Author's response to reviews

Title: Efficacy of platelet rich fibrin in the reduction of the pain (check) and swelling after impacted third molar surgery. Randomized multicenter split-mouth clinical trial.

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Author's response to reviews: see over
Dear Editor-in-Chief,

We’d like to thank you and your reviewer’s kind comments and supportive contributions. We reevaluated our manuscript, and tried to clarify according to reviewer’s suggestion meticulously. As a result, the following changes have been made in the manuscript point-by-point and the changes marked as colored texts (red) in the manuscript. We revised the manuscript according to the changes recommended by all reviewers.

We are resubmitting our paper to you for our review. If you have any further comments, we can take into consideration them. The entire manuscript was proofread again by native speakers of English as recommended by the reviewers.

I hope the revised paper would meet your criteria and merits publication in the Journal of Head and Face Medicine.
Once again, thank you very much for your kind concern.

King Regards

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Reviewer 1:

Was the examiner blinded to the study.

- Thank you for giving us an opportunity to clarify this issue. The examiners were blinded to the study and explanation has been added to the materials and methods. “The postoperative evaluations were performed by surgeons that were blinded to the operative procedures, in order to eliminate unwanted bias.”

Were all wisdom teeth fully impacted

- Yes all the wisdom teeth were fully impacted and this information has been added to the text.

It would be better to use 3D optical scanner to measure the facial swelling

- Thank you very much for this valuable contribution. We would agree so however the funding of the study did not support such expenses. This point has been mentioned as limitations of our study in the Discussion as “Also the use of 3-D optical scanner for the measurements of facial swelling might have given more precise recordings however the funding of the study did not support such expenses.”
- Statistical analyses were performed again with Wilcoxon test.

Reviewer 2:

Thank you very much for this valuable contribution. But we have some divergences with these comments, so we manage to revise our manuscript without harming the unity of the manuscript:

*It is recommended to provide a suitable null hypothesis.*

- Thank you for giving us an opportunity to clarify this issue. We have provided a null hypothesis. "The null hypothesis tested was that PRF would effect the postoperative swelling and pain positively."

*The text do not describe a method for blinding for evaluator.*

- Blinding the evaluator has been added to the material and methods as “The postoperative evaluations were performed by surgeons that were blinded to the operative procedures, in order to eliminate unwanted bias.”

*Sample size method and sample method of including patients are missing*

- Thank you for giving us an opportunity to clarify this issue. Sample size calculation has been explained in the materials and method section as “Based on previously treated trial cases we conducted a power analysis (Power and Precision software, Biostat, Englewood, NJ, USA). The findings indicated a minimum sample size of n = 50, based on an α of 5% and a power of 80%. Considering a possible loss of about 10% of patients, we used 56 participants.”
The evaluation of pain in this case is difficult and the conclusion probably was wrong, because the patients have not the capacity for discriminate what side is worst in the pain scale at the same time.

- We agree that evaluation of pain is difficult in this study design however it has been mentioned as a limitation of the study in the discussion as “There are some limits to our study; the present study was conducted on bilaterally removed third molars at the same session the results of pain might have been influenced by the control side.”

I recommended a new analysis using a mixed model or a correction like Bonferroni, probably the difference after a new analysis will not result significant.

- Statistical analyses were performed again with Wilcoxin test.

It is suggested to include study’s strengths and weaknesses and future directions.

- In the discussion a paragraph about the limits of the present study has been added “There are some limits to our study; the present study was conducted on bilaterally removed third molars at the same session the results of pain might have been influenced by the control side. Also the use of 3-D optical scanner for the measurements of facial swelling might have given more precise recordings however the funding of the study did not support such expenses. We recommend that further studies investigating this manner should consider the mentioned limitations of the present study.”

I propose the follow title: Efficacy of platelet rich fibrin in the reduction of the pain (check) and swelling after impacted third molar surgery. Randomized multicenter split-mouth clinical trial.
- Thank you very much for bringing up this important issue. The title has been changed according to your recommendation.

Reviewer 3:

- Thank you very much for valuable contributions and comments. Reviewer 3 made the corrections on the document. The changes recommended by the referee has been added to the text that can be observed as red.

10 ml of venous blood was collected (who did this blood collection??)

- Thank you for giving us an opportunity to clarify this issue. We have tried to clarify our perspective on this subject matter. "Prior to the extractions, 10 ml of venous blood was collected from each patient by a surgical nurse and was placed in glass-coated plastic tubes".

Was the extractions made in two different periods? In both the blood was collected?

- We have tried to clarify this subject. "All patients underwent bilateral removal of 3rd molar in single appointment that were the same degree of surgical difficulty "

Figure 1 This should be figure 2.

- Thank you very much for bringing up this important issue. We have missed this mistake. According to your suggestion we have changed the sentence, and it can be observed as track changes in the manuscript.

All statistical analysis has several problems. First authors should perform normality test for further choose parametric or non-parametric test.
- Thank you very much for bringing up this important issue. Statistical analyses were performed again with Wilcoxin test. Also the tables has been improved following the new statistical work.

Reviewer 4:

Sample size justification should be given

- Thank you very much for this valuable contribution. We would think that this could be the explanation of the question. Sample size calculation has been explained in the materials and method section as “Based on previously treated trial cases we conducted a power analysis (Power and Precision software, Biostat, Englewood, NJ, USA). The findings indicated a minimum sample size of n = 50, based on an \( \alpha \) of 5% and a power of 80%. Considering a possible loss of about 10% of patients, we used 56 participants.”

No mention of statistical method for evaluation of pain:

- Statistical analysis were renewed and described as “Statistical analysis was performed using the software program SPSS 20.0 (SPSS 20.0 for Windows; SPSS Inc., Chicago, IL, USA), at a significance level of \( \alpha = 0.05 \). For analysis of swelling the Shapiro–Wilk test was used to evaluate the distribution of the data (normal or non-normal), the Wilcoxon test for paired samples was used since the data were not normally distributed. Regarding the pain statistical analysis were performed by using one–way analysis of varience (ANOVA). If there were
difference between the measurements, the data were analyzed by the Paired Sample test.”

There should a mention of the blood withdrawn

- We have tried to clarify our perspective on this subject matter. It was mentioned in the text as “10 ml of venous blood was collected from each patient by a surgical nurse”

Mention the type and number of suturing

- Thank you very much for giving us the opportunity to clarify this matter. “Both extraction cavities were primarily closed with 3-4 interrupted sutures using 3.0 silk sutures” has been added to the manuscript.

Singh et al. study mentioned as significant result clarity should be brought.

- In the discussion part it was mentioned that The present study found no significant difference between PRF and control sides in terms of pain which is similar to Singh et al.

Spelling errors

- We have corrected the spelling error and it can be seen in the manuscript as track changes.

Conclusion in abstract and at the end overstated as both vertical and horizontal reduction in swelling whereas results show only reduction in horizontal swelling. Conclusion should be specific based on the results.

- Conclusion has been revised as “As a conclusion, PRF seems to be efficient on postoperative horizontal swelling after third molar surgery. PRF might be used on a routine basis after third molar extraction surgery. Studies with a larger sample
that will need a bilateral third molar removal that will be extracted in different sessions with a longer follow-up is warranted to obtain a more statistically meaningful results with respect to bone regeneration.”