Author’s response to reviews

Title: Photobiomodulation therapy on the palliative care of temporomandibular disorder and orofacial/cervical skull pain: study protocol for a randomized, controlled clinical trial

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Response to reviewers' comments:

Reviewer # 1:

1. “Dear authors, thank you for submitting your study protocol for Trials Journals. Whilst the study design of great interest, it has weakness, which are - unfortunately - highlighted by the manuscript”.

Answer: Thank you for the important comments. The authors really appreciate the opportunity to review the manuscript and make it better. All comments were considered and changes and/or answers are included in the present document.

2. “A comprehensive text revision is advised, including review of the English language, as grammatical and typing mistakes (such as repeated words) appear through the text.

Answer: The entire manuscript was reviewed concerning the English language, grammatical and typing mistakes.

3. “Introduction: Overall the introduction is well structured, but in my opinion the authors failed in stating the gap in the literature. In the end of the introduction the authors state that "Although there are many studies that report the effects of PBM therapy on TMD, there is still no consensus regarding its effectiveness and which are the best parameters of PBM therapy and which are the locations of the points to be used to apply the laser for the reestablishment of the functions of the stomatognathic system.” The problem here is that this study protocol will not test or help establishing the parameters indicated, nor the locations points for laser application. My advice is
to review this sentence in order to make clear how your study will contribute in answering questions that are not yet clarified.”

Answer: The Introduction session was reviewed and rewritten in order to make clearer the objectives of the study. Part of the text ("Although there are many studies that report the effects of PBM therapy on TMD, there is still no consensus regarding its effectiveness and which are the best parameters of PBM therapy and which are the locations of the points to be used to apply the laser for the reestablishment of the functions of the stomatognathic system.") was rewritten as "Although there are many studies that report the effects of PBM therapy on TMD, there is still no consensus on the potential of the PBM therapy using low power laser on decreasing orofacial/cervical skull pain caused by TMD".

4. “Objectives: The authors state that one of the objectives of this research project is to verify: "If the PBM therapy using low power laser is effective on the palliative care, of TMD and orofacial/cervical skull pain." The word "effective" is defined as "adequate to accomplish a purpose; producing the intended or expected result", and therefore can lead to different interpretations. If I understood well, you will verify if the therapy is effective in terms of pain reduction. My suggestion is that you make it more clear.

Answer: Authors agree with the reviewers’ comment and have rewritten the sentence, as follows. The sentence "If the PBM therapy using low power laser is effective on the palliative care of TMD and orofacial/cervical skull pain." was changed to “If the PBM therapy using low power laser is effective on the palliative care of TMD and orofacial/cervical skull pain by decreasing pain in masticatory muscles and orofacial/cervical regions.”

5. “Methods/ Design: Study design: You state that: "The researches, the participants and the statistician will be blinded to the treatments groups (active or placebo).” In this case, who are the researches? Operators? Examiners? How many are they?”

Answer: The text was rewritten, as follows, in order to make clear the topic addressed by the reviewer.

"The researches (F.R.C.; R.Q.B.) in charge of the laser application on participants, the participants and the statistician will be blinded to the treatments groups (active or placebo). Other researcher (P.M.F.), not involved with laser application, will be in charge of setting the equipments for each experimental group: active and placebo (without emission of laser light).”

6. “ Randomization: Who will be responsible for patients randomization/ allocation to the groups? The operator? One of the evaluators? Someone else not enrolled in the research?”

Answer: The randomization/allocation to the groups will be made by one of the researchers, not involved with the clinical procedures. The information was added to the text as follows: “This
procedure will be repeated 4 times. A researcher (P.M.F.), not involved with the clinical steps, will be in charge of randomization/ allocation of patients to the groups.”

7. “Sample Calculation: Sample size calculation should be based on your primary outcome analysis. Your sample size was calculated taking a 50% magnitude of effect among the groups; however it is not clear what kind of test you used here or why you choose this effect size. Can you support this based on the literature? Also, why did you not increase the sample size in order to compensate for possible drop-outs.”

Answer: The text was rewritten, as follows, in order to make clear the topic addressed by the reviewer and we introduced new information. The new text is:

“The sample size was calculated based on the main outcome and assuming a Type I error of 5%(significance level), Type II error of 20% (80% test power) and 50% of magnitude of effect among groups, the total number of participants will be 200 individuals. [17], who will be allocated in 2 groups (active or placebo).

Despite the data available in the literature we take them into account to use the magnitude of effect of 50% among groups.

We will consider increase the sample size in order to compensate for possible drop-outs in case of compromise the results.

When concluding the treatment of all 200 subjects, researchers will consider to include more participants (increase the sample size) to compensate for possible drop-outs. If necessary, the inclusion will be made by adding a new block with participants of both experimental groups (PBMT and placebo), randomly assigned to each of the proposed therapies.”

8. “Outcome measure: Who will be responsible for the measurements? The examiner(s) will be trained and calibrated? How is this going to be done? Also, for all outcomes measured (such as VAS scale, Sleep quality assessment, quality of life). It is not clear when those outcomes will be measured (only before intervention, before and after?). In the flowchart, as well as in the schedule enrolled there is more information about it, but it should also be better explained in the text. Also, the figure 2 needs to be called in the text.”

Answer: Information was added to the text, as suggested by the reviewer.

9. “Statistical analysis: Statistical analysis needs some more detail. What tests you will apply for each outcomes? Are you planning to perform correlation tests or even build regression models in order to verify the interaction (association/correlation) of variables that are going to be collected?”

Answer: We change the test with new informations The new text is:
“Before performing the statistical analysis, the data will be placed in a spreadsheet and randomly checked by one of the authors (an author who did not insert the data in the spreadsheet) to verify if there was an error in the transcription of the data.

In order to present the characteristics of the participants, a descriptive statistic will be used. Demographic data and clinical characteristics will be compared, for continuous variables, by using the Wilcoxon test or the t-test; for the categorical variables by the Fisher's exact test or Chi-square test will be performed.

All results will be analyzed using 95% confidence intervals, with a significance level of 5%. The data also analyze the results according with intention to treat analyses (ITT). No interim analyses will be performed because this trial have a short time of intervention for each participant.”