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

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BACKGROUND

- Hypoxic ischemic Encephalopathy (HIE) remains the leading cause of neonatal seizure
- Neonatal seizures often requires antiepileptic drugs (AEDs) yet these drugs are associated with long-term neurodevelopmental concerns
- Clinical evidence shows that AEDs may be discontinued prior to discharge without harmful outcomes but clinical practice is variable
- Understanding the long-term neurodevelopmental concerns of infants with HIE who remain on AEDs after discharge would inform clinical guidelines for discontinuation

HYPOTHESIS

Infants with HIE who remain on AEDs at discharge will have significantly worse neurodevelopmental outcomes despite of severity of illness

METHODS

- A retrospective cohort study of infants diagnosed with moderate/severe HIE
- 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 were analyzed using Chi-square, Fisher exact, and Student's t-test as well as Poisson and logistic regression with significance set at $p<0.05$

RESULTS

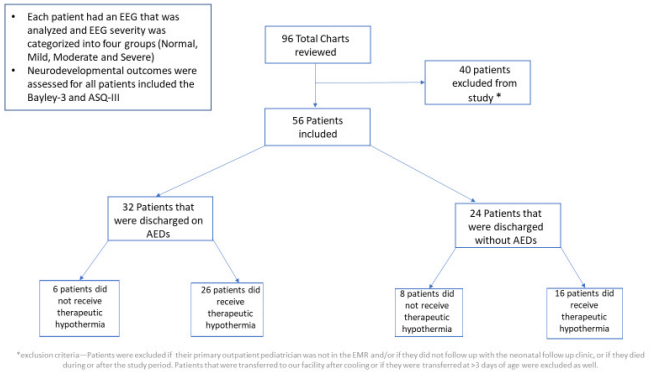


Figure 1. Flow diagram of patient inclusion and exclusion

Patient Characteristics	Off AEDs at discharge (%) N = 32	On AEDs at discharge (%) N = 24	p -value
Male Gender	**66.67**	**33.33**	**0.022**
Hypoglycemia	13.33	7.69	0.67
Sepsis	10	11.5	>0.99
Hypotension	30	42.3	0.34
Mode of Ventilation			0.054
Intubated	40	80	
CPAP	10	8.85	
High Flow Nasal Canula	6.7	0	
Nasal Canula	10	3.9	
Room Air	20	3.9	
10 min Apgar Score (Median (25th-75th percentile)‡	5 (4 - 7)	5 (4 - 7.5)	0.666
Length of Stay (Median (25th-75th percentile), days)‡‡	**11 (2 – 92)**	**21.5 (7 – 56)**	**0.0014**
HIE finding on MRI	**13**	**73**	**<0.0001**
HIE Grade			**<0.0001**
Mild	**43**	**7.6**	
Moderate	**13**	**38.5**	
Severe	**0**	**53.85**	
Abnormal Background EEG (during rewarming)	64.29	76.67	0.390
Antiepileptic Medication at Discharge	27.78	54.55	0.066
Antiepileptic Medication at 3 Months of Age	**37.50**	**78.95**	**0.037**

† Chi-square or Fisher Exact test, †† Student T-test, ‡ Mann-Whitney U-test, ‡‡ Poisson Regression

Table 1. Patient characteristics in relationship with neurodevelopmental outcome. Normal was defined as an ASQ score >50 and Bayley scores >75

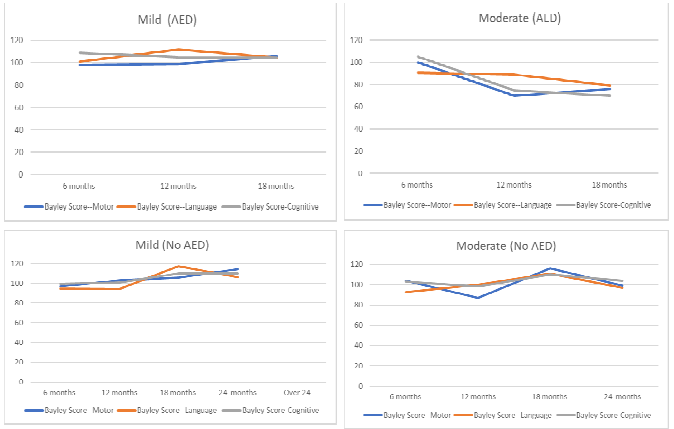
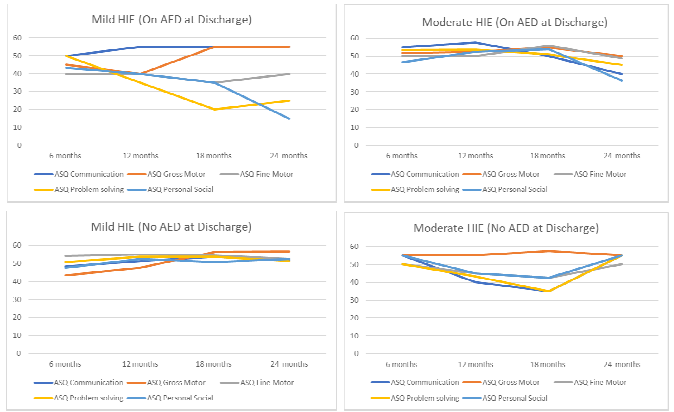


Figure 2. Bayley-III (Top) and ASQ-3 (Bottom) results over time in mild and moderate HIE on and off of AEDs. Use of AEDs at discharge was significantly associated with worse neurodevelopmental outcomes



CONCLUSION

- Extended AED use in infants diagnosed with HIE is associated with worse neurodevelopmental outcomes when corrected with illness severity.
- Trial of discontinuation of AEDs should be considered in infants with HIE prior to hospital discharge

Alexandra Wilson has documented no financial relationships to disclose or Conflicts of Interest to resolve.