Reviewer’s report

Title: Caffeine is a Risk Factor for Osteopenia of Prematurity in Preterm Infants: A Cohort Study

Version: 1 Date: 07 Nov 2016

Reviewer: David R. Weber

Reviewer's report:

1) Thank you for the clarifying that two readers reviewed films. I still think it would be appropriate to provide the results of interrater reliability analyses.

2) Regarding question of how OP changed over time - I don't think this question has been adequately answered. Figure 1 shows probability of OP by caffeine dose. I understand that cumulative dose goes up with time, but there is a lot of variability in duration in the population (60 +/- 45 days) so I don't think this plot is necessarily showing the effect of time on OP in the entire cohort. Can't you plot probability of OP against time (weeks)? If caffeine exposure is important, I would expect that plot (OP vs time) to look different than figure 2 (OP vs caffeine weeks).

3) Perhaps I am misunderstanding how you handled "time" in your longitudinal models - maybe this can be clarified in methods section?

   - The basic question I would like to know is: "does OP score get worse (or probability of OP become more likely) in this cohort over time", irrespective of caffeine or other covariates… I think that would help readers interpret your findings.

4) I still don't see the n values in the figures or legends…

5) Are the probabilities shown in figures 1 and 3 statistically different between the two gestational age groups? If so, can you provide confidence intervals, p-values, or some other means of denoting statistical differences in the figures?

6) I found the discussion in the "response to reviewer 1" of why no caffeine unexposed patients were included to be informative, I would recommend including an abbreviated version in the text of the manuscript.

7) I like the discussion of potential mechanism for the dose*gestational age interaction - I would just recommending changing "can" to "may" in line 48, page 16, since you didn't actually measure ½ life in this study.
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.

Yes

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

No

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 recommend additional statistical review

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