Author’s response to reviews

Title: omega-3 Fatty Acids are protective against Paclitaxel-Induced Peripheral Neuropathy: A Randomized double-blind placebo controlled trial

Authors:

Zohreh Ghoreishi (zohreh_ghoreishy@yahoo.com)
Ali Esfahani (ali_sfhn@yahoo.com)
Abolghasem Djazayeri (djazavery@yahoo.com)
Mahmoud Djalali (jalalimahmood@hotmail.com)
Banafsheh Golestan (bgolestan@tums.ac.ir)
Hormoz Ayromlou (ayromlouh@tbzmed.ac.ir)
Shahriar Hashemzade (shahriar_90@yahoo.com)
Mohammad Asghari Jafarabadi (m.asghari862@gmail.com)
Vahid Montazeri (vahidmontazeri@yahoo.com)
Seyed Ali Keshavarz (sakeshavarz2012@gmail.com)

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Author’s response to reviews: see over
Dear editor in-chief

We read the comments provided by the reviewers carefully and we tried to response all of them point-by-point.

The article has been text edited by a native English editor, Ms. Rebecca Pike, from the University of Essex, UK and the certification letter has been attached as a separate file.

The manuscript was reorganized based on the guidelines of BMC Cancer. In addition, title page was written again according to the standards for preparing a title page introduced by BMC series medical journals.

The technical corrections have been highlighted in the text to be easily identified.

Best Regards,

Seyed Ali Keshavarz
The manuscript was reorganized based on the guidelines of BMC Cancer.

The within group changes have been omitted in the sections of results and conclusions.

No statistically significant differences were observed between the two study groups in incidence and severity of the PIPN according to the changes of serum DHA levels, and it was stated in the results. But, there was a significant difference between the two groups based on the changes of serum EPA and DHA, which could be an indicator of the participants’ compliance. These results and the method used have been added to the sections of Methods, Results, and Conclusions.

We intended to say that rTNS scale is well correlated with the other common neurotoxicity scales in general. It was mentioned to emphasize the accuracy and precision of rTNS scale to evaluate the peripheral neuropathy both in clinical and research settings. Some corrections have been made.

Sample size was determined based on primary information for vibratory perception threshold (VPT) obtained from the study by Okuda et al [1] (as they evaluated the efficacy of omega-3 fatty acids on diabetic peripheral neuropathy) using the following data:

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<tr>
<td>mean1</td>
<td>13.30</td>
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<td>SD1</td>
<td>6.4</td>
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<tr>
<td>mean2</td>
<td>9.5</td>
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<tr>
<td>SD2</td>
<td>1.80</td>
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</tbody>
</table>

Moreover, according to Pocock[2], a power of 80% is the least acceptable power to determine the sample size.

The between group differences in incidence and severity of PIPN have been explained below the Table 1. Table 2 and 3 were re-drawn and p values were computed using analysis of covariance in order to assess between group differences.

Primary and secondary outcome measures were declared in the new revision.

The new revision of the manuscript has been edited by a native English editor and the certification letter has been attached.

References

Primary and secondary outcome measures were declared in the new revision.

"The group matching according to age" has been omitted and it was mentioned that there was no statistical difference between two groups according to age.

The placebo soft gels in our study had no fishy taste and it has been noted as one of the study limitations in the new revision.

We aimed to show the summary of the study design based on the population who completed the study in the first flow diagram. In this revision, the flow chart was re-drawn to reflect design, whole study population, and the drop-outs.

Sample size was determined based on primary information for vibratory perception threshold (VPT) obtained from the study by Okuda et. al. [1] (as they evaluated the efficacy of omega-3 fatty acids on diabetic peripheral neuropathy) using the following data:

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</table>

It was computed as 23.24 (≈24) per group. This number was increased to 28 per group to accommodate the anticipated 20% dropout rate, although more patients were enrolled. According to Pocock SJ. [2], a power of 80% is the least acceptable power to determine the sample size. However, the small sample size was mentioned as one of the possible limitation of the study.

The manuscript was reorganized based on the guidelines of BMC Cancer.

The psychological status of the patients was not assessed and it was stated as another limitation of the study.

In a study performed by Cao et al[3], it has been emphasized that "erythrocyte membrane is a better index for monitoring long-term intake of omega-3 fatty acids whereas plasma phospholipids are more sensitive to short term changes in the intake of omega-3 fatty acids and may be thus be more useful in the monitoring the compliance of individuals in intervention studies with fish oil supplementation" (P 2271).

No statistically significant differences were observed between the two study groups in incidence and severity of the PIPN according to the changes of serum DHA levels, and it was stated in the results. But,
there were a significant difference between the two groups based on the changes of serum EPA and DHA, which could be an indicator of the participants’ compliance. These results and the method used have been added to the sections of Methods, Results, and Conclusions.

10- The limitations of the work have been expanded to the mentioned comments.

11- The positive influences of omega-3 fatty acids in prevention of the wide range of psychiatric, arrhythmic, and neurological disorders such as major depression. Schizophrenia, dementia, Alzheimer, and Parkinson have been discussed in P.13. Additionally, the direct and indirect effects of omega-3 fatty acids on neuropathic pain were discussed in page 13.

12- The new revision of the manuscript has been edited by a native English editor and the certification letter has been attached.

References