Antiseizure medication at discharge in infants with hypoxic-ischaemic encephalopathy: an observational study

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Background:

- Antiseizure medications (ASMs) are potentially neurotoxic and adversely effect neurodevelopmental outcomes, independent of seizure burden.
- In 2011, the WHO recommended discontinuation of ASMs without a taper after 72 hours without seizure in infants with a normal EEG and neurological examination
- While the risk of epilepsy following acute symptomatic seizures in neonates is higher than in the general paediatric population. the incidence of epilepsy following acute symptomatic seizures, particularly when related to hypoxic-ischaemic encephalopathy (HIE), is relatively low (4%–18%) and frequently does not develop for months to years after birth.

Questions:

What is the association between discharge with or without ASM and death or moderate or severe disability in infants with HIE and seizures?

Study design:

- Retrospective study of infants enrolled in three National Institute of Child Health and Human Development Neonatal Research Network Trials of therapeutic hypothermia (22 US centers)
- Patients: Infants with HIE who survived to discharge and had clinical or electrographic seizures treated with ASM.
- Exposures: ASM continued or discontinued at discharge.

Results:

Of 302 infants included, 61% were continued on ASMs at discharge (range 13%–100% among 22 centres). Electroencephalogram use occurred in 92% of the cohort. Infants with severe HIE comprised 24% and 22% of those discharged with and without ASM, respectively. The risk of death or moderate-to- severe disability was greater for infants continued on ASM at discharge, compared with those infants discharged without ASM (44% vs 28%, adjusted OR 2.14; 95% CI 1.13 to 4.05).

Primary outcome:

Post discharge death or moderate-to-severe neurodevelopmental disability, based on neurodevelopmental assessment at 18–22 months.

Conclusion

In infants with HIE and seizures, continuation of ASM at discharge varies substantially among centres and may be associated with a higher risk of death or disability at 18–22 months of age.

Table 2 Hospital course

Characteristic	Discharged home on ASM	
	No (n=118)	Yes (n=184)
Severity of HIE*		
Moderate	92 (78%)	139 (76%)
Severe	26 (22%)	44 (24%)
Hypotension	37 (31%)	60 (33%)
Hypothermia treatment		
Normothermia	36 (31%)	54 (29%)
Hypothermia 33.5°C × 72 hours	25 (21%)	51 (28%)
Hypothermia 32°C × 72 hours	15 (13%)	18 (10%)
Hypothermia 33.5°C × 120 hours	14 (12%)	17 (9%)
Hypothermia 32°C × 120 hours	14 (12%)	11 (6%)
Hypothermia ≥6 HOL	14 (12%)	33 (18%)
Persistent pulmonary hypertension	33 (28%)	34 (18%)
Oliguria or anuria	28 (24%)	43 (23%)
Hepatic dysfunction	25 (21%)	36 (20%)
Bloodstream infection/septicaemia	2 (2%)	4 (2%)
Use of EEG	103 (87%)	174 (95%)
Presence of EEG seizure among infants with EEG†	28/82 (34%)	74/127 (58%)
Days receiving oxygen (days)‡	5 (2-13)	6 (2-13)
Length of stay (days)§	17.5 (11-24)	17 (12–25.5)
Abnormal neuroexam at discharge	51 (46%)	98 (57%)
Any abnormal additional findings at discharge	43 (39%)	71 (42%)
Discharge on tube/gavage feeds	23 (19%)	50 (27%)

Data given as n (%) unless otherwise specified.
*Severity of HIE is missing for one infant.
†Presence of EEG seizure is missing for 68 infants, as data were not available for the IH Study.
‡Days of oxygen defined as need for any supplemental oxygen (>0.21) by any means for any portion of the day.
§Length of stay defined as number of days between infant's date of birth and date of discharge or transfer.
ASM, antiseizure medication; EEG, electroencephalogram; HIE, hypoxic-ischaemic encephalopathy; HOL, hour of life; IH, induced hypothermia.