

1. GENERAL COMMENTS:

The important significance of the review provides the evidences that chromium does not belong in the treatment arsenal of diabetes as supplementation. This is good for the readership in the WJD.

However, the review is not well structured and the evidences about recommendation to not use chromium as supplementation in Type 2 diabetic patients only come from limit amount studies.

It is important to add more findings from other studies and make better systematic review. Therefore, it is difficult to accept this review for publication in WJD as the present form. Furthermore, this review is quite short; therefore it is suggested to publish as mini-review if author make a proper revision according to the comments.

Reply: First of all, we would like to thank the reviewer for the time and effort he or she invested in our manuscript. We think the manuscript has improved after incorporating the suggestions by the reviewer. We agree that it is suitable to publish it as a mini review. We have tried to incorporate the suggestions into the manuscript. Specific changes are outlined below.

2. Abstract: This abstract is too simple and should be structured better.

Reply: We have restructured the abstract.

3. Introduction: The introduction is not well structured. The advantage and disadvantage for using chromium should be briefly mentioned in the introduction. Otherwise, we cannot understand the title of the review very well if author did not briefly mention why chromium supplementation is not effective in improving glycemic control.

Reply: We agree with the reviewer. We have extended the introduction.

4. Physiology: From the data of physiology, it seems that chromium (trivalent chromium) is very important for glucose metabolism and the function of insulin and insulin receptor. This does not support the conclusion of present review. How authors can explain this contradiction with the evidence of some clinical data, which showed no use of chromium in the type 2 diabetic patients.

Reply: We have added information in the discussion on chromium measurement and chromium status to better explain this.

5. Case reports: In this case reports section, authors describe in more detail in one case report and state that the chromium supplementation is very important. For the review, authors should look for more literatures related to case reports that were used chromium as supplementation and find out positive and negative data.

Reply: We added more case reports and tried to emphasize that the cases all had risk factors for chromium deficiency.

6. Clinical evidence: The evidences authors provided here seems not support to use chromium as supplementation for type 2 diabetic patients. But the evidences mainly come from the review by Balk et al and the second Dutch, double blind trial. Also many other trials that authors have omitted in the review. If author can look for literatures related the clinical studies about the supplementation of chromium in type 2 diabetic patients, the review should be written better.

Reply: We added several references regarding other markers of glycemic control. We added extra remarks that we focused on trials investigating HbA1c. We added extra studies concerning weight and fasting blood glucose and also regarding safety.

At beginning of this section, only one animal study was mentioned here, it may be too simple. It is suggested that authors should provide a separated paragraph to mention the animal studies of supplementation of chromium.

Reply: We added an extra paragraph concerning animal data on safety of chromium supplementation to the section on chromium physiology.

Discussion:

Do we have to be worried that a low chromium status contributes to hyperglycemia our patients?

Authors indicated that “For the average patients with type 2 diabetes the answer is; no. Trivalent chromium is highly available in food and the occurrence of severe chromium deficiency seems unlikely.”. However, In the physiology section, authors mentioned that whole grain products, such as bread (not white), legumes, nuts, and some spices contain low concentrations of trivalent chromium. Please explain.

Reply: We acknowledge that this could have led to confusion. We changed highly available into sufficiently available.

Authors also mentioned that “The sparse evidence that chromium supplementation might have effects on glycemic control is derived from studies with important methodological flaws”. Authors should point out what methodological flaws in these studies and should provide references.

Reply: We added references from the Anderson and Balk study to this part. We added extra information on the bias in the Anderson study to the discussion of the evidence.

Recommendations

At the end of this section, author concluded that “For patients with type 2 diabetes in general, it should be concluded that at this moment, there is no role for supplementation of chromium”. Same reasons as authors mentioned in recommendations section, this conclusion maybe too early to make without knowing the status of chromium in the body of diabetic patients and the bioavailability of different forms of chromium.

Reply: We agree with the reviewer and changed the conclusion

References: The references cited are too few for the review; authors should provide more relevant literatures. Furthermore, the format of references should follow the instruction of WJD. Authors did not read the Instruction to Authors in WJD very well when they prepare the manuscript.

Reply: we changed the style the references.