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Review Article

Plasma-Rich-Fibrin Role in Dentistry

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Abstract

Platelet rich fibrin (PRF) is an improved version of Platelet Rich Plasma (PRP), a fibrin matrix which consists of growth factors and cytokine, can serve as a resorbable membrane facilitating wound healing. It is a second-generation platelet concentrate which is prepared from the patient's own blood free of any anticoagulant. This article enriches the benefits and role of plasma-rich fibrin in dentistry.

Keywords: Platelet Growth Factor; Maxillofacial Surgery; Graft Material; Periodontal Lesions

Introduction

Platelets regenerative abilities were first described in 1974 [1] where the growth factors play an important role to wound healing. In a study of Gassling., *et al.* PRF membranes resulted to be better to collagen membranes (Bio-Gide) in proliferation and suitable for serving as a scaffold for periosteal tissue engineering [2]. Platelets play an important role not only in the regeneration of the wound, thanks to fibrin matrix which works as healing material, but also in hemostasis [3]. These growth factors stimulate the stem cells to produce new host tissue very quickly and this is why platelet rich fibrin is so effective in the post-treatment healing process and plays a key role in tissue regeneration.

In transfusion medicine, platelet concentrates are used to prevent serious bleeding due to severe thrombocytopenia or it's prophylactic usage for patients undergoing coronary bypass grafting in cardiovascular services [4].

PRF (Platelet Rich Fibrin) was first used in 2001 by Choukroun., *et al*. [12] in oral and maxillofacial surgery and is currently considered as a new generation of platelet concentrate. It's a natural fibrin matrix from autologous blood and shows high cicatricial capacity. Its membranes favor and support the healing process due to slow polymerization mode [8].

PRF is the new generation of PRP (or platelet rich plasma) which creates a fibrin matrix or scaffolds for new tissue construction rich in platelet-derived growth factors, but also many other vascular proteins and enzymes part of this PRF mesh such as mesenchymal stem cells, VEGF (vascular endothelial growth factors), leukocytes, TGF β1(transforming growth factor β1) etc [5,12]. PRF accelerate the healing process and also optimizes bone grafting results [6,7].

The PRF Procedure

The PRF procedure begins drawing the patient's own peripheral blood. Than the blood is placed in a centrifuge for 10 minutes (low speed centrifugation system) without anticoagulant in a 10 ml vacutainer. During the centrifuge process, the blood coagulates and is separated into three distinct layers: the upper straw-colored

acellular plasma, middle portion containing the fibrin clot, and red-colored lower portion containing red blood cells. Only the middle portion is collected, which is the PRF. The upper layer acellular plasma and the bottom layer of RBC) are removed and discarded. While, the middle layer is the fibrin mesh which contains platelets [8,9].

The mechanism involved here is the fibrinogen concentrated in the upper part of the tube combines with the circulating thrombin when centrifuged to form fibrin. So, fibrin clot stays between the upper layer of acellular plasma and the lower one containing red blood cells. The time between blood collection to its transfer for centrifuging should be short, in order to avoid it's coagulation before the process, especially when it is taken without any anticoagulant [10] Once separated from the clot, the PRF may be withdrawer and we can put this layer into a plug, or use it as a membrane depending on how and in what treatment do we need it [11].

PRF Role in Dentistry

PRF is basically used in various disciplines of dentistry to repair various lesions and regenerate dental and oral tissue. In recent times a lot of research has been done on PRF and numerous cases have been reported regarding the use of PRF clot and membranes: in oral surgery for bone augmentation, sinus lifts etc. and in periodontics to correct gingival recession, guided bone regeneration, periapical lesions etc. It has also been used for regeneration in open apex, regenerative pulpotomies, periapical surgeries etc [13].

PRF can be used in maxillofacial surgery as a filling material in extraction sockets acting as a stable blood clot for neovascularization and accelerated tissue regeneration. This can be used to improve wound healing in immunocompromised and diabetic patients. PRF stimulates coagulation (with thrombospondin) and wound closure, it can be used as an adjuvant in patients on anticoagulant therapy [14].

According to a study of Simonpieri., et al. PRF can be used successfully as the sole filling material during sinus lift and implantation and seems to be a reliable surgical option promoting natural bone regeneration [26].

PRF maybe used also in combination with beta tricalcium phosphate without bone graft in chronic periodontal lesions and sinus lift procedures [27].

A combination of PRF with bone substitutes and other adjuncts may be necessary in residual defects where one or several walls are missing or damaged in order to provide an adequate reconstruction of bone volume. Since PRF is an optimized blood clot, the fibrin increases the bond between the graft materials acting as a 'sticker' between them and serves as a physiological linkage between the wound tissues thanks to its healing properties [14]. The fibrin mesh promotes cellular proliferation, migration creating biologically links between tissues, remodeling their structure.

The PRF fibrin membrane, thanks to its elasticity and strength, can be used as a membrane for guided bone regeneration (GBR). Its matrix architecture covers and stabilizes bone graft material and operative site in general [13]. Simonpieri., *et al*. [25] 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.

PRF membranes acts as a "biological joining material" between grafts and surgical site acting as a matrix which leads to the process of angiogenesis and migration of osteoprogenitor cells to the graft [28].

While in periodontics, PRF has been used to treat gingival recession, intra-bony defects and periapical lesions. Some studies show the use of PRF gel and PRF membrane in combination with a bone graft for treating a tooth with a combined periodontics-endodontic lesion [15]. To cover the defect are used two layers of PRF membrane because are very thin, inhomogeneous and leucocytes and platelet aggregates are believed to be concentrated in end of the membrane. So, it can be used two layers of membrane in opposite sense in order to prevent the resorption of the membrane and to allow the entire surgical area to be exposed to leucocytes and platelet aggregates [15]. The rapid healing and regenerative properties of growth factors of PRF membrane can be used successfully in periodontal therapy, in gingival recession as a coverage in exposed root surfaces in mandibular process with a flap that covers this membrane over the exposed surface [16].

PRF can stimulate the osteogenic differentiation of the human dental pulp cells by up regulating osteoprotegerin and alkaline phosphatise expression promoting the healing of bone processes defects. PRF also releases growth factors such as platelet-derived growth factor and transforming growth factor which promote periodontal regeneration. These facts emphasize the role of PRF in reparative dentin formation [17].

Studies have shown that PRF can be used on periapical inflammatory lesion in cases of pulp tissue necrosis and can be used as a membrane for the treatment of this lesion inducing dental regeneration and as scaffolds accelerating bone repair [15]. Use of PRF in regenerative pulpotomy procedures can be done where coronal pulp is removed and the pulp wound is covered by PRF followed by sealing it with MTA and GIC [18]. Also, some case reports show that the PRF membrane usage as a matrix shows to speed up the process of periapical healing lesions. Use of a membrane can prevent the extrusion of material [18]. According to Keswani., *et al*, PRF can also been used in cases of big periapical lesions after surgeries to repair bone defects by filling them, as matrix in tissue ingrowth guiding proliferation, migration of cells and as scaffolds in order to enhance the microvascularization of necrotic pulp [19].

Advantages and disadvantages of its uses

Some studies have demonstrated that PRF is a healing biomaterial with a great potential for bone and soft tissue regeneration, without inflammatory reactions and may be used alone or in combination with bone grafts, promoting hemostasis, bone growth, and maturation [20]. This autologous matrix demonstrated in the in vitro studies a great potential to increase cell attachment [7]. Simonpieri., *et al.* reviewed advantages of the use of PRF as it acts as a stabilizing sheath and offers mechanical sustenance, such as the regeneration through PRF membranes both the bone volume and gingival tissue. They also reported satisfactory clinical results related to reshaping the whole alveolar bone and the restoration of gingival volume and peri-implant bone, achieving adequate mechanical and aesthetic properties [25].

Comparing to PRP it has several advantages over it: it's a minimized autologous blood manipulation [29,30] including easier preparation. This entire process is natural, without any external manipulation leading to the absence of any immunological reaction [8,29]. So, it's not required a chemical manipulation of the blood, which makes it strictly an autologous leukocyte-platelet-rich fibrin matrix [8,22]. which acts as a biodegradable scaffold [23] that favors the development of microvascularization and is able to guide epithelial cell proliferation and migration to its surface [8].

It has a natural fibrin mesh with growth factors within that may keep their activity for a relatively longer period and stimulate tissue regeneration [7]. Used as a membrane, it avoids a donor site surgical procedure and results in a reduction in patient discomfort during the early wound-healing period [32]. It is an economical and quick option compared with recombinant growth factors when used in conjunction with bone grafts [31] It can be used in combination with bone grafts or as one layer, depending on the manipulation [21,25]. Comparing to PRP, it's more efficient and shows better clinical results [33].

While talking about disadvantages: The success of the PRF protocol depends on blood collection time and its way on to the centrifuge [8]. The final amount available is low because it is an autologous blood [30] and for the process is needed a glass-coated tube to achieve clot polymerization [34]. It exists possible refusal of treatment by the puncture required for blood collection (Wani 2014).

Conclusion

PRF is the new generation of platelet concentrates and has potential applications in medicine and dentistry too. It can be used alone or in combination with grafts or other biomaterials. Although the mechanisms how growth factors work is not clearly understood yet, PRF shows to have beneficial outcomes and satisfactory clinical results giving new perspectives of treatment in dentistry field.

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