

Author's response to reviews

Title: Assessment of soy phytoestrogens' effects on bone turnover indicators in menopausal women with osteopenia in Iran: a before and after clinical trial

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Author's response to reviews: see over

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Dear Dr Hiromichi Kumagai

Thank you for your nice and faithful comments on the manuscript "Assessment of soy phytoestrogens' effects on bone turnover indicators in menopausal women with osteopenia in Iran: a before and after clinical trial" (MS: 1272750712737803). We revised the manuscript according to the reviewers' comments, hope to satisfy them. The changes have been highlighted in the text. Also detailed list of revisions and point by point response to the reviewers is as follow:

Reviewer #1

1.General: There are other clinical studies done on bone density with soy phytoestrogens. How is this paper different? Make sure all relevant papers are cited.

As soy cultivated in Iran is of different variety, namely “Gorgan” compared to other studies and because the Iranian food habits and food pattern is different which might affect the metabolism of nutrients and isoflavones, this study was conducted to assess its effects compared to other countries. Furthermore there are still contradictions, in the literature regarding the role of soy isoflavones which justify implementation of this study.

2. Pg 4 “Reduced bone density ...” Ref 2 is incorrect

There was a typographic error, it was corrected in page 4, paragraph 1.

3. Pg 4 “Today estrogen therapy, especially bisphosphonates, calcitonin ...” these compounds are not estrogens.

We corrected the sentence on page 4; paragraph 2, as followed: Today estrogen therapy and drugs like bisphosphonates, calcitonin and raloxifene...

4. Pg 4 “only 3-8% of menopausal women...” this is different values than ref 11 says

The values were corrected according to Ref 7 (after correcting some parts of the article, Ref 11 was changed to Ref 7). On page 4, paragraph 2.

5. Pg 4 “Soy is part of Asian traditional diet”... use original sources

It was corrected according to your comment on page 4, paragraph 3.

6. Pg 4 “Estrogen like compounds such as isoflavones....” Ref 12 is incorrect

We added two related references instead of Ref 12 on page 4, paragraph 4.

7. Pg 5 "... were screened..." State what they were screened for. Did you accept anyone or did you want certain bone density levels?

We screened the subjects with osteopenia that is normal subjects and those with osteoporosis were excluded from the study. The sentence that shows our inclusion criteria was added in page 5, line 12.

8. Pg 5 "calorimetrically" this should be colorimetrically

It was a typographic error and was corrected in page 6, line 4.

9. Pg 6 "women with osteopenia" there is no mention in the manuscript before this that the women had osteopenia.

We mentioned it in Title and subjects and methods, on page 5.

10. Pg 6 "Comprehensive human studies ... there seems to be positive effect on bone formation" Where does this info come from

We changed the first part of discussion based on your comment and 4 new references (21-24) were added on page 6, line 24.

11. Pg 6 "Animal models such as monkey ..." There are estimates of human conversion of isoflavones to equol are available. Use these.

Based on correction in comment 10, we added these estimates, page 7, line 8.

12. Pg 7 "Other seral indicators.." This should be serum indicators.

We used the adjective form of the word "serum" but if the reviewer prefers "serum" it is all right with us.

13. Pg 7 "... and even reduction" Ref 27 shows no reduction or change in bone formation

It was a typographic error and was corrected on page 7, line 26.

14. Pg 10, Change the format of the references for Nutrition Journal

We have done it based on the format of the references of Nutrition Journal.

15. Pg 10, Ref 10 – Adlercreutz, H

We corrected it.

16. Pg 11, Ref 17 Correct page numbers 1364s-1368s

We corrected it according the format of Nutrition Journal.

Reviewer# 2

1. The author should change the tone and conclusion of the manuscript according to the following discussion.

Total Al-Pase in serum is an insensitive marker for bone formation compared to bone-specific Al-Pase (BAP) or intact osteocalcin (BGP), so these latter markers are generally used. In this study, serum osteocalcin is not changed during the study, indicating that soy protein may not enhance bone formation. With regard to bone resorption, urinary DPD, a sensitive marker, is reduced during the study. Hence, I consider that soy protein may reduce bone resorption significantly, but not enhance bone formation.

We changed the conclusion according to your comment on page 8, line 5.

2. Table 1. Please unify the format of data description.

It was edited according to your comment.

3. Table 3. The unit for TALP is incorrect. Data representation for IGFBP3 should be rearranged.

We corrected the unit for TALP and rearranged data representation for IGFBP3, on page 16, Table 3.

4. There are many grammatical and typographic errors. The manuscript is recommended to be reviewed by a native English speaker.

The manuscript was reviewed by an expert in English language.

Kind Regards,
Bagher Larijani, MD