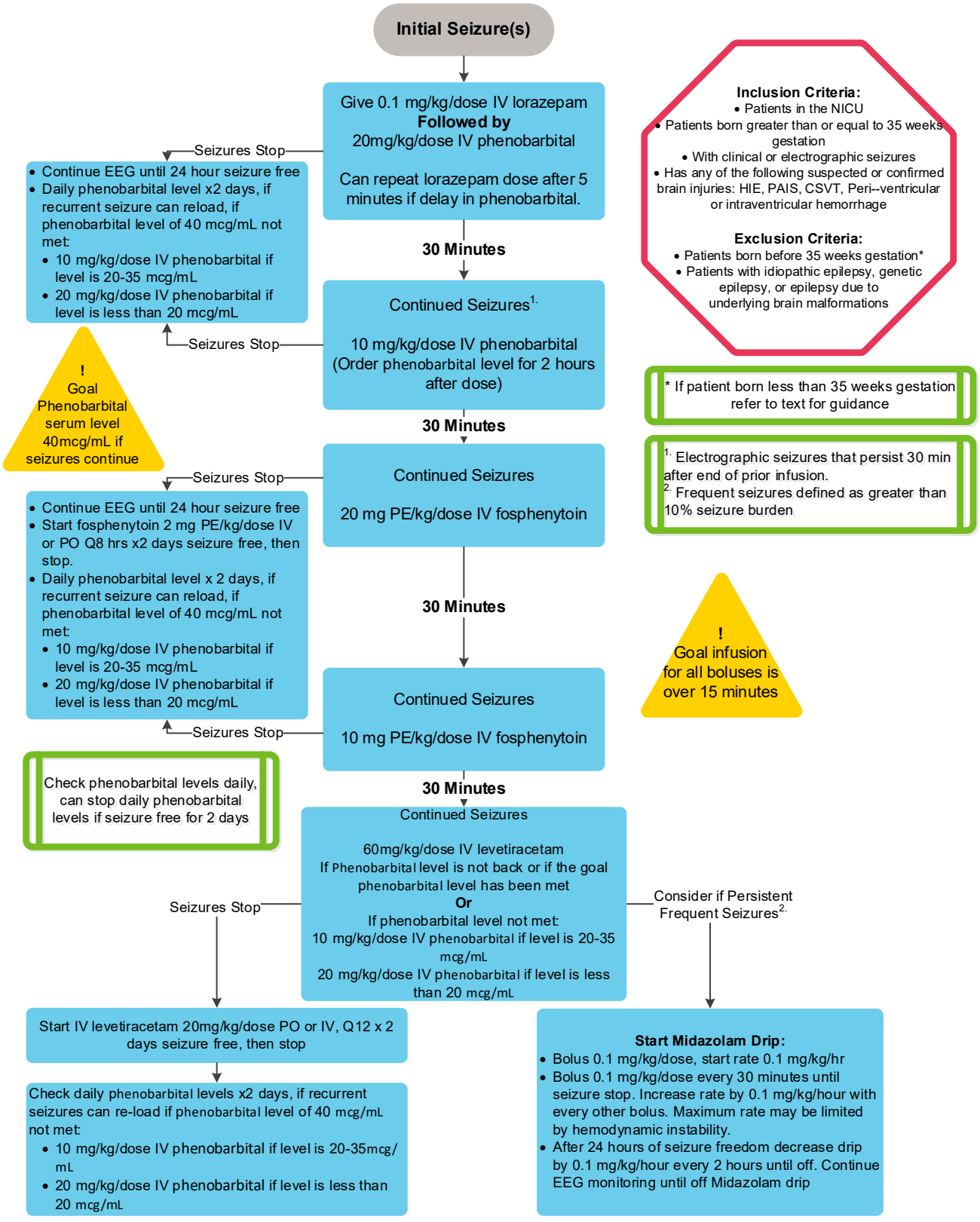
Neonatal Seizures after Acquired Brain Injury

Treatment of Symptomatic Seizures in Term and Late Pre-term Neonates

ALGORITHM:



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TARGET POPULATION

Inclusion Criteria

Patients in the NICU born at greater than or equal to 35 weeks gestation* who have clinical or electrographic seizures and have any of the following known or suspected acquired brain injuries:

- Perinatal Hypoxic Ischemic Encephalopathy (HIE)
- Perinatal Arterial Ischemic Stroke (PAIS)
- Cerebral Sinus Venous Thrombosis (CSVT), with or without venous infarct or hemorrhage
- Peri-ventricular or intra-ventricular hemorrhage

* If patient born less than 35 weeks see exclusion criteria below for details

Exclusion Criteria

- Neonates with idiopathic epilepsy, genetic epilepsy, epilepsy due to underlying brain malformations.
- Infants outside of the neonatal period (older than 28 days of life). See Status Epilepticus Clinical Pathway
- This guideline is intended to apply to late pre-term and term neonates. The treatment principles in this guideline may be applied to neonates born earlier than 35 weeks gestation at provider discretion. However, data is lacking regarding the efficacy of standard anticonvulsants in preterm infants, as well as the long-term effects of both anticonvulsant use and seizures on the preterm neonatal brain.
- Neonates at outside NICUs awaiting transfer to CHCO: for neonates with suspected seizures at outside hospitals, who are awaiting transport to CHCO, or are in transport to CHCO, we recommend treating with an initial 20 mg/kg/dose of IV phenobarbital. An additional 10mg/kg/dose of IV phenobarbital may be given if suspected seizures do not stop within 30 minutes of the initial infusion. However, further treatment should be done in the setting of continuous EEG monitoring to correctly identify seizures and so further medication boluses without EEG confirmation of seizures should be used with caution.

BACKGROUND | DEFINITIONS

THE GOALS OF TREATING NEONATAL SEIZURES ARE TO MINIMIZE SEIZURE BURDEN WHILE MINIMIZING CUMULATIVE ANTICONVULSANT EXPOSURE.

Definitions

- Acute Symptomatic Seizures- seizures occurring within one week of a brain injury.[1]
- Remote Symptomatic Seizures- seizures occurring more than one week after a brain injury.

- Intermittent seizures- recurrent seizures in which the seizure burden is less than 10% for a specific period of time.
- Frequent seizures- recurrent seizures in which the seizure burden is equal to or greater than 10%.
- Seizure burden- percentage of any given epoch of time taken up by electrographic seizure activity.
- PAIS- perinatal arterial ischemic stroke
- CSVT- cerebral sino-venous thrombosis
- ICH- intracranial hemorrhage.
- Seizure – "rhythmic spike wave activity" lasting greater than 10 seconds, with or without clinical correlate.

Roles and Responsibilities:

- When a continuous EEG is felt to be indicated by the NICU team, it is the responsibility of a NICU team member to call the neurology fellow on call to request the EEG.
- Once the EEG is running it is the responsibility of the on-call neurology team to monitor the EEG for seizures and to notify the NICU team once seizures are identified.
- Once seizures are identified and the algorithm is initiated, it is the responsibility of the neurology team to monitor for resolution of seizures, and to notify the NICU team when it is appropriate to move to the next step in the algorithm.
- It is the responsibility of the NICU team to order the appropriate medications when recommended by the on-call neurology team.

Background

Seizures in Neonates with acquired brain injury

Seizures are common in neonates with acquired hypoxic and/or ischemic brain injury. Examples of this type of brain injury associated with seizures in neonates are HIE, PAIS, ICH, and CSVT.[2,3] Excitatory neuronal transmission is critical for maturation of neural networks, and studies in rodents suggest that the younger brain has an increased propensity for seizures due to overdevelopment of the excitatory neurotransmitter systems, and underdevelopment of inhibitory systems[4,5] Therefore, the neonatal brain is particularly susceptible to generating seizures after ischemic insult. Furthermore, neonates are more likely than older children to have subclinical seizures, and in particular to have subclinical seizures after anticonvulsant therapy.[6]

There is considerable debate in the literature as to whether recurrent seizures after neonatal brain injury exacerbate injury and independently contribute to outcome.[7,8] Neonates who develop seizures after brain injury have worse outcomes compared to neonates who do not, but it is difficult to determine whether poor outcome is due to more severe injury, and perhaps seizures are simply a secondary consequence of that injury. In animal models of perinatal HIE, there is conflicting data as to whether induced seizures exacerbate histological injury after HIE, with some studies showing larger injury with seizures,[9] and others showing no difference between animals with and without seizures.[10] Imaging studies in human neonates suggest that seizures exacerbate energy failure in watershed regions after HIE.[11] Worse developmental outcome in children with seizures may be related to reduced neurogenesis after neonatal seizures.[12] Recently, Glass et al found that seizures were associated with worse neurodevelopmental outcome in neonates when controlling for injury size,[13] suggesting that seizures do confer additional injury.

Neonatal seizures after acquired brain injury tend to be self-limited in most cases. In a study evaluating the temporal evolution of seizures of HIE, the median age when maximum seizure burden occurred was 23 hours of life, with majority of seizures resolving within 18-53 hours of onset.[14] There is less data regarding the time frame of acute symptomatic seizures after PAIS or ICH, but these are likely to be self-limited as well. There is evidence that neonatal seizures after acquired brain injury significantly increase the risk of later life epilepsy.[15] However, there is not any research to suggest that treating children with anticonvulsants after the acute symptomatic phase prevents developing remote symptomatic epilepsy. Therefore, treatment for seizures due to perinatal brain injury can likely be limited to a short duration.

Traditionally, the primary anticonvulsants used to treat neonatal seizures have been barbiturates (phenobarbital), fosphenytoin, and benzodiazepines (midazolam, diazepam, and lorazepam). Both barbiturates and benzodiazepines act by opening GABA receptors, which in a more mature brain increases the seizure threshold through chloride influx, thereby hyperpolarizing neurons. However, there is evidence from animal research that in the neonatal brain the chloride gradient is reversed, and so GABA activation is actually excitatory rather than inhibitory.[16] This may explain why some studies evaluating the efficacy of phenobarbital have shown relatively poor seizure control with phenobarbital, only 43%.[17] Interestingly, phenytoin had equally poor efficacy. However, in these early studies, relatively low loading doses were used. In studies in which sequential loading doses were used in order to obtain higher serum levels, the efficacy of phenobarbital increased to up to 77%.[18-20] In addition, the initial studies showing a poor response rate to phenobarbital and fosphenytoin were conducted prior to therapeutic hypothermia being the standard of care, and there is evidence that, at least for phenobarbital, response rate is higher in the setting of hypothermia (66%).[19] Fosphenytoin and phenobarbital together may have marginally increased efficacy when combined in patients who fail monotherapy to control seizures.[17] Levetiracetam has increasingly been used in neonatal seizures. There have been no large studies examining the safety and efficacy of levetiracetam in treating neonatal seizures. Some smaller studies suggest that in the acute treatment period, there are not obvious adverse outcomes. These same studies claim efficacy; however, treatment is considered successful if seizures are controlled within a week of starting levetiracetam, a time frame in which most symptomatic neonatal seizures cease regardless of treatment.[21,22] Overall there is very little data regarding the efficacy of levetiracitam for treating neonatal seizures.

There has long been evidence that anticonvulsants have some neurotoxicity in the developing brain. Animal studies have demonstrated apoptosis (programmed cell death) after administration of phenobarbital, phenytoin and several different benzodiazepines.[23] Studies of children with febrile seizures randomized to treatment with phenobarbital vs. placebo found significantly lower IQ in children treated with phenobarbital, an effect that persisted after cessation of treatment.[24,25] However, in these studies, patients were treated for two years, and it is unclear whether much shorter treatment durations have similar long-term effects on IQ. More recent animal studies suggest that phenobarbital treatment might actually confer some neuroprotection after perinatal HIE.[26] At this point, it is uncertain whether anticonvulsant therapy is overall detrimental to the developing brain, but the potential for long-term neurodevelopmental effects necessitate using these therapies with caution and limiting length of treatment when possible.

Algorithms to standardize the treatment of neonatal seizures are being used more frequently. Studies of short term outcomes when treatment algorithms are used suggest that this approach may reduce the frequency of status epilepticus and minimize cumulative anticonvulsant exposure,[27] as well as reducing time to treatment and overall seizure burden.[28]

In summary, neonatal seizures are very common after acquired brain injury, and cumulative research supports that seizures may have negative effects on long-term outcome. There is very limited data on efficacy of different anticonvulsants in neonates, but better efficacy may be reached with sequential medication loading doses. Anticonvulsants may be detrimental to the developing brain, and seizures after acquired perinatal brain injury typically resolve within 5 days of onset. Therefore, defined endpoints for treatment are needed.

INITIAL EVALUATION

Neonates undergoing therapeutic hypothermia per CHCO Pathway

Initial EEG monitoring and MRI per CHCO clinical pathway

- Hypoxic Ischemic Encephalopathy

Neonates with new onset seizures of unclear etiology:

NOTE: WHILE THE FULL TREATMENT ALGORITHM IS MEANT TO APPLY SPECIFICALLY TO NEONATES WITH SEIZURES AFTER ACQUIRED BRAIN INJURY, THE INITIAL WORKUP AND MANAGEMENT CAN BE APPLIED TO ALL NEONATES WITH SEIZURES, REGARDLESS OF ETIOLOGY.

- Serum glucose and electrolytes.
- Sepsis workup per neonatologist's discretion.

- MRI of the brain without contrast.
- Start continuous EEG monitoring: Order continuous EEG monitoring STAT. Call on-call neurology resident to let them know about the patient and the order.
- If phenobarbital was given at an OSH, please check level upon admission to CHCO.
- Continuous cardiorespiratory monitoring

CLINICAL MANAGEMENT AND THERAPUETICS

Initial seizure management

- Initial management is meant for patients with suspected repeated clinical seizures, electrographic seizures on EEG, or pattern concerning for seizure on an EEG.
- Initial treatment with 0.1mg/kg/dose of IV lorazepam AND 20 mg/kg/dose of intravenous phenobarbital while etiologic workup is started.

Subsequent seizure management for patients with confirmed PAIS, HIE, CSVT or ICH

Each subsequent step in the algorithm should be initiated if electrographic seizures do not stop, or if they recur within 30 minutes of completing the prior step.

- If seizures continue after initial phenobarbital load, give an additional 10mg/kg/dose IV phenobarbital load. Draw phenobarbital level two hours after infusion.
- If continued seizures (while awaiting phenobarbital level), give 20 mg PE/kg of IV fosphenytoin.
- If continued seizures (while awaiting phenobarbital level), give an additional 10 mg PE/kg of IV fosphenytoin.
- If seizures continue after a cumulative fosphenytoin dose of 30 mg PE/kg, and if still awaiting serum phenobarbital level, OR if serum phenobarbital level is greater than 40 mcg/mL, give 60 mg/kg/dose of IV levetiracetam.
- If continued seizures and serum phenobarbital level is 20-35 mcg/mL, give 10 mg/kg/dose of IV phenobarbital. If serum phenobarbital level is less than 20 mcg/mL, give 20 mg/kg/dose of IV phenobarbital.
- If *intermittent seizures* persist after completing the algorithm (maximum seizure burden less than 10% in the 1.5 hours after the last bolus infusion), consider starting maintenance anticonvulsant therapy for a short period (see below). Phenobarbital levels should be checked daily until seizure free for 2 days. If intermittent seizures persist and level is less than 20 mcg/mL, can re-load 20 mg/kg/dose of phenobarbital; if level is 20-35 mcg/mL, can give 10 mg/kg/dose of phenobarbital. Goal phenobarbital level in the setting of continued seizures is 40 mcg/mL. If phenobarbital level is 40 mcg/mL or greater and frequent seizures persist, initiate a midazolam drip (see next bullet).
- If *frequent seizures* continue after completing the algorithm (seizure burden greater than 10%), consider starting a midazolam drip. This should be discussed with the NICU attending. Recommended midazolam dosing: 0.1 mg/kg/dose bolus followed by a starting rate of 0.1 mg/kg/hour. A bolus of 0.1 mg/kg/dose should be given up to every 30 minutes for continued seizures. The midazolam drip rate should be increased by 0.1 mg/kg/hour with every other bolus (i.e. rate increase up to once per hour). There is no recommended maximum midazolam drip rate; however, the maximum rate may be limited by hemodynamic or respiratory instability, and the benefits of continued treatment should be weighed against the potential harm of increased supportive care at the discretion of the providers involved. Once 24 hours of seizure freedom has been reached, midazolam can be decreased by 0.1 mg/kg/hour every two hours until drip is off. EEG monitoring should be continued through weaning of the drip. If seizures recur, can give additional boluses of phenobarbital, levetiracetam, or fosphenytoin, as appropriate.
- Midazolam drip can be weaned more slowly if it is considered by NICU or Neurology providers that the patient is at risk for withdrawal seizures or other benzodiazepine withdrawal symptoms.

Maintenance anticonvulsants:

- If complete or partial response to fosphenytoin, can start 2 mg PE/kg Q8 hours (6 mg PE/kg/day), PO or IV until 48 hours of seizure freedom, then stop. If seizures persist beyond 5 days of onset, consider transitioning to a different anticonvulsant, such as levetiracetam (15-30 mg/kg/dose BID, PO or IV), phenobarbital (5mg/kg/dose daily, PO or IV) or topiramate (5-7.5 mg/kg/dose BID, PO)).
- If complete or partial response to levetiracetam, can start 20 mg/kg/dose Q12 hours PO or IV (40 mg/kg/day), until 48 hours of seizure freedom, then stop.

Cessation of Anticonvulsants:

- As most acute symptomatic seizures are self-limited, we recommend that maintenance anticonvulsants, if started, are discontinued 48 hours after seizure freedom.
- A longer course of anticonvulsant therapy can be used at the discretion of providers if the patient is considered high risk of recurrent seizures (eg temporal lobe hemorrhage). However, in most cases, cessation of treatment should be strongly considered prior to discharge if electrographic seizures stopped within the acute phase.

Length of EEG monitoring:

- EEG monitoring should continue until 24 hours of seizure freedom. Routine EEGs can be repeated after cessation of anticonvulsants to confirm seizure freedom.

LABORATORY STUDIES | IMAGING

- Continuous EEG monitoring should be started for any neonate with suspected seizures and continued until the patient is 24 hours seizure free.

HIE

- Patients with diagnosed HIE, continuous EEG should be done for the first 24 hours after arrival to CHCO. If electrographic seizures are captured, continuous EEG monitoring should be continued through cooling and re-warming, or until the patient is 24 hours seizure free (if seizures persist through rewarming).
- In patients with mild HIE who do not have seizures in the first 24 hours of EEG monitoring, continuous EEG can be discontinued and the patient can be followed with amplitude integrated EEG (aEEG). Conventional EEG should be re-initiated if concern for seizures on aEEG or for clinical seizures. If no further concern for seizures, an extended inpatient EEG (2-4 hours) should be done on DOL 4-5, after the MRI scan, for prognostic purposes.
- Patients with moderate or severe HIE should be monitored with continuous EEG throughout hypothermia and re-warming.

REFERENCES

1. Beghi, E., et al., Recommendation for a definition of acute symptomatic seizure. Epilepsia, 2009. 51(4): p. 671-675.
2. Tekgul, H., The Current Etiologic Profile and Neurodevelopmental Outcome of Seizures in Term Newborn Infants. PEDIATRICS, 2006. 117(4): p. 1270-1280.
3. Glass, H.C., et al., Contemporary Profile of Seizures in Neonates: A Prospective Cohort Study. The Journal of Pediatrics, 2016. 174: p. 98-1030.
4. Sanchez, R.M. and F.E. Jensen, Maturational Aspects of Epilepsy Mechanisms and Consequences for the Immature Brain. Epilepsia, 2001. 42(5): p. 577-585.
5. Brooks-Kayal, A.R., Rearranging Receptors. Epilepsia, 2005. 46(s7): p. 29-38.
6. Scher, M.S., et al., Uncoupling of EEG-clinical neonatal seizures after antiepileptic drug use. Pediatric Neurology, 2003. 28(4): p. 277-280.
7. Kwon, J.M., et al., Clinical seizures in neonatal hypoxic-ischemic encephalopathy have no independent impact on neurodevelopmental outcome: secondary analyses of data from the neonatal research network hypothermia trial. Journal of child neurology, 2010. 26(3): p. 322-328.
8. Glass, H.C., D.M. Ferriero, and S.P. Miller, Correspondence on "Clinical Seizures in Neonatal Hypoxic-Ischemic Encephalopathy Have No Independent Impact on Neurodevelopmental Outcome: Secondary Analyses of Data From the Neonatal Research Network Hypothermia Trial". Journal of Child Neurology, 2011. 26(4): p. 532-532.
9. Wirrell, E.C., et al., Prolonged Seizures Exacerbate Perinatal Hypoxic-Ischemic Brain Damage. Pediatric Research, 2001. 50(4): p. 445-454.
10. Towfighi, J., et al., Effect of seizures on cerebral hypoxic–ischemic lesions in immature rats. Developmental Brain Research, 1999. 113(1-2): p. 83-95.
11. Campbell, C., et al., Seizure-associated brain injury in term newborns with perinatal asphyxia. Neurology, 2002. 59(7): p. 1119-1120.
12. McCabe, B.K., et al., Reduced neurogenesis after neonatal seizures. The Journal of neuroscience : the official journal of the Society for Neuroscience, 2001. 21(6): p. 2094-2103.
13. Glass, H.C., et al., Clinical Neonatal Seizures are Independently Associated with Outcome in Infants at Risk for Hypoxic-Ischemic Brain Injury. The Journal of pediatrics, 2009. 155(3): p. 318-323.
14. Lynch, N.E., et al., The temporal evolution of electrographic seizure burden in neonatal hypoxic ischemic encephalopathy. Epilepsia, 2012. 53(3): p. 549-557.
15. Fox, C.K., et al., Neonatal seizures triple the risk of a remote seizure after perinatal ischemic stroke. Neurology, 2016. 86(23): p. 2179-2186.
16. Dzhala, V.I., et al., NKCC1 transporter facilitates seizures in the developing brain. Nature Medicine, 2005. 11(11): p. 1205-1213.
17. Painter, M.J., et al., Phenobarbital Compared with Phenytoin for the Treatment of Neonatal Seizures. The New England Journal of Medicine, 1999. 341(7): p. 485-489.
18. Gilman, J.T., et al., Rapid sequential phenobarbital treatment of neonatal seizures. Pediatrics, 1989. 83(5): p. 674-678.
19. van den Broek, M.P.H., et al., Pharmacokinetics and Clinical Efficacy of Phenobarbital in Asphyxiated Newborns Treated with Hypothermia. Clinical Pharmacokinetics, 2012. 51(10): p. 671-679.
20. Venkatesan, C., et al., Epilepsy Following Neonatal Seizures Secondary to Hemorrhagic Stroke in Term Neonates. Journal of Child Neurology, 2015. 31(5): p. 547-552.
21. Ramantani, G., et al., Levetiracetam: Safety and efficacy in neonatal seizures. European Journal of Paediatric Neurology, 2011. 15(1): p. 1-7.
22. Yau, M., E. Fung, and P. Ng, Response of levetiracetam in neonatal seizures. World journal of clinical pediatrics, 2015. 4(3): p. 45-49.
23. Bittigau, P., et al., Antiepileptic drugs and apoptotic neurodegeneration in the developing brain. Proceedings of the National Academy of Sciences, 2002. 99(23): p. 15089-15094.
24. Farwell, J.R., et al., Phenobarbital for Febrile Seizures — Effects on Intelligence and on Seizure Recurrence. New England Journal of Medicine, 1990. 322(6): p. 364-369.

25. Sulzbacher, S., et al., Late cognitive effects of early treatment with phenobarbital. Clinical pediatrics, 1999. 38(7): p. 387-394.
26. Barks, J.D., et al., Phenobarbital Augments Hypothermic Neuroprotection. Pediatric Research, 2010. 67(5): p. 532-537.
27. Harris, M.L., et al., Standardized Treatment of Neonatal Status Epilepticus Improves Outcome. Journal of Child Neurology, 2016. 31(14): p. 1546-1554.
28. Srinivasakumar, P., et al., Treating EEG Seizures in Hypoxic Ischemic Encephalopathy: A Randomized Controlled Trial. PEDIATRICS, 2015. 136(5).

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REVIEW | REVISION SCHEDULE

Scheduled for full review on date here August 3, 2021.

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