Regeneration, Reconstruction & Restoration **Review**

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Platelet-Rich Fibrin in Periodontal Treatment and Implant Dentistry: A Narrative Review

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Abstract

Platelet-rich fibrin (PRF) is a second-generation platelet derivative characterized by a dense fibrin network enriched with cytokines and growth factors. Its preparation includes involves centrifugation of autologous blood without anticoagulants that form a concentrated fibrin matrix, which could be inserted directly into the site of injury or used as a membrane for specific applications. Higher concentrations of growth factors in PRF lead to faster periodontal regeneration and higher clinical attachment gain, along with new bone formation. Thus, it's widely used in periodontal treatment. PRF has also shown promising results in implant dentistry. This review aims to summarize the current knowledge concerning the applications of PRF in periodontal treatment and implant dentistry and highlight its potential to improve clinical outcomes in these fields.

Keywords: Platelet-rich fibrin, Periodontal regeneration, Dental implant.

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1. Introduction

Platelets are discoid-shaped and small cell fragments derived from megakaryocytes (1). Platelets are the first arriving cells at the place of tissue injury. They also have diverse roles in hemostasis, wound healing, vessel constriction, and clot retraction. Activated platelets release their α granules, which contain various growth factors such as vascular endothelial growth factor (VEGF), platelet-derived growth factor (PDGF), insulin-like growth factor (IGF-1), and transforming growth factor (TGF-β) (2). Each of these growth factors has a fundamental role in wound healing. TGF-β inhibits the osteoclasts and shifts the differentiation of the progenitor cells toward osteoblastic and endothelial cells. PDGF acts in angiogenesis, chemotaxis, and proliferation of progenitor cells. IGF-1 provides the needed osteocalcin for matrix synthesis by increasing its expression and also aids the proliferation of osteoblasts (3). Upon the release of said factors and their binding to their receptors, they altered the expression of genes in target cells and, therefore, caused rapid healing (2).

Platelet-rich fibrin (PRF) is one of the platelet derivatives that consists of a dense fibrin scaffold enriched by growth factors and cytokines and can promote tissue regeneration and repair (4,5). It was suggested that PRF could be employed in tissue engineering for its unique roles in 1) angiogenesis (happens through the proliferation of endothelial cells), 2) Immune control (defined by functions such as chemotaxis and the degranulation of leukocytes), 3) the entrapment of stem cells in PRF's fibrin structure, and 4) the coverage of the wound with epithelialization (6).

In recent years, several studies have investigated the application of PRF in different medical and dental treatments (7-9). Periodontal treatments and implant dentistry also benefit from this bioactive material. In periodontal treatment, PRF was used in tissue engineering and regeneration, enhancing the healing process (2,3,7). In dental implant dentistry, using this autogenous material aimed to improve healing, stability, and the augmentation process for proper implant placement (4,8,9). This study aimed to review the different applications of PRF in periodontal treatments and implant dentistry.

2. PRF Preparation

The PRF, the second generation of plasma concentrations, was

invented by Choukroun and consists of leukocytes, growth factors, fibrin matrix, and platelets. Its preparation starts with centrifuging the obtained autologous blood at 2,700 and 3,000 rpm for 10 to 12 minutes (3), and there is no need to add an anticoagulant to the sample and which is centrifuged at 2,700 and 3,000 rpm for 10 to 12 minutes. It is noteworthy that the blood collection process and transfer to centrifuge tubes have to be accomplished quickly (maximum within 90 seconds) otherwise, the obtained PRF will not be clinically usable (10). Centrifugation results in three layers: red blood cells in the lowest layer, the acellular plasma layer at the upper level, and the platelet-rich fibrin in the middle. The PRF clot is removed from the tube and immediately applied to the site of interest (11).

The advantages of PRF are that it is a completely autologous product, the absence of bovine thrombin, the simplicity of the process, and less need for technical skills, along with low costs. Moreover, its dense fibrin network resulted in a slower degradation rate and extended release of growth factors (up to 7 days) (10). Furthermore, the preparation of PRF can be in the shape of a highly flexible membrane. By causing pressure between two sterile gauzes, the fluids in the PRF clot are extracted, and thus the desired membrane is achieved (11). However, its disadvantages are the low amount of PRF obtained in each session, and it requires immediate use after preparation to prevent losing its structural integrity (10).

The assembly of fibrin fibrillae in PRF formation is one a crucial factor causing the difference between PRP and PRF that distinguishes Platelet-rich plasma (PRP) from PRF. The fibrin fibrillae in PRP are made with bilateral junctions and high thrombin concentrations, which result in a firm network that contains fewer cytokines and permits fewer cells to migrate to the site of healing. Fibrin fibrillae of PRF, on the other hand, form equilateral junctions, leading to a less firm fibrin network and also higher entrapments of cytokines, as well as a more permeable environment for cellular migration (11).

Due to several leukocytes incorporated in it, PRF is also known as leukocyte and platelet-rich fibrin (L-PRF) (12). Various techniques used in the preparation of PRF lead to the making of different types of PRF, each with distinct characteristics and clinical applications (10-17), which are further discussed in Figure 1.

3. PRF in periodontal treatments

3.1. Periodontal regeneration

Periodontitis is an inflammatory disease resulting in periodontal attachment and alveolar bone destruction, and regeneration of lost periodontal tissue is the final goal of periodontal treatment. Following periodontal treatment, clot formation begins the healing process, which continues with proliferative and maturation stages. During the healing process, growth factors assist in the proliferation and migration of cells along with the formation of blood vessels (13,14). As mentioned before, the fibrin network in PRF holds higher concentrations of growth factors and inhibits their proteolysis. This leads to the prolonged activity of said stimulating factors and, thus, faster tissue regeneration (15). PRF was used for periodontal regeneration in infra-bony defects. It was used alone or in combination with graft material or may be used during guided tissue regeneration (GTR) (16). Reduction in pocket depth (PD), clinical attachment gain, and new bone formation were significantly

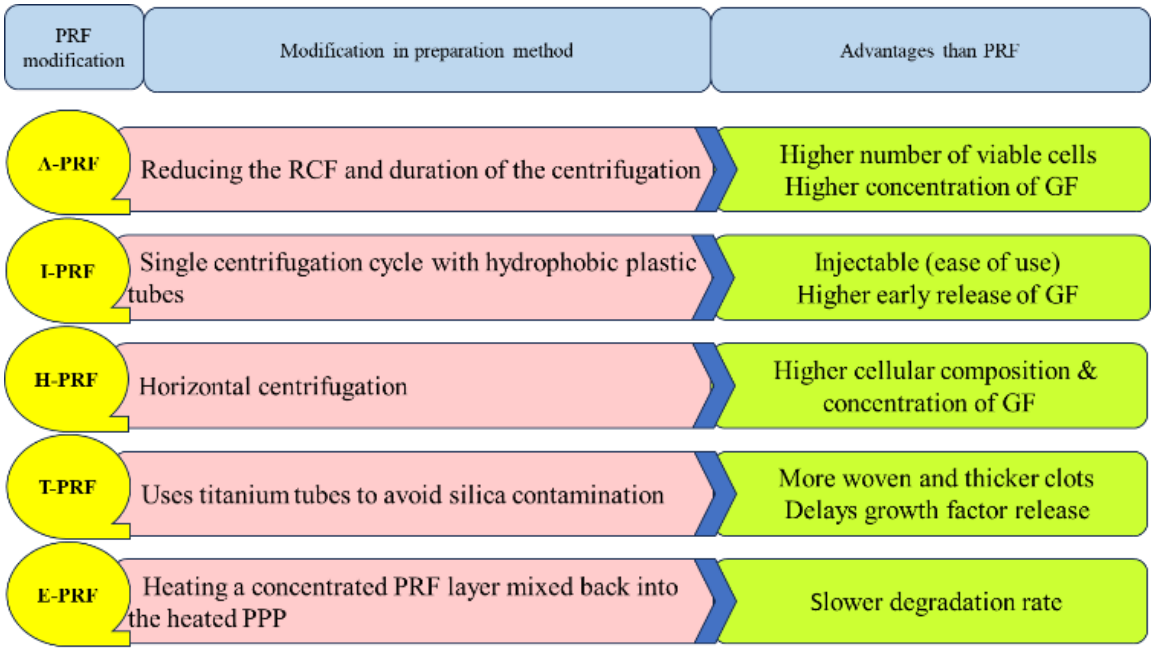

Figure 1. Different types of PRF and their advantages. A-PRF = Advanced platelet-rich fibrin, E-PRF = Extended platelet-rich fibrin, GF = Growth factor, I-PRF = Injectable platelet rich fibrin, H-PRF = Horizontal platelet-rich fibrin, L-PRF = leucocyte- and platelet-rich fibrin, PPP = platelet-poor plasma, RCF = Relative centrifugal force, T-PRF = Titanium-prepared platelet-rich fibrin.

higher in patients who received PRF (16,17).

3.2. Gingival augmentation / root coverage Periodontal

People with a thin gingival biotype with a minimum zone of attached gingiva have a more profound response to inflammation, trauma, and restorative and orthodontic treatments. In addition, they predispose to gingival recessions (18). As a result, in many situations, it is necessary to augment the gingiva, and a free gingival graft is a gold standard for this reason (18). Gingival recession is another mucogingival problem in which the root is exposed in the oral cavity. Therefore, the patient is at risk of aesthetic problems and root caries. To overcome this problem, connective tissue graft (CTG) is a gold standard treatment modality. Both the FGG and CTG techniques need harvesting tissue, typically from the hard palate, which is time-consuming and associated with postoperative discomfort at the donor site (7).

PRF can be used as a bioactive matrix in the augmentation of the gingiva where there is a lack of keratinized tissue or in the treatment of gingival recession (18,19). It was shown that the application of PRF alone or in combination with a coronally advanced flap or connective tissue grafts (CTG) increased the speed of soft tissue healing and decreased the depth of the gingival recession (20). However, the Clinical efficacy of using PRF instead of CTG is limited (21). CTG is still a gold standard for the treatment of gingival recession; nevertheless, using PRF alone can reduce patients' fear and postoperative pain (7).

3.3. Periodontal wound healing

Several conditions open wounds left in the oral cavity after periodontal treatments like gingivectomy, gingivoplasty, or harvesting a free gingival graft from the hard palate mucosa (22,23). Wound healing after these procedures happens as secondary wound healing, and epithelial migration from the gingival margins begins 24 to 36 hours after surgery. Complete epithelization of the wound surface happens within about 14 days, and complete healing occurs around 30 days. To accelerate tissue repair and reduce patients' discomfort, several techniques were introduced, including hemostatic agents, low-dose lasers, and herbal products (22,23).

Bahar et al. reported that I-PRF accelerates wound healing after gingivectomy and gingivoplasty (22). They claimed that this adjunctive treatment modality contributes to the patient's comfort and quality of life. The use of PRF membrane following free gingival graft harvesting from the hard palate was also reported, which can improve wound healing, accelerate palatal wound reduction, reduce postoperative pain, and affect quality of life (23,24).

4. PRF in implant dentistry

4.1. Dental implant stability

Dental implants are a widespread and predictable treatment modality for replacing missing teeth (25). Osseointegration is a vital aspect of measuring the success of dental implants. Primary and secondary stability are essential for the success of dental implant treatment. Primary stability, which is achieved at the time of implant surgery, is determined by many factors, including bone density, implant design, and surgical technique. However, secondary stability is determined by tissue response to dental implants and bone healing (26). It was shown that the proximity between bone and dental implant increases in the presence of PRF, especially in the early phase (27). The meta-analysis showed that in the presence of PRF, a significantly higher implant stabilization (using ISQ value) was achieved (26). Shortening the duration of the healing period and waiting time for prosthetic rehabilitation of dental implants are other advantages of using PRF during dental implant placement (28,29). Also, using PRF during immediate implant placement resulted in higher bone quality (Hounsfield unit) compared with preoperative bone quality after 3 months (30).

4.2. Peri-implant soft tissue augmentation

The presence of attached keratinized tissue around dental implants and its thickness affects peri-implant health. Lack of this tissue is associated with peri-implant inflammation, plaque accumulation, and esthetic problems (25,31). Like soft tissue augmentation around teeth, FGG and CTG are the most predictable techniques used to increase the width and thickness of soft tissue around dental implants (25,31). Therefore, the disadvantages of harvesting tissue from the hard palate (that was mentioned previously) are still present (7). When PRF is used for soft tissue augmentation around dental implants, it's not only successful in increasing the width of keratinized tissue but also reducing surgical time and postoperative pain and discomfort (32,33). However, the results of FGG were significantly higher than PRF in terms of gingival augmentation (33).

4.3. Maxillary sinus grafting

The maxillary posterior area has a unique situation; alveolar ridge resorption, as well as, maxillary sinus pneumatization after tooth extraction, leads to a deficient alveolar ridge. However, the maxillary sinus space allowed the clinician to use it for sinus floor elevation. This procedure can be done through a lateral window or transrectal approach (34). However, PRF used in combination with bone graft substitute in sinus floor elevation procedures, Qiu et al, in a systematic review, claimed that the application of PRF in sinus grafting neither has significant effects on new bone formation nor maxillary sinus floor height elevation (35).

Interestingly, researchers have shown that PRF can be used alone as a grafting material during sinus elevation procedures (36-38). Aoki et al. showed histologic evidence of new bone formation in sinus grafting with PRF alone (38). Moreover, using PRF can reduce post-operative complications and the healing period, besides improving bone volume and density in the maxillary sinus (6,39).

The Schneiderian membrane is the lining mucosa of the maxillary sinus cavity which is respiratory in nature. One of the complications of maxillary sinus elevation is Schneiderian

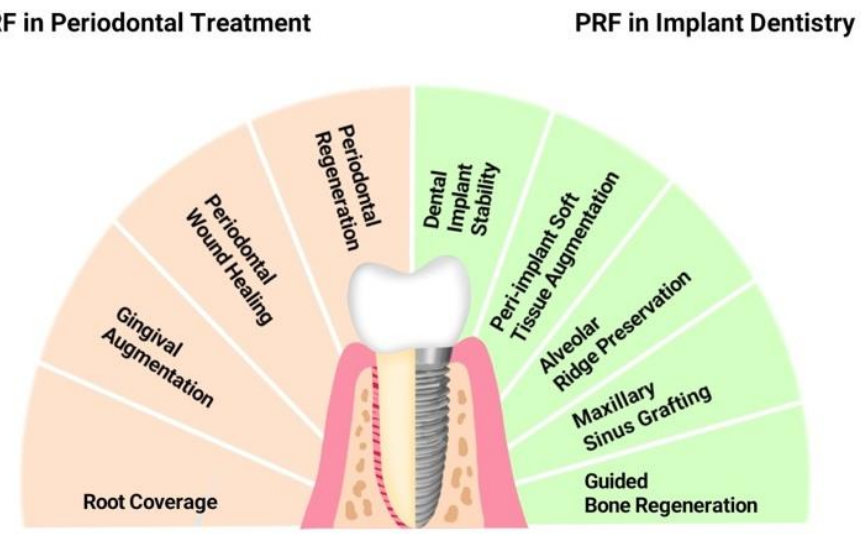

Figure 2. The application of platelet-rich fibrin in periodontal treatment and implant dentistry.

membrane perforation. It was reported that applying PRF in combination with collagen membranes was effective for sealing perforations and enhancing membrane repair (40).

4.4. Alveolar ridge preservation

Alveolar ridge preservation is a technique to prevent or limit post-extraction alveolar ridge resorption. Besides the limitation of post-extraction alveolar ridge dimensional changes, this procedure is usually aimed at the enhancement of new bone formation within the extraction socket during healing time as well as the progression of soft tissue healing at the entrance of the socket to preserve the external alveolar ridge contour (41). Studies showed that dental implantation in extraction sites grafted with most of the different bone substitutes must be postponed for 4 to 6 months. It was shown that using PRF in alveolar ridge preservation techniques decreased this waiting time and thus lowered the overall duration of implant treatment. Furthermore, radiographic measurements showed that PRF increased bone density and aids in preserving the alveolar ridge by intervening with the resorption of its width and height (43). Although Amer et al. showed similar clinical results regarding alveolar ridge preservation when using graft material with or without PRF, they claimed that the PRF group significantly preserves keratinized tissue width and lessens postoperative pain score (44).

4.5. Guided bone regeneration (GBR)

A prerequisite of dental implant placement is the presence of sufficient bone in an ideal place, especially in the reconstruction of the esthetic zone. Therefore, the treatment plan usually begins with planning the desired prosthetic reconstruction and then placing the implants in the three-dimensional position (45). Insufficient alveolar bone can occur in horizontal, vertical, or both dimensions as a result of postextraction changes, congenital disorders, trauma, or surgical defects (45,46). To date, GBR is the most widely used method to augment bone, allowing the placement of dental implants in areas lacking sufficient bone for standard dental implant placement (45). In this technique, a space, provided and maintained by barrier membranes, is filled with autogenous bone or bone substitute materials. Depending on the defect size and form, GBR may be done simultaneously with dental implant placement or several months before (staged) (45,47).

PRF was incorporated in horizontal or vertical, and simultaneous or staged GBR techniques. Isik et al showed that using PRF in GBR with simultaneous implant placement leads to thicker augmented bone (47). Arora et al's meta-analysis reported that using PRF as a part of the GBR technique increased horizontal ridge width and reduced the rate of bone resorption. Moreover, postoperative discomfort may be slightly improved (8). Tony et al reported that combining graft material with i-PRF and providing sticky bone predictably can replace collagen barrier membrane in horizontal ridge augmentation (46). It seems that combining PRF in GBR resulted in the enhancement of the migration of osteogenic cells and angiogenesis, along with the inhibition of the entry of unwanted cells in bone defects; therefore, PRF can be a great material in guided bone regeneration (48).

5. Conclusions

PRF is an easily obtained autogenous platelet concentration with a unique fibrin structure and high concentration of growth factors. In this review, the application of PRF in periodontal treatment and implant dentistry was summarized (Figure 2). PRF can be used alone or in combination with other biomaterials to aid in periodontal and bone (for

preparing a proper site for dental implant placement) regeneration. One of the strengths of using PRF is reducing post-operative pain and discomfort in most treatment approaches. However, PRF was a useful biomaterial in the mentioned treatments, but is still far from the gold standard, and further research is needed to overcome these problems.

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Ethics
Not applicable.

Using artificial intelligence (AI)
It is declared by the authors of this manuscript that no generative artificial intelligence (AI) or AI-assisted technologies were used to generate content, ideas, or theories during the writing process of this work.

Author contributions
Asal Khodabandehloo: Data curation, Writing-Original draft, Writing -Review & editing.
Fazele Atarbashi-Moghadam: Conceptualization, Supervision, Writing-Review & editing.

Conflict of interest
The authors declare no conflict of interest.

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