Reviewer’s report

Title: Lack of efficacy of pomegranate supplementation for glucose management, insulin levels and sensitivity: evidence from a systematic review and meta-analysis

Version: 0 Date: 07 Aug 2017

Reviewer: Asad Abbas

Reviewer's report:

This study is a systematic review and meta-analysis of studies exploring the effect of pomegranate products on glycemic control, insulin levels, and sensitivity.

Diabetes mellitus/glucose intolerance is a chronic disease in which various alternative treatments of unproven efficacy are often tried either alone or in combination with other medications. There have been claims about the efficacy of pomegranate products which are put to scrutiny in this study, which makes the study relevant.

Title:

1. The PRISMA guidelines state that manuscript should be identified as meta-analysis and systematic review, please include that in the title. As fasting blood insulin was one of the primary outcomes, it should be included in the title.

Abstract:

2. Abstract is succinct and summarizes the study, however it should be updated to include the changes that I have described below.

Background:

3. While the scope of problem of diabetes mellitus and importance of glycemic control is described appropriately, majority of studies included in this trial are not done on diabetic individuals. The background should include more details about the insulin resistance and primary prevention in healthy individuals.

4. The sentence, Line 113, "Encouraging findings from experimental research…" needs references to more than one study, so does the next sentence, line115, "several observational studies…” in which references to all the original studies should be provided.
5. The next sentence, Line 116, should be rephrased to "However, the effects of pomegranate on insulin and glucose metabolism in humans are inconsistent and their precise role in the management of hyperglycaemia has not been fully established". The sentence also need references.

6. The last sentence describes the objective of the study. This should be done under a separate sub-heading and primary and secondary objectives need to be more explicitly described with reference to participants, interventions, comparators, and outcomes (PICO)

Methods:

7. Is the protocol for review available to public and were there any deviations from the protocol?

Eligibility Criteria:

8. The eligibility criteria should precede search strategy in the manuscript.

9. The eligibility criteria should be described under separate subheadings of types of study, participants, intervention and outcome measures. The inclusion criteria do not define the type of participants which must be included.

Data Sources and Search strategy:

10. There is inadequate description of the search strategy. Please mention who was involved in the creation of search strategy, and was it peer reviewed?

11. Please provide a draft of search strategy of at least one database either in the main text or as an appendix.

12. Please mention if the trial registers were searched for ongoing trials and whether PROSPERO was searched for ongoing or recently completed related systematic reviews. Was the search restricted to studies in English language?

Data Extraction:

13. The description of data extraction process is inadequate. Please describe the mechanisms that were used to manage data in the review including use of computer programs or software
if any. Please describe the selection process, who was involved in the selection and data extraction and how were the differences (if any) resolved.

Assessment of methodological quality:

14. The risk of bias tool used to assess the methodological quality is robust and used appropriately, however, there is indirectness of evidence in terms of differences in population and differences in intervention, due largely to a lenient inclusion criteria, there is also inconsistency in effect and effect size across studies. While subgroup analysis and meta-regression will help address some of these issues, a tool like GRADE that helps rate quality of evidence for each outcome across studies taking into account the above factors is needed to help make more objective decisions about the results.

Statistical analysis

15. Choosing a meta-analysis model based on statistical heterogeneity is not recommended [1]. There exist significant clinical and methodological differences in the pooled studies to warrant the use of random effect model only.

Results:

Identification of studies:

16. The boxes in figure one needs to be rearranged. The text in line 199 need to be revised so it describes what's represented in the figure.

17. Please explain why this 2013 study by Banihani et al was not included [2].

Study characteristics

18. Please mention the names of studies studying the outcome of interest in the text.

Overall effect of pomegranate on glucose control and insulin sensitivity

19. The study was Cerda et al does not mention fasting blood glucose as the outcome measure, were the authors contacted to confirm that glucose measured was actually fasting?
20. The subgroup analyses and sensitivity analysis is adequate and takes into account most confounders.

Discussion:

21. Discussion should provide more information on how pomegranate came to be used in the prevention and management of diabetes including more references for studies in human and animals.

22. Include examples of other herbal medications used in diabetes, and discuss if their use can cause any potential harm.

Figures:

23. Figure 1 should be corrected as above

24. Figure 3 should include number of participants for each study, their mean and SD (or as applicable). Each forest plot should be labeled to indicate the model of meta-analysis used.

Language errors:

25. There are several language errors throughout the manuscript that need editing.

REFERENCES


Level of interest
Please indicate how interesting you found the manuscript:

An article whose findings are important to those with closely related research interests
Quality of written English
Please indicate the quality of language in the manuscript:

Not suitable for publication unless extensively edited

Declaration of competing interests
Please complete a declaration of competing interests, considering the following questions:

1. Have you in the past five years received reimbursements, fees, funding, or salary from an organisation that may in any way gain or lose financially from the publication of this manuscript, either now or in the future?

2. Do you hold any stocks or shares in an organisation that may in any way gain or lose financially from the publication of this manuscript, either now or in the future?

3. Do you hold or are you currently applying for any patents relating to the content of the manuscript?

4. Have you received reimbursements, fees, funding, or salary from an organization that holds or has applied for patents relating to the content of the manuscript?

5. Do you have any other financial competing interests?

6. Do you have any non-financial competing interests in relation to this paper?

If you can answer no to all of the above, write 'I declare that I have no competing interests' below. If your reply is yes to any, please give details below.

I declare that I have no competing interests

I agree to the open peer review policy of the journal. I understand that my name will be included on my report to the authors and, if the manuscript is accepted for publication, my named report including any attachments I upload will be posted on the website along with the authors' responses. I agree for my report to be made available under an Open Access Creative Commons CC-BY license (http://creativecommons.org/licenses/by/4.0/). I understand that any comments which I do not wish to be included in my named report can be included as confidential comments to the editors, which will not be published.

I agree to the open peer review policy of the journal