Efficacy of Platelet-Rich Fibrin After Mandibular Third Molar Extraction: A Systematic Review and Meta-Analysis



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Purpose: To assess the effect of platelet-rich fibrin (PRF) on the healing process of the alveolar socket after surgical extraction of the mandibular third molars.

Materials and Methods: PubMed, the Cochrane Central Register of Controlled Trials, Scopus, and relevant journals were searched using a combination of specific keywords ("platelet-rich fibrin," "oral surgery," and "third molar"). The final search was conducted on November 2, 2015. Randomized controlled clinical trials, as well as controlled clinical trials, aimed at comparing the effect of PRF versus natural healing after extraction of mandibular third molars were included.

Results: Five randomized controlled trials and one controlled clinical trial were included. There were 335 extractions (168 with PRF and 167 controls) in 183 participants. Considerable heterogeneity in study characteristics, outcome variables, and estimated scales was observed. Positive results were generally recorded for pain, trismus, swelling, periodontal pocket depth, soft tissue healing, and incidence of localized osteitis, but not in all studies. However, no meta-analysis could be conducted for such variables because of the different measurement scales used. The qualitative and meta-analysis results showed no significant improvement in bone healing with PRF-treated sockets compared with the naturally healing sockets.

Conclusions: Within the limitations of the available evidence, PRF seems to have no beneficial role in bone healing after extraction of the mandibular third molars. Future standardized randomized controlled clinical trials are required to estimate the effect of PRF on socket regeneration.

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Extraction of mandibular third molars is the most common procedure performed by oral-maxillofacial surgeons.¹ The surgical procedure may be associated with considerable postoperative side effects and complications, which include pain, trismus, edema, infection, and dry sockets.²⁻⁶

Platelet-rich plasma (PRP) was found to reduce pain, swelling, and alveolar osteitis (AO), as well as improve soft and hard tissue healing, after mandibular third molar extractions.⁷⁻⁹ However, placing PRP is a timeconsuming technique, and it has poor mechanical properties that have discouraged many surgeons from routinely using it after extractions.¹⁰

Platelet-rich fibrin (PRF) is a second generation of the platelet concentrate. It is prepared with a simplified, inexpensive process and without biochemical blood handling.¹¹ It is an autologous soluble biologic material that does not introduce foreign material into

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© 2017 American Association of Oral and Maxillofacial Surgeons 0278-2391/17/30107-6 http://dx.doi.org/10.1016/j.joms.2017.01.022 the surgical site and prevents consequent foreign-body inflammatory responses.^{12,13}

Similar to natural healing, slow polymerization during PRF preparation generates a fibrin network that enhances cell migration and proliferation. Being a reservoir of platelets, leukocytes, cytokines, and immune cells, PRF was reported to allow slow release of cytokines—transforming growth factor, plateletderived growth factor, vascular endothelial growth factor, and epidermal growth factor—which play a critical role in angiogenesis, tissue healing, and cicatrization.^{11,13-15}

Moreover, PRF has multiple applications in implant and dentoalveolar surgery. PRF may be used alone or combined with bone grafts as a socket preservation material and for treatment of periodontal bony defects.¹⁶⁻²¹ PRF is used to enhance tissue healing and to minimize postoperative inflammatory complications after mandibular third molar extractions.^{12,22-28}

To date, there is no evidence that summarizes the effect of PRF application on bone healing after mandibular third molar extractions. This study was conducted to systematically review and critically analyze the available evidence on the effect of PRF on tissue healing and potential complications after mandibular third molar extractions.

Materials and Methods

SEARCH STRATEGY

An electronic search was conducted in the following databases (from August 20 to November 2, 2015): PubMed, the Cochrane Central Register of Controlled Trials, and Scopus. The online databases of *Journal of Oral and Maxillofacial Surgery, International Journal of Oral and Maxillofacial Surgery, British Journal of Oral and Maxillofacial Surgery,* and *Journal of Cranio-Maxillo-Facial Surgery* were searched manually. "Platelet-rich fibrin," "oral surgery," and "third molar" were the keywords used for the electronic search. The reference lists of similar reviews were manually checked for studies that met the inclusion criteria.

The inclusion criteria included all English-language randomized clinical trials (RCTs) and controlled clinical trials that compared the effect of PRF application on fresh extraction sockets of mandibular third molars versus natural socket healing. Non-English-language studies, retrospective studies, case series, case reports, animal studies, and review studies were excluded. Studies that evaluated the role of PRF in extraction sockets of teeth other than the mandibular third molars, as well as studies that compared PRF as a socket filling with other biologic material, also were excluded. The following data were collected for each study (when available): authors, publication year, country of origin, study design, mean age, age range, malefemale ratio, medical status, participants, surgical sessions, closure technique, tooth angulation, bone removal, bone removal device, operation time, cointerventions, follow-up period, blood collection protocol, and outcome variables (Tables 1,2). Two researchers (E.A. and F.A.) independently reviewed the included articles and collected the data. Disagreements between the reviewers were resolved by consensus.

QUALITY ASSESSMENT

The quality assessment of the included studies was performed following the guidelines from the *Cochrane Handbook for Systematic Reviews of Interventions* and the PRISMA (Preferred Reporting Items for Systematic Reviews and Meta-Analyses) protocols.^{32,33} The Cochrane Collaboration's tool for assessing risk of bias in RCTs was used to assess the quality of the included articles.³⁴

META-ANALYSIS

The meta-analysis standard scale was used to evaluate one common outcome (bone healing with bone scintigraphy) in 2 studies $only.^{30,31}$

ASSESSMENT OF HETEROGENEITY

Heterogeneity among studies was estimated by the Cochrane test for heterogeneity and the I^2 statistic. The χ^2 test was used to determine the presence of statistical heterogeneity. Heterogeneity was considered statistically significant at P < .10. The interpretation of the I^2 statistic depended on the Cochrane Collaboration recommendations.³⁵

Results

STUDY SELECTION

The electronic and manual searches identified 242 articles, of which 60 were duplicates and were excluded. The abstracts of the remaining 182 articles were screened, and the full text of the related studies was read by both researchers for potential inclusion. Of 13 full-text studies reviewed for potential inclusion, only 6 met the inclusion criteria and were assessed for reliability.^{22,26,27,29:31} The other 7 articles were excluded for the following reasons: One study was a retrospective study²³; one study compared PRP with PRF¹²; in one study, the prepared material was PRP gel, although the title mentioned it was PRF²⁴; data analysis was not reported in one study³⁶; and in three studies, multiple extractions were performed other

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