Platelet-Rich Fibrin (PRF): A New Approach to Tissue Repair?

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Abstract
The healing process of lesions is complex and involves chemical and biological agents. After lesion, repair is initiated and divided into tissue inflammation, proliferation, and remodeling. Following tissue damage by different agents, inflammation characterized by the migration of defense cells, such as macrophages, occurs. After this inflammation, coagulation by platelets, fibrin, and fibrinogen naturally begins by the process of tissue repair, which consists of the deposition of connective tissue in the injured area. This process depends on the release of cytokines, growth factors, and elimination of aggressors and dead tissue, roles played mainly by macrophages recruited to the injury site. At the same time, as a repair procedure, there is a decrease in vascularization and some fibroblasts with the presence of act filaments, the myofibroblasts that give scar contraction capacity. The Fibrin Rich Plasma (PRF) is a natural matrix originated from a simple and inexpensive protocol in which blood is withdrawn and placed under specific conditions, providing a fibrin network. This fibrin gel is a new type of platelet concentrate with great healing properties. PRF is the concentrated type that is more similar to the natural clot because it does not require anticoagulants, since it is obtained from pure blood. It has been found that such material is favorable for an effective development of healing without the inflammatory excess. Thus, a proposal of this communication and show how possible uses of the PRF in certain processes of cutaneous healing, as a new therapeutic approach without treatment of lesions.

ABBREVIATIONS

INTRODUCTION
Although the large development of new drugs for the therapy of pathologies, such as osteonecrosis, malignant hypercalcemia, and osteoporosis [1-4], solid tumors [5], and persistent full-thickness idiopathic macular hole [6], the side effects and exacerbated immune response remain a great problem for the patients.

In this context, the fibrin-rich plasma (PRF) or autologous platelet concentrate is considered a second-generation platelet concentrate [7] that functions as an important healing promoting agent since it promotes the migration of endothelial cells and fibroblasts. It carries all the favorable biological components for healing present in the blood, such as growth factors: fibroblast growth factor (FGF-2), vascular endothelial growth factor (VEGF), platelet-derived growth factor (PDGF), and transforming growth factor beta (TGF-β) [8]. Studies of Dohan et al. [9], showed that significant amounts of these factors were found even 7 days after obtaining and applying PRF to the injured tissue, with the peak of release in the first 24 hours and slowing down to the fifth day.

In the last two days, significant amounts of these molecules have been released, but in a slower way. The gradual and prolonged release of growth factors, unlike platelet rich plasma, degraded a few hours after application, favors a better healing or repair of injured tissue [9].

Fibrin is the activated form of fibrinogen, a molecule present in plasma that plays important roles in wound hemostasis, as it promotes platelet aggregation by creating a protective barrier during coagulation. In the tissue repair process, angiogenesis (formation of new vessels) occurs in the injured area through a mechanism that involves the release of growth factors VEGF, PDGF, FGF through the fibrin matrix. These factors promote the recruitment and migration of endothelial cells that will participate in the structure of the new vessels. The fibrin concentrate stimulates the release of these factors, improving the revascularization of the injured tissue [10]. During angiogenesis, new tissue formation occurs simultaneously in order to replace the injured one. This formation depends on the migration of fibroblasts and synthesis of collagen, forming a granulation tissue and later the scar tissue rich in collagen. Growth factors, chemokines and cytokines such as interleukin-5 (IL-5) and tumor necrosis factor (TNF) are primarily released by macrophages [11]. PRF, in promoting the production of these molecules and the proliferation and recruitment of fibroblasts and endothelial cells, is an agent that facilitates the healing of wounds and can be...
used in the clinic to repair several types of tissues. Developed by Choukroun et al. [8], the technique of obtaining the PRF draws attention for its easiness, practicality and low cost. It is divided into simple steps which, however, require technique and speed, since no type of anticoagulant is used. The protocol for obtaining PRF is very simple and the ability is shown in the speed that the collection should be done and immediately the centrifugation, since the absence of anticoagulant would cause the formation of coagulation cascades in the sample, rendering it ineffective [7]. After centrifugation, the tube is observed in three distinct parts: the acellular plasma at the top; the PRF platelet concentrate in the medium; and red blood cells in the background. The equatorial part of the sample is withdrawn and used (PRF). The absence of thrombin in the PRF preparation allows the conversion of fibrinogen to fibrin to occur naturally, slowly, allowing a gradual release of the signaling molecules such as growth factors and endothelial cells and fibroblasts. This gradual release allows better performance in the repair of the lesion [12].

This new complementary treatment with autologous platelet concentrates is being developed, focusing in the improvement of the healing. Among these new therapies, autologous platelet concentrates have come into use for treating bisphosphonate-related osteonecrosis of the jaw, and it has been found that specific growth factors improve angiogenesis. Furthermore, it has been shown that PRF could stimulate collagen production, production of anti-inflammatory agents, initiate vascular internal growth and help heal tissue lesions, leading to the reduction in pain and tumefaction B [13-16].

Despite advances in different oral surgical techniques which use hemostatic compounds, the use of materials that induce good healing is still a problem. There is a wide variety of hemostatic materials, such as collagen membranes, cellulose and synthetic adhesives, and within this therapeutic arsenal, fibrin membranes emerge as a good therapeutic option, since they correspond to a natural biological product whose mechanism involves the fibrin polymerization during artificially amplified hemostasis [17]. However, over a long period of time, these fibrin membranes have been criticized because they are derived from blood. Simpler tools concerning the production of autologous fibrin have been developed [18].

Hematological studies have shown that these structures are specific, since a small plaque formed in the acellular supernatant, the platelet poor plasma, does not have the same effects. Also, histological analysis confirmed the distribution of different structures in the centrifuged collection tube, such as: accumulate in the lower part of the fibbrillation clot, especially at the junction between red corpuscles (red thrombus) and the body PRF itself. The PRF matrix aggregates glycosaminoglycans (heparin, hyaluronic acid) from blood and platelets, and glycosaminoglycans have a strong affinity for circulating small molecules (such as platelet cytokines) and a strong ability to integrate cell migration and repair processes [19].

CONCLUSION

These observations open important perspectives for the understanding of new approaches, since PRF is not only a platelet concentrate, but also an immunological cluster capable of stimulating and activating defense mechanisms. It is also very likely to promote the regulation of the inflammatory process, since in many surgical procedures treated with PRF the activation of cytokines originating from the fibrin network and released during the remodeling of this matrix occurs.

REFERENCES


