Wisconsin Perinatal Quality Collaborative (WisPQC)

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Extended Antiepileptic Drug Use for Neonatal Seizures Due Hypoxic-Ischemic Encephalopathy Is Associated with Poor Neurodevelopmental Outcomes

Primary Author: Name: Alexandra Wilson, MD
Organization: Medical College of Wisconsin
Email: ahwilson@mcw.edu

Additional Authors: Michael Kim; Samuel Adams, MD; Ke Yan; Jian Zhang; Erwin Cabacungan, MD; Susan Cohen, MD

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Introduction: Hypoxic-ischemic encephalopathy (HIE) remains the most common cause of neurologic disease in term infants. Neonatal seizures due to HIE often require treatment with antiepileptic drugs (AEDs). There is evidence that AEDs may be discontinued prior to discharge without harmful outcomes. Clinical practice remains variable despite limited difference in neonatal seizure recurrence. Understanding the long-term outcomes of infants with HIE who remain on AEDs after discharge could better inform clinical guidelines for discontinuation.

Hypothesis: Extended use of AEDs is a risk factor for poor neurodevelopmental outcomes in infants born with HIE.

Methods/design: A retrospective cohort study of infants diagnosed with moderate/severe HIE was performed between 1/1/2013-12/31/2018. Ages and Stages Questionnaire- 3rd edition (ASQ3) and Bayley Scales of Infant Development- 3rd Edition (Bayley-III) results were collected from pediatrician well-child and neurodevelopmental follow-up visit documentation respectively. Patient characteristics including the extended use of AEDs was analyzed using Chi-square, Fisher exact, Student's t-test and Mann-Whitney U-test as well as Poisson regression with significance set at $p<0.05$.

Results: In our cohort, 95 infants were diagnosed with moderate/severe HIE. After excluding infants who died or were lost to follow up, 51 patients had documentation of neurodevelopmental outcomes (54%). Use of AEDs at 3 months of age was significantly associated with neurodevelopmental impairment on ASQ3 and Bayley-III assessment (adjusted OR 7.37, 95% CI 1.05 - 51.48, $p<0.05$). Other significant risk factors for poor neurodevelopmental outcomes included male gender, longer hospital length of stay (11 vs 23 days), increased duration of mechanical ventilation (1 vs 3.5 days), and severe MRI findings but were not significant when adjusted for other factors.

Conclusions: Extended AED use in infants diagnosed with HIE is a significant risk factor for worse neurodevelopmental outcomes. These results suggest that early discontinuation of AEDs may be beneficial. Because factors that reflect increased illness severity were also associated with poor outcomes, further investigations are needed to help risk-stratify infants who may benefit most from early discontinuation of AEDs.