Reviewer’s report

Title: Efficacy of Levetiracetam for Neonatal Seizures in Preterm Infants

Version: 0 Date: 10 Oct 2017

Reviewer: Sarah Mulkey

Reviewer's report:

I thought this was a well thought out retrospective study which addresses an important area in the treatment of neonatal seizures among preterm newborns. Some areas to improve the manuscript:

1. In the abstract background, I am not sure about the word "controversial". I agree that efficacy is not as good as we would like, but there are fairly agreed upon recommendations for the management of neonatal seizures. Suffice it to say that there is not a standard anti-seizure drug protocol for the treatment of neonatal seizures; however phenobarbital continues to remain as the usual first line agent despite its mediocre efficacy and side effect profile.

2. The background section can be made more concise.

3. Background sentence "neonatal seizures occur more often during the neonatal period than any other time of life." This should simply say, Seizures occur during the neonatal period more often.

4. Consider using the newer term "anti-seizure medication" as opposed to anti-epileptic medication as preferred by the ILAE.

5. In Introduction, levetiracetam, studies by RH. Haas should be cited in sentence discussing pharmacokinetics and safety profile.

6. Results section, first paragraph can be shortened. Birth weight ranges are all presented in Table 1, so do not need to write out.

7. Results, Onset of Neonatal seizures: Neonatal seizures occurred from 30 min to 45 day after birth seems different than the enrollment criteria of seizures within 28 days or within the neonatal period. The timing of seizures mentioned in that paragraph may also go into Table 1 and shorten the results text.

8. Results, response to AED treatment section. Table 1 is mentioned for the response to treatment with LEV, but I did not see those results in Table 1. Did you mean Figure 1?

9. Discussion, "due to cerebral pathology, preterm infants of less than 30 weeks have a higher incidence of seizures...". This statement needs a reference. Did you look at this in your own data among the included infants? Are seizures in this group increased due to brain immaturity?

10. Discussion can be made more concise. For example, too much detail presented in paragraph beginning with, "Antiepileptic drugs such as N-methyl-D-aspartate..."

11. How do your findings of efficacy compare to that of phenobarbital for first line in preterm newborns? I think that is a big question among clinicians that care for preterm newborns who may be considering changing to use levetiracetam over phenobarbital as first line.

12. It may be good to point out that the pk study of R. Hass (Ref 26-Sharpe CM et al) suggests that a q8 hour dosing schedule be used in the first week of life as opposed to q12 (twice daily) for newborns. This study was performed though in term newborns.

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.

Unable to assess

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

Yes

**Are you able to assess any statistics in the manuscript or would you recommend an additional statistical review?**
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I am able to assess the statistics

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