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The Use of Platelet-Rich Plasma and Platelet-Rich Fibrin in Dentistry and Orofacial Harmonization: A Literature Overview

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Abstract

PRF (Platelet-Rich Fibrin) is a by-product of obtaining Platelet-Rich Plasma (PRP). Both are widely used in the medical and dental fields, being used mainly as adjuvant therapy in regenerative procedures. In dentistry, PRP is widely used in maxillofacial surgeries. PRF is widely used in bone grafting for dental implants and soft tissue grafts, such as connective tissue grafts, and recently it has also gained prominence in the area of orofacial harmonization. PRP and PRF are concentrates that contain growth factors such as Transforming Growth Factor Beta (TGF-β), Insulin-like Growth Factor type 1 (IGF 1), Platelet-Derived Growth Factor (PDGF), Vascular Endothelial Growth Factor (VEGF), Fibroblast Growth (FGF), Epidermal Growth Factor (EGF) and Platelet-Derived Epidermal Growth Factor (PDEGF), with important utility in the medical-aesthetic area, accelerating tissue repair results. In cases of facial rejuvenation surgery and resurfacing and also in percutaneous collagen stimulation procedures, the use of these concentrates improves the ageing aspect of the face, smoothing expression lines and improving volume and skin texture. Thus, this work seeks to elucidate the results found in the literature regarding the use of concentrates such as PRP and PRF, making a comparison of clinical use found in published scientific papers.

Keywords: Ageing; Growth Factors; Platelet-rich plasma

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Introduction

Tissue healing and regeneration are the main goals in aesthetic medical procedures. Much has been studied about autologous concentrates and their clinical applications. Therapy using autologous platelets gained popularity in 1990; Since then, many areas have sought to study the medical benefits of these concentrates [1]. Platelet concentrates have been used for more than 60 years in humans, showing promising results, since these platelets are obtained from the patient's own blood. Platelet-Rich Fibrin (PRF) is part of the second generation of concentrates and is simpler to obtain when compared to Platelet-Rich Plasma (PRP). Currently, these concentrates are becoming increasingly specific, which favors their use in several areas, among which they have been investigated as a tool for aesthetic procedures in the orofacial region [2].

Platelet precursor cells are megakaryocytes, which are large hematopoietic cells present in the bone marrow. These megakaryocytes fragment into small discoid corpuscles known as platelets in the blood. The histological diameter of platelets ranges from 1 μm to 4 μm; they are colorless and non-nucleated with moderately refractive bodies. The average lifespan of a platelet is a few days, approximately 5 to 10 days. Platelets are a source of growth factors that are important in the treatment and regeneration of wounds, since they have mitogenic and angiogenic capacity. However, with the evolution of medicine and dentistry, the use of platelet concentrates has gained importance in tissue regeneration processes. Fibrin glue has long been used in periodontal surgery and is being replaced by PRP. PRP has also been widely used in aesthetic dermatology and since 2001 a new generation of PRF platelet concentrates is gaining ground when compared to the previously used platelet concentrates [3].

Basically, blood is composed of 55% plasma and 45% of this plasma consists of water and soluble proteins, electrolytes and metabolites. The most notable soluble constituent is fibrinogen, a clotting protein. Also, in addition to plasma, red blood cells (erythrocytes) and white blood cells (leukocytes) make up the rest of the cells that make up whole blood. Erythrocytes are the most

abundant components, comprising about 44% of the total blood composition, while leukocytes constitute the layer that corresponds to approximately 1% of the total cells present. The blood centrifuge technique consists of centrifuging the whole blood, by which the components present are separated according to their density. The red blood cells accumulate in the lower part of the tube as they have a higher density, whereas the leukocyte concentrate settles in the upper part. Also in this separation process, anticoagulants or enzyme supplements can be used to separate the components of PRP.

In facial surgeries and invasive treatments, it is convenient to use PRF at the surgical site; this results in an acceleration of wound healing and attraction of mesenchymal stem cells to the site, helping in collagen remodeling and support, thus providing more effective tissue regeneration. PRF injections improve the appearance of scars and stimulate hair growth where hair follicles are most inactive [1]. It is also known that plasma proteins present in PRF can be coagulated through heat to form a gel capable of improving the appearance of 'box' scars, especially in cases of patients who contracted chickenpox [4]. Also, PRF is widely used in surgical treatments of drug-induced osteonecrosis and closure of oroantral communications, providing positive results in terms of mucosal healing and improved quality of life for the patients [5].

The aim of the study was to review the literature on the use of PRP and PRF in various areas of dentistry and medicine, emphasizing its use in dentistry and orofacial harmonization.

Materials and Methods

Searches were performed thru scientific literature enrolled in mayor scientifical databases: SciELO, PubMed, and Google Scholar. No date of publication or language has been defined. The aim of the present study was to review the literature on the use of PRP and PRF in various areas of dentistry and medicine, emphasizing its use in dentistry and orofacial harmonization.

Discussion

Restoring skin tone and reversing the effects of genetic ageing by non-surgical methods are modalities that have attracted much attention due to the reduced risk of complications and sufficiently satisfactory treatment results in most cases. Advances in therapies with laser, especially fractionated CO_2 (Carbon Dioxide), platelet concentrates and micro-needling, have repercussions on many studies on the wound repair process [1].

PRF represents the second generation of platelet concentrates that have gained prominence in recent years in pro-regeneration processes. This biomaterial is an autologous component which is easy to prepare, has a minimal cost and has a prolonged release of growth factors, along with other advantages over the traditional first-generation PRP concentrate. Several protocols have been presented for the preparation of PRF, each providing the required amount of growth factors and other biomolecules necessary for wound healing [7]. The studies available in the literature regarding PRP for use in dermatological treatment are controversial, especially with regard to aesthetics. The absence of randomized clinical trials and protocols for the preparation and application of PRP also mean it is difficult to make recommendations based on evidence of PRP and skin rejuvenation [8].

Basically, PRF supplies the characteristics of PRP and has the advantage of not requiring the use of anticoagulants or external substances to stabilize the concentrate, which can generate immunogenic reaction and hypersensitivity reactions, being considered more reliable for its purpose in aesthetic protocols [9]. Although there are few specific studies, the results indicate that injectable PRF has been shown to be effective when used in orofacial aesthetic procedures; effectively responding to tissue regeneration and has several areas of application within dentistry, including bone augmentation in implant dentistry, maxillary sinus lift and periodontal aesthetics, among others.

When using PRP in oral surgery, found a clear benefit, which was the ability to stimulate bone repair and formation. However, the use of bovine thrombin that is used in the PRP protocol is often dangerous, since antibodies V and XI, and thrombin factors, which contribute to coagulopathy, can form. In 2001, PRF was first used by Choukroun [2], specifically in oral and maxillofacial surgery, being called the modern form of platelets. This is an autologous fibrin matrix that has many benefits compared to PRP, including better storage and delivery of chemical hemotherapy. In this sense, PRF emerges as a natural, viable, inexpensive and quite satisfactory alternative with promising results.

The main advantage of PRF is that it has a simple preparation protocol when compared to PRP. Consequently, the benefits of PRF in wound and bone healing, its antibacterial and anti-hemorrhagic effects, associated with low risk of its use and the availability of preparation methods and low cost, should encourage more dentists to adopt this technology in their practices for the benefit of their patients. The Table 1 demonstrates the advantages and disadvantages of using PRF.

Specifically in orofacial harmonization, there are few studies in the literature that compare the use of platelet aggregates in facial rejuvenation, and those that are available have an undefined or high risk of bias. There is a need to conduct more well-designed clinical studies comparing the use of platelet aggregate injections associated or not with facial rejuvenation techniques [10]. About the selection of use, and as described, PRP having a faster release of growth factors than PRF, does not maintain this release for a long period, whereas PRF releases some factors more slowly and remains for a longer time [1].

The use of autologous therapies based on platelets in different dermo-aesthetic fields such as skin rejuvenation, acne scar reduction and contour correction, among others, is not something new.

Table 1: PRF's advantages and disadvantages of use.

Advantages	Disadvantages
It is a fully autologous product Minimizes blood handling Does not require the use of anticoagulants Contains growth factors, leukocytes and cytokines involved in the repair process It has a slow and prolonged release of growth factors, similar to what occurs in the repair process It is inexpensive and involves a single centrifuge process	Preparation success mainly depends on blood handling speed Short working time Unable to store PRF preparation As it is an autologous product, it cannot be used in other patients.

Table 2: Growth factor's roles.

Growth Factors	Action Mechanism
Platelet-derived growth factor (PDGF)-PDGF AA, PDF BB	Mitogenic for blasts and smooth muscle cells Chemotactic for mesenchymal stem cells, fibroblasts, smooth muscle cells, macrophages, mono-thrombin-activated, neutrophils, and platelets Fibroblast proliferation and migration Believed to regulate cell growth and division in wound healing
Vascular and endothelial growth factor	Mediates the synthesis and deposition of the extracellular matrix, promoting angiogenesis Chemotactic for endothelial cells Mitogenic for endothelial cells and keratinocytes Believed to increase the permeability of blood vessels to improve tissue nutrition
Transforming growth factor beta (TGF-β)-TGF-β1, TGF-β2, TGF-β3	Mediates the formation of extracellular matrix Migration of keratinocytes in re-epithelialization Stimulates angiogenesis Stimulates the production of type I and type III collagen Stimulates fibroblast and mesenchymal stem cell proliferation
Metalloproteinase tissue inhibitor (TIMP1 and 2)	Regulates enzymatic activity, preventing the degradation of collagen and hyaluronic acid
Fibroblast growth factors (FGF)-FGF-2, FGF-4, KGF (FGF-7), FBF-9	Stimulates and mediates angiogenesis Endothelial and fibroblast proliferation and migration Synthesis and secretion of fibronectin Believed to promote skin cell growth and tissue repair Hepatocyte growth factor Inflammatory Mediates formation of extracellular matrix Believed to promote three-dimensional tissue growth Believed to promote cell growth and multiplication
Hepatocyte growth factor	Mediates formation of extracellular matrix Believed to promote three-dimensional tissue growth
Insulin-like growth factor (IGF)-IGF1, IGFBP1, IGFBP2, IGFBP3, IGFBP6	Believed to promote cell growth and multiplication
Placental growth factor	Believed to promote endothelial cell growth
Bone morphogenetic protein	Believed to promote nerve and cell development in developing tissue
Interleukins-15 different interleukin relatives, including IL-10 and IL-13	Believed to play a critical role in wound formation and healing
Colony-stimulation factors	Believed to induce secretion of other cytokines

However, current knowledge about their eventual safety profile and potential risks and adverse effects are still under study, and research is still recent and is expanding. Some challenges still persist with regard to traditional studies involving proteomic characterization of platelets, to fully understand the biomolecular mechanism behind the regenerative effect of these therapies. Furthermore, the establishment of biological dosages for these therapies is also a current field of study [6].

Therapeutic use of PRP stimulates the storage and release of platelets, growth factors and collagen synthesis. Thus, recent studies have investigated treatments with topical and injectable PRP solutions. The results obtained in a study with 12 women, who analyzed the improvement of wrinkles, increase of hydration and improvement of skin texture, were positive in just 1 month of treatment. After 6 months of treatment with topical and injectable PRP, there was a change in skin texture and reduction of wrinkles, pigmentation and telangiectasias [8]. *In vitro* studies in animals and patients treated with PRP are also promising to improve the healing process. However, there is a need for more evidence for reliable and efficient protocol formulations. These studies would also seek to associate factors of growth to hyaluronic acid, developing a synergistic and more effective combination in rejuvenation treatments and aesthetic protocols.

To overcome the limitations offered by PRP, PRF was developed in 2001, and, in plastic surgery, solid PRF has benefit in healing soft and bone tissue as well as fat. However, there are still limited studies on its use for facial rejuvenation [11]. Basically, PRF supplies the characteristics of PRP, presenting the advantage of not needing the use of anticoagulants or external substances to stabilize the concentrate. It was found that with PRP, growth factors are almost totally released 15 min after injection, requiring a greater number of sessions at more frequent intervals, when compared to PRF. The injectable PRF was developed to contain platelets, B lymphocytes, monocytes, stem cells, neutrophils and growth factors distributed in a three-dimensional mesh, also considered a very important factor in wound healing [12].

PRF has attracted significant interest in the dental scenario due to its regenerative proposal in healing processes. Basically, this mechanism is due to the high release of growth factors to promote the wound healing and regeneration process. The Table 2 demonstrates the mechanism of action of the main and supplementary growth factors. The use of PRF can be considered broad, since its use extends both in the dental area of bone grafts, orofacial harmonization, and oral and maxillofacial surgeries, as well as in dermatological and regenerative medicine [13].

The process of obtaining biological blood products (PRF and PRP) is influenced by supplier techniques and a lack of standardization in procurement protocols. The use of PRF, according to the authors of the present work, still remains controversial, as there is a lack of standardization in preparing this concentrate. Basically, the results obtained by PRP and PRF would be significantly similar; however, they differ by the types of external additives used and the amount of

growth factors released in a period of time, PRP releasing them faster than PRF [14]. Knowing that the results for these autologous blood concentrates are similar, further studies will be necessary to provide a scientific basis for their properties and limitations [15].

PRP is considered an adjuvant therapy for resurfacing procedures, being a potential inducer of the repair process after procedures such as micro-needling, CO_2 laser and radiofrequency; in addition to being associated with treatments with chemical peels [16]. PRF may be a better option when compared to PRP as it has similar growth factor release behavior with the natural process of clotting and wound healing. It is important to distinguish the different types of PRP preparations, as in most published studies these concentrates are commonly referred to as just PRP.

In some studies, when compared to PRP, the use of PRF was postulated to produce better results, as the release of growth factors occurs over a longer period of time. In summary, PRF has been used to treat periorbital wrinkles, glabellar creases, malar enlargement and zygomatic arch enhancement. When compared to PRP, PRF achieved significantly better results for treating wrinkles, texture, elasticity, smoothness and barrier function of the skin, since it promoted an increase in dermal thickness and volume, when applied three times a week for 12 weeks. PRF has also been shown to be more effective in the treatment of superficial and deep wrinkles, as well as in cases of reduction of hypertrophic scars and acne scars [17].

In a study with 22 patients who underwent facelift and autologous fat grafting, injections in the fat graft plane showed significant improvement in the aesthetic result and recovery after lifting surgery, when compared to the control group. Platelet concentrate preparations (L-PRP) were also combined with fractional CO_2 laser resurfacing [14]. The results obtained were a significant improvement and shortened the duration of post-procedure erythema, edema and crusts, in addition to increased dermal thickness. Today the platelets are known for a myriad of functions, such as cytokine signaling, chemo-release of growth factors, mesenchymal stem cells and mitogenesis, thus contributing significantly to tissue renewal. Furthermore, systematic reviews have also assumed a broad-based approach in categorizing all PRPs, excluding their apparent differences. These obscurities have confused the literature due to the lack of standardization, thus allowing the term 'PRP' to be mispromoted, regardless of product concentration or quality [18].

On other hand, the effect of PRP on tissue regeneration has been supported by *in vitro* and *in vivo* studies, which suggest a positive impact on the differentiation and migration of various cell types. PRP is also used in combination with autologous and halogenic bone grafts, providing better bone graft results. As mentioned, the lack of standardization, observed at the level of preparation of the product, characteristics and form of application, results in great difficulty in comparing studies and drawing conclusions about the real efficacy and adverse effects of its use. Also, future perspectives, mainly in the field of tissue engineering, aim to take advantage of platelet functions to develop new therapeutic strategies. A recent proposal aims to use platelets as Trojan horses for drug delivery or biological therapies, due to their biocompatibility and the possibility of targeting specific sites [19].

Conclusion

There is no consensus in the literature on which type of concentrate, PRP or PRF, is better, much less on effective application and concentration protocols. Both are autologous components obtained from blood, differing only in some aspects of preparation, such as platelet concentration, centrifugation technique, and the quantity and release of growth factors. Although the ability to stimulate tissue repair of both biomaterials is widely reported, more randomized clinical studies should be carried out in order to indicate the clinical practice of professionals.

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