Reviewer's report

Title: Practice variation in anti-epileptic drug use for neonatal hypoxic-ischemic encephalopathy among regional NICUs

Version: 2 Date: 14 Feb 2019

Reviewer: Jarred Garfinkle

Reviewer's report:

The authors aim to assess intercenter variability around the treatment, and to some extent, the diagnosis of neonatal seizures in neonates with HIE.

Abstract: no issues

Introduction: no issues. Only a comment that it may be worth providing evidence from other diseases or populations that identifying ICV is the first step in improving care.

The discussion of seizure management is important, but can be found in review articles.

Methods: No issues. One comment:

How were aEEG results surmised from chart review? My own experience is that aEEG results are not always adequately documented in the medical chart. Is it possible that some "clinical seizures" were also detected on aEEG but not documented in the chart as such? Lack of aEEG documentation could, perhaps, explain the high rate of "clinical seizures."

Results:

- Page 9: Was there a standardized definition of status epilepticus across centres?

- Did the proportion of babies with mild and/or moderate encephalopathy increase over time? Perhaps this could account for the reduction in AED use over time, and the stability over time of electrographic seizure rate despite increase in cEEG usage.
Discussion:

Page 14: "Our data reinforce that cEEG should be obtained in all mild cases of encephalopathy as EEG seizures would indicate that the eligibility for TH had been met." Would aEEG not be sufficient? If aEEG demonstrates continuity and/or SWC, would the baby still need a cEEG? I'm not sure that the data provided here reinforces need for cEEG in all babies with mild HIE, particularly since this study looks at quaternary hospitals only. Need for cEEG in every baby with mild encephalopathy may suggest that all babies with mild encephalopathy should be transferred to a quaternary care centre.

Page 14: "That some clinical seizures did not have EEG correlates" may be better phrased as "That some clinical seizures occurred in the absence of electrographic seizures." Again, I would like to know if the authors were confident in their ability to discern aEEG seizures from chart review.

Page 17, last paragraph: It may not be worth speculating as to the higher unadjusted rate of seizures in neonates who were selectively head-cooled since the practice is of course centre-specific and the analysis here did not adjust for centre. Perhaps this hypothesis can be further explored in a separate analysis.

Overall, I am not sure that the cost analysis of AEDs is helpful in achieving their stated objective. I understand that calculating cost is novel, but I'm not sure it adds to the paper. The cost appears to refer to the cost of the drugs only, which is minimal, and does not represent the costs associated with seizure detection and other aspects of seizure management.

Are the methods appropriate and well described?
If not, please specify what is required in your comments to the authors.

Yes

Does the work include the necessary controls?
If not, please specify which controls are required in your comments to the authors.

Yes

Are the conclusions drawn adequately supported by the data shown?
If not, please explain in your comments to the authors.

Yes
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