Research Article

APPLICATION OF PLATELET-RICH FIBRIN (PRF) IN ORAL SURGICAL PROCEDURES

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Abstract

In 2000, Choukroun pioneered the use of platelet-rich fibrin (PRF). PRF is considered a second generation platelet concentrate. It is a fibrin mesh structure that stores a variety of growth factors and cytokines and gradually releases them during remodeling. PRF has a wide variety of applications in the field of oral surgery due to its biological potential to accelerate the wound-healing process and tissue regeneration. This review mentioned a number of possible PRF implementations in different oral surgical procedures. This review is based on the literature analysis of current oral surgical procedures including mandibular third molar surgery, preservation of extraction sockets, maxillary sinus augmentation, dressing, dental implant installation, osteonecrosis of jaw, oroantral communication closure, and periodontal surgery. These findings demonstrate that RPF can be employed widely in different types of oral surgical procedures.

Keywords: Fibrin, oral surgical procedures, platelet-rich fibrin (PRF).

I. Introduction

Platelet-rich fibrin (PRF) has been considered a significant surgical supplement in oral surgical interventions since its first introduction by Choukroun [1] in 2000. In particular, this biological material first attained notice in the field of dentistry research after the introduction of five major studies [2–6] in 2006. There have been over 500 scientific studies reported on this topic to date [7]. Third molar extraction, alveolar ridge preservation following tooth extractions, sinus lift surgery, alveolar cleft reconstruction, dental implant installation, surgical management of medication-related osteonecrosis of the jaw (MRONJ), and management of oroantral communications are some of the potential application fields for PRF in oral surgical practice [8-14].

PRF is a platelet concentration that is prepared without the need for biochemical blood processing [15]. It has three important features: First, platelets and their effective growth factors become confined to the fibrin matrix during the normal polymerization

mechanism [3]. Second, leukocytes and their cytokines play a role in the healing process, contributing to anti-infective activities and immunological modulation [16]. Finally, natural polymerization provides the uniformity and intricacy of the fibrin matrix structure without the requirement of any anticoagulant or gelling substance [17]. PRF is a major source of angiogenesis-promoting growth factors like transforming growth factor β (TGF- β) and vascular endothelial growth factor (VEGF). Platelet-derived growth factors (PDGFs), which serve as a key controller for collagen formation and mesenchymal cell migration and proliferation, are still plentiful in platelets [3, 5, 17]. The concept and impacts of PRF will be addressed through this review to determine its clinical employment in oral surgical interventions.

History of PRF

Platelet-rich plasma (PRP) is the first material to contain the growth factor. While PRP is made chemically by adding a coagulant to blood, it has several disadvantages, including the necessity for two centrifugation cycles and prompt growth factor release [18].There are several disadvantages to PRP, which led to the birth of PRF, a new type of platelet concentrate that overcomes most of the drawbacks of PRP [15].Choukroun's PRF is a three-dimensional biomaterial made up of leukocytes and platelets with a distinctive configuration [19].PRF is a fibrin mesh framework that accumulates and eventually discharges a range of growth factors and cytokines throughout remodeling[3]. Leukocytes, cytokines, glycoproteins [20], as well as growth factors like transforming growth factor β1, platelet-derived growth factor, vascular endothelial growth factor, and glycoproteins, namely thrombospondin-1, form a complex fibrin matrix in PRF [21]. Leukocytes seen in the PRF help growth factors migrate [21]. Because it has the ability to accelerate the healing process, PRF is an excellent autologous tissue regeneration material with a wide range of therapeutic workouts in the field of oral surgery.

PRF types and preparation

In general, there are two forms of PRF: solid and liquid. Choukroun and colleagues developed the solid PRF as the first variant of PRF [1]. For L-PRF preparation, the two most frequent procedures were centrifugation at 3000 rpm for 10 minutes [2] and centrifugation at 2700 rpm for 12 minutes [22]. The constituents and structure of the PRF could be changed by applying a different centrifugal force [23]. Advanced PRF (A-PRF) and injectable PRF (I-PRF) can be made by reducing the centrifugal force. More neutrophils are present in A-PRF, which can induce monocytes to develop into macrophages and provide more growth factors to aid bone regeneration [24-26]. I-PRF has a lesser consistency than PRF and is mostly used to decrease the complexity of using bone biomaterials [27]. To avoid the health hazard caused by silica particles in glass tubes during blood centrifugation, Tunalı et al. [28] produced titanium-prepared PRF (T-PRF) by using a titanium tube instead of a glass tube. T-PRF has a tighter and thicker fibrin structure and a longer release time of growth factors than PRF, which may be more conducive to tissue regeneration. Table-1 summarizes some accepted PRF preparations such as L-PRF [2, 22,] A-PRF [24], T-PRF [28], and I-PRF [29]. Venipuncture is a procedure that must be carried out to collect blood. Blood must be drawn into 10-cc blood collection tubes. The amount of blood that should be used per volume of defect varies according to the technique. In most cases, 10 to 100 cc of blood is required. When compared to glass

tubes, plastic tubes trigger clotting factors less. The protocol will determine which option is used. This technique's effectiveness is largely dependent on the speed at which blood is collected and delivered to the centrifuge. After all, without an anticoagulant, blood appears to coagulate quite instantly upon touch with the tube glass, and centrifugation takes at least a few minutes to concentrate fibrinogen in the middle and upper parts of the tube. The best way to attain a clinically useful PRF clot is to approach it rapidly [30]. The centrifugation will differentiate the blood into acellular plasma in the upper layer, a PRF layer in the middle, and a red blood cell layer in the lowermost stratum. PRF is formulated during centrifugation as a result of a normal and gradual polymerization [3]. Where the time required for acquiring blood and initiating centrifugation is too long, failure usually happens. The fibrin can polymerize diffusely in the test tube, resulting in a slight blood clot of no durability [31].

Table 1: PRF preparations that are commonly used

PRF preparations	Rotations per minute	Centrifugation force (g)	Duration (minutes)
L- PRF [2]	3000	400	10
L- PRF [22]	2700	-	12
A- PRF [24]	1500	208	14
I-PRF [29]	700	60	3
T-PRF [28]	3500	-	15

L- PRF, Leukocyte-PRF; A- PRF, Advanced-PRF; I-PRF, Injectable-PRF; T-PRF, Titanium-prepared PRF.

Benefits of platelet-rich fibrin (PRF) over platelet-rich plasma (PRP)

In comparison to PRP, PRF provides a lot of advantages, including a lower cost and ease of application. Moreover, it enables the rapid and efficient processing of numerous concentrates, that is, without the need for additives or artificial conditions [30].Apart from PRPs, PRF does not degrade rapidly following implementation; rather, the solid fibrin matrix remodels gradually in a manner comparable to that of a normal blood clot. This system collects platelets and leucocytes efficiently and preserves the leucocytes within. However, platelets are stimulated during the process, resulting in a considerable amount of platelet and growth factors being incorporated in the fibrin matrix [3, 4]. PRF has a fine and versatile three-dimensional structure that is more conducive to cytokine enmeshment and cell movement [32]. PRF also plays a role in the process of haemostasis[33, 34]. It has recently been demonstrated that the application of PRF as a healing agent has tremendous potential in various aspects of dentistry [35].

Platelet-rich fibrin application in oral and maxillofacial surgery

Mandibular third molar surgery

The most frequent treatment executed by oral and maxillofacial surgeons is the removal of mandibular third molars [36]. Pain, trismus, swelling, infection, and alveolar osteitis (AO) are all possible unwanted effects and consequences of the surgical treatment [37]. In mandibular third molar surgery, PRF appeared to speed up both soft tissue [38, 39]

and bone healing [38, 40]. The postoperative pain [38, 39, 41-43] and swelling [8, 38, 39, 41] was also reduced following employment of PRF after extraction. The lower incidence of AO was reported in several studies following the application of PRF after mandible third molar extraction [39, 42, 44].

PRF effects on alveolar osteitis

Acute alveolar osteitis (AO), often known as dry socket, is a painful and debilitating illness that affects people who have had their teeth extracted. Crawford [45] was the first to propose the term "dry socket" in 1896. Several terms have been used in the past to define it in publications [46, 47]. Blum [48] defines it as "pain in and around the extraction site that worsens in any period between 1st and 3rd days postoperatively following the removal of the tooth, followed by partial or completely dissolved clots within the extracted socket, with or without bad breath." On the 3rd and 7th postoperative days, several studies reported that the use of PRF decreased pain significantly caused by AO, as well as improved wound healing at the end of the 2nd week [49, 50].

Alveolar ridge preservation

After teeth are extracted, the alveolar ridge develops considerable 3-dimensional resorption [51]. As a result, it's critical to keep the alveolar ridge's width and height after tooth removal, particularly if implant rehabilitation is planned. After tooth removal, the purpose of alveolar ridge maintenance is to keep the tooth socket soft and hard tissue unaltered [9]. Improved bone fill, fast soft tissue repair, mature bone, reduced ridge width loss, and increased bone density are thought to be some of the benefits of PRF [52]. There were several studies conducted to assess the effects of PRF on alveolar ridge/tooth socket preservation following tooth extraction. The PRF effects were compared to either naturally healing sockets [53, 54] or bone substitutes like beta-tri-calcium phosphate (β-TCP) [55] or demineralized freeze-dried bone allograft (DFDBA) [56]. The PRF was also employed in combination with DFDBA to evaluate the effects on alveolar ridge preservation [9, 57]. Enhanced bone fill and diminished alveolar bone width resorption were observed employing clinical and radiological measures when PRF was applied to speed socket wound healing following tooth removal [53, 54]. After tooth extraction, PRF alone or in combination with DFDBA is an effective biomaterial for preserving ridge height, enhancing new bone formation, and maintaining bone mineral density [9, 56]. However, socket preservation was also achievable with either autologous PRF or β-TCP with collagen [55].

Dental implantology

The application of L-PRF to the implant surface is recommended to increase bone reproduction in order to enhance osseointegration, as well as to improve the durability of endosseous implants [12]. Furthermore, placing L-PRF over an implant surface enhances soft tissue thickness, which improves peri-implant tissue integrity and reduces peripheral bone loss [58]. During the healing phase, Tabrizi et al. [12] assessed the implant stability implanted in the posterior maxilla, with or without the application of PRF. At 2 weeks, 4 weeks, and 6 weeks after implant installation, meaningful effects on implant stability were concluded across the groups [12]. In a split mouth RCT, the PRF effect was assessed on immediate implant stability following tooth extraction. The implant stability of PRF-treated implants was much better. Furthermore, the PRF group had less marginal bone resorption [59].

Hamzacebi et al. [60] found that using PRF to treat peri-implant bone loss outperformed traditional flap surgery in terms of clinical outcomes.

Maxillary sinus floor lift and augmentation procedures

Adequate bone quantity and quality are definitely required for effective implant installation. Significant difficulties during dental implant placement are caused by a paucity of bone in the posterior maxilla, which is caused by a combination of alveolar bone loss following tooth extraction, pneumatization of the maxillary sinus, and periodontitis. This condition is presently being addressed by augmentation of the alveolar ridge height via bone grafting, accompanied by maxillary sinus lift surgery [61]. Choukroun et al. [6] intended to assess the possible role of PRF in a mixture with freeze-dried bone allograft (FDBA) to improve bone restoration in sinus floor elevation. The test group's histologic study of harvested bone specimens was examined after four months, whereas the control group's was analyzed following eight months of bone allograft. From a histologic standpoint, the findings showed that using FDBA and PRF to augment the sinus floor reduced the healing period (by four months) before implant insertion [6]. The combination of L-PRF with the deproteinized bovine bone mineral (DBBM) into the maxillary sinus augmentation permitted earlier implant installation (4 months) with more new bone formation than DBBM itself after 8 months of the healing process [10].

Alveolar cleft reconstruction

One of the most frequent congenital defects affecting the oro-facial area is cleft lip and palate. During the mixed dentition phase, repair of the alveolar cleft with bone grafting is a desirable supplementary treatment [62]. Among the several graft materials used for cleft restoration, autogenous bone is usually favoured [63]. Grafting from the anterior iliac crest, ribs, symphysis, and tibia are all sources of autogenous bone [64]. PRF is a great source of autologous cytokines and growth factors that is widely employed in clinical research for regenerative medicine. Shawky et al. [11] looked at how PRF impacted bone density and the percentage of new bone generation in unilateral maxillary alveolar cleft repair. PRF and autogenous anterior iliac crest bone graft (AICBG) were applied in test group, while just autogenous AICBG was employed in the control group. In the PRF group, the percentage of newly produced bone increased by a statistically meaningful level [11]. When compared to AICBG, Movahedian et al. [65] assessed the efficiency of a combination of symphysis bone, allograft, and PRF in the repair of alveolar clefts. The authors found that a mixture of chin symphysisautograft, allogeneic bone material, and PRF is effective for bone regeneration in small to moderate-sized alveolar clefts [65]. Dayashankara et al. [66] compared cases between AICBG and cases treated by two newly created types of PRF: I-PRF and A-PRF were mixed with AICBG for secondary alveolar bone grafting. When combined with AICBG, I-PRF and A-PRF appear to improve bone growth in alveolar clefts more than AICBG alone [66].

Osteonecrosis of the jaw

The causes of osteonecrosis of the jaw (ONJ) are several. Antiresorptive and antiangiogenic medications, and also high-dose radiation, are the most frequent associations. A case reported for Bisphosphonate-related ONJ was published for the first time [67]. ONJ is frequently accompanied with poor vascularization, and the focus is frequently to

achieve reepithelization and vascularization of bone. PRF possesses angiogenic characteristics that help to induce angiogenesis and the development of new blood vessels [4]. The efficacy of the PRF on subjects with medication-related osteonecrosis of the jaw (MRONJ) was studied by Szentpeteri et al. [13]. The PRF with traditional surgery group showed significant outcomes than those who were solely treated with traditional surgery in terms of remission, stage improvement, and recurrence rate [13]. Surgical therapy of MRONJ with supplemental local PRF treatment showed to be quite successful and effective, particularly when all necrotic bone can be readily excised in the initial stages [68].

Oroantral communications closure

Oroantral communication (OAC) is an accessible passage between the oral cavity and the maxillary sinus that is most frequently caused by maxillary posterior tooth extraction [69]. Surgical approaches are generally the most prevalent method for closing OAC [70]. To seal an OAC, the buccal advancement flap, palatal rotational flap, and buccal fat pad procedures are commonly employed. Bilginaylar [14] stitched up PRF clots to the gingiva to prevent them from moving to the sinus and to stabilize the post-extraction tooth socket cavity. During the extraction site follow-up, adequate granulation tissue and epithelialization of the oral mucosa were detected [14]. Gülsen et al. [71] showed that PRF clots can effectively seal OAC. Furthermore, when compared to buccal advancement flap surgery, the application of PRF clots for the instant sealing of acute oroantral communications resulted in minimal pain and no swelling [72]. PRF is a biological fibrin-based material that can be used to facilitate cell migration into a wound. Growth factors are also useful in encouraging tissue regeneration since they are functional for a prolonged period of time. As a result, the concept of employing PRF as a biocompatible material for OAC closure was born [73]. The application of PRF for prompt sealing of acute OAC will enable OAC management to be less traumatic and simpler, and it will reduce the requirement for specialized surgical skills [14, 71].

Gingival recession treatment

The apical movement of the gingival margin approaching the cement-enamel junction is known as gingival recession. Because both the cementum overlaying the root and the dentin are uncovered in the oral cavity, it causes aesthetic issues and unpleasantness [74]. Periodontal plastic surgery aims to provide not only complete and consistent coverage of visible root surfaces, but also to provide less aggressive procedures that promote regenerative recovery, lower postoperative unpleasantness, and improve patient comfort [25, 76]. Miller class I and II recessions have the best potential for clinical benefit and provide the most comprehensive coverage [77]. For Miller I and II recession deficits, a connective tissue graft (CTG) combination with a coronally advanced flap (CAF) is regarded as the ideal standard [78, 79]. When compared to CTG-treated gingival recessions, the application of a PRF membrane in gingival recession correction reduced postoperative discomfort for patients [80]. Incorporating i-PRF into the CAF and CTG treatments resulted in an increase in keratinized tissue thickness and a decrease in recession depth [81]. T-PRF is a non-invasive procedure that can be applied to correct several Miller class I and II gingival recession deficiencies [82]. However, the inclusion of PRF had no effect on the outcomes of CAF

and CTG interventions for Miller class I and II recessions [78, 83].

Treatment of periodontal intra-bony defects

Periodontitis is a chronic inflammatory condition marked by inflammation and the eventual loss of tooth supporting structures induced by pathogenic bacteria [84]. Alveolar bone resorption is a characteristic clinical presentation of periodontal disorders and a diagnostic hallmark incident that can result in vertical and/or horizontal bone deficiencies, mobility of teeth, and possibly tooth loss [85]. It is generally recognized that standard open flap debridement (OFD) is ineffective in regenerating tissues damaged by chronic periodontitis [86]. The application of PRF in periodontal regeneration techniques has reported a number of benefits. Patel et al. conducted a study to compare the regenerative effects of the PRF and OFD on periodontal intrabony defects (PIBD) [87]. In addition, the PRF with OFD is compared to OFD alone [88, 89]. When compared to the OFD, the PRF exhibited significant improvements in clinical parameters such as bone fill, probing depth reduction, and soft tissue healing [87]. Furthermore, when PRF was used with conventional OFD, there was more bone fill than when conventional OFD was used alone [88]. Both autologous PRF and TPRF were found to improve clinical indicators and radiological findings in the management of PIBD [89]. Several trials evaluated the effect of PRF in combination with enamel matrix derivative (EMD) [90], decalcified freeze-dried bone allograft (DFDBA) [91], 1% alendronate [92], porous hydroxyapatite graft [93], 1.2% rosuvastatin[94], and 1% metformin [95] for the treatment of PIBD in chronic periodontitis and reported better clinical parameter findings like clinical attachment level gain and probing depth reduction. Galav et al. [96] compared PRF with autogenous bone graft for the management of PIBD in patients with chronic periodontitis. Both autogenous bone graft and PRF can be used to restore damaged periodontal tissues in a predictable manner. However, autogenous bone grafts are more effective than PRF in terms of bony defect filling [96].

Dressing agent

Eldibany [34] conducted a study to assess the efficacy of PRF and hemcon dental dressing (HDD) in patients with cardiac disease receiving warfarin following tooth extraction. The PRF and HDD were filled into extracted tooth sockets after completion of atraumatic extraction. PRF acts as a haemostatic agent and promotes tissue regeneration and wound repair, allowing for a rapid revival without major painful incidents. Hassan et al. [97] covered and protected the palatal donor site with a variety of palatal dressings, including PRF, hyaluronic acid, and gelatin sponge. As outcome variables, pain, post-operative bleeding, and wound healing were listed. In terms of cost, pain relief, hemostasis, and healing effects, PRF showed a better outcome than both hyaluronic acid and gelatin sponge [97].

PRF as intracapsular injection in temporomandibular joint (TMJ)

The potential of I-PRF to discharge larger concentrations of different growth factors to promote better fibroblast migration and expression of PDGF, TGF-β, and collagen-1 was observed. The clinical effects of liquid PRF on individuals with TMJ pain and dysfunction were investigated in a study [98]. At 2-week intervals, 48 TMJs from 37 patients with painful internal derangement (ID) (Wilkes' classification I–V) were introduced with 1.5–2cc liquid PRF into the

upper joint space. At different periods of follow-up, 69% of TMJs exhibited a notable pain reduction. The liquid PRF injections demonstrated the best response in ID stages IV and V. In most individuals with painful TMJ ID, liquid PRF has long-standing analgesic benefits [98].

II. Conclusion

There is a wealth of publications on the application of PRF, with the majority of studies favoring PRF treatment over the control group. Although there is no definitive PRF methodology, it has numerous applications in oral and maxillofacial surgery. The majority of these studies yielded encouraging outcomes. To validate surgical rationale, further randomized controlled trials and standard techniques are required.

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