Platelet Growth Factors In Dermatology, More Than A Growth-factor Therapy

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Introduction & Objective:

In recent years, the use of platelet-rich plasma (PRP) has increased eminently in a range of diseases. Platelet-rich plasma is a highly concentrated autologous solution of plasma prepared from a patient's own blood. PRP contains platelets which release numerous growth factors that may be useful in several dermatologic conditions. The application of platelets and their associated growth factors opened new possibilities for the treatment of skin complaints including ulcers, alopecia, acne scarring and lipoatrophy.

The aim of the authors is first, to explain the mechanism of action of PRP in tissue regeneration and secondly to refer to their experience of the use of PRP in different dermatological indications[1-5].

Methods

Six patients came to us with dermatologic complaints (tab 1). Three of whom suffered from severe and extensive burns on the upper limbs , two were affected by burns to the face, one suffered from a chronic wound of the skin, another was affected by universal alopecia. Five out of six patients were treated with one application of topical platelet gel and its fluid part, the last with intradermal injection of fluid PRP. The patient with alopecia underwent eight PRP intradermal injections once a month and she is still undergoing treatment because of the extent of her alopecia(figg3a,3b,4a,4b,4c,5a,5b,5c.

To prepare PRP, a small amount of blood is drawn from the patient's vein and collected in sterile tubes with citrate as anticoagulant (fig 2a). The tubes are then centrifuged in a conventional centrifuge. A low centrifugation speed is recommended in order to prevent an early fragmentation of the platelets and the subsequent early release of the secreted proteins. When the blood is centrifuged, it separates into three layers with different densities: the lower layer, consists of red blood cells, the middle layer of white blood cells and platelets, and the upper layer of plasma. The plasma phase, in turn, can be sub-divided into three sections according to the number of platelets: the platelet-poor section, the intermediate section with a medium concentration of platelets, and the platelet-rich one (Fig. 2b). In order to achieve platelet degranulation and the subsequent release of the growth factors and other bioactive molecules, the lower fraction of the plasma phase will be activated by calcium gluconate (fig2c). The product obtained will be then administered by injection or as a gel[7,8].

Tab 1

Baseline Characteristics	
Total number pts	6
Mean-age (years)	38,16
Male (number)	2
Female (number)	4

Fig 2a

Fig 2c

Fig 2b

Platelet-poor plasma PPP

Platelet-rich plasma PRP

Red blood cells

As mentioned above , PRP is prepared in various forms. Pure PRP is the most commonly used form consisting of a buffy coat with a large number of platelets with little leukocytes. PRP contains various growth factors collected within alpha granules and dense granules. Alpha granules contain seven fundamental growth factors: the platelet derived growth factors (PDGFaa, PDGFbb, and PDGFab), transforming growth factor beta (TGFβ1 and 2), epithelial growth factor (EGF), and vascular endothelial growth factor (VEGF), while dense granules contain adenosine diphosphate (ADP), serotonin and calcium[9] (tab.2).

Tab 2

Classification and Functions of Bioactive Molecules Present in Platelet-Rich Plasma.

Category	Proteins	Function
Adhesive proteins	Von Willebrand factor, fibrinogen, fibronectin, vitronectin, tamminin-8	Cell interaction, hemostasis, composition of extracellular matrix
Coagulation factor and associated proteins	Factor V/Va, multimerin, protein S, high-molecular weight kininogen, antithrombin III, tissue factor pathway inhibitor	Thrombin production and regulation
Fibrinolytic factors and associated proteins	Plasminogen, α-2 antiplasmin, histidine-rich glycoprotein, α-2 macroglobulin	Plasmin production and vascular remodeling
Proteases and antiproteases	Ttissue inhibitors of metalloproteases 1-4 (TIMP 1-4), metalloproteases 1, 2, 4, 9, C1 inhibitor, α-1 antitrypsin	Angiogenesis, vascular modeling, coagulation regulation
Growth factors	PDGF, TGF-β 1 and 2, EGF, IGF-1, VEGF, bFGF, HGF, BMP-2, 4, 6, CTGF	Chemotaxis, cell proliferation and differentiation, angiogenesis
Chemokines, cytokines, and others	IL8, FasL, endostatins, osteonectin, bone sialoprotein	Regulation of angiogenesis, vascular modeling, cell interactions, bone formation
Antimicrobial proteins	Thrombocidins	Bactericidal and fungicidal properties
Membrane glycoproteins	Most of the components of the plasma membrane	Platelet aggregation and adhesion, protein endocytosis, inflammation, thrombin generation, platelet-leukocyte interactions
Others	Chondroitin 4 sulfate, albumin, immunoglobulins, semaphoring	Promote angiogenesis, cartilage regeneration, fibrin production, and platelet adhesion

Adapted from Anitua et al[10]

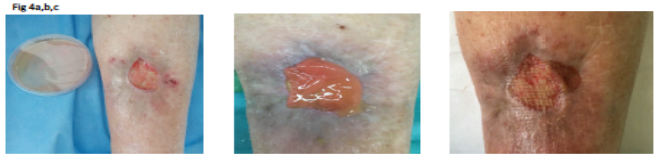
Fig 3a

Phases of PRP-gel treatment for the extensive burn

Fig 3b

After one application of PRP gel

Fig 4a,b,c



Phases of PRP-gel treatment for the extensive burn

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Fig5a

Before

Fig5b

Before

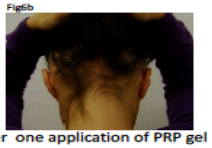
Fig5c

After one application of PRP gel

Fig6a

Before

Fig6b



After one application of PRP gel

Results & Conclusions

In the last decade, several smaller studies have highlighted the favorable effects of PRP as a bio-regenerator in many applications in different fields of medicine, including dermatology. These bioactive molecules, have different important functions in local regeneration (see table 2) including wound healing, angiogenesis and antibacterial properties. Some proteins (fibrin, fibronectin, and vitronectin) also promote cell adhesion, necessary for cell migration and for proliferation and 3-dimensional growth of tissues.

Therefore, PRP has effects not only directly related to the target cells owing to the various growth factors but also has a wider effect as an extracellular matrix for the stimulation and repair and/or regeneration of the tissue[4,10].

Although a small group of patients was treated with the PRP technique, we can definitely consider the aforementioned technique effective and safe, thus, since its first application, we could see a rapid healing of wounds as well as a visible improvement in the area affected by alopecia.

So far no relevant side effects have been documented including infectious diseases which is due to the autologous nature of PRP, which is considered to be a safe product owing to the lack of potential risk of disease transmission. Furthermore, no evidence of either oncogenic potential or systemic effects of PRP has been reported and it is in line with what can be seen in literature[11].

In conclusion, PRP application has demonstrated effectiveness in numerous skin complaints and it would seem to be a promising therapy for several other skin diseases. Nonetheless, more clinical studies are needed to support its efficacy and safety and to standardize the technique.

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