



## KEY ADVANCES PRACTICE ADVANCE

# Pediatric Status Epilepticus Management (for children > one month of age)

New July 2024

Why is this topic important? Convulsive status epilepticus is a common neurological emergency in childhood that is associated with significant economic burden, morbidity, and mortality.(1) Management guidelines that highlight the importance of rapid assessment, stabilization, and treatment aim to reduce the associated morbidity and mortality. Unfortunately, therapies are often delayed or underdosed (2,3,4) and poor adherence to the recommended guidelines leads to worse outcomes.(5)

**How will this change my clinical practice?** An expedited, stepwise approach to the management of pediatric status epilepticus using appropriately dosed therapies is critical to optimizing clinical outcomes in children.

#### **Synopsis Focus Points:**

For pediatric status epilepticus, defined as seizure activity > five minutes and/or ongoing seizure on presentation to Emergency Medical Services (EMS)/Emergency Department (ED) or one seizure without full recovery, following a stepwise process that starts with the administration of benzodiazepines via IV/IM/IO/IN as first-line therapy will help lead to early cessation of seizure activity and reduction of poor outcomes.

### **Background:**

Management guidelines for the treatment of status epilepticus in children exist to assist in the delivery of critical therapies in a timely fashion to avoid the potential adverse sequela of continued seizure activity.(2) Resolving the seizure activity as soon as possible is important because they become increasingly difficult to stop as they continue, thus increasing the risk for morbidity and mortality. Current guidelines recommend stepwise antiseizure medication administration with up to two doses of benzodiazepines being delivered within the first five to ten minutes of seizure onset, followed by additional antiepileptic medications if required.

While benzodiazepines are well known to be the first-line therapy for status epilepticus, there is evidence that they are often underdosed in the EMS and ED settings regardless of drug, route of

administration, or patient weight.(4) It is known that adherence to the recommended guidelines is correlated with improved clinical outcomes. Unfortunately, there are often several challenges and barriers that are encountered to administering appropriate dosages of medications, including lack of intravenous access. While the intravenous route may be preferred, delays in administration of the benzodiazepine are important to avoid, so the intramuscular or intranasal route should also be considered early.

Selection of second-line therapies may generate uncertainty in providers, but the current evidence clearly demonstrates that the recommended options are all safe and effective.(6,7,8) There is no statistical significance found among levetiracetam, fosphenytoin, and sodium valproate when cessation of seizure activity in children is compared. Given their similar efficacies, levetiracetam is often preferred due to its favorable safety, side-effect profile, medication interactions, and ease of administration.

A representation of the current recommendations for the management of pediatric status epilepticus (for patients > one month of age) follows:

#### 0-5 minutes:

- Initial assessment includes airway, breathing, circulation (ABCs), cardiopulmonary monitoring, and finger-stick glucose.
- Consider investigation of potential causes of provoked seizures (e.g., trauma, infection, electrolyte derangements, sub-therapeutic antiepileptic prescriptions, and intoxicants). This should not delay therapies.

#### 5-15 minutes:

- Give appropriate dose of benzodiazepine promptly.
  - o If no IV/IO access, then give midazolam 0.2 mg/kg/dose IM/Intranasal (max 10 mg)
    - May consider standardized IM/IN doses based on weight: 5 mg/dose for 13-40 kg; 10 mg/dose for > 40 kg.
  - o If IV/IO access, then:
    - Midazolam 0.2 mg/kg/dose IV/IO (max 10 mg/dose) OR
    - Lorazepam 0.1 mg/kg/dose IV/IO (max 4 mg/dose)
- A second dose of benzodiazepine may be given if seizure activity continues five minutes after the first dose was given.

#### >15 minutes:

- Second-line antiepileptic medication should be given if seizure activity continued after benzodiazepine administration.
- All second-line antiepileptic medications have similar efficacy for pediatric status epilepticus.
- Levetiracetam has a favorable side-effect profile and may be given rapidly.
  - Levetiracetam 60 mg/kg/dose (max 4,500 mg/dose)
  - Valproic acid 40 mg/kg/dose (max 3,000 mg/dose)
    - Rate of 1.5-3 mg/kg/min, max 20 mg/min
  - o Fosphenytoin 20 mg phenytoin equivalents/kg/dose (max 1,500 mgPE/dose)
    - Rate of 2 mgPE/kg/min, max 150 mgPE/min
  - Phenytoin 20 mg/kg/dose (max 1,500 mg/dose)
    - Rate of 1-3 mg/kg/min, max 50 mg/min

- Phenobarbital 20 mg/kg/dose (max 1,000 mg/dose)
  - Rate of 1mg/kg/min, max 30 mg/min
- Continued seizure activity or concern for nonconvulsive status epilepticus should lead to use of a third-line agent.
- Third-line agents and dosing:
  - Midazolam:
    - Loading dose 0.2 mg/kg IV at 2 mg/minute;
    - Infusion at 0.05-2 mg/kg/hour
  - Propofol:
    - Loading dose 1-2 mg/kg IV, administered over 1-2 min;
    - Infusion at 30-200 mcg/kg/minute
  - Phenobarbital:
    - Loading dose 20 mg/kg IV; rate 1mg/kg/min, max 30 mg/min
    - Maintenance dose of 5 mg/kg IV given at 12 and 24 hours
  - Ketamine:
    - Loading dose 0.5 mg/kg given over 60 seconds, may repeat every 3-5 minutes up to 3 mg/kg;
    - Infusion of 0.1-0.5 mg/kg/hr
- Airway protection should be considered as risk for apnea increases with use of additional sedating medications.

#### References:

- 1. Gurcharran K, Grinspan ZM. The burden of pediatric status epilepticus: epidemiology, morbidity, mortality, and costs. *Seizure*. 2019;68:3-8. doi:10.1016/j.seizure.2018.08.021. Epub 2018 Aug 29. PMID: 30270121.
- 2. Jones KEA, Howells R, Mallick AA, Paul SP, Dey I. NICE guideline review: epilepsies in children, young people and adults NG217. *Arch Dis Child Educ Pract Ed.* 2023;108(6):416-421. doi:10.1136/archdischild-2022-324427. Epub 2023 Jun 20. PMID: 37339862.
- 3. Gaínza-Lein M, Fernández IS, Ulate-Campos A, Loddenkemper T, Ostendorf AP. Timing in the treatment of status epilepticus: from basics to the clinic. *Seizure*. 2019;68:22-30. doi:10.1016/j.seizure.2018.05.021. Epub 2018 Jun 1. PMID: 29884518.
- 4. Sathe AG, Underwood E, Coles LD, Elm JJ, Silbergleit R, Chamberlain JM, Kapur J, Cock HR, Fountain NB, Shinnar S, Lowenstein DH, Rosenthal ES, Conwit RA, Bleck TP, Cloyd JC. Patterns of benzodiazepine underdosing in the Established Status Epilepticus Treatment Trial. *Epilepsia*. 2021;62(3):795-806. doi:10.1111/epi.16825. Epub 2021 Feb 10. PMID: 33567109; PMCID: PMC8075113.
- 5. Srivastava K, Suryawanshi VR, Yerrapalam N, Panda BK. Compliance with status epilepticus management protocol and effect on clinical outcomes in children with status epilepticus. *Eur J Hosp Pharm.* 2023;30(3):147-152. doi:10.1136/ejhpharm-2021-002721. Epub 2021 Jun 28. PMID: 34183455; PMCID: PMC10176975.
- Dalziel SR, Borland ML, Furyk J, Bonisch M, Neutze J, Donath S, Francis KL, Sharpe C, Harvey AS, Davidson A, Craig S, Phillips N, George S, Rao A, Cheng N, Zhang M, Kochar A, Brabyn C, Oakley E, Babl FE; PREDICT Research Network. 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. doi:10.1016/S0140-6736(19)30722-6. Epub 2019 Apr 17. PMID: 31005386.
- 7. Lyttle MD, Rainford NEA, Gamble C, Messahel S, Humphreys A, Hickey H, Woolfall K, Roper L, Noblet J, Lee ED, Potter S, Tate P, Iyer A, Evans V, Appleton RE; Paediatric Emergency Research in the United Kingdom & Ireland (PERUKI) Collaborative. Levetiracetam versus phenytoin for

- second-line treatment of paediatric convulsive status epilepticus (EcLiPSE): a multicentre, openlabel, randomised trial. *Lancet*. 2019;393(10186):2125-2134. doi:10.1016/S0140-6736(19)30724-X. Epub 2019 Apr 17. PMID: 31005385; PMCID: PMC6551349.
- 8. Chamberlain JM, Kapur J, Shinnar S, Elm J, Holsti M, Babcock L, Rogers A, Barsan W, Cloyd J, Lowenstein D, Bleck TP, Conwit R, Meinzer C, Cock H, Fountain NB, Underwood E, Connor JT, Silbergleit R; Neurological Emergencies Treatment Trials; Pediatric Emergency Care Applied Research Network Investigators. Efficacy of levetiracetam, fosphenytoin, and valproate for established status epilepticus by age group (ESETT): a double-blind, responsive-adaptive, randomised controlled trial. Lancet. 2020;395(10231):1217-1224. doi:10.1016/S0140-6736(20)30611-5. Epub 2020 Mar 20. Erratum in: Lancet. 2023;401(10387):1498. PMID: 32203691; PMCID: PMC7241415.
- Messahel S, Bracken L, Appleton R. Optimal management of status epilepticus in children in the emergency setting: a review of recent advances. *Open Access Emerg Med.* 2022;14:491-506. doi:10.2147/OAEM.S293258. PMID: 36158897; PMCID: PMC9491331.

Notes: Practice Advance synopses should be built from a strong body of evidence, that likely includes a systematic review. The synopsis will include a recommendation that should be similar in wording to how GRADE recommendations are given. These should not be controversial recommendations and essentially all emergency physicians should be adopting them. The impact or "effect size" should be substantial and no significant harm should be associated with this gain.

#### **Resources for Additional Learning:**

EMS for Children innovation and Improvement Center Pediatric Education and Advocacy Toolkit. <a href="https://emscimprovement.center/education-and-resources/peak/peak-status-epilepticus/trekk-eiic-pediatric-status-epilepticus-practice-quideline/">https://emscimprovement.center/education-and-resources/peak/peak-status-epilepticus/trekk-eiic-pediatric-status-epilepticus-practice-quideline/</a>

PedEM Morsels: Non-Convulsive Status Epilepticus. <a href="https://pedemmorsels.com/non-convulsive-status-epilepticus-in-children/">https://pedemmorsels.com/non-convulsive-status-epilepticus-in-children/</a>

EMRA: Management of Pediatric Seizures. <a href="https://www.emra.org/emresident/article/pediatric-seizure/">https://www.emra.org/emresident/article/pediatric-seizure/</a>

#### **Authors**

Sean Fox, M.D. (Lead)

#### **Editors**

Christopher Carpenter, M.D.; Christopher Edwards, PharmD.; Marianne Gausche-Hill, M.D.; Stephen Hayden, M.D.; Samuel Keim, M.D., M.S.; John Marshall, M.D., M.B.A.; Ernest Wang, M.D.