

Clinical Success of Platelet-rich Fibrin and Mineral Trioxide Aggregate (MTA) or MTA-like Agents in Healing of Periapical Lesion in Nonsurgically Treated Pulpless Immature Permanent Teeth: A Systematic Review

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ABSTRACT

Background: The chances of extrusion of mineral trioxide aggregate (MTA) are quite high if apical barrier is not present in immature pulpless permanent teeth. Platelet-rich fibrin (PRF) enriched with platelets and growth factors serves to accelerate the wound healing of periapical lesion in immature pulpless permanent teeth and also serves as internal matrix to condense MTA. **Aim:** The aim of the present study was to comprehensively review the clinical success of MTA+PRF in healing of periapical lesions in immature pulpless permanent teeth. **Materials and Methods:** An electronic search for systematic review was conducted in Pubmed/Medline (www.ncbi.nlm.nih.gov), Cochrane (www.cochrane.org), Scopus (www.scopus.com) databases upto 15th January 2020 related to the healing of periapical lesions in permanent teeth with immature apices when combination of MTA+PRF was used. A sample of 10 relevant studies and case reports were identified in our search out of 65. The sampling method was simple random technique. The studies and case reports with Randomised Controlled Trials(RCTs), Invitro studies, Case reports and animal studies in healing of periapical lesion were included in our comprehensive systematic review. **Results:** The search showed that the combination of MTA+PRF showed faster and definite periapical lesion healing in immature permanent teeth. The follow-up period was also recorded in all the relevant studies and case reports. **Conclusion:** Accelerated bone filling was seen in healing of periapical lesions when MTA+PRF was used.

KEYWORDS: Apexification, immature teeth, pulp regeneration, regenerative endodontics, revascularization

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INTRODUCTION

Root canal treatment for teeth with immature apices poses a significant challenge because of thin dentinal walls and open apices. The standard root canal treatment cannot be achieved due to open apex. The alternative treatment, revascularization/revitalization or apexification, has been advocated.^[1]

Root end closure (revascularization) for immature pulpless teeth is an accepted treatment protocol. The outcome of revascularization depends on the survival

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of stem cells adjacent to the root canal system. The clinical outcome of revascularization remains unpredictable, and the management is also challenging. The outcome of treatment needed multiple visits and longer time.^[2]

Apexification is defined as mechanical induction of calcific barrier in teeth with incomplete root development. Calcium hydroxide, Ca(OH)₂, has been always the first choice of material but the treatment with Ca(OH)₂ needed longer time and multiple appointments. Poor patient compliance in keeping follow-up appointments and failure to maintain temporary seal may result in reinfection. For these reasons, one-visit apexification has been advocated.^[3]

The one-step or one-visit apexification can be achieved by nonsurgical compaction of mineral trioxide aggregate (MTA) or MTA-like agents (Biodentine), thereby creating artificial apical stop. MTA is composed of tricalcium silicate, tricalcium aluminate, tricalcium oxide, and silicone oxide, and it sets in 4–5 h. It has been shown to promote periapical tissue healing and periodontal healing. But in wide open apex cases, it may be extruded beyond the apex.^[4] Therefore, an apical matrix is used for controlled placement of MTA at the apical third. Number of materials such as collagen calcium phosphate,^[5] proplast,^[6] and freeze-dried dentin,^[7] have been used as internal matrix followed by condensation of MTA.

Platelet-rich fibrin (PRF) developed by Choukroun and Dohan,^[8] contains strong fibrin membrane enriched with platelets and growth factors. It serves to accelerate the wound healing and also serves as internal matrix to condense MTA.^[9]

This study was a systematic review to assess the success rate of autologous PRF, which acts as an internal matrix for one-step apical barrier placement of MTA or MTA-like agents (Biodentine) in healing periapical lesions of immature pulpless permanent teeth.

MATERIALS AND METHODS

PROTOCOL

This article was designed according to the Cochrane criteria (Cochrane Handbook for Systematic Reviews of Interventions, version 5.1.0) for elaborating systematic review.^[10]

ELIGIBILITY CRITERIA

The inclusion criteria were (1) randomized controlled trials as well as prospective and retrospective trials, (2) studies (*in vivo* and *in vitro*) and case reports that evaluated the success rate of autologous PRF and

MTA) in healing of periapical lesions in pulpless immature permanent teeth, (3) studies published in English language, and (4) animal studies. Exclusion criteria included any articles that failed to meet the inclusion criteria. Letters to editor and reviews were excluded from this study.

OUTCOME

The outcome of this review was to assess the clinical success of PRF and MTA in healing periapical lesion in pulpless immature permanent teeth.

STRATEGY OF SEARCH

Information sources: An electronic search was conducted in PubMed/Medline (www.ncbi.nlm.nih.gov), Cochrane (www.cochrane.org), and Scopus (www.scopus.com) databases up to January 15, 2020. The search structure followed the pediatric and endodontics journals: *Dental Traumatology*, *International Journal of Pediatric Dentistry*, *Pediatric Dentistry*, *Journal of Endodontics*, *International Endodontic Journal*, *Journal of American Dental Association*, and *Australian Endodontic Journal*. The keywords “Apexification,” “Pulp Regeneration,” “Regenerative Endodontics,” “Revascularization,” and “Immature Teeth” were used. The search includes all the articles from the start date of each source until January 15, 2020 [Figure 1 and Table 1].

RESULTS

Risk of bias assessment: Bias was not assessed for the outcomes because majority of the cases were case reports. Only three studies were included.

In the results of the literature search referring to clinical studies and case reports of clinical success of healing of periapical lesions in the permanent teeth with open apices with PRF and MTA or MTA-like materials, 10 articles have been found. Among the variables are the year of the study or case report, type of the study, and conclusion of the study or case report.

DISCUSSION

Kathuria *et al.*^[11] reported the use of PRF and MTA in healing of periapical lesion in permanent mandibular second molar. The PRF matrix prevented the extrusion of MTA in periradicular tissues. PRF, an autologous fibrin, consists of platelets and cytokines within fibrin mesh, which are released progressively over a period of 7–10 days. PRF and MTA together promoted osseous filling in the lesion due to the release of platelet derived growth factor, insulin like growth factor, and transforming like growth factor. Thus the combination

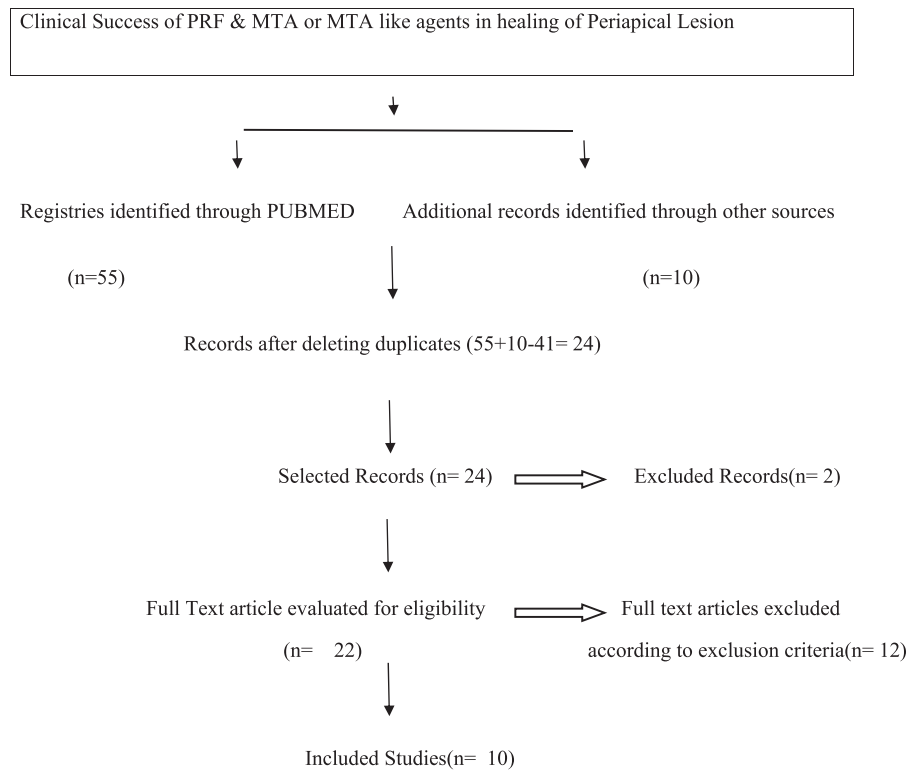


Figure 1: Diagrammatic representation of clinical success of platelet-rich fibrin and mineral trioxide aggregate (MTA) or MTA-like agents in healing of periapical lesion in immature pulpless permanent teeth

Table 1: Studies implicating the success of platelet-rich fibrin and mineral trioxide aggregate (MTA) or MTA-like agents in healing of periapical lesion

Serial number	Authors' name	Year	Type of study	Conclusion
1.	Kathuria <i>et al.</i> ^[11]	2011	Case report	Faster periradicular healing and complete resolution of symptoms occurred with MTA and PRF as apical barrier in mandibular second permanent molar. Follow-up was of 18 months.
2.	Rudagi and Rudagi ^[12]	2012	Case report	Successful healing of periradicular tissues with MTA and PRF as an internal matrix. Follow-up was of 12 months (with 2-month interval).
3.	Khetrupal <i>et al.</i> ^[13]	2013	Case report	PRF acts as a fibrin bandage serving as a matrix to accelerate the healing of wound edges. Combination of PRF and MTA has been demonstrated to be an effective alternative for creating root end barrier and to induce faster periapical healing. Follow-up period was of 9 and 12 months
4.	Yadav <i>et al.</i> ^[14]	2015	Case report	Faster periapical healing of tissues when MTA and PRF was used in combination in a failed revascularization case. Follow-up period was for up to 24 months.
5.	Woo <i>et al.</i> ^[15]	2015	<i>In vitro</i> study	Combination of PRF and MTA has a synergistic effect on stimulation of odontoblastic differentiation of human dental pulp stem cells via modulation of BMP/Smad signaling pathway.
6.	Tawfik <i>et al.</i> ^[16]	2015	Descriptive study	Perforation defects with periapical lesion healed more effectively when MTA and PRF were used together.
7.	Pawar <i>et al.</i> ^[17]	2015	Case report	Periapical lesion healed in failed attempt of revascularization, when MTA and PRF were used together.
8.	Goel <i>et al.</i> ^[18]	2017	Case report	Periradicular lesion healed faster in a tooth with dens invaginatus when combination of PRF and Biodentine was used.
9.	Khanduri and Kurup ^[19]	2018	Case report	PRF used as an internal matrix over which sealing material was placed. PRF and MTA together helped in the healing of periapical lesion. PRF and MTA provides good apical sealing ability because of release of calcium and hydroxyl ions from set matrix. Follow-up of 30 months showed good bone filling using CBCT.
10.	Nazife and Aricloglu ^[20]	2019	Descriptive study	CBCT was used for the assessment of bone healing in 40 participants, which were divided into four groups of (1) MTA, (2) PRF, (3) MTA +PRF, and (4) control. Statistically significant difference was seen in healing of periapical lesion between MTA + PRF and other group agents. MTA + PRF showed better healing in comparison with other materials.

of MTA and PRF promotes faster periapical healing.

Rudagi and Rudagi^[12] reported that PRF as a matrix and MTA as an apical barrier could be considered as a good option for creating artificial root end barrier. The follow-up of 12 months showed reduction in the size of periapical lesion, and the patient was completely asymptomatic.

Khetrpal *et al.*^[13] presented a successful report of three cases in which PRF was used as a “Modified Matrix” for the condensation of MTA. PRF acts as a fibrin bandage serving as a matrix to accelerate the healing of wound edges. Combination of PRF and MTA has been shown to be an effective alternative for creating root end barrier and to induce faster periapical healing. The follow-up period was of 9–12 months.

Yadav *et al.*^[14] carried out the technique of revascularization in an 18-year-old female. But the technique failed with grade 1 mobility to the affected tooth and symptomatic apical periodontitis. The failure was in the form of formation of periapical lesion and inhibition of root growth. Placement of PRF followed by condensation of MTA in a failed case of revascularization was attempted. The tooth was obturated with GuttaFlow. Clinical and radiographic examination was carried out at 1, 3, 6, 9, 18, and 24 months. The combination of PRF and MTA showed predictable and reproducible results with the healing of periapical lesion.

Woo *et al.*^[15] conducted an *in vitro* study in which combination of MTA and PRF showed synergistic effect on the stimulation of odontoblastic cell differentiation via the modulation of BMP/Smad signaling pathway.

Tawfik *et al.*^[16] conducted a study on 192 teeth of 12 dogs in which perforation defects covered with MTA and PRF showed reduced inflammatory response and improved periapical healing.

Pawar *et al.*^[17] reported healing of periapical lesion in a failed attempt of revascularization, when MTA and PRF were used together.

Goel *et al.*^[18] reported that periradicular lesion healed faster in a tooth with dens invaginatus when combination of PRF and Biodentine was used. Biodentine (MTA-like agent) showed good sealing ability, high compressive strength, excellent biocompatibility, very short setting time (6 min), and better handling properties. To prevent overfilling, PRF was used as the apical matrix. PRF has been shown to be osteoinductive and osteoconductive.

Nazife and Aricoglu^[20] carried out a cone beam computed tomography (CBCT)-based study for the

assessment of bone healing in four groups. The MTA + PRF showed better bone fill and density in comparison with other groups in healing of periapical lesion.

CONCLUSION

To conclude, PRF when used as an apical barrier along with MTA or MTA-like agents in nonsurgical management of pulpless immature permanent teeth, accelerated bone filling was seen from the different studies and case reports. Thus, it helps in “guided tissue repair” and bone regeneration. However, histological studies are required to see the quality of newly formed bone, and long-term clinical trials are required to know the effects of combination of MTA + PRF.

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CONFLICTS OF INTEREST

There are no conflicts of interest.

AUTHOR CONTRIBUTIONS

Not applicable.

ETHICAL POLICY AND INSTITUTIONAL REVIEW BOARD STATEMENT

Not applicable.

PATIENT DECLARATION OF CONSENT

Not applicable.

DATA AVAILABILITY STATEMENT

Not applicable.

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