Author's response to reviews

Title: A systematic review and meta-analysis of the effect and safety of ginger in the treatment of pregnancy-associated nausea and vomiting

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Author's response to reviews: see over
Dr Nagaraj Nagathihalli
Nutrition Journal Editorial Team

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REVISIONS: MS: 5815604521146107 - A systematic review and meta-analysis of the effect and safety of ginger in the treatment of pregnancy-associated nausea and vomiting

The authors wish to thank the reviewers for the constructive comments to improve the manuscript and for the opportunity to revise the document to be considered for publication. Below please find a list of responses to the reviewers' comments/critiques and reference to the changes that have been made in the manuscript, as relevant.

Reviewer #1: Ronna L Chan

Major compulsory revisions:

“Methods, Types of studies and participants: It was indicated by the authors that ‘studies were selected regardless of publication status’. Please provide clarification in regards to publication status.”

As per the study protocol, the authors planned to include studies regardless of publication status. Ongoing and unpublished trails (as for example available at www.currentcontrolledtrials.com), were thus considered for inclusion, but none were relevant for inclusion in this systematic review. Therefore, to avoid further confusion in this regard, the authors decided to remove this sentence from the paper (as in the end no unpublished data were included) (removed on page 7 under “Types of studies and participants”).

“Methods, Types of studies and participants: The authors indicated that publications included in this systematic review and meta-analysis consisted of women who varied in maternal age and gestational age of pregnancy. Published literature has shown associations between gestational age and the presence and severity of NVP. Likewise, gestational age of pregnancy (e.g. later) is often an indication on the health of the pregnancy and adverse pregnancy outcomes (e.g. spontaneous abortion or SAB) can be influence by maternal age. Please comment on these inclusion criteria and the potential influences by these variables on analyses results on the association between ginger use and NVP and on the association between ginger use and SAB”
The authors acknowledge the fact that maternal age and stage of pregnancy can indeed affect the prevalence of Nausea and Vomiting of Pregnancy (NVP) or adverse outcomes, such as spontaneous abortion. These events may, however, indeed still occur in any pregnancy stage or maternal age. As is relevant for all Systematic Reviews (SRs), we could only include and analyze the trails (and the specific methodology they employed) that are available. Not all trails specified gestational stage or maternal age. Therefore, our criteria were to include women who were suffering from NVP, regardless of age or stage of pregnancy, to include as many subjects as possible (small clarification included on page 7). This systematic review reported very few cases of adverse events and side effects. Ginger did not pose a risk for any major side-effects or adverse events occurring, thus no risk for any serious complications detrimental to the mother or fetus.

“Results, General response to treatment: Please provide information on variables measured for general response to treatment.”
The authors note this comment with appreciation and have added additional paragraphs on pages 18 and 19 highlighted in blue, to indicate new text.

Minor Essential Revisions
“Abstract, under results: “Ginger did not pose …..or vitamin B6 (RR=0.49, 95% CI: 0.17-1.42).” Awkward wording, please reword.”
The authors note the comment and made relevant changes. See yellow highlighted text on page 2.

“Introduction and Rational for Review, first and second paragraphs: Reorder references to ascending order.”
The authors note this comment with appreciation; all references were corrected to be in ascending order throughout the document.

“Subgroup and sensitivity analyses: For consistency throughout the manuscript, please indicate dosages in milligram instead of gram or if the authors prefer, in gram instead of milligram.”
The authors note this comment with appreciation; all dosages were corrected to be indicated in milligrams.

“Discussion, Primary outcomes – symptomatic relief of nausea: Citations are needed for the “various individual studies concluded that ginger had beneficial effects on nausea....”
Noted and corrected, highlighted in yellow on page 24.
Reviewer #2: Maretha M Opperman

Major Compulsary Revisions

“The forest plot and Table 1, which describe the characteristics of the included studies, are very comprehensive and easy to understand. However, significance of the main results have not been indicated in Table 1. It will be helpful if significance can be indicated e.g. Chittumma - Ginger was significantly/non-significantly more effective than vitamin B6 for relief from NVP.”

The authors note this comment with appreciation. The authors edited Table 1 to include significance (or not) in the last column, highlighted in blue to indicate new text.

“In some instances, as discussed in the manuscript, it is not always preferable to use forest plots for reporting results. It will therefore make more sense to me if the studies, which were pooled in a meta-analysis, are tabulated. The reason be that it is difficult to follow the natural flow of the results. It also takes quite some time to read through the results. It would be of great help if the results can be summarized in a table and only the most important findings emphasized in the text. Please see suggestions below on how to compile the suggested table.

Table 2: Pooled estimates of effect size (95% confidence intervals) expressed as weighted mean difference for the effects of ginger vs placebo”

The authors note this comment and welcome the excellent suggestion to reduce text and to summarize results. The authors have retained a limited number of forest plots (for variety) and further summarized all adverse events and side-effects for all comparisons in a new Table 2. Minimal text was retained, with the majority deleted and summarized in Table 2. See page 19 and 22 highlighted in yellow to indicated edited text.

“The first paragraph of the discussion is merely a repetition of the limitations of the study. This paragraph should be incorporated under the heading “Strengths and limitations of the study”.

Noted with appreciation. The whole discussion section was edited. Strengths and limitations paragraph also edited on page 28.

“The authors need to ensure that the discussion is not just a repetition of results or facts mentioned in the introduction. Authors should also employ other literature on ginger and pregnancy for the discussion.”

Noted with appreciation. Discussion paragraphs edited and highlighted in yellow to indicate edited text and blue to indicated new text, on page 24-28.
“The authors should perhaps reconsider the necessity of this review OR approach this topic from a different angle because the following peer reviewed articles with very similar objectives were published in the recent past:


Please comment on how this specific manuscript can further contribute to the topic of ginger and pregnancy apart from the publications indicated above.”

Thank you for this important comment. We feel our systematic review makes an important and original contribution as compared to the mentioned reviews ours is the only one to include all comparisons (placebo, Vitamin B6, dimenhydrinate and metoclopramide) whereas the mentioned reviews only compared ginger to placebo (in both cases also including one study comparing ginger to Vitamin B6). We have thus considered all comparators and active ingredients. Our systematic review is the most up-to-date (last search July 2013) and includes 12 individual trails (compared to 4 and 6 in the other 2 mentioned systematic reviews).

To paint the full picture we have added these 2 systematic reviews to our discussion section and reference list. Please see the edited discussion section: Yellow highlighted text on page 26, and blue highlighted text on page 26 and 27.

Minor Essential Revisions

“The author can be trusted to make these. For example, missing labels on figures, the wrong use of a term, spelling mistakes.”

The authors thank the reviewer for these comments. The labels on the figures were according to the specification of Nutrition Journal, added at the end of the manuscript text, and not below each figure. The authors did, however, add the labels to ease the reviewing process. The manuscript as a whole was checked for spelling/grammar errors and corrections made as appropriate.

“H. pylori change to Helicobacter pylori and abbreviated as H. pylori”

Noted and corrected. Highlighted in yellow to indicate edited original text.

“Zingiber officinale Roscoe not Zingiber Officinale Roscoe”

Noted and corrected. Highlighted in yellow to indicate edited original text.
“Indicate in text references briefly e.g. [8-12] not [8, 9, 10, 11, 12]”
Noted and corrected. Highlighted in yellow to indicate edited original text.

“Second line from below, page 26: The term “significantly” is not used in the correct context here. Significance means p<0.05 which is not the case with the reported results. Please also check the rest of the manuscript where the term “significantly” is used.”
Noted and corrected throughout the document.

The authors thank the reviewers for their time in providing constructive comments to improve this manuscript. We hope that these comments, additions and revisions address the reviewers’ critiques satisfactorily. We look forward to receive feedback on our revised manuscript.

Yours sincerely,

Estelle Viljoen
(On behalf of the author team)

Footnotes:
- Yellow highlight in the manuscript indicates edited original text.
- Blue highlight in the manuscript indicates new text added based on the reviewers’ comments.