Author's response to reviews

Title: A Systematic Review and Meta-Analysis of the Use of Oral Zinc in the Treatment of Hepatic Encephalopathy

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Author's response to reviews:

Dear Editor,

We read your kind comments for the article entitled "A Systematic Review and Meta-Analysis of the Use of Oral Zinc in the Treatment of Hepatic Encephalopathy"

Regarding the Editor's comments the following suggestions were considered

English language correction are requested
- The language was reviewed and corrected.

Abstract/text.Database “The Cochrane Library”, it is better to substitute this with “CENTRAL “both in abstract and text.
- The term CENTRAL was used in the abstract and the manuscript.

Measures of treatment effect and data analysis- Line 122-124 “The trials were explored to identify variations in the randomization process. The preferred design was a simple parallel group design, although other designs such as cluster randomized trials, crossover trials, and repeated measurements during the trial were also analyzed. “This sentence is really unclear.
- We appreciate your suggestion. This sentence was cryptic and did not provide additional information, was deleted.

Assessment of heterogeneity, line 130-131 “Whenever heterogeneity was detected, subgroup analysis was performed to assess the effect of potential sources of heterogeneity on the main results. “ This was not done. Heterogeneity is 50% in the Forest plot for the number connection test results, but where is sub-grouping reported?
- We perform subanalysis by year of the study and sample size, but no
differences were observed. This sentence was included in the manuscript "Some heterogeneity of effects (I²=50%) was observed, and stratified analyses were conducted by year of the study and sample size, but no change in the direction or significance of the effect was observed (data not shown)."

Assessment of reporting biases line 133 “A funnel plot estimating the precision of trials (plot of logarithm of the RR against the sample size) was used to evaluate asymmetry and to detect potential publication bias. In addition, the standard normal deviate (SND), defined as the RR divided by its standard error, was regressed against the estimate’s precision (regression equation: SND = a + b # precision) to quantify the bias captured by the funnel plot. “ This is not reported in the result section, where are reporting bias reported?

- This information was included in the manuscript. The next sentence was included "The funnel plot shows no evidence of publication bias (additional figure 2)."

Sensitivity analysis – line 140 “We analyzed the data using both fixed-effect and random-effect model meta-analyses. When both models produced similar estimates, the fixed-effect result is reported; otherwise, we report the results from both analyses. Outcomes were analyzed as reported in the trial, either per protocol or as an intention-to-treat analysis. “ results of the fixed-effect compared to random-effect model meta-analyses are not reported in the text.

- This analysis was included as addition figure 1.

“The available trials had important methodological flaws “ this sentence is in contrast with what stated in results: line 166-168” Risk of bias within studies The risk of bias was unclear in all trials due to lack of information, and was not possible to assess if the trials were on high or low risk of bias “

-This sentence is confused and was changed to "Available trials studied heterogeneous outcomes and failed to measure critical outcomes such as quality of life. This hinders the ability to draw conclusions about the value of oral zinc supplementation in the treatment of hepatic encephalopathy"

Needs some language corrections before being published

-English language correction was done.