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Platelet Rich Fibrin and Periodontal Tissue Regeneration

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Abstract

Introduction: The regeneration of grade II furcation defects has always been unpredictable especially in terms of complete bone fill. The use of biologic mediators, such as growth factors; has been increased in the last two decades. Naturally most of these growth factors are in platelets and are secreted upon platelet activation giving the platelets a crucial role in wound healing and regeneration of injured tissues besides their hemostatic functions. Platelet rich fibrin (PRF) is an autologous healing biomaterial composed of afibrin clot matrix entrapping leukocytes, cytokines, living progenitor cells, and platelets and capable of releasing various growth factors. Aim of this study was to summarize the use of platelets rich fibrin on periodontal regeneration of furcation defects.

Results: The combination of PRF with bone graft material showed higher vascularization, better bone fill with thick bone trabeculae and PDL fibers regeneration in bifurcation defect area.

Conclusion: The addition of PRF to bone grafting material with guided tissue regeneration procedures was found to be effective in enhancing Angiogenesis and facilitating cellular events that are favorable for periodontal regeneration.

Keywords: Platelet rich fibrin; Angiogenesis; Periodontal regeneration; Bone; Furcation defects

Introduction

Growth factors are substance (proteins) capable of stimulating cellular growth, proliferation, healing, and cellular differentiation. Most of the growth factors are stored naturally in platelets and are secreted upon platelet activation giving the platelets a crucial role in wound healing and regeneration of injured tissues besides their hemostatic functions [1]. Thus, the idea of using platelet concentrates to promote tissue healing and periodontal regeneration has been raised.

Numerous techniques of autologous platelet concentrates have been developed since and applied in oral and maxillofacial surgery. These concentrates can be divided mainly into two generations; the first generation incorporates the platelet-rich plasma (PRP) while the second generation involves the platelet-rich fibrin (PRF) [2].

Platelet-Rich Plasma (PRP)

Marx et al. [3] introduced PRP as a type of platelet concentrate that can act as a source of biologic mediators and growth factors. He incorporated the PRP with cancellous bone marrow grafts in mandibular reconstructions. He observed that addition of PRP accelerated the rate and degree of bone formation. It was believed that PRP can release various growth factors that showed crucial chemo tactic and mitogenic effects promoting and modulating tissue healing, regeneration, and cell proliferation [4].

Platelet Rich Fibrin (PRF)

In 2001, French doctor Choukroun J developed the PRF [5]. It was classified as a second generation platelet derivative, unlike PRP; PRF is a strictly autologous fibrin matrix containing a large quantity of platelets and leukocytes. Its preparation technique does not require artificial or exogenous biochemical modifications like the use of anticoagulants or bovine thrombin or any other jellifying agent.

The PRF clot is obtained by inducing a natural polymerization process during centrifugation without the addition of anticoagulants, and due to this the obtained fibrin clot has a very dense fibrin network in which Platelets and leukocytes are

entrapped and activated in a natural mechanism; thus releasing growth factors and cytokines in a slow rate during a period of 7 days or more [6]. This slow releasing mechanism makes PRF very distinguishable from PRP preparation protocols because platelets in PRP are activated in a brutal way ;thus the sudden release of growth factors in large quantities over a short period of time, and a very light fibrin network is produced [7].

Classification of PRF Products

According to leukocyte content Dohan et al; classified PRF into pure PRF (P-PRP) or leucocyte poor PRF and leucocyte-rich PRF (L-PRF) [2].

Leukocyte-Poor Or Pure Platelet-Rich Fibrin (P-PRF) Concentrates

In this category, there is only one method available. The Fibrinet PRFM kit by Cascade Medical (New Jersey, USA). The company claims that the system produces a 'natural' platelet concentrate owing to the absence of bovine thrombin. However, doubts has been raised because the blood is mixed with anticoagulant and separation gel, leading to what could be considered unnatural conditions. This protocol is similar to other typical L-PRP protocols. The main difference is that only very low amounts of leucocytes are collected owing to the specific separator gel used in the method. However, the platelet collection efficiency is high and the preservation of the platelets during the procedure seems to be acceptable, but studies demonstrating the efficiency of Fibrinet PRFM are not yet available [2].

Leukocyte-rich PRF (L-PRF) Also named Choukroun's PRF, Advanced PRF (A-PRF), and commonly named PRF Membrane

Developed by Dohan & Choukroun [5]. The PRF Box (Process Ltd., Nice, France) is commercially available to prepare the PRF membrane. The PRF clot is placed on the grid in the PRF box and covered with compressor lid which squeezes out the fluid from the clot. The membranes formed using this method had constant thickness of 1mm which remains hydrated for several hours. The serum exudates are also collected under the grid for further use. The serum exudates expressed from the clot is rich in proteins such as vitronectin and vitronectin. These exudates may be used to hydrate graft materials, rinse the surgical site, and store autologous graft [8].

However, another alternative to obtain a PRF membrane developed by Raja et al, [9] is by pressing the clot between two gauzes thereby squeezing out the fluids in the fibrin clot. Toffler et al. showed that the PRF clot can also be slowly compressed in a cylinder in the PRF box with an opposing piston to obtain PRF plugs measuring 1 cm in diameter. Which can be used in socket preservation procedures?

Releasing Kinetics Differences between PRP and PRF

He et al. [10] studied the expression of alkaline phosphatase (ALP) and induction of mineralization under the effects of PRP and PRF in vitro. He concluded that the gradual release of autologous growth factors expressed a stronger and more durable effect on proliferation and differentiation of rat osteoblasts than PRP in vitro.

Saluja et al. [11] concluded that the limited potential of PRP to stimulate bone regeneration is due to its quick release of growth factors, just before the cell outgrowth and population occurs from the surrounding tissue.

This was also observed by Hatakeyama et al. [12] after he compared the effect of Platelet poor plasma (PPP), PRP with that of PRF in promoting bone maturation in extraction sockets of dogs. He stated that PRF was found to promote bone maturation in extraction sockets in dogs. He observed abundant osteogenic cells in PRF group more than PPP and PRP groups.

The regenerative ability of PRF

Angiogenesis "The formation of new blood vessels inside the wound" underlies the success of tissue regeneration, as the newly formed blood vessels are crucial in the delivery of oxygen, nutrients, and crucial cells from nearby tissues in the hypoxic microenvironment of healing wounds [13]. Steinbrech et al [14]. Observed a high expression of VEGF growth factors that is believed to be found responsible for regulating angiogenesis in the hypoxic microenvironment of healing bone.

Yoon et al. [15] conducted immunostaining intensity for VEGF in regenerating cranial defect in rabbits he found that VEGF intensity was consistently higher in the experimental group; in which PRF was used, than in the control group at all experimental time points leading to more red bone marrow formation. Also, Diss et al. [16] observed that PRF directly promotes angiogenesis when it was used as grafting material for sinus floor elevation.

Change et al. [17] observed that PRF promoted human PDL formation in periodontal infrasonic defects by; increasing extra cellular signal protein kinase phosphorylation (p-ERK), stimulating the production of osteoprotegerin (OPG) and increasing alkaline phosphatase (ALP) activity around periodontal ligament fibroblasts. They concluded that PRF can increase PDL proliferation thus improving periodontal tissue regeneration.

Moreover, Chang et al. [18] stated that the same mechanisms of p-ERK, OPG and ALP also had led to osteoblasts differentiation and proliferation favoring bone formation. Similarly Huang et al. [19] reported that PRF stimulates osteogenic differentiation of the human dental pulp cells by up regulating OPG and alkaline phosphatase expression.

Tsai et al. [20] related the regenerative abilities of PRF to the growth factors released by the platelets entrapped within, such as PDGF and TGF. These factors can promote periodontal regeneration by stimulating specific cell differentiation and proliferation in a specific manner. He stated that PRF had induced cell proliferation of osteoblasts and periodontal ligament cells while suppressing oral epithelial cell growth during a 3-day

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culture period. Concluding that these cell type-specific actions may be beneficial for periodontal regeneration.

PRF has been extensively studied in the last few years testing its regenerative ability in both experimental and clinical studies. Simon et al. [21] evaluated the effects of PRF and DFDBA in socket preservation procedures in 4 dogs. He observed better bone fill of PRF groups after 3 weeks in comparison to DFDBA groups. Bölükbaş et al. [22] observed more bone formation in PRF and Biphasic calcium phosphate (BCP) than in BCP group alone in a period of 40 days in surgically created defects in sheep tibia. Also , Yilmaz et al. [23] conducted an experimental study to show the effectiveness of using PRF and β-TCP each alone or in combination in bone regeneration in surgical defects created in a tibia of a pig. The histological results showed more new bone formation in the defects grafted with PRF mixed β-TCP than in the defects grafted with either β-TCP or PRF alone.

Thakkar et al. [24] conducted a clinical and radiological study comparing socket preservation using DFBDA alone or in combination with PRF. They concluded that although DFDBA is considered as an ideal graft material, the combination group showed less ridge width reduction, while regarding the reduction in ridge height, no statistical difference was observed between the two groups at different intervals.

In a study conducted by Pradeep et al. [25] a significantly greater probing depth PD reduction and clinical attachment gain with the use of PRF in the study group, when compared to the control group, where only the open flap debridement OFD procedure was employed.

Lekovic et al. [26] also concluded that PRF had improved the clinical parameters CAL gain and PD reduction of human infrabony periodontal defects when combined with Bovine porous bone mineral xenograft. Bansal et al. [27] also stated that the combination of PRF with DFDBA demonstrated better results in probing pocket depth reduction and clinical attachment level gain as compared to DFDBA alone in the treatment of periodontal infrasonic defects. Sharma et al. [28] concluded in a randomized controlled clinical trial that all clinical and radiographic parameters showed statistically significant improvement at the sites treated with PRF and OFD compared to those with OFD alone

Several studies had shown the advantages of using PRF for GTR either alone or combined with bone graft material. PRF application was shown to create a well vascular zed space, facilitating cellular events that are favorable for periodontal regeneration including bone formation. This could be attributed to its inherited osteoconductive and osteoinductive properties. Based on the previous literature we can conclude that the use of PRF would be beneficial specifically for bone regeneration and generally for periodontal regeneration.

Conflict of Interest

There is no conflict of interest exist with any of the authors.

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