycemia, hyponatremia, hypocalcemia)
    - Toxic ingestion
- Febrile (22%)
- Idiopathic (15%)
- Progressive encephalopathy (3%)[4,5]

Complications

- Cardiovascular
    - Hypertension
    - Tachycardia
    - Increased cardiac output
    - Stimulation secondary to sympathetic discharge
- Hypoxia
    - Impaired ventilation
    - Increased oxygen consumption
    - Aspiration
    - Airway obstruction
- Metabolic acidosis
- Respiratory acidosis
- Hyperpyrexia
- Hyper/hypoglycemia
- Uncommon
    - Neurogenic pulmonary edema
    - Rhabdomyolysis
    - Pneumonia
    - Shock[6]

Assessment and Diagnosis of SE

Assessment Performed Simultaneously to Rapid Seizure Control

- History key elements
    - History of seizure disorder, especially if refractive to treatment
    - Medications, maintenance antiepileptic drugs
    - Recent medications given outside of emergency room for current episode (i.e. diastat, lorazepam, etc.)
    - Recent illness or suspected infection
    - Toxic exposures
    - Possible head trauma

- Physical exam key elements
    - Airway patency and breathing
    - Color and perfusion
    - General responsiveness, Glascow Coma Scale (GCS)
    - Type of seizure activity
    - Evidence of trauma
- Laboratory evaluation[4]
    - All patients
        - Stat serum glucose and electrolytes, specifically sodium, calcium, magnesium
            - Abnormal in 6% of patients
            - Will need correction before any pharmacologic treatment will be successful
        - Antiepileptic drug levels low in 32% of patients with known epilepsy
    - As indicated
        - BUN/Cr for drug dosing
        - Coagulation panel for suspected trauma or bleeding
        - Liver function test
        - Toxicology evaluation
            - Urine drug screen
            - Consider rare screens like isoniazid, lithium, etc. if applicable and available.
        - If suspected infection
            - Complete blood cell count (CBC)/blood culture
            - Lumbar puncture and cerebrospinal fluid (CSF) cultures; central nervous system (CNS) infections appear in 12% of patients.
            - Herpes simplex virus polymerase chain reaction (HSV PCR)
            - Additional encephalitis serologies
- Neuroimaging
    - Computerized tomography (CT) is only helpful for trauma or suspected bleeding.
    - Magnetic resonance imaging (MRI) is the best test and good for tumors, infections, and congenital anomalies.
        - Especially important in new-onset seizures with SE
        - Wait until patient is hemodynamically stable.[5]
        - Probably best obtained later at pediatric tertiary care center
        - Eight percent (8%) of patients with new-onset seizures have imaging abnormality.[6]
- Electroencephalogram (EEG) monitoring
    - Continuous EEG monitoring needed for persistent altered mental status
    - Even if clinical seizure stops, ruling out subclinical seizures is required.

Differential Diagnosis

SE is a clinical diagnosis based on definitions above; remember there are a large number of conditions that could present with a “spell” that may be confused with SE.[3]

- Dystonia
- Gastroesophageal reflux disease (GERD)
- Baclofen withdrawal syndrome
- Cardiogenic syncope
- Conversion disorder
- Breath holding spell
- Other, multiple causes of unresponsiveness

Management of SE

Initial Stabilization

- Stay calm! Follow your ABCs (Airway, Breathing, and Circulation).
- Position patient for airway patency.
- Monitors: pulse oximetry, cardiopulmonary
- Supplemental oxygen
    - Mild-to-moderate hypoventilation is expected.
    - Remember, "*Plastic doesn't treat seizure;*" do not intubate until necessary and neuromuscular blockade ≠ seizure termination.
    - Forget the blood gas; "GCS < 8 rule" does not apply.
- IV access, antecubital if possible; if unable to obtain expediently, place an intraosseous (IO) line for medication delivery.
- Watch and wait. Many seizures abort spontaneously within a few minutes.[7]
- If the patient has not stopped seizing after 4-5 minutes, begin treatment.
- If the patient has an electrolyte abnormality, correct that as soon as possible.
    - Treat hyponatremia immediately with 5 ml/kg of 3% saline
    - Treat hypoglycemia immediately with 5 ml/kg of D10W.[1]

Pharmacologic Seizure Termination

- Benzodiazepines
    - First-line agents for SE[6]
    - Includes lorazepam, midazolam, diazepam
    - Stimulates GABA receptors
    - Benzodiazepine-sensitive GABA receptors are internalized as SE continues; 20-fold decrease in potency of benzodiazepines after 30 minutes in SE[6]
    - IV is preferred route for all benzodiazepines.
    - Midazolam can also be given via intramuscular, intranasal (atomizer), and buccal routes.
    - Diazepam can be given via rectum (gel or IV formulation).
    - Recommendations to increase efficacy and reduce side effects are
        - Use IV lorazepam preferentially if IV access available.
        - Use intranasal midazolam if no IV available.
        - Use rectal diazepam if IV *and* midazolam are not available.[8]
    - Dosing

Table 1. Dosing

	Lorazepam	IV	0.1 mg/kg	(max 5 mg/dose)
	Midazolam	IV/IM	0.2 mg/kg	(max 10 mg/dose
		IN/Buc	0.3 mg/kg	
	Diazepam	IV	0.2 mg/kg	(max 10 mg/dose)
		Rectal	0.5 mg/kg	(max 20 mg/dose)

    - Need to wait 4-5 minutes between doses
    - If there is no response after 2-3 doses, this class is unlikely to work.
    - Side effects include sedation and respiratory depression; cumulative with dosing.[8]

- Fosphenytoin
    - Second-line agent for SE
    - Slows the recovery of voltage gated sodium channels

    - Dosage is a 20 mgPE/kg IV bolus over ~7 minutes (3 mg/kg/min with a maximum of 150 mg PE/minute).
    - Can re-dose with another 10 mg/kg
    - Side effects
        - Thrombophlebitis
        - Hypotension
        - Cardiac arrhythmias
    - Fosphenytoin converted to phenytoin in serum
    - May use phenytoin if fosphenytoin is unavailable.
        - Much more caustic
        - Has more side effects
        - Must be infused slowly (1 mg/kg/min)
- Levetiracetam (Keppra®)
    - Commonly regarded as a new second-line agent
    - Multiple mechanisms of action
    - Dosed at 40 mg/kg IV over ~10 minutes
        - This is common practice at ACH.
        - Published recommendations range from 20-50 mg/kg for loading dose.[9,10]
    - Can re-dose with another 20 mg/kg.
    - Side effects include sedation at high doses.
    - Fewer complications than many other antiepileptic drugs but must adjust dosing with decreased renal function
    - Consider using this medicine early if patient is maintained on Keppra® at home.

- Phenobarbital
    - Third-line agent, but commonly used in neonatal seizures
    - Enhances GABA activity
    - Dosed at 20 mg/kg IV bolus over ~20 min
    - Can re-dose with another 10mg/kg
    - High incidence of respiratory suppression and sedation
- Valproic acid
    - Third-line agent
    - Enhances GABA and modulates sodium/calcium channels
    - Dosed at 20 mg/kg IV bolus over ~5-10 minutes
    - Rare side effects of
        - Hyperammonemia
        - Hepatotoxicity
        - Encephalopathy

Antibiotics

- If the patient has a suspected infection, consider early administration of antibiotics.
- IV administration of broad-spectrum coverage for pathogens causing meningitis

Transferring a Patient

- The decision to transfer a patient to a higher level of care must always be determined by the referring provider based on their expertise, comfort, and their facility's resources.
- Patients with known history of seizure, whose seizure has been aborted with either first or second line agents, who regain consciousness and do not appear to be at risk for subclinical seizures, and who have a physician willing to admit them for observation, may reasonably remain at a local hospital.

- All other patients should be considered for transport to higher level of care.
- All federal Emergency Medical Treatment and Active Labor Act (EMTALA) regulations must be followed when arranging transfer.

Refractory Status Epilepticus – Options for Practitioners at Tertiary Care Centers

- Seizure duration >1-2 hours and resistant to >2-3 anticonvulsants
- Will usually require
    - Pediatric intensive care unit (ICU)
    - Hemodynamic support
    - Respiratory support with intubation
    - Continuous EEG monitoring
- Frequent complications and high morbidity[1]
- Little pediatric data from case reviews and retrospective and adult studies
- Treatment options for refractory SE
    - Midazolam continuous infusion
        - Start with 0.2 mg/kg bolus then begin 0.1 mg/kg/hr infusion.
        - May repeat boluses and increase infusion to max 2 mg/kg/hr.
    - Thiopental (barbiturate coma)
        - Anesthetic
        - Thiopental metabolized to pentobarbital
        - 5 mg/kg IV bolus followed by 3-5 mg/kg/hr infusion
        - Serious side effects
            - Hypotension
            - Respiratory depression
            - Decreased cardiac contractility
            - Immune suppression
    - Propofol
        - Anesthetic
        - GABA receptor activity, different than benzodiazepines and barbiturates
        - Side effects
            - Respiratory suppression
            - Hypotension
            - Propofol infusion syndrome: metabolic acidosis
            - Rhabdomyolysis
            - Cardiac failure
            - Renal failure
        - Dosed at ~10 times typical sedation infusion rates
    - Inhaled anesthetics
        - Desflurane/isoflurane
        - Better safety profile with long-term administration
        - Hypotension is a side effect.
    - High dose phenobarbital
    - Ketamine
        - NMDA receptor antagonist, independent of GABA
        - Possibly neuroprotective
        - Debated effects on intracranial pressure[5]

Figure. Emergency Department Management of Pediatric Status Epilepticus

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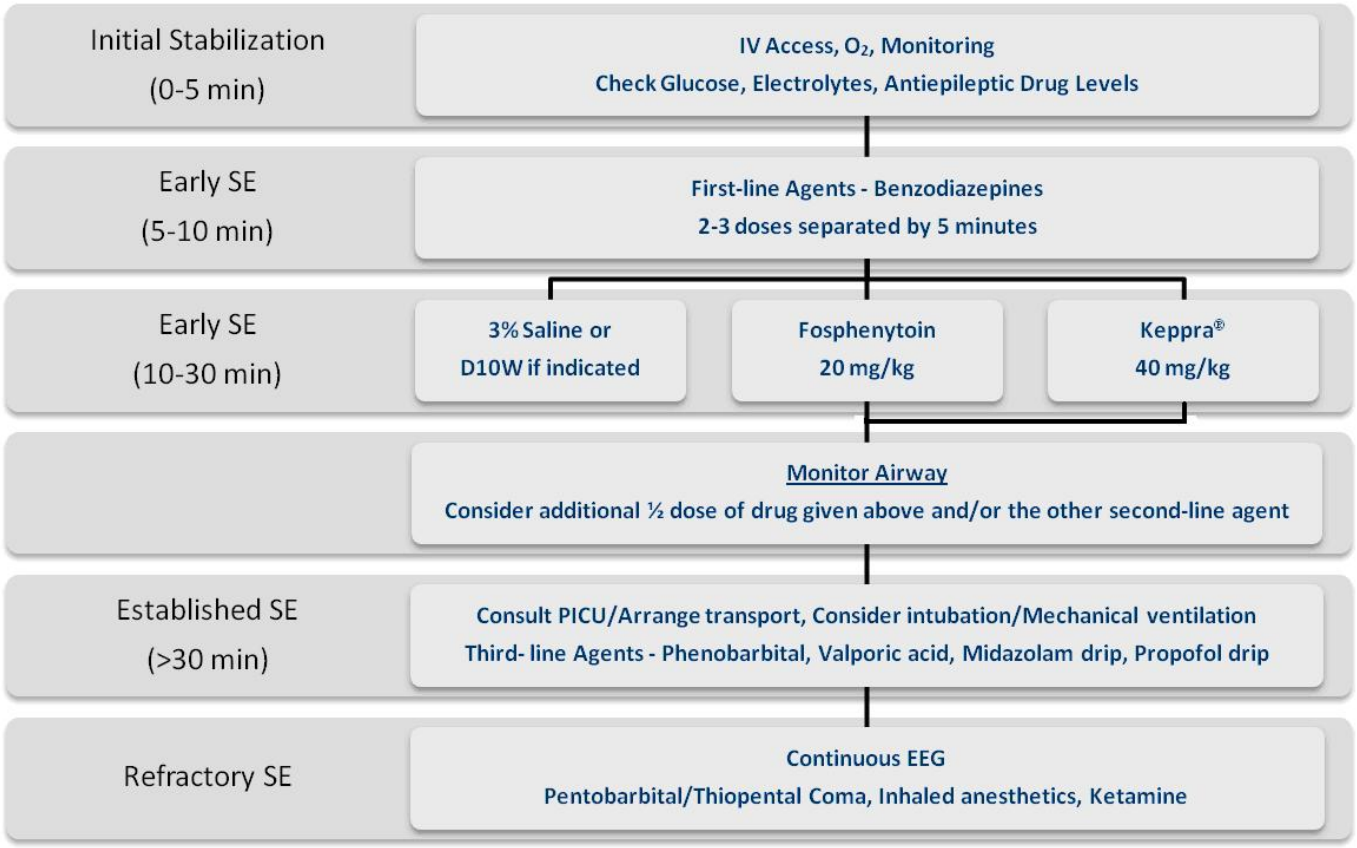

Table. Most Common Antiepileptic Drugs and Dosing for Pediatric Status Epilepticus

Drug	Route	Dosage	Max Dose	Supplemental Dose
Lorazepam	IV	0.1 mg/kg	5 mg/dose	
Midazolam	IV/IM	0.2 mg/kg	10 mg/dose	
	IN/Buc	0.3 mg/kg		
Diazepam	IV	0.2 mg/kg	10 mg/dose	
	Rectal	0.5 mg/kg	20 mg/dose	
Fosphenytoin	IV	20 mg/kg		10 mg/kg
Levetiracetam	IV	40 mg/kg		20 mg/kg
Phenobarbital	IV	20 mg/kg		
Valproic acid	IV	20 mg/kg		

This guideline was developed to improve health care access in Arkansas and to aid health care providers in making decisions about appropriate patient care. The needs of the individual patient, resources available, and limitations unique to the institution or type of practice may warrant variations.

References

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