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OPEN PEER REVIEW

Effect of Zinc and Vitamin E on Blood Testosterone and Inflammatory Markers in Male Patients Undergoing Heart Surgery

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About this report

This open peer review (OPR) report shows the public comments made on this article during peer review, by the reviewers, the associate editor and the editor-in-chief, for every revision round, together with the authors' replies. Comments appear only with the consent of the people who wrote them. Reviewers who chose to sign their report are named; the others are shown as "Referee". Comments are edited for language only, and confidential remarks to the editors are not included.

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1 Original submission

1 comment · 24 Apr 2024

Referee 1 Reviewer

MAJOR REVISION 24 Apr 2024

I am writing to express my opinion regarding the revised manuscript titled " Effect of zinc and vitamin E on blood testosterone and inflammatory markers in male heart surgery patients", which was recently submitted to International Journal of Endocrinology and Metabolism. Having thoroughly reviewed the manuscript, I would like to share my thoughts on its major revision.

Sincerely,

The manuscript should be edited by a native English speaker.

In the introduction, there is a lack of RCT evidence with details of the disease, dose, etc.

What are the side effects of zinc and vitamin E?

How many patients were excluded for any reason?

There is no information regarding the sample size formula and the power of the study.

A CONSORT diagram should be added.

If the significance level is 0.05, why is there a tendency at nonsignificant levels…?

How were the assessments performed? Which kit was used, who performed the assessments, etc.?

Table 2 should be discussed.

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Revision 1

AUTHORS' RESPONSE TO REVIEWERS

Authors' reply to reviewers

The next pages contain the authors' point-by-point reply to the comments of this revision round, as submitted with the revised manuscript. It is published as the authors wrote it.

Reviewers' Comments:

Reviewer 1:

I am writing to express my opinion regarding the revised manuscript titled " Effect of zinc and vitamin E on blood testosterone and inflammatory markers in male heart surgery patients", which was recently submitted to International Journal of Endocrinology and Metabolism. Having thoroughly reviewed the manuscript, I would like to share my thoughts on its major revision.

Sincerely,

Comment: The manuscript should be edited by native English speaker.

Response: Thank you. The text has been edited and changes in sentences are indicated by highlighting.

Comment: In introduction, there is lack of RCT evidence with details of disease, dose and etc

Response: The introduction section also included additional details pertaining to the disease and dosage. Please refer to lines 49-53.

Comment: What are the side effects of zinc and vitamin E?

Response:

Oral vitamin E has been demonstrated to exhibit minimal toxicity in both animal and human studies. It has been demonstrated that short-term (30-day) vitamin E supplementation in an oral dose of 800 mg (>800 IU) does not result in adverse effects on hepatic or renal function, hematological status, or intermediary metabolism in healthy older subjects (Am J Clin Nutr.

1994 60(5):704-9. doi: 10.1093/ajcn/60.5.704). Longer-term studies with higher doses of vitamin E (1200-200 IU/day) in patients who had undergone coronary angioplasty (J Am Coll Nutr. 1992;11(1):68-73. doi: 10.1080/07315724.1992.10718198.) or in patients with Parkinson's disease also reported no side effects (N Engl J Med. In 1993, the New England Journal of Medicine (NEJM) published a study (328(3):176-83. doi: 10.1056/NEJM199301213280305). One of the principal adverse effects associated with high doses of zinc is the disruption of the absorption of other minerals, particularly copper. Nevertheless, it has been demonstrated that zinc supplementation (30 mg per day) for 14 weeks had no effect on copper and ceruloplasmin status in healthy men. (Biol Trace Elem Res. 2003;93(1-3):75-86. doi: 10.1385/bter:93:1-3:75.).

Although the doses of zinc and vitamin E in the present study were higher than the Dietary Reference Intake values, they were not higher than the Tolerable Upper Intake Levels. Moreover, the recommended dietary amounts are intended for individuals in good health, and the amount required during acute illness may differ. Consequently, given the brief duration of the current study (3 weeks), it was not anticipated that the use of supplements would result in adverse effects. For this reason, no clinical or laboratory evaluations were conducted in the present study to assess the potential for adverse effects.

Comment: How many patients were excluded for any reason?

Response: A total of 13 patients (all women) from the zinc-vitamin E group and 13 patients (all women) from the placebo group were excluded from this study. This additional explanation has been incorporated into the results section. Please refer to lines 139-142.

Comment: There is no information regarding the formula of sample size and power of study.

Response: The rationale behind the sample size has been incorporated into the methodology section. Please refer to lines 119-123.

Comment: Consort diagram should be added.

Response: It was added (Figure 1).

Comment: If the significant level is 0.05, why for non-significant levels, there is tendency…..

Response: In various sections of the manuscript text where the phrase "there was tendency" or "tended to" was employed, the phrase "no significant difference" was substituted and highlighted.

Comment: How were the assessments? Which kit, by whom and etc.

Response: More details have been added; have a look at subsections 3.3 and 3.4.

Comment: Table 2 should be discussed.

Response: The findings pertaining to Table 2 were also discussed. Please refer to lines 186-193.

Reviewer 2:

The manuscript entitled "Effect of zinc and vitamin E on blood testosterone and inflammatory markers in male heart surgery patients" was reviewed.

Considering the aim and findings of the study, this secondary analysis of a previously published article is not suitable for publication in the IJEM as an original research paper.

What is the rationale for inclusion of testosterone concentrations which can change significantly in the perioperative period due to several reasons?

Response:

The comment that multiple factors influence hormone levels, including testosterone, is accurate. Nevertheless, the mere fact that a factor undergoes significant changes in the postoperative period for various reasons does not preclude its evaluation. Coronary artery bypass grafting (CABG) is a major surgical procedure that results in significant alterations in hormonal and biochemical factors. The modulation of certain of these factors may have a beneficial impact on the surgical outcome. In fact, the rationale for including testosterone in the study was its observed decrease in the postoperative period. As previously stated, this decrease has been demonstrated to be associated with adverse effects. In the present study, efforts were made to ensure that confounding factors affecting testosterone levels in the two study groups were similar. This included ensuring that the evaluation was performed only on male subjects, that the type of surgery was the same, that age was not different, and that body weight was adjusted in the statistical analysis.

Comment: Is the unit of serum cortisol depicted in Figure 1 (ng/mL) correct?

Response: Thank you for your attention. The value was subsequently corrected to micrograms per deciliter (µg/dL)

Associate Editor's Comments:

Associate Editor 1:

The reviewers have requested substantial changes in several part of the manuscript, especially for more clear description of the method, that require a major revision. English editing is also required.

Response: Thank you. The comments were addressed to the greatest extent possible, and any necessary corrections were implemented. Additionally, the text was edited for grammatical correctness and clarity in the English language.

2 Revision 1

1 comment · 28 May 2024

Referee 1 Reviewer

MINOR REVISION 28 May 2024

Having thoroughly reviewed the revised manuscript and the authors'
responses to my inquiries and comments, I would like to share my thoughts on its acceptability
for publication after a minor revision to add the response to the comment “What are the side effects of zinc and vitamin E?” to the text.
Sincerely,

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Revision 2

AUTHORS' RESPONSE TO REVIEWERS

Authors' reply to reviewers

The next pages contain the authors' point-by-point reply to the comments of this revision round, as submitted with the revised manuscript. It is published as the authors wrote it.

Reviewers' Comments:

Reviewer 1:

Having thoroughly reviewed the revised manuscript and the authors' responses to my inquiries and comments, I would like to share my thoughts on its acceptability for publication after minor revision of adding the response of comment “What are the side effects of zinc and vitamin E?” in text.

Sincerely,

Response: Thank you. It was added (lines 259-274).

Associate Editor 1:

The reviewer has suggested a minor correction that need to be made before publication.

Response: Thank you. The task was completed.

3 Revision 2

0 comments

No public comments in this round.