Author's response to reviews

Title: What is the easier and more reliable dose calculation for iv Phenytoin in children at risk for developing convulsive status epilepticus, 18 mg/kg or 20 mg/kg?

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Author's response to reviews: see over
Cover letter 22-03-2013

Dear Catherine Olino and Elena Chiappini for Biomedcentral
Re our manuscript “What is the easier and more reliable dose calculation for iv Phenytoin in children at risk of developing convulsive status epilepticus, 18 mg/kg or 20 mg/kg?”

Responses to reviewers comments:

Reviewer 1 Philippe Hubert
Essential revisions
1. Corrected “sequelae”
2. Added “(SHO)”
3. Corrected “collected”
4. Added “hypotension”

Discretionary revisions
5. Substituted in line with the suggestion “Objective: With the convulsive status epilepticus in children guideline due for renewal, we wondered if a Phenytoin dose of ‘20 mg/kg’ would be easier to calculate correctly and therefore safer than the previously recommended ‘18 mg/kg’ dose. An educational exercise was therefore undertaken to assess the ease of dose calculation.”
6. We preferred to keep original “The 2000 guideline...”

Reviewer 2 Anna Rosati
Discretionary revision
7. Added discussion of need for a study comparing 18 mg/kg vs 20 mg/kg. We now discuss this question and recommend that an RCT would be too costly and cumbersome for such a minor difference in dose, but that routine surveillance (clinical audit) would be useful to compare 18 mg/kg and 20 mg/kg as used in different units, at least major adverse events would be recorded this way.

Reviewer 3 Arif Khan
Essential revisions
8. We have added more detail on the effect of the randomised order.

Discretionary revisions
9. We have now referenced the Summary of Product Characteristics.
10. The variable regimes used in different hospitals is well known but we could not find a suitable primary reference, we have stated this in the introduction, ref 8, and ref 7 also includes this observation.
11. We found no studies, we think it is clearly enough stated as it is.
12. We think our phrase about errors greater than 10% is adequate.
13. Reference 7 is 2000, the working party have not published a revision yet, however the international Advanced Paediatric Life Support course, recently changed their recommendation to phenytoin 20 mg/kg. We have explained this recent development in a subsequent paragraph, and reference 20.
14. We do not think we should say which guidelines should adopt 20 mg/kg, rather we recommend this dose and present evidence that this dose is less prone to calculation error.
15. The Cochrane reviews do not cover phenytoin for this indication, the difference between 18 and 20 mg/kg is so small as to be unlikely to give an overall pharmacological difference,
especially if weights are estimated rather than measured as will happen in an emergency with a convulsing child. This discussion has been expanded to include that point.

16. Related research recommendations are now discussed as suggested by reviewer 2.

Essential correction

17. “Sequeleae” now corrected.

Your required changes

1 Ethics: This was not experimental research, this was an educational exercise, so no ethics committee approval was required. This is now stated in the methods.

2 Consent: no written consent was obtained, this was not clinical research, and the exercise took about 5 minutes for each participant. This is now stated in the methods.

3. Competing interests: section added

4. Authors information: section added

5. Title page: revised

6. Abstract: revised

7. Acknowledgements: added, study was unfunded

8. Figure titles: revised

With best wishes

William

Whitehouse