

# Impact of platelet-rich fibrin (PRF) on mandibular third molar surgery recovery: an article review

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## Abstract

**Background:** Extraction of impacted mandibular third molars is the most frequent procedure performed by oral surgeons. This procedure may be associated with considerable postoperative complications including pain, trismus, edema, surgical site infection as well as alveolar osteitis (AO).

Platelet-rich fibrin is characterized by the slow polymerization during its preparation that generates a fibrin network very similar to the natural one that enhances cell migration and proliferation.

**Materials and Methods:** The aim of this article is to investigate the effect of PRF on lower third molar extraction. Pain, swelling, trismus, alveolar osteitis (AO), and osteoblastic activity were extracted to evaluate the effect of PRF. Also, narrative review of clinical outcomes from different articles published on Pubmed, Medscape, Cochrane Library and Google Scholar are included.

**Results:** Being a reservoir of platelets, leukocytes, cytokines and immune cells, PRF is reported to allow slow release of cytokines; TGF, PDGF, VEGF, and EGF which play a critical role on angiogenesis and tissue healing and cicatrization. PRF also reported to enhance angiogenesis, support immunity, and to enhance the coverage of injured tissues through its positive effect on epithelial cells and fibroblasts.

Although, PRF preparation is simple, inexpensive process, and requires no additives, rapid blood handling is an important factor in success of its preparation. Failure in quick handling of the blood sample results in a diffuse polymerized fibrin within the glass tube and only a small blood clot without consistency will be obtained.

**Conclusion:** The evidence supports the use of PRF as socket preservation materials to enhance soft tissue healing and reduce postoperative complications. However, there is no evidence to date to support the positive effect of autologous materials in hard tissue regeneration.

**Keywords:** Platelet-rich fibrin, cytokines, alveolar osteitis.

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## I. Introduction

In oral surgery, the operation of the impacted third molar is one of the most common surgical procedures performed by oral and maxillofacial surgeons. After the impacted third molars are removed in the early postoperative stage, patients usually present complications such as pain, swelling, and trismus. These inflammatory complications are crucial for patients and surgeons in order to develop the customized strategy for reducing the risk of complications and improving postoperative healing. Several attempts using platelet-rich plasma administration, preoperative and postoperative antibiotics, cryotherapy, wound draining, the use of different kinds of flaps, and osteotomy using high- or low-speed rotary instruments, postoperative ice packs, analgesics, corticosteroids, and laser have been made to reduce the postoperative outcome of the removal of the third molar post-surgery.

## II. Materials and methods

It was made a literature research through the electronic database: PubMed, Medscape, Cochrane Library and Google Scholar. A systematic and comprehensive search was performed, using a combination of keywords and medical subheadings: “platelet-rich fibrin” or “PRF”, “oral surgery”, and “third molar”. The publications obtained from the search were reviewed on inclusion and exclusion criteria, in order to accurately and qualitatively define the study review. Inclusion criteria used in this review search are: published studies written in English and studies for which the full text is available for review, to be a review article. Exclusion criteria are: studies that are duplicates. In this way, the definition of considered studies was limited.

### III. Results

Platelet-rich fibrin can play an important role in oral and maxillofacial surgery, implant dentistry, periodontal regeneration and post-extraction site preservation. The fibrin is a reservoir of platelets that will slowly release growth factors and cytokines, which are the key factors for regeneration of the bone and maturation of the soft tissue. Platelet-rich fibrin (PRF) is an autologous platelet concentrate prepared from the patient's own blood at the dentist's office just before the oral/dental procedure. Platelets are the second-most numerous corpuscles in the blood. They are cytoplasmic fragments that lack core derived from megakaryocytes. Their lifetime is between 7 and 10 days, and the normal peripheral blood concentration is  $150-450 \times 10^9/L$ . These unactivated platelets are biconvex discoid structures shaped like a lens with dimensions of approximately  $2.0-4.0$  by  $0.5 \mu m$  and a mean volume of 7-11 fl.

Platelets are formed by a peripheral area, which corresponds to a phospholipid membrane, a series of microtubules, and a very extensive canalicular system connecting the surface to the cytoplasm. Glycogen granules, mitochondria, lysosomes, peroxisomes, and various types of inclusions, including alpha and dense granules, can be identified within the cytoplasm.

Platelet-rich fibrin (PRF) is a novel strategy for concentrating the platelets (the preparation process without thrombin), which can be used for the enhancement after tooth extraction and residual cyst bone formation and promotion of the wound epithelialization. The PRF originates from the slow, gradual polymerization occurring during centrifugation. This is the second generation of immune platelet concentrate, collected as single fiber membrane protein components of the blood sample.

Whitman in 1997, was the first to introduce the use of platelet-rich plasma in oral surgical procedures, reporting great advantages because it enhances osteoprogenitor cells in the host bone and bone graft. However, using it also presents risk because bovine thrombin, which is used to handle PRP, may generate antibodies to factors V, XI, and thrombin that could cause coagulopathies that may endanger life.

These components are utilized for healing and immune regulation, especially, fibrin matrix in which, growth factors (vascular endothelial growth factor (VEGF), transforming growth factor (TGF)-A1, platelet-derived growth factor (PDGF)-AA, and insulin-like growth factor 1, leukocytic cells, and their cytokines such as, interleukin (IL)-4, IL-6, IL-1A, and tumor necrosis factor (TNF)) are enmeshed. PRF is the second generation of platelet concentrates (PRP is the first generation). It is characterized by slow polymerization during preparation, which produces a fibrous protein network similar to the natural cells in order to enhance cell migration and proliferation. As a reservoir of platelets, cytokines, leukocytes, and immune cells, PRF allows a sustained release of cytokines such as VEGF, PDGF, TGF, and epidermal growth factor (EGF) that play a key role in vascular and tissue healing and scarring. PRF also enhances angiogenesis, supports immunity, and increases the coverage of the injured tissue by enhancing the positive effects on epithelial cells and fibroblasts. In oral and maxillofacial regions, PRF is widely used in simple graft or combination with allograft or xenograft. In addition, the PRF clots are used for the flapless treatment of acute sinus perforations. The extraction for socket preservation, intrabony defects, and periodontal problems are the other indications of PRF usage.

Complications following third molar surgery are not uncommon. Pain and delayed healing are perhaps the most frequently encountered complications. AO is a painful and relatively common complication that necessitates intervention for treatment. Relief of postoperative pain is an essential criterion in the overall success of tooth extraction. In addition, most of the potential postoperative complications are in fact manifested as pain.

In research done by Faez Saleh Al-Hamed et al. about clinical effects of PRF revealed that PRF significantly reduced postoperative pain and analgesic consumption following surgical removal of impacted third molars. This, although could not be detected clinically, could reflect a better and faster healing of the extraction sockets. The decrease in pain or analgesic consumption, although statistically significant for few postoperative days, should be considered with caution because it is based on the subjective visual analogue scale, pain sensation, and response to analgesics, which differ from patient to another.

In another study Xu Xiang et al. evaluated the effect of PRF on the healing process of the alveolar socket after surgical extraction of the mandibular third molars by meta-analysis. The current results showed that the local application of PRF during lower third molar extraction prevented postoperative complications. Subsequently, the pain and swelling were relieved and the incidence of alveolar osteitis was reduced. However, according to their research there is no significant difference was observed in trismus, osteoblastic activity, and soft tissue healing between the PRF and non-PRF groups.

Furthermore, Choukroun et al. conducted a study in which they wanted to see the potential of using PRF in conjunction with freeze-dried bone allograft with (FDBA) to enhance bone regeneration in a maxillary sinus lift procedure. The results showed a decreased healing time prior to implant placement. From the histological point of view, this healing time was reduced by half - from 8 months to 4 months; however, large-scale studies are needed to validate these results. Additionally, the addition of PRF to the bone graft can lead to a reduction of the volume of bone substitute used and seems to improve revascularization of the graft by

supporting angiogenesis. Simonpieri et al. suggested using a mix of PRF with a bone graft, placing in bone defects, or, in cases of immediate implants, covering it with several PRF layers, noting good clinical results.

Yilmaz et al. histologically and stereologically compared the healing effects of  $\beta$ -TCP and PRF, alone and in combination, in standardized bone defects in pig's tibiae. The results showed that when  $\beta$ -TCP and PRF were used together, the newly formed bone was significantly greater than when used both separately. In addition, PRF may act as a biologic adhesive to hold the particles together, facilitating the manipulation of the bone grafts.

One of the latest innovations in oral surgery is the use of platelet concentrates for in vivo tissue engineering applications: 1) platelet-rich plasma (PRP) and 2) platelet-rich fibrin (PRF). Platelet concentrates are a concentrated suspension of growth factors found in platelets, which act as bioactive surgical additives that are applied locally to induce wound healing.

#### IV. Discussion

The results of our search was conducted to assess the effect of PRF on the healing process of the alveolar socket after surgical extraction of the mandibular third molars. Also, the results obtained from our search showed a beneficial effect of PRF in relieving pain and swelling and reducing the incidence of alveolar osteitis after extraction of an impacted lower third molar.

The physiological additives modulate the inflammation and increase the therapeutic effect postoperatively; the use of fibrin adhesives has been documented in the past three decades. However, due to the risk of cross-infection and cumbersome protocols for preparation, the use of these additives has been controversial.

#### V. Conclusion

PRF is the newest and most popular technique to accelerate healing in dentistry. During most large implant dental conventions and meetings in oral and maxillofacial surgery, periodontics, endodontics, implantology and bone regeneration, the number of speakers presenting successful cases increases every year. Everyone dentist involved in regenerative procedures and the manufacturing of PRF, are obligated to use only materials and supplies that guarantee patients' safety and, at the same time, eliminate the clinician's liability risks.

In conclusion, from the literary data that were the subject of our research, our study confirmed that PRF only reduces some of the postoperative complications but not prevent them. PRF administered after third molar extraction significantly relieved pain, swelling, and reduced the incidence of alveolar osteitis. Therefore, further studies with a larger dataset and well-designed models are essential to validate the current findings.

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