Pediatric Prolonged Seizure Clinical Pathway

Jan 2022

Outcomes/Goals	1. Rapid identification and treatment of pediatric patients with status epilepticus 2. Create a team-oriented approach to treatment of status epilepticus. 3. Cessation of seizure activity
INCLUSION Criteria	Patients aged < 18 years who present with a single, prolonged convulsive seizure lasting >5 minutes or repetitive seizures without return to neurological baseline
EXCLUSION Criteria	Age < 29 days
NURSE documentation	Onset of seizure. Fever history. Recent injury or illnesses. History of seizure activity
INTERVENTIONS Initiate on arrival	ESI Triage level II Ensure ventilation / provide supplemental oxygen Establish IV / IO access POC glucose Cardiac / SaO2 monitoring Consider intubation as seizure duration progresses and additional treatment is required; strongly consider when at 3rd and 4th line therapies
DIAGNOSTICS	Bedside CBG; CMP, CBC, consider blood culture, blood gas, urine studies if clinically indicated Consider head CT or lumbar puncture if trauma or CNS infection suspected
PHYSICIAN (LIP)	
Fluids (if indicated)	Normal Saline bolus 20 ml/kg
Medication **1st Line Treatment**	**IV Access:** **Lorazepam** 0.1 mg/kg IV (max 4 mg) **Diazepam** 0.2mg/kg IV (max 10mg) **No IV Access:** **Midazolam** 0.2mg/kg IM (max 10 mg) **Midazolam** 0.3-0.4mg/kg IN (max 10mg) Repeat dose q 5 minutes x 1 for continued seizure activity
Correct hypoglycemia PRN	D10W 5ml/kg **IF** CBG <50
2nd Line Treatment (Give 5 minutes after 2nd benzo dose)	**Levetiracetam** (Keppra) 60 mg/kg IV (max dose 4500 mg) **Alternatives:** **Fosphenytoin** 20 mg/kg IV (max 1500mg) **Valproic acid** 40 mg/kg IV (max 3000mg) **Lacosamide** 10mg/kg IV (max 400mg)
3rd Line Treatment Options	**Phenobarbital** 20 mg/kg IV (maximum dose 1000 mg) OR Direct to Continuous Infusion (see below, '4th line treatment')
4th Line Treatment Refractory Status	**Midazolam infusion** 0.2 mg/kg bolus, then 0.1 mg/kg/hr gtt. If > 10 minutes, rebolus and increase by 0.1mg/kg/hr. Repeat q10 minutes up to 0.5 mg/kg/hr
DISPOSITION	Consult PICU / Pediatric Neurology Prepare family/Patient for admission if second line agent required

Clinical Pathway Decision Making Process

Pediatric Prolonged Seizure

Jan 2022

ESTABLISH:
IV/IO
Adequate ventilation/ provide supplemental oxygen
SaO2/cardiac monitoring

→

OBTAIN:
CBG, CBC, CMP, consider blood gas, blood culture, urine studies
Consider head CT, lumbar puncture

→

ADMINISTER:
Isotonic saline infusion 20mg/kg
Dextrose (D10) if CBG < 50

INITIAL TREATMENT

IV/IO access:

- **Lorazepam** 0.1 mg/kg slow IV push (max. 4 mg)
- **Midazolam** 0.2mg/kg IV (max 10 mg)

No IV/IO access

- **Midazolam** 0.4 mg/kg Intranasal **OR** 0.2mg/kg IM (max 10 mg)

REPEAT BENZO IN 5 MINUTES X 1 IF SEIZURE CONTINUES

ORDER 2nd Line AGENT CONCURRENT WITH SECOND BENZO DOSE

2nd LINE TREATMENT

Start 2nd line Agent 5 Minutes After Last Benzo

Levetiracetam (Keppra) 60 mg/kg IV (max 4500mg)

Alternatives:
Fosphenytoin 20 mg/kg IV (max 1500mg)
Valproic acid 40 mg/kg IV (max 3000mg)
Lacosamide 10mg/kg IV (max 400mg)

Consult Neurology +/- PICU

Infuse all IV medications over 10 minutes

3rd LINE TREATMENT

Phenobarbital 20 mg/kg IV (max single dose 1000 mg)
OR
Direct to Continuous infusion (see below)

Consider Intubation

4th LINE TREATMENT

Refractory Status

Midazolam infusion
0.2 mg/kg bolus, then0.1 mg/kg/hr gtt. If > 10 minutes, re-bolus and increase by 0.1mg/kg/hr. Repeat q10 minutes up to 0.5 mg/kg/hr

Intubation
Arrange for EEG
Admit to PICU

Prolonged Pediatric Seizure

Goals of Clinical Pathway

1. Rapid identification and treatment of pediatric patients with status epilepticus
2. Create a team-oriented approach to efficient and timely treatment of status epilepticus.
3. Cessation of seizure activity

Refractory Status, Benzodiazepines, and Second-Line Agents

Refractory Status Epilepticus (RSE) has a mortality rate that ranges from 32-77% and is compounded by other co-morbid conditions and multiple organ dysfunctions. RSE may cause irreversible brain injury.

Benzodiazepines are first line therapy for status epilepticus. Delay in initiation of therapy with benzodiazepines is associated with a higher frequency of death, longer seizure duration, and more frequent hypotension, underscoring the importance of early administration. If two adequate doses of benzodiazepines do not abort the seizures, further doses of benzodiazepines are likely to cause respiratory depression and less likely to terminate the seizure compared to alternative agents. Lorazepam, diazepam, and midazolam all have good efficacy as first line agents.

Several studies in recent years have compared fosphenytoin, valproic acid, and levetiracetam as second-line agents for status epilepticus. The ConSept Trial was a multicenter study that showed levetiracetam was not inferior to fosphenytoin in terms of seizure cessation in children with refractory SE (50% vs 60%). ESETT was a large multicenter trial in the US comparing fosphenytoin, levetiracetam, and valproic acid; all medications resulted in seizure cessation in about 50% of patients, with numerically higher rates of hypotension and intubation in the fosphenytoin group (though not statistically significant). The EcLiPSE trial compared levetiracetam and phenytoin in children with refractory SE, with seizure cessation in 70% vs 64%, respectively. All trials used higher doses of levetiracetam than are often customarily used, ranging from 40-60mg/kg. In light of this data, and given its safety profile and ease of administration, levetiracetam is the preferred choice for 2nd line agents in the DCH Peds ED.

Why Propofol is Used with Caution in Pediatric Status Epilepticus

The development of propofol infusion syndrome, an irreversible chain of events associated with significant morbidity and mortality, is a concern. Propofol infusion syndrome was first described in 1992 by Parke et al. Since then, numerous case reports and reviews have been published. Reports of severe acidosis and movement disorder after propofol use in infants have caused a significant decrease in its use within that age group. Metabolic acidosis may be a complication related to prolonged use of propofol, explaining the rarity of this complication in short surgical anesthesia. In contrast, metabolic acidosis in children with prolonged propofol use for sedation and treatment of SE has been reported. Also worrisome is the association of propofol-related metabolic acidosis in patients receiving the ketogenic diet.

References:

Gaínza-Lein M, Sánchez Fernández I, Jackson M, et al. Association of Time to Treatment With Short-term Outcomes for Pediatric Patients With Refractory Convulsive Status Epilepticus. JAMA Neurol 2018; 75:410.

Glauser T, Shinnar S, Gloss D, et al. Evidence-Based Guideline: Treatment of Convulsive Status Epilepticus in Children and Adults: Report of the Guideline Committee of the American Epilepsy Society. Epilepsy Curr 2016; 16:48.

Dalziel SR, Borland ML, Furyk J, et al. Levetiracetam versus phenytoin for second-line treatment of convulsive status epilepticus in children (ConSEPT): an open-label, multicentre, randomised controlled trial. Lancet.2019;393(10186):2135-2145.

Kapur J, et al. Randomized Trial of Three Anticonvulsant Medications for Status Epilepticus. N Engl J Med. 2019 Nov 28;381(22):2103-2113.

Hanna JP, Ramundo ML. Rhabdomyolysis and hypoxia associated with prolonged propofol infusion in children. Neurology 1998; 50:301.