Reviewer's report

Title: Efficacy of N,N'bis-(2-mercaptoethyl)isophthalamide on mercury intoxication: A randomized controlled trial

Version: 0 Date: 27 Sep 2017

Reviewer: Erik Jørs

Reviewer's report:

Dear Authors!

Thank you for your article, it is of importance to ASGM miners and others suffering from mercury poisoning. It should be published but I think some major revisions needs to be done before the paper is ready for publications. My comments you can see below.

The paper test the therapeutic effect of a chelating agent (NBMI) to lower symptoms and signs of mercury poisoning and to decrease mercury burden in the body by improving the excretion of mercury.

Abstract: no comments

Background: no comments

Methods:

line 104-110

Discretionary revision - It might be of value to include the numbers of individuals with urine samples collected, number of individuals with mercury levels >15myg/l and number of individuals included meeting the selection criterias. I know you have this information in fig 2 as an appendix, but for the reader it might be easier to have this information here.

line 128-134

Major revision - I miss an explanation of possible mercury exposure during the testing - were persons all included allowed or not allowed to continue mining, burning amalgam etc. Because if some were exposed to mercury during this trial and others not, or they were exposed to a different degree then the interpretation of the results in the study becomes very difficult. An explanation is needed and it needs to be taken up in the Discussion as it can have an impact on symptoms and mercury levels in blood and urine.
Minor revisions - I suggest you either present the 'total fatigue score' or 'the mental and physical fatigue scores' as presenting all three scores is a repetition taking up too much space in Results without giving any additional information.

You make a comparison between baseline and day 15, why not also include baseline and day 45?

Major revisions You summarise continous variables in mean, SD, median, range (min-max) in the tables 1-3. Again it takes a lot of space and I think presenting only mean or median value with range (min-max) is sufficient.

You use the Wilcoxon test to compare two independent samples (threatment group with placebo group) - I think the correct test would be a t-test if data are normally distributed or a Mann-Whitney non-parametrical test for such a comparison. The Wilcoxon test you can use to compare the same group (same sample) before an after treatment, which is also relevant for you as you can compare the test results within the same group at baseline with the results at day 15 and with day 45 to see if any significant change has occurred. Or if normally distributed you can use the paired t-test.

Results

Minor revision - I think some of this information belongs to Methods.

You mention fig 2 but where is fig 1, and you might move this flow chart fig 2 into Methods as it is quite informative.

Major revision Table 1 In text you call it table I in headline to table you call it table 1 and this difference is seen for all tables and text please correct so you use the same nomenclature.

In table 1-3 you should simplify it as said above with only mean (or median) and Range I suggest. In table one you can leave out sex and ethnicity as all are males and hispanic of origin (although I would think some were native indian as well?). You can just mention in text all included were males and of hispanic origin. What is missing in table is BMI as you mention it in Discussion it should be included here as well. In table 2 you have both yes and no numbers and percentages, to save space you could only mention the 'yes numbers' then reader will now the 'no numbers' as well. In all tables 1-3 I miss the p-values to see the significant differences between the three groups.
Major revision I suggest you only present the MIS and then move the individual score items to the annex or present them in a table.

In table 3 you present baseline data on mercury in urine and MIS score, this table could be changed into two tables to present data from three groups on scores (MIS, catsys, and fatique) at baseline, day 15 and 45 in one table and biomonitoring values at baseline, day 15 and 45 in another table. I think it would give a better overview.

Major revision Here is a repetition from Methods, it should only be in Methods.

Table 5 if you believe adjusted myg/g creatinine is the most correct way to present urine mercury - then why present the unadjusted urine measures of Hg? I miss some p-values in this table.

Discussion

Minor revision - I think you statement of a clear positive effect is too optimistic - what we have seen is an improvement in physical fatigue score and unadjusted Hg in urine in the 300 mg group. And as you later point out there might be some problems with measuring subjective symptoms - so I suggest to modify this statement.

Major revision - In the discussion I miss a discussion on what should be expected when treating with NBMI - I could imagining an increase of blood and urine levels of Hg as it is released from the fat tissue into blood and eventually into the urine or if it goes fast you might expect a decrease after or during the treatment? Some discussion about this would be nice to have especially for readers who are not familiar with chelating treatment of Hg poisonings.

Major revision - I think we miss a good paragraph on strengths and weaknesses of this study at the end of the discussion although some are mentioned. But the size of the study is clearly a limitation, and different Hg exposures during the trial if that is the case is another serious limitation.

Best regards, and hope to see a corrected manuscript soon,
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