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Treatment of sinus membrane perforations during sinus lift surgeries using leukocyte and platelet-rich fibrin: a report of three cases

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Treatment of sinus membrane perforations during sinus lift surgeries using Platelet-Rich Fibrin: A case series.
Journal of Clinical and Translational Research

Dear Prof. Dr. Salgado-Peralvo,

Reviewers have now commented on your paper. You will see that they are advising that you revise your manuscript. If you are prepared to undertake the work required, I would be pleased to reconsider my decision.

For your guidance, reviewers' comments are appended below.

If you decide to revise the work, please submit a list of changes or a rebuttal against each point which is being raised when you submit the revised manuscript. Also, please ensure that the track changes function is switched on when implementing the revisions. This enables the reviewers to rapidly verify all changes made.

Your revision is due by Jul 19, 2022.

To submit a revision, go to https://www.editorialmanager.com/jctres/ and log in as an Author. You will see a menu item call Submission Needing Revision. You will find your submission record there.

Yours sincerely

Michal Heger
Editor-in-Chief
Journal of Clinical and Translational Research

Reviewers' comments:

Reviewer #1: The present study titled: "Treatment of sinus membrane perforations during sinus lift surgeries using Platelet-Rich Fibrin: A case series." Investigated the use of PRF for sinus perforations. It's actually a good study but has some limitations.

1) In the introduction, much more literature on PRF should be described including the fact that PRF has already been used for the repair of the lateral windows. This case series presents nice outcomes with good data but the concept has been well published in the literature. Please cite this previous research.

2) Generally speaking, there are only 20 references, many of which are extremely old ones. Please update this with relevant citations to read more like a paper to be published in 2022.

3) There is no mention of the PRF tube types used in this study. This has a great impact on final outcomes. Please see the following study and it should be a discussion point in the discussion of this manuscript.
BMC Oral Health. 2021 Mar 19;21(1):135. doi: 10.1186/s12903-021-01497-0.

4) The protocol of PRF is not well described. In a recent consensus paper, researchers asked that articles written on PRF be described a certain way. It is not possible to report simply the RPM and time without more data. Please read the following
PMID: 30730050, DOI: 10.1002/JPER.18-0553

DOI: 10.4103/GFSC.GFSC_23_18

5) The discussion should focus on ways to improve PRF quality with more cells.

Reviewer #2: #First of all, I think your paper should focus on cases that were repaired by PRF alone. For small perforations, repair with PRF alone has been shown to be simple and effective. For large perforations, however, sutures and collagen membranes alone are not sufficient, and the intent to combine PRF with them should be described with a bit more discussion.
#From your paper, it is difficult to distinguish whether the role of PRF is repair or bone augmentation. So the use of PRF in the lateral window site seems to have nothing to do with treatment of perforation
#Do you have any other intraoperative Figures of the perforation being repaired with PRF? It's not clear from these Figures that the PRF is repairing the perforation.
No abbreviations are listed. p3 l2 "SLS", l6 "DI", l22 "CM"
Reference [21] is not listed.

Reviewer #3: The manuscript aimed to show the results of using PRF in the treatment of Schneiderian membrane perforations occurring during sinus augmentation procedures with a lateral

window approach. It is a case series study. The results are interesting, however no innovative or novel information (technique) is presented. Other comments:

Introduction:

Is the un-ruptured Schneiderian membrane "essential" for the high survival rates for implants placed into augmented sites? According to a recent systematic review (Díaz-Olivares et al., 2021), the membrane perforation had no impact on implant survival rates- 97,68% with membrane perforation and 98,88% without membrane perforation.

"PRF is a polymerised matrix with a tetramolecular structure containing a large number of leukocytes and platelets (approximately 70% and 95% of the initial clot, respectively)." The composition depends on the protocol of PRF preparation used. This information should be mentioned.

Case presentation

The following parameters must be included regarding PRF preparation (Miron et al., 2019 - Standardization of relative centrifugal forces in studies related to platelet-rich fibrin): 1) dimensions of the rotor (radius at the clot and end of the tube); 2) rotor angulation for the tube holder; 3) RCF value calculated at either the RCF-minimum,RCF-clot, or RCF-maximum; 4) composition and size of tubes used to produce PRF; and 5) centrifugation model used.

How bone compaction and maturation was evaluated using CBCT?

Discussion

A recent publication in this topic should be included. The Effectiveness of L-PRF in the Treatment of Schneiderian Membrane Large Perforations: Long-Term Follow-Up of a Case Series. de Almeida Malzoni CM et al., 2021. J Oral Implantol. 2021 Feb 1;47(1):31-35. doi: 10.1563/aaid-joi-D-20-00044.

Conclusion

Your study does not allow the following conclusion: "Although there are no significant differences between repaired and intact SM, radiologically, greater bone compaction and maturation is observed in the latter, which could translate into less primary stability of DIs placed in sinuses in which SM perforation occurred." This information should be discussed in the discussion section.

Reviewer #4: Submitted case series reported a treatment method for the most frequent intrasurgical complication of sinus lifting procedure-Schneiderian membrane perforation. However, the manuscript has some drawbacks that need further clarification.

* The conclusion has overexpressed the findings. Also, conclusion is too general when it is commented on cost which not all 3 cases treated with only PRF.
* Information on surgeon's experience, presence of pathology within the sinus and the use of certain medications, systemic status, smoking status should be given.
* The discussion should include information on sinus perforation management strategies considering perforation size and location.
* The authors would benefit on manuscript structure if they follow CARE guidelines.
* Page 3, line 15: (n=2) belongs to patient or implant?
* Different techniques to different size of the perforations has been applied, therefore it is hard to

give a common conclusion to all.
* How could the authors make a statement on "greater bone compaction and maturation"? Which parameter did they consider?

Authors' response

Re: revision JCTRes-D-22-00059

Madrid, Spain, 12 July 2022

Dear Editor-in-Chief, Prof. Dr Michal Heger,

Thank you for allowing us an opportunity to resubmit a revised version of our manuscript entitled "Treatment of sinus membrane perforations during sinus lift surgeries using Platelet-Rich Fibrin: A case series".

All modifications were highlighted in yellow in the text. Moreover, every modification or revision of the reviewers´ comments is detailed per the comments below in red italics.

We are grateful for the useful comments of the reviewers, as a result of which the paper has been considerably improved.

On behalf of the authors, kindest regards,

Dr. Angel-Orión Salgado-Peralvo.

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REVIEWER COMMENTS

Reviewer 1:
The present study titled: "Treatment of sinus membrane perforations during sinus lift surgeries using Platelet-Rich Fibrin: A case series." Investigated the use of PRF for sinus perforations. It's actually a good study but has some limitations.
Dear reviewer,

Thank you for taking the time to review our manuscript and helping us improve the quality of our work. After analysing your comments, we proceed to answer them one by one:

1. In the introduction, much more literature on PRF should be described including the fact that PRF has already been used for the repair of the lateral windows. This case series presents nice outcomes with good data, but the concept has been well published in the literature. Please cite this previous research.
   We appreciate your comment, however, the purpose of our manuscript is to describe the use of L-PRF for sealing SM perforations. However, in the last paragraph of the discussion, we indicate the other uses for which L-PRF can be used in sinus elevations, particularly: (1) as a grafting material, and (2) for sealing lateral antrostomy. In addition, we have added further updated references in the introduction and discussion and, in the latter, we have alluded to other studies that used L-PRF in the treatment of SM perforations.

2. Generally speaking, there are only 20 references, many of which are extremely old ones. Please update this with relevant citations to read more like a paper to be published in 2022.
   The authors added a larger number of bibliographical references, and these were updated.

3. There is no mention of the PRF tube types used in this study. This has a great impact on final outcomes. Please see the following study and it should be a discussion point in the discussion of this manuscript.
   BMC Oral Health. 2021 Mar 19;21(1):135. doi: 10.1186/s12903-021-01497-0.
   The type of tubes used (glass-coated plastic tubes of the blood of 10 mL [Process® for PRF], without anticoagulants or other additives) was added in the Case Presentation (third paragraph). In addition, the influence of the type of tubes used on the L-PRF clots obtained was discussed in the discussion, following your recommendation.

4. The protocol of PRF is not well described. In a recent consensus paper, researchers asked that articles written on PRF be described a certain way. It is not possible to report simply the RPM and time without more data. Please read the following PMID: 30730050, DOI: 10.1002/JPER.18-0553 DOI: 10.4103/GFSC.GFSC_23_18
   Following your comment, the protocol used was described in the third paragraph of the Case Presentation with reference to the article by Miron et al. (2019): "Six glass-coated plastic tubes of blood of 10 mL (Process® for PRF), without anticoagulants or other additives are withdrawn and centrifuged at 2,700 rpm for 12 mins (RCF-clot= 408 g), using an LC-04P centrifugation device (Zenith Lab® CO, LTD. Jiangsu, CN) (48º rotor angulation, 50 mm radius at the clot, 80 mm at the maximum). Six L-PRF clots were produced and dehydrated to obtain membranes in a PRF Box (Salvin®, Charlotte, CN, USA)".

5. The discussion should focus on ways to improve PRF quality with more cells.
   In the penultimate paragraph of the discussion, a paragraph was added specifying modifications of the technique to achieve a higher number of cells in the PRF clots.

Reviewer 2:

Dear reviewer,
Thank you for taking the time to review our manuscript and helping us improve the quality of our work. After analysing your comments, we proceed to answer them one by one:

1. First of all, I think your paper should focus on cases that were repaired by PRF alone.

In this article, we describe the treatment of three patients, two of whom underwent bilateral SLSs, which offers the possibility of being able to compare the results between sinuses with SMs "repaired" with L-PRF and those not repaired. The authors believe that focusing only on the first, eliminating the comparison, would detract from valuable information.

2. For small perforations, repair with PRF alone has been shown to be simple and effective. For large perforations, however, sutures and collagen membranes alone are not sufficient, and the intent to combine PRF with them should be described with a bit more discussion.
   Following your recommendation, it is explained in the discussion why the use of collagen membranes (paragraph 7 of the discussion) or sutures (paragraph 8 of the discussion) was not sufficient to repair SMs and was combined with L-PRF.

3. From your paper, it is difficult to distinguish whether the role of PRF is repair or bone augmentation. So, the use of PRF in the lateral window site seems to have nothing to do with treatment of perforation.
   The protocol used by the authors in SLSs always includes the use of L-PRF because, in the event of perforation of the SM during the procedure, L-PRF is available to seal it easily (this is specified at the beginning of paragraph 7 of the discussion). Therefore, we take advantage of the fact that we perform the technique and use L-PRF for other purposes, i.e. by mixing it with a bone graft for regeneration of the subsinusal cavity and, in addition, to seal the lateral antrostomy. So we use it not only for reparation but also for bone regeneration.

4. Do you have any other intraoperative Figures of the perforation being repaired with PRF? It's not clear from these Figures that the PRF is repairing the perforation.
   Unfortunately, we do not have any more figures illustrating the sealing of the SM perforations.

5. No abbreviations are listed. p3 l2 "SLS", l6 "DI", l22 "CM"
   All abbreviations have been listed in this modified version.

6. Reference [21] is not listed.
   Reference [21] was added (Dragonas et al. https://doi.org/10.1016/j.ijom.2018.06.003.)

Reviewer 3:

Dear reviewer,
Thank you for taking the time to review our manuscript and helping us improve the quality of our work. After analysing your comments, we proceed to answer them one by one:

1. The manuscript aimed to show the results of using PRF in the treatment of Schneiderian membrane perforations occurring during sinus augmentation procedures with a lateral window approach. It is a case series study. The results are interesting, however no innovative or novel information (technique) is presented.
   The uniqueness of the present study lies in the fact that we make recommendations on various ways of resolving SM perforations depending on their dimensions. We also describe less graft material compaction at 6 months post-surgery, a previously undescribed finding, which we relate to the "septic theory" described by Choukroun et al. (DOI: 10.1097/ID.0b013e318181349a). These authors observed that, when they mixed the graft biomaterial in SLSs with a topical antibiotic (metronidazole), greater biomaterial compaction occurred than when they did not.

Introduction:

2. Is the un-ruptured Schneiderian membrane "essential" for the high survival rates for implants placed into augmented sites? According to a recent systematic review (Díaz-Olivares et al., 2021), the membrane perforation had no impact on implant survival rates- 97,68% with membrane perforation and 98,88% without membrane perforation.
   The authors have modified this paragraph in the introduction, stating that it is essential that the SM is intact and with continuity, i.e. we have deleted "must be healthy and without perforations", as this may have led to misinterpretations, such as that implants placed in sinuses with repaired SM may have lower survival rates.

3. "PRF is a polymerised matrix with a tetramolecular structure containing a large number of leukocytes and platelets (approximately 70% and 95% of the initial clot, respectively)." The composition depends on the protocol of PRF preparation used. This information should be mentioned.
   This consideration was added in the penultimate paragraph of the discussion.

Case presentation

4. The following parameters must be included regarding PRF preparation (Miron et al., 2019 - Standardization of relative centrifugal forces in studies related to platelet-rich fibrin): 1) dimensions of the rotor (radius at the clot and end of the tube); 2) rotor angulation for the tube holder; 3) RCF value calculated at either the RCF-clot, or RCF-maximum; 4) composition and size of tubes used to produce PRF; and 5) centrifugation model used.
   In accordance with your comment, the protocol used in the third paragraph of the Case Presentation has been described with reference to the article by Miron et al. (2019): "Six glass-coated plastic tubes of blood of 10 mL (Process® for PRF), without anticoagulants or other additives are withdrawn and centrifuged at 2,700 rpm for 12 mins (RCF-clot= 408 g), using an LC-04P centrifugation device (Zenith Lab® CO, LTD. Jiangsu, CN) (48º rotor angulation, 50 mm radius at the clot, 80 mm at the maximum). Six L-PRF clots were produced and dehydrated to obtain membranes in a PRF Box (Salvin®, Charlotte, CN, USA)".

5. How bone compaction and maturation was evaluated using CBCT?
   It was assessed visually, by the appearance observed between CBCT at 6 months after SLSs were performed, comparing sinuses with repaired SMs to the opposite side where no SMs were perforated. Figure 5 was added for a better understanding.

Discussion

6. A recent publication in this topic should be included. The Effectiveness of L-PRF in the Treatment of Schneiderian Membrane Large Perforations: Long-Term Follow-Up of a Case Series. de Almeida Malzoni CM et al., 2021. J Oral Implantol. 2021 Feb 1;47(1):31-35. doi: 10.1563/aaid-joi-D-20-00044.
   Following your recommendation, this reference was included in the discussion (paragraph 9).

Conclusion

7. Your study does not allow the following conclusion: "Although there are no significant differences between repaired and intact SM, radiologically, greater bone compaction and maturation is observed in the latter, which could translate into less primary stability of DIs placed in sinuses in which SM perforation occurred." This information should be discussed in the discussion section.
   We have added a section in the "discussion" (paragraph 9) in which we explain, by means of the "septic theory", this reduced "compaction" of the graft material in cases where the SM was repaired by L-PRF. According to this explanation, the graft would contain air

bubbles caused by the presence of anaerobic bacteria. These bacteria would colonise the graft material through the perforation of the SM and the longer surgical time required to repair it. The conclusions were also modified by specifying this fact.

Reviewer 4:

Submitted case series reported a treatment method for the most frequent intrasurgical complication of sinus lifting procedure-Schneiderian membrane perforation. However, the manuscript has some drawbacks that need further clarification.

Dear reviewer,

Thank you for taking the time to review our manuscript and helping us improve the quality of our work. After analysing your comments, we proceed to answer them one by one:

1. The conclusion has overexpressed the findings. Also, conclusion is too general when it is commented on cost which not all 3 cases treated with only PRF.
   In line with your comment, we have modified the conclusions (both in the specific section at the end of the manuscript and in the abstract).
2. Information on surgeon's experience, presence of pathology within the sinus and the use of certain medications, systemic status, smoking status should be given.
   Information on the surgeon's experience was added at the beginning of paragraph 3 of the Case Presentation section, and in table 1, information on the systemic status, medications, and smoking status of all included patients was added..
3. The discussion should include information on sinus perforation management strategies considering perforation size and location.
   Strategies for the management of SM perforations were added at the beginning of paragraph 7 of the discussion.
4. The authors would benefit on manuscript structure if they follow CARE guidelines.
   Minor modifications were made to adapt the manuscript to the CARE guidelines.
5. Page 3, line 15: (n=2) belongs to patient or implant?
   This refers to the fact that two implants were placed in position 2.6. For clarification, this was specified (n= 2 DIs).
6. Different techniques to different size of the perforations has been applied, therefore it is hard to give a common conclusion to all.
   In line with your comment, we have modified the conclusions (both in the specific section at the end of the manuscript and in the abstract).
7. How could the authors make a statement on "greater bone compaction and maturation"? Which parameter did they consider?
   We have added Figure 5. This figure compares the radiological appearance at baseline and at 6 months postoperatively in patients with repaired and unrepaired SM in both repaired and unrepaired sinuses in patients who underwent bilateral SLSs.
   We also tried to explain this finding in the discussion (paragraph 9) through the "septic theory". So, the graft would contain air bubbles caused by the presence of anaerobic bacteria. These bacteria would colonise the grafted material through the perforation of the SM and through increased surgical time. The conclusions were also modified by specifying this fact.

2nd Editorial decision

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27-Jul-2022

Ref.: Ms. No. JCTRes-D-22-00059R1
Treatment of sinus membrane perforations during sinus lift surgeries using Leukocyte- and Platelet-Rich Fibrin: A case series.
Journal of Clinical and Translational Research

Dear authors,

I am pleased to inform you that your manuscript has been accepted for publication in the Journal of Clinical and Translational Research.

You will receive the proofs of your article shortly, which we kindly ask you to thoroughly review for any errors.

Thank you for submitting your work to JCTR.

Kindest regards,

Michal Heger
Editor-in-Chief
Journal of Clinical and Translational Research

Comments from the editors and reviewers: