Evaluation and Management of Status Epilepticus in Infants < 30 Days of Age in the NICU, Special Care Nursery, Newborn Nursery, or Neonatal Transport

Approved by SSM Health Cardinal Glennon Clinical Practice Guidelines Committee July 25, 2024 and the SSM Health Pediatric Clinical Program September 23, 2024

Clinical Practice Guideline:
Evaluation and Management of
Status Epilepticus in Infants < 30 Days of Age
in the NICU, Special Care Nursery, Newborn Nursery, or Transport

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INCLUSION CRITERIA
- Infants of any gestational age who are < 30 days of age with clinical concern for status epilepticus or confirmed status epilepticus on EEG
- Infant is hospitalized in the post-delivery care setting (NICU, Nursery, Special Care Nursery, or Transport)

Status Epilepticus: seizure activity for greater than 5 minutes OR 2 or more seizures within 30 minutes

EXCLUSION CRITERIA
- Infants > 30 days of age in any care settings
- Infants of any age presenting with Status Epilepticus in an Acute Care Setting (Emergency Department, Inpatient Floor, PICU) following discharge from the NICU/Nursery/Special Care Nursery

INCLUSION CRITERIA MET

EVALUATION
May occur prior to or concurrent with treatment
- Assess ABC's, intervene as indicated
- Establish IV access, if not already available
- Laboratory Studies

CMP	Magnesium
CBC w/ Differential	Blood cultures
Blood gas	Ammonia
Consider Lumbar Puncture*	Meconium Drug Screen

** = If febrile, hypothermic, or clinical concern for infection*

- Head ultrasound
- Consult Pediatric Neurology
- Initiate video EEG (if not already started)

ADMINISTER FIRST LINE THERAPY

IV Phenobarbital Load
20mg/kg over 15 minutes

Seizures stopped 20 minutes post-load?

YES
- Continue video EEG monitoring for 24 hours
- Consider further workup for underlying cause of seizure (See *Box 1*)
- Do not initiate maintenance anti-seizure medication if no further seizure activity

NO

CONSIDER SECOND PHENOBARBITAL LOAD

At the discretion of the treating team, repeat IV Phenobarbital 20mg/kg over 15 minutes
OR
Proceed to next step of algorithm and second-line therapy

Seizures stopped 20 minutes post-load?

YES
- Continue video EEG monitoring for 24 hours
- Pursue workup for underlying cause (see *Box 1*)
- Consider maintenance anti-seizure medication with one of the following, dosing depending on response
  - Phenobarbital 5mg/kg/day divided twice daily
  - Levetiracetam 40-60mg/kg/day divided twice daily
  - Fosphenytoin 5mgPE/kg/day divided twice daily
- Consider medication levels for adjustment at least 2 hours post-load(s)

NO

ADMINISTER SECOND LINE THERAPY

IV Fosphenytoin* 20mg PE/kg over 15 minutes
OR
IV Levetiracetam 60mg/kg over 15 minutes

** = Caution when using in a patient with cardiac pathology*

Seizures stopped 20 minutes post-load?

YES
- Continue video EEG monitoring for 24 hours
- Pursue workup for underlying cause (see *Box 1*)
- Consider maintenance anti-seizure medication with one or more of the following, dosing depending on response
  - Phenobarbital 5mg/kg/day divided twice daily
  - Levetiracetam 40-60mg/kg/day divided twice daily
  - Fosphenytoin 5mgPE/kg/day divided twice daily
- Consider initiating Pyridoxine per Pediatric Neurology discretion
  - 100mg IV or PO load, followed by 30mg/kg/day divided twice daily, IV or PO, for 3-5 days
- Consider Pyridoxal 5'-phosphate (PLP) if unresponsive to Pyridoxine per Pediatric Neurology discretion
- Consider medication levels for adjustment at least 2 hours post-load(s)

NO

ADMINISTER THIRD LINE THERAPY
Use whichever agent was not used as second line above

IV Fosphenytoin* 20mg PE/kg over 10 minutes
OR
IV Levetiracetam 60mg/kg over 5 minutes

** = Caution when using in a patient with cardiac pathology*

Seizures stopped 20 minutes post-load?

YES
- Continue video EEG monitoring for 24 hours
- Pursue workup for underlying cause (see *Box 1*)
- Consider maintenance anti-seizure medication with one or more of the following, dosing depending on response
  - Phenobarbital 5mg/kg/day divided twice daily
  - Levetiracetam 40-60mg/kg/day divided twice daily
  - Fosphenytoin 5mgPE/kg/day divided twice daily
- Consider initiating Pyridoxine per Pediatric Neurology discretion
  - 100mg IV or PO load, followed by 30mg/kg/day divided twice daily, IV or PO, for 3-5 days
- Consider Pyridoxal 5'-phosphate (PLP) if unresponsive to Pyridoxine per Pediatric Neurology discretion
- Consider medication levels for adjustment at least 2 hours post-load(s)

NO

ADMINISTER FOURTH LINE THERAPY
IV Midazolam bolus 0.15mg/kg
followed by
Midazolam 0.05mg/kg/hr infusion,
titrate up to 2mg/kg/hr as tolerated

Discuss Pyridoxine administration with Pediatric Neurology
100mg IV load

- Continue video EEG monitoring
- Pursue workup for underlying cause (see *Box 1*)
- Once seizure-free for 24 hours, initiate wean of midazolam infusion
- Transition to maintenance anti-seizure medication with one or more of the following, dosing depending on response and neurology preference
  - Phenobarbital 5mg/kg/day divided twice daily
  - Levetiracetam 40-60mg/kg/day divided twice daily
  - Fosphenytoin 5mg/kg/day divided twice daily
- Consider continuing or initiating Pyridoxine at the discretion of Pediatric Neurology
  - 100mg IV or PO load, followed by 30mg/kg/day divided twice daily IV or PO, for 3-5 days
- Consider Pyridoxal 5'-phosphate (PLP) if unresponsive to Pyridoxine per Pediatric Neurology discretion

DISCHARGE PLANNING AND FOLLOW-UP
- Weaning of maintenance medications should begin after 5-7 days of electroclinical or electrographic seizures, unless there is a contraindication (identified genetic condition or malformation on neuroimaging)
- Neurology will provide guidance on the order of weaning for patients on multiple therapies
- Infants being discharged from the NICU on multiple medications should follow up with Neurology
- Infants being discharged from the NICU off medications or on a single medication can follow up with Nursery Follow-Up Clinic

Box 1: Further Workup
- Epilepsy Gene Panel (if no provoking factor identified)
- Genetics consult if significant family history or dysmorphic features
- Metabolic workup
  - Lactate
  - Pyruvate
  - Urine organic acids
  - Serum amino acids
  - Carnitine profile
  - Acylcarnitine
  - Ammonia
- MRI Brain with and without contrast
- MR Spectroscopy

SSMHealth Cardinal Glennon Access Center Transfer Line
888-229-2424

1. SSMHealth Cardinal Glennon CPG Home

2. Resources

a. Abend NS, Wusthoff CJ. Neonatal Seizures and Status Epilepticus. *Journal of Clinical Neurophysiology*. 2012;29(5):441-448.
b. Bamgbose O, Boyle F, Kean AC, Stefanescu BM, Wing S. Tolerability and Safety of Lacosamide in Neonatal Population. *Journal of Child Neurology*. 2023;38(3-4):137-141.
c. Glass HC, Soul JS, Chang T, et al. Safety of Early Discontinuation of Antiseizure Medication After Acute Symptomatic Neonatal Seizures. *JAMA Neurology*. 2021;27(7):817-825.
d. Pin JN, Leonardi L, Nosadini M, et al. Efficacy and safety of ketamine for neonatal refractory status epilepticus: case report and systematic review. *Front Pediatr*. 2023;11:1189478.
e. Pressler R, Abend NS, Auvin S, et al. Treatment of seizures in the neonate: Guidelines and consensus-based recommendations-Special report from the ILAE Task Force on Neonatal Seizures. *Epilepsia*. 2023;64(10):2550-2570.
f. Sharpe C, Reiner GE, Davis SL, et al. Levetiracetam versus Phenobarbital for Neonatal Seizures: A Randomized Controlled Trial. *Pediatrics*. 2020;145(6):e20193182.

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