Reviewer’s report

Title: Nutritional adequacy of a novel human milk fortifier from donkey milk in feeding preterm infants: study protocol of a randomized controlled clinical trial

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Reviewer: Paulina Correa-Burrows

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This paper describes a RCT aiming to investigate whether donkey milk could be a suitable ingredient for developing a human milk fortifier for the nutrition of preterm infants. So far, donkey milk has only been tested as an alternative for children allergic to cow's milk protein. The research question is well crafted and contains all the major elements to properly assess the quality of both the intervention and its findings: population, intervention, comparisons, and primary and secondary outcomes. The trial has ethical approval and was duly registered. The fact that the trial is single-blind is reckoned by the authors, but there's nothing they can do about it. The introduction provides all the essential elements to properly understand the rationale of the study. The protocol is well written, no language editing is needed, and it was easy to read it, so the findings should be easily communicated to a non-academic audience, let's say, parents, clinicians and policymakers. All competing interest have been disclosed. I just have a few minor suggestions which are mostly intended to add to the paper.

1. Methods section: Please, state the trial was registered and provide the registration number.

2. Methods section >> Page 8, Line 58 >> Informed written consent should not be considered an inclusion criteria because this is an ethical requirement. Inclusion criteria refers to characteristics that the prospective participants must have if they are to be included in the study.

3. Methods section >> Page 10, Line 57 >> Outcome measures: the number of feeding intolerance episodes is reported as both a primary and secondary outcome. Is that a slip-up?

4. Methods section >> Page 12 Line 51 >> Statistical analysis: The whole statistical analysis will be probably done using SAS, not just the model fitting.

5. Methods section >> Page 12 >> Statistical analysis: The type of statistical test to compare groups will depend on the type of variable (continuous or categorical) and their distribution. If the primary variable is the number of episodes of intolerance, the variable is ordinal and a Mantel-Henzel test should be used. In the case of the secondary outcome variables, when comparing by groups the statistical test in the bivariate analysis will depend again on the type of variable and its distribution. It would also be convenient to compare these variables. It seems reasonable to start with a bivariate analysis and if it is
necessary to adjust for other influences to move to the linear model. In all outcome types, it will be necessary to use repeated measures analysis not only in the case of the secondary outcomes, to account for the correlation that exists between the observations in the same individual. I think it would be much easier for the authors to be assisted by a statistician to write this section.

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An article of importance in its field

**Quality of written English**
Please indicate the quality of language in the manuscript:

Acceptable

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