Dear Editors and Reviewers:

Thank you very much for your careful review and constructive suggestions with regard to our manuscript "Pulp revascularization on an adult mandibular right second premolar: a case report with a three-year follow-up" Manuscript NO.: 73971. Those comments are helpful for us to revise and improve this article.

We have revised and improved the manuscript according to the reviewer's comments. In the revised version of our manuscript, revised portion are highlighted in yellow and the replies to the reviewer's comments are showed by using the comment function of office.

We appreciate for Editors/Reviewers' warm work earnestly and hope that the corrections will meet with approval. Please feel free to contact us with any questions and we are looking forward to your consideration.

The main corrections in the paper and the replies to the reviewer's comments are as follows:

Comments from Reviewer 1:

Scientific Quality: Grade B (Very good)

Language Quality: Grade B (Minor language polishing)

Conclusion: Accept (General priority)

Specific Comments to Authors: method of pulp revascularization need to be mentioned in the title it is not clear what is the reason for incomplete root formation in a 26 years old patient to follow up case radiographically it is much more reliable to use CBCT line 174 please add reference page 177 it is much more accurate to say we have inadequate evidence's instead of no evidence's page 180 reference required it is not clear in the discussion section the role of cefaclor antibiotic, bacteriologically what is the mean reason of its use IROOTBP role is not clear in the healing process suggested scaffolds and its forms alo need to be clear

Reply:

Thank you very much for your comment. We are very glad that our manuscript was approved.

Comment 1: method of pulp revascularization need to be mentioned in the title <u>Reply:</u>

Thank you very much for your advice. At present, pulp revascularization has been used as a specific method treatment in regenerative endodontic therapy. As far as we know and consult the relevant reference, there is no more specific description of this method. The morphology of the patient's mandibular right second premolar is abnormal, and there was an abnormal central cusp. Soon after eruption, it was in frequent contact with the contralateral teeth, and over time, the abnormal central cusp was broken. It was the infection and necrosis of dental pulp and the necrosis of dental papilla tissue, which then affects the continuous development of tooth root.

Comment 2: it is not clear what is the reason for incomplete root formation in a 26 years old patient

Reply:

Thank you very much for your comment. The morphology of the patient's mandibular right second premolar is abnormal, and there was an abnormal central cusp. Soon after eruption, it was in frequent contact with the paired jaw teeth, and over time, the abnormal central cusp was broken. It was the infection and necrosis of dental pulp and the necrosis of dental papilla tissue, which then affects the continuous development of tooth root.

Comment:3: to follow up case radiographically it is much more reliable to use CBCT

Reply:

Thank you very much for your comment.



Preoperative view



Postoperative view

Comment 4: line 174 please add reference

Reply:

Thank you very much for your comment. We made a revision to this in our revised manuscript and cited reference. Please check it.

Original version (Discussion section, Line 173, Page 11):

.....However, it is a material of high cost and difficult clinical manipulation. In addition, clinical treatment and follow-up visits found that apical barrier technology caused less root development, no thickening of the root wall or extension of root length.

Revised version (*Background* section, *Line 173, Page 11*):

.....However, this technology has a high cost and difficult clinical manipulation. In addition, clinical treatment and follow-up visits found that apical barrier technology

caused less root development and no thickening of the root wall or extension of the root length [15].

Comment 5: page 177 it is much more accurate to say we have inadequate evidence's instead of no evidence's

Reply:

Thank you very much for your comment. We made a revision to this in our revised manuscript. Please check it.

Original version (Discussion section, Line 178, Page 11):

.....However, there is no literature to support that pulp revascularization has a good effect on adult patients with immature roots with open apical teeth [12].

Revised version (*Background* section, *Line 178, Page 11*):

.....However, there is inadequate literature to support that pulp revascularization has a good effect on adult patients with immature roots and open apical teeth [15]

Comment 6: page 180 reference required it is not clear in the discussion section the role of cefaclor antibiotic, bacteriologically what is the mean reason of its use <u>Reply:</u>

Thank you very much for your comment. We made a revision to this in our revised manuscript. Please check it.

Original version (Discussion section, Line 198, Page 12):

The common complication of revascularization is tooth discolouration. Previous studies have suggested that tooth discolouration is related to the triple antibiotic paste. Minocycline is considered to form a chelate with calcium ions in dentinal tubules, which changes the refractive index of teeth and causes tooth discolouration [14].

Revised version (Discussion section, Line 198, Page 12):

A common complication of revascularization is tooth discoloration. Previous studies have suggested that tooth discoloration is related to the triple antibiotic paste. Minocycline is considered to form a chelate with calcium ions in dentinal tubules, which changes the refractive index of teeth and causes tooth discoloration [17]. Cefaclor is an antibiotic alternative to minocycline. Thibodeau et al [18]. and Dabbagh et al [19]. proposed replacing minocycline with cefaclor and reported successful regenerative treatment using this technique.

Comment 7: IROOTBP role is not clear in the healing process suggested scaffolds and its forms alo need to be clear

Reply:

Thank you very much for your comment. We made a revision to this in our revised manuscript. Please check it.

Original version (Discussion section, Line 204, Page 12):

In this case, there was no obvious discolouration of the affected teeth, which may be because cefaclor was used instead of minocycline and iRoot BP was used instead of MTA.

Revised version (*Discussion* section, *Line 204, Page 12*):

In this case, there was no obvious discolouration of the affected teeth, which may be because cefaclor was used instead of minocycline and iRoot BP was used instead of MTA. Some studies have found that iRoot BP promotes increased alkaline phosphatase activity compared with MTA, and iRoot BP has better biocompatibility and repair performance and promotes the expression of factors related to odontogenic differentiation, so it has a higher biomineralization ability and induces dentin differentiation [21].

Comments from Reviewer 2:

Scientific Quality: Grade A (Excellent) Language Quality: Grade A (Priority publishing)

Conclusion: Minor revision

Specific Comments to Authors: The paper is very interesting, however, before acceptance, authors should discuss in a more accurate way the state of the art about stem cells applicatin in dentistry. Indeed, they should cite the following papers: - PubMed ID32188154 - PubMed ID32811413 - PubMed ID33386051 Moreover they should emphasize the potential role of chlorexidine in managing stem cell implantation procedures. Please cite DOI10.23805/JO.2019.12.01.20

Reply:

Thank you very much for your comment. We are very glad that our manuscript was approved.

Comment 1: The paper is very interesting, however, before acceptance, authors should discuss in a more accurate way the state of the art about stem cells applicatin in dentistry. Indeed, they should cite the following papers: - PubMed ID32188154 - PubMed ID32811413 - PubMed ID33386051

Original version (*Introduction* section, *Line 52, Page 3*):

During the treatment process, it is best to protect the residual dental pulp tissue, dental pulp stem cells and apical papillary stem cells.

Revised version (*Introduction* section, *Line 52, Page 3*):

During the treatment process, it is best to protect the residual dental pulp tissue, dental pulp stem cells and apical papillary stem cells. Studies have shown that stem cells that isolated from various problems of the oral cavity have emerged as important sources for bone and dental regulation, given stem cells plasticity, they can differentiate into specific cell lineages with a capacity of almost unlimited self-renewal and release of trophic / immunomodular factors.[8-10]

Comment 2: Moreover they should emphasize the potential role of chlorexidine in managing stem cell implantation procedures. Please cite DOI10.23805/JO.2019.12.01.20

Reply:

Thank you very much for your comment. Since chlorhexidine was not used in this case, the potential role of chlorhexidine in the implementation procedure of managing stem cells was not emphasized. However, through the reference given by the reviewer, we know that chlorhexidine is widely used in daily clinical practice for its bactericidal and bacteriostatic properties are associated with high durability, it binds well to teeth and oral mucosa, and its progressive release can be maintained for up to 12 hours. Its wide range of antimicrobial effects makes it the most effective, and hence the most extensively used, product available for the control of dental plaque, for the prevention of gingivitis and for the management of post-surgical infection. We will try to use chlorhexidine in future cases and discuss the potential role of chlorhexidine in the management of stem cell implementation procedures.

4 LANGUAGE POLISHING REQUIREMENTS FOR REVISED MANUSCRIPTS SUBMITTED BY AUTHORS WHO ARE NON-NATIVE SPEAKERS OF ENGLISH

As the revision process results in changes to the content of the manuscript, language problems may exist in the revised manuscript. Thus, it is necessary to perform further language polishing that will ensure all grammatical, syntactical, formatting and other related errors be resolved, so that the revised manuscript will meet the publication requirement (Grade A).

Authors are requested to send their revised manuscript to a professional English language editing company or a native English-speaking expert to polish the manuscript further. When the authors submit the subsequent polished manuscript to us, they must provide a new language certificate along with the manuscript.

Reply:

According to the editor's instruction, we have revised the manuscript carefully. In addition, we have used the language editing service and obtained the certificate with the help of editors of Editage by AJE. We hope that the language is now acceptable for the next review process.



Editing Certificate

This document certifies that the manuscript

Pulp revascularization on an adult mandibular right second premolar: a case report with Three-year follow-up

prepared by the authors

Yeqing Yang, Junkai Zeng, Chong Jiang, Buling Wu, Ming Chen

was edited for proper English language, grammar, punctuation, spelling, and overall style by one or more of the highly qualified native English speaking editors at AJE.

This certificate was issued on March 16, 2022 and may be verified on the AJE website using the verification code 8122-1782-437B-A782-0248.



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