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REVIEW ARTICLE

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Platelet-Rich Fibrin in Oral Surgery and Endodontic Procedures as a Regenerative Biomaterial: A Review Article

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Abstract

Background: One of the major challenges in clinical research is to incorporate materials and procedures into dentistry that can improve clinical outcomes, increasing percentages of success. Platelet-rich fibrin (PRF) is a surgical, biological additive prepared by manipulation of autologous blood, which stimulates and regulates inflammation during and after oral surgery. This study aims to assess the potential benefits of using PRF in modern oral and endodontic surgery to accelerate radiographic healing and reduce postoperative discomfort.

Methods and Results: Electronic literature research was conducted using the biomedical search engine "National Library of Medicine," PubMed/MEDLINE database from March 2000 to June 2023. To obtain results that involved the whole scope of dentistry and PRF, the keywords used for the search were "PRF," "PRF in dentistry," and "PRF on apical surgery." The articles were selected by reviewing the titles and abstracts of the articles with the word "platelet-rich fibrin (PRF)." Articles related only to clinical applications in general dentistry and its different application fields were hand-searched in applicable, significant journals, and reference lists of included studies were broadcast with no language limitation. The inclusion criteria set for this review were as follows: all case reports, case series, original research papers, review papers, in vitro/in vivo studies, animal studies, and controlled clinical trials on PRF used in dentistry-related studies.

Current studies, in vitro and in vivo, have confirmed safe and encouraging results, without opposing outcomes, related to the use of PRF alone or in a mixture with other biomaterials. The use of PRF treatment has been shown to enhance and promote natural tissue healing support.**(International Journal of Biomedicine. 2023;13(4):213-220.)**

Keywords: platelet-rich fibrin • endodontic procedures • apical surgery

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Abbreviations

MTA, mineral trioxide aggregate; **PRF**, platelet-rich fibrin; **i-PRF**, injectable PRF; **PRP**, platelet-rich plasma; **PRGF**, plasma rich in growth factors.

Introduction

One of the major challenges in clinical research is to incorporate materials and procedures into dentistry that can improve clinical outcomes, increasing percentages of success.[1] Platelet-rich fibrin (PRF) is a surgical, biological additive prepared by manipulation of autologous blood, which stimulates and regulates inflammation during and after oral surgery.[2] As a biomaterial, it appears to provide natural and satisfactory alternative results and low risks. The possibility of accelerating bone regeneration in periapical and other surgical defects might be of great interest to clinicians to proceed with soft and hard tissue regeneration for complete healing after oral surgery.

Based on a literature review, PRF is a very important factor that promotes and regulates inflammation during and after oral surgery.[1,2] PRF, which is emerging as a biological revolution in dentistry, is an immune and platelet concentrate with specific composition, three-dimensional architecture, and associated biology that collects all the constituents of a blood sample to favor wound healing and immunity.[3]

This study aims to assess the potential benefits of using PRF in modern oral and endodontic surgery to accelerate radiographic healing and reduce postoperative discomfort.

Materials and Methods

Electronic literature research was conducted using the biomedical search engine "National Library of Medicine," PubMed/MEDLINE database from March 2000 to June 2023. To obtain results that involved the whole scope of dentistry and PRF, the keywords used for the search were "PRF," "PRF in dentistry," and "PRF on apical surgery."

The articles were selected by reviewing the titles and abstracts of the articles with the word "platelet-rich fibrin (PRF)." Articles related only to clinical applications in general dentistry and its different application fields were hand-searched in applicable, significant journals, and reference lists of included studies were broadcast with no language limitation. The inclusion criteria set for this review were as follows: all case reports, case series, original research papers, review papers, in vitro/in vivo studies, animal studies, and controlled clinical trials on PRF used in dentistry-related studies.

Platelet Concentrate Evolution

The regenerative potential of platelets was reported in the 1970s, and hematologists created the term PRP to describe plasma with a platelet count above that of peripheral blood, which was initially used as a transfusion product to treat patients with thrombocytopenia.[4,5]

In the 1980s, fibrin glue was the first blood-related product used in surgery, and at that time, fibrin glue was used as a hemostatic agent and surgical glue. Many authors then stated that it was used because of its positive effects on tissue healing.[6]

Platelet-rich plasma (PRP) was available during the 1990s, with the rapid development of techniques and equipment. In oral surgery, the first PRP study was introduced by Whitman et al. in 1997.[7] Later, at the beginning of the 2000s, PRF was presented for endodontic surgery as an autologous fibrin with a large quantity of platelets and leukocyte cytokines. This product can be used to improve wound healing in immune-compromised and diabetic patients. Additionally, as PRF stimulates coagulation and wound closure, it can be used as an adjuvant in patients on anticoagulant therapy.[8]

The PRF concept, as described in France by J. Choukroun in 2001,[9] is a second-generation platelet concentrate used for its ability to improve tissue repair and regeneration. It was presented as a replacement for PRP, which is known as a first-generation platelet derivative, as it is simpler and safer than PRP.[1] Choukroun et al. reported that platelets and leukocyte cytokines are important in the key role performance of this biomaterial; nonetheless, the fibrin matrix supporting them was very helpful in constituting the determining elements responsible for the real therapeutic potential of PRF.[1,9] Choukroun's PRF is a biomaterial used by itself and as an adjunct to grafts. It has been successful as it delivers high doses of growth factors and has anti-inflammatory properties. PRF is of great promise in dentistry, ranging from implantology, sinus lift procedures, and treatment of endodontic and periodontal lesions to regeneration of necrotic pulp. PRF is used to fill bony defects after periapical surgeries such as root-end resection.[10]

Protocol for PRF Preparation

According to Choukroun's original protocol that tries to collect platelets and the released cytokines in a fibrin clot, the PRF protocol requires only centrifuged blood without any addition of anticoagulant and bovine thrombin. Formerly, 10ml of whole blood sample was taken without anticoagulant in a 10 mL glass or glass-coated plastic tube and then immediately centrifuged at 3,000 rpm for 10 minutes.[9,10] The protocol tries to accumulate platelets and the released cytokines in a fibrin clot.[11] The plasma machine for preparation was a T-Lab Centrifuge (S-106) PRP, PRF Swing Rotor. Then, the blood sample settles into three layers: a straw-colored fraction of acellular platelet-poor plasma at the peak level, a PRF clot at an intermediate level, and a red fraction of red blood cells at the base level. Driving out the fluids trapped in the fibrin matrix by squeezing the PRF clot between pieces of sterile dry gauze, medical practitioners will obtain a highly resistant, autologous PRF membrane (a highly promising biomaterial) for multiple clinical usages.[12]

Advantages of the Clinical Application of PRF

PRF is autologous, derived from the patient's own blood, and is safe and fast. Therefore, disease transmission is not an issue, and PRF technology is readily available. It is easy to prepare and use, and it can be produced immediately by a chairside procedure. Currently, it is widely applicable in dentistry and financially realistic for both the patient and the clinician. The most important advantage is that there is no risk of a rejection reaction (no foreign body response). It provides the surgical wound area or defect not only with a matrix or scaffold permitting cell migration into the defect area, but also crucial biological signals or growth factors that can accelerate the wound healing and regeneration process.[12,13]

Benefits of PRF Compared to PRP and PRGF

The benefits of PRF are that it is simpler to produce and does not require blood manipulation: no additives, no

anticoagulants, no animal thrombin or calcium chloride, unlike PRP and PRGF. PRF produces a larger share of blood product over the share of blood taken that contains more healing factors, more stem cells, and less trauma. The benefits of PRF treatment in wound and bone healing, its antibacterial and antihemorrhagic effects, the low risks with its use, and the availability of easy and low-cost preparation methods encourage more clinicians to adopt this technology to benefit their patients.[12,13]

PRF has wide applicability, from dentistry to medicine, with excellent results in the short term. All studies have shown its safety in maxillofacial applications. Recently, much research has been done on PRF, and numerous cases have been reported regarding the use of PRF clots and PRF membranes. Most research has focused on using PRF in oral surgery for bone augmentation, sinus lifts, and avulsion sockets;[13-15] and in periodontics to correct intrabony defects, gingival recession, guided bone regeneration, and periapical lesions. Some case reports have shown that a combination of PRF gel, hydroxyapatite graft, and guided tissue regeneration plays a very important role during endodontic procedures for regeneration in open apex, regenerative pulpotomies, and periapical surgeries.[14-17] Platelet concentrates have been used extensively in oral and craniofacial interventions for hard tissue regeneration and soft tissue healing. In addition, these concentrates could decrease inflammatory complications, such as pain and swelling due to the inhibition of cytokine secretion.[18]

Platelet concentrates today are used in many orofacial disciplines, such as endodontic regeneration, osteoradionecrosis, closure of oro-antral communication, oral ulcers, and temporomandibular disorders.[19]

Endodontic Procedures

Endodontic failures are the most common reason periapical lesions are caused, and the main reason is the persistence of bacteria (intracanal and extracanal). Studies have shown that as the size of the lesion increases, so does the risk of root canal therapy failure after treatment.[20]

This increased risk is probable because as the size increases, so does the probability that the lesion may have evolved to be cystic by nature.[21] Infection, inflammation, and bone resorption are closely related to apical periodontitis development. Biochemical mediators are released locally to stimulate the immune response during inflammatory events.[22] The integrity of bone tissues depends on maintaining a delicate equilibrium between bone resorption by osteoclasts and bone deposition by osteoblasts.[23] With advances in surgical techniques, the outcome of surgical endodontic treatment appears to be more promising and predictable than before. Apical surgery is now considered a predictable treatment option to save a tooth with apical pathology that cannot be managed by conventional, nonsurgical endodontic procedures.[24]

Different natural materials have been used: bone grafts platelet-rich plasma (PRP), bone morphogenic proteins (BMPs), platelet-derived growth factor (PDGF), parathyroid hormone, and enamel matrix protein derivative (EMD) which have been locally applied to promote the healing potential of the surgical site.[25] Therefore, PRF can be used in a common form with mineral trioxide aggregate (MTA) as an alternative for creating artificial root-end barriers and to induce faster periapical healing in cases with large periapical lesions.[15]

The use of PRF in the form of a membrane can prevent the extrusion of material. PRF can also be used in regenerative pulpotomy procedures, in which the coronal pulp is removed, and the pulp wound is covered with PRF and then sealed with MTA and glass ionomer cement. Clinical data have shown that the healing outcome of apical surgery in teeth with permanent restorations is better than in teeth with temporary restorations.[26,28]

Regenerative Endodontic Procedures

In certain aspects of surgical endodontics, such as the treatment of periapical lesions and the regeneration of pulp (in the case of a tooth with a previously necrotic pulp with an open apex), PRF could be used as an ideal scaffold material for the repair and regeneration of the tissue since it acts as a matrix for the migration of cells.[28-30]

PRF also promotes the revascularization of teeth by releasing growth factors. The three criteria for the success of any regenerative procedures, including regenerative endodontics, are stem cells, signaling molecules, and an ideal scaffold. A study conducted by Huang found that there was a proliferation of human dental pulp cells and increased protein expression of osteoprogenin and alkaline phosphatase activity in cases where PRF was used.[31]

Shivashankar et al.[32] reported a case of revitalization of a tooth with necrotic pulp and an open apex, where PRF was the biomaterial he used. Once the inflammation subsides, the dental pulp cells differentiate into odontoblast-like cells under the influence of Hertwig's epithelial root sheath. It was reported that revitalization of a necrotic infected immature tooth was possible when PRF was used as a biomaterial for regenerating the pulp-dentin complex under conditions of total canal disinfection.[32]

Based on the literature, the difference between natural blood clots and PRF is that the latter is more homogeneous and stable, and is easier to handle and place in the indicated local area. PRF can be used as a scaffold in the regenerative endodontic treatment of traumatized immature nonvital teeth.[33] Slow polymerization during PRF preparation generates a fibrin complex similar to the natural linkage (in vitro). Unlike the other platelet concentrates, PRF can progressively release cytokines during fibrin matrix remodeling.[34]

Six studies[15,32,35-38] present a total of 55 patients who were treated with PRF by placing it into the dental canals or in the periradicular lesions. One study reported five patients with incomplete healing. Two patients did not respond to treatment;[38] in the remaining 48 patients, complete resolution and bone regeneration of the apical lesions were achieved. The treated pathologies were immature teeth with necrotic pulps, acute chronic apical abscess, and suppurated chronic apical periodontitis.

Recently, Lin et al.[39] demonstrated that the healing of periapical tissues is a "programmed event." More than the size of the lesion, it is the microenvironment consisting of the progenitor/stem cells, extracellular matrix, and bioactive molecules that play a crucial role in tissue regeneration or scar formation during wound healing.

One potential method to improve the disinfection performance is by using atmospheric-pressure cold plasmas.[39-41]

However, due to the shape of the narrow channel geometry of a root canal, which typically has a length of a few centimeters and a diameter of one millimeter or less, for better efficacy in killing bacteria, plasma should be generated inside the root canal. Hereafter, when plasma is generated inside the root canal, all kinds of reactive agents, including short-life pieces, such as charge particles, could play some roles in the death of bacteria. Lu et al. used a reliable and user-friendly plasma-jet device that could generate plasma inside the root canal.[42]

Another study by Hiremath et al.[43] described and reported affirmative results with pulpotomy using PRF. The effectiveness of this method must be demonstrated in long-term trials with larger sample sizes to justify its use in treating pulpitis. Pulpotomy with PRF could be a substitute treatment for MTA or other materials.

Bains et al.[44] reported the applicability of PRF for managing iatrogenic perforation of the pulpal floor in the furcation region of the first mandibular molar; PRF and MTA appeared to be most favorable materials for good long-term clinical results. Regenerative endodontics has been used in different root canal procedures, including apexification, apexogenesis, pulpotomy, and endodontic apical surgery.[45]

In recent studies, researchers have enhanced periapical bone regeneration, root development, and pulp vitality. In addition, a comprehensive, systematic review of clinical evidence showed that applying PRF is a successful procedure in treating immature teeth. Although the level of evidence was weak, reports were included, and further well-designed studies with longer follow-up periods are needed.[45]

The following brief literature review on the various applications of PRF in endodontic therapy considered a variety of methods that have been performed, such as mechanical cleaning, irrigation, laser irradiation, ultrasound, and application of hypochlorite and other antibacterial compounds. Regenerative endodontic procedures are widely being added to the current armamentarium of pulp therapy procedures.[31,46-50] These biologically based procedures are designed to restore the function of a damaged and nonfunctioning pulp by stimulation of existing dental pulp stem and progenitor cells present in the root canal under conditions that are favorable to their differentiation.[47,48]

Recent case reports have shown that the combined use of PRF and MTA as root-filling material is beneficial for the endodontic management of an open apex.[51,52]

Revascularization and Revitalization

Revascularization is the most studied and successful approach to regenerative endodontics.[51] Revitalization of necrotic infected immature teeth is possible under conditions of total canal disinfection combined with the additive effect of PRF.[52,53] PRF is proposed as an ideal biomaterial for regenerating the pulp-dentin complex because it is a potentially valid scaffold material containing leukocytes and growth factors to facilitate tissue healing and regeneration in immature necrotic teeth in children.[51-53] The repair and regenerative potential of PRF and enhanced cellular metabolism with laser biostimulation, in combination with the sealing ability of MTA, enhance the clinical success in pulpotomy and apexification procedures.[51] Revitalization, revascularization, and regenerative pulp therapies still need to be validated with robust clinical trials.[52,53]

Endodontic Surgery (apical surgery)

PRF clots (gels) serve as an ideal scaffold in root-end surgical procedures to enhance soft tissue healing and bone regeneration.[15,54,55] Other researchers have reported that PRF may not necessarily improve the outcome of treatment.[56]

It has been suggested that the combination of PRF and β-TCP for bone augmentation in the treatment of periapical defects is also more effective at increasing healing time than using bone substitute material alone.[57] PRF combined with an alloplastic bone substitute has been successfully used for managing combined endodontic-periodontal lesions.[58]

Oral and Maxillofacial Surgery

PRF represents a revolutionary step in the platelet gel therapeutic concept. Post-extraction socket augmentation and healing along with the filling of avulsion sockets with PRF lead to very favorable results when bone walls are intact.[57,58] A combination of PRF with bone substitutes and other adjuncts may be necessary for residual defects where one or several walls are missing or damaged to provide an adequate reconstruction of bone volume. PRF increases the cohesion between the graft materials, as fibrin acts as a physiological glue between the wound tissues. In cases of wide sockets and lesions where primary closure is difficult, PRF membranes can be used as a covering and protective membrane that promotes re-epithelialization of the site and accelerates the merging of the wound margins. The elasticity and strength of the PRF membrane make it easy to suture.[58-60]

The healing and remodeling of an extraction socket is highly dependent on the initial stabilization of the blood clot and quick closure of the gingival wound. This can be achieved by placing a fibrin plug in the socket and closing it with a fibrin membrane. PRF will act as a stable blood clot for neovascularization and accelerated tissue regeneration. PRF is recommended as a useful procedure to reduce the early adverse effects of inflammation, such as postoperative pain, and to promote soft tissue healing and bone regeneration processes.[60-64]

Clinical situations where post-extraction socket augmentation with PRF was specifically indicated for early or delayed implant placement, and immediate post-extraction implant placement improved the strength of bone integration to dental implants.[65-74]

PRF led to aggregate tissue regeneration, making healing more effective and capable in both hard and soft tissue. Using it to regenerate tissues can repair much damage caused by peri-implant recessions, and maxillary sinus lift helps in rapid healing by accelerating the bone integration of the implants.[75-79]

There are several advantages to using PRF, such as easy and simplified chairside preparation of PRF, cost-effectiveness, release of relatively constant concentrations of growth factors over a period of 7 days, and rapid and excellent healing of the periodontium. Many studies of PRF have found it to be more efficient and with fewer controversies about its final clinical results than PRP.[74]

Anilkumar et al.[80] reported on PRF as a potential novel root coverage approach for treating gingival recession in mandibular anterior teeth using a combined laterally positioned flap technique and PRF membrane. The major differences between PRP and PRF glues are attributable to the gelation mode. Fibrin and CPRP adhesives use bovine thrombin and calcium chloride association to initiate the last phase of coagulation and polymerization of sudden fibrin. The advantage of PRP is the release of significantly more proteins at earlier time points, whereas PRF displayed a continual and steady release of growth factors over a 10-day period. Moreover, in general, it was observed that the new formulation of PRF (A-PRF) released significantly higher total quantities of growth factors than traditional PRF. Based on these findings, PRP can be recommended for fast delivery of growth factors, whereas A-PRF is better suited for long-term release.[80] Another study favored PRF over PRP, and the results from the present study favored the use of naturally formulated i-PRF over traditional PRP with anticoagulants.[79,81]

Further investigation into the direct role of fibrin and leukocytes contained within i-PRF is therefore warranted to better elucidate their positive role in i-PRF on tissue wound healing. The results from the present study favored the use of naturally formulated i-PRF over traditional PRP with anticoagulants.[81]

Other Clinical Applications

PRF is used in different fields. It has been shown to produce as much as a 10-fold decrease in osteomyelitis infections.[82] To reduce post-extraction complications in medically compromised cases, PRF can be used to minimize post-extraction pain and bleeding, close oro-antral fistulas, manage oro-antral communications, etc. However, a split-mouth control study devoted to evaluating the efficacy of PRF on postoperative edema and pain after impacted mandibular third molar surgery has found that using or not using PRF to reduce postoperative pain and edema in third molar surgery were equally successful.[83-86]

Conclusion

Current studies, in vitro and in vivo, have confirmed safe and encouraging results, without opposing outcomes, related to the use of PRF alone or in a mixture with other biomaterials. It has several indications and advantages to be used in dentistry and medicine. Currently, the use of PRF treatment has been shown to enhance to enhance and promote natural tissue healing support.

This review article attempted to summarize the use of PRF accepted as a minimally invasive technique with low risk and satisfactory clinical results in oral and maxillofacial surgery.

Competing Interests

The authors declare that they have no competing interests.

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