Reviewer’s report

Title: Effects of valproic acid on skeletal metabolism in children with epilepsy: a systematic evaluation and meta-analysis based on 14 studies

Version: 0 Date: 19 Aug 2019

Reviewer: Research Square

Reviewer's report:

STATISTICAL REVIEWER ASSESSMENT:

Is the study design appropriate for the research question (considering whether the analyzed population accurately reflects the design and whether you see any problems with control/comparison groups, e.g., likely confounders)?

No - there are minor issues

Are methodologies adequate and well implemented (considering whether assumptions are addressed and whether analyses are robust)?

Yes - methodologies are adequate and well implemented, assumptions are addressed, analysis is robust

Are the analyses adequately communicated (considering whether reporting details are adequate and whether figures and tables are well labeled and described)?

No - there are minor issues

Does the interpretation accurately reflect the analyses without overstatement (considering whether limitations/bias are acknowledged and whether accurate descriptors, e.g., 'significant', are used)?

Yes - interpretation accurately reflects analyses, limitations/bias are acknowledged, accurate descriptors are used

Could an appropriately REVISED version of this work represent a statistically sound contribution?

Probably - with minor revisions

STATISTICAL REVIEWER COMMENTS:

The authors performed a systematic review and meta-analysis according to PRISMA statement. Overall, the study is performed well and there is no flawed mistake. The study has sufficient steps according to PRISMA statement, including searching, screening, data extraction, quality assessment, and data analysis. The authors used a relevant scale (the Newcastle-Ottawa Scale) to assess the quality
of included studies and sufficient statistical analysis methods. However, the statistical method should be clarified more about the sensitivity analysis. In addition, the authors should not combine different outcome in a meta-analysis (figure 2, 3, 4, and 5).

REQUESTED REVISIONS:

I hope these below comments could make this manuscript better:

1- In the abstract, the authors should report the effect size (SMD and 95% CI) along with (or instead of) the p-value.

2- In the statistical analysis section, the sensitivity analysis should be clarified more, eg which method was used to perform the sensitivity analysis.

3- In the results section, the heterogeneity test section might be added to each of the outcomes analysis, instead of separating into a section.

4- In figure 2, 3, 4 and 5, there should be no "overall" result from meta-analysis. These 8 outcomes should be analyzed separately.

5- There are several typos needed to revise.

ADDITIONAL REQUESTS/SUGGESTIONS:

No

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

No

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

No

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?
If an additional statistical review is recommended, please specify what aspects require further assessment in your comments to the editors.

I am able to assess the statistics
Quality of written English
Please indicate the quality of language in the manuscript:

Acceptable

Declaration of competing interests
Please complete a declaration of competing interests, considering the following questions:

1. Have you in the past five years received reimbursements, fees, funding, or salary from an organisation that may in any way gain or lose financially from the publication of this manuscript, either now or in the future?

2. Do you hold any stocks or shares in an organisation that may in any way gain or lose financially from the publication of this manuscript, either now or in the future?

3. Do you hold or are you currently applying for any patents relating to the content of the manuscript?

4. Have you received reimbursements, fees, funding, or salary from an organization that holds or has applied for patents relating to the content of the manuscript?

5. Do you have any other financial competing interests?

6. Do you have any non-financial competing interests in relation to this paper?

If you can answer no to all of the above, write 'I declare that I have no competing interests' below. If your reply is yes to any, please give details below.

This reviewer has been recruited by a partner organization, Research Square. Reviewers with declared or apparent competing interests are not utilized for these reviews. This reviewer has agreed to publication of their comments online under a Creative Commons Attribution License attributed to Research Square and was paid a small honorarium for completing the review within a specified timeframe. Honoraria for reviews such as this are paid regardless of the reviewer recommendation.

I agree to the open peer review policy of the journal. I understand that my name will be included on my report to the authors and, if the manuscript is accepted for publication, my named report including any attachments I upload will be posted on the website along with the authors' responses. I agree for my report to be made available under an Open Access Creative Commons CC-BY license (http://creativecommons.org/licenses/by/4.0/). I understand that any comments which I do not wish to be included in my named report can be included as confidential comments to the editors, which will not be published.

I agree to the open peer review policy of the journal