Neonatal Seizure Treatment Care Guideline

Inclusion Criteria:
- Suspected seizure activity
- Neonates (0 - 28 days of life) ≤ 44 weeks corrected gestational age
- Admitted to 4S NICU

Exclusion Criteria: Patients outside 4S NICU, at this time

Assessment: For suspected seizure

- Assess airway, breathing and circulation
- Monitor vital signs and treat as necessary

Consult neurology and communicate the following:
- Semiology of event of concern to include but not limited to the following:
  - The presence of loss or alteration of consciousness
  - Vital signs during the episode
  - Are any movements rhythmic or non-rhythmic
  - Are any movements continuous or discontinuous
  - Amplitude of movements
  - Frequency of movements
  - Generalized or focal nature of movements
- Perinatal history, Family History, Neurologic Examination
- Obtain following labs: Point of care glucose, CBC with diff/platelets, CMP to include Calcium, Magnesium and Phosphorous.
- Infectious workup per NICU.
- Place order for continuous EEG monitoring if, after consulting with neurology, it is determined to be necessary.

If clinical concern for seizures high or seizure confirmed on EEG, proceed to the following

Remove patients from pathway if concerning events are captured on EEG and are deemed non-epileptic.

Interventions

- Treat electrolyte disturbance if present (such as hypoglycemia, hypocalcemia, hyponatremia)
- **If seizures,** first-line anti-seizure medication – Phenobarbital 20 mg/kg IV
  - **If additional seizures,** give Phenobarbital 20 mg/kg IV

- **If additional seizures,** second-line anti-seizure medication – Fosphenytoin 20 mg/kg IV ***OR*** Levetiracetam 60 mg/kg IV (see below)

- **Consider obtaining the following labs:**
  - 2-hour post load phenytoin level
  - Albumin level at the time of phenytoin level (if recent level not available)
  - Phenobarbital random level (at same time of phenytoin level)

- **If additional seizures,** give alternative second-line (Fosphenytoin IV 20 mg/kg ***OR*** Levetiracetam IV 60 mg/kg if not previously given)

- **If additional seizures**
  - Additional phenobarbital loads to achieve therapeutic levels of phenobarbital ***OR***
  - Additional fosphenytoin loads to achieve therapeutic levels of fosphenytoin ***OR***
  - If prior anti-seizure medications (ASMs) have been optimized and patient continues to seize consider the following based on seizure burden and neurology recommendations
    - Additional Levetiracetam 60 mg/kg IV
    - Lacosamide 10 mg/kg IV
    - Midazolam 0.1 mg/kg IV bolus followed by 0.1 mg/kg/hr - titrate to efficacy

- Patients who have had seizures generally stay connected to EEG until seizure free for approximately 24 hours. Patients can be discontinued earlier per NICU/Neurology discretion should benefit of obtaining a study in this 24 hour period outweigh the risk of earlier discontinuation of the EEG.

Approved Evidence Based Medicine Committee
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Recommendations/ Considerations

- Anti-seizure medication (ASM) levels:
  - Administering two consecutive phenobarbital loading doses of 20 mg/kg IV can result in higher therapeutic levels. Therefore, consider not obtaining ASM levels after the second loading dose of phenobarbital when these doses have been given in close succession.

- Obtain levels of ASMs in the following scenarios:
  - If seizures persist and there is a need to determine if ASM levels can be optimized..
  - When it is necessary to assess if ASM levels are supratherapeutic and potentially impacting clinical status.

- Maintenance of ASM, per Neurology Recommendation:
  - The need for maintenance ASM is based on clinical status, serum ASM levels (if available), and the risk for seizure recurrence.
    - **Phenobarbital:** If needed, the typical starting dose is 3 - 5 mg/kg/day PO, administered once or divided twice daily. Maintenance therapy with phenobarbital is usually initiated 12 hours after last loading dose.
    - **Fosphenytoin:** If needed, the typical starting dose is 5 mg/kg/day PO, divided twice daily, and typically initiated 12 hours or longer after last loading dose.
    - **Levetiracetam:** Maintenance dosing is 40 mg/kg/day PO, divided q8h.

- In the setting of Hypoxic-ischemic encephalopathy (HIE):
  - If seizures resolve after phenobarbital loading, consider not starting maintenance ASM if the seizures are considered acute symptomatic seizures.

- For guidance on the duration of continuous EEG monitoring, please refer to the CHOC Care Guideline titled ‘Critical Care Continuous EEG (CCEEG-LTM) Care Guideline’.

- If a channelopathy is suspected, initiate a sodium channel blocker as a second-line ASM (fosphenytoin or oxcarbazepine). In neonates with cardiac disorders, levetiracetam may be preferred as a second-line ASM. If channelopathy is the likely cause for seizures due to family history, then fosphenytoin or oxcarbazepine (sodium channel blocker) may be the first-line ASM.

- If the etiology of seizures is unclear and seizures persist after second-line ASM, consult metabolics and genetics, and initiate the following treatments until genetic testing/biochemical markers exclude pyridoxine dependent epilepsy:
  - **Pyridoxine:** 15 - 30 mg/kg/day PO, divided three times daily.
  - **Folinic acid:** 3 - 5 mg/kg/day PO, divided two times daily.
    - Pyridoxine and Folinic acid can be started prior to second-line ASM failure if clinical features or EEG characteristics suggest pyridoxine-dependent epilepsy.

- In the setting of acute symptomatic seizures, anti-seizure medications (ASMs) should be discontinued prior to discharge to home unless the clinical team determines benefits of continuing ASMs outweigh the risk of discontinuing them.

- Episodes that are concerning for seizure activity should be treated as such. Treatment of suspected seizure activity should not be delayed until neurophysiologic (EEG) characterization.

Discharge Criteria

- If the patient is found to have EEG-confirmed seizures, they will need a neurology follow-up appointment scheduled prior to discharge from the hospital. Neurologist to determine the timeframe for follow-up.

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References

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