

Role Platelet-Rich Plasma (PRP) in Management of Acne Scar

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Abstract

Background: Inflammatory acne can cause different types of scars. These scars negatively affect patient's relational and social life. The abnormal production or degradation of collagen that occurs in healing processes leads to various types of acne scars. In most cases (80–90%), there is a degradation of collagen at the dermal level which results in atrophic scarring. More rarely, there is an increased production of collagen which causes hypertrophic or keloid scars. Platelet-Rich Plasma is used with variable success for the treatment in specialties of dermatology, plastic surgery and aesthetics, ear-nose-throat surgery, orthopedics, sports medicine, gynecology and ophthalmology. Platelet-rich plasma (PRP) came into the acne scar management picture after platelet-derived growth factor (PDGF) was shown to promote wound healing, angiogenesis, and tissue remodeling. Platelet-rich plasma modalities are minimally invasive and have the advantages of short downtime and low cost. Platelet-rich plasma is derived from autologous blood containing other factors, such as transforming growth factor, vascular endothelial growth factor, and insulin-like growth factor that upon activation lead to collagen induction which may ultimately enhance the remodeling of atrophic acne scars.

Keywords: Acne scars, Platelet-Rich Plasma.

Introduction

Acne has been reported in 30% of acne patients, although mild to moderate scarring has been reported in up to 95% of these patients (1).

Acne scarring is often the result of delayed and/or inadequate medical treatment, However, it can be developed despite appropriate medical therapy. Collagen and other tissue damage, secondary to inflammation of acne, leads to permanent skin texture changes and fibrosis. Scars typically proceed through a cascade of wound healing phases: inflammation, granulation, and remodeling (2).

Acne scarring is a therapeutic challenge as many treatments may be only partially effective, leading to patient disappointment and frustration (2). The detrimental effects of

acne scarring are not limited to impaired cosmetic appearance. Rather, acne scarring has also been associated with depression and other mental health disorders, suicidal ideation, emotional debilitation, embarrassment, poor self-esteem, and general social impairment (2).

Eighty to ninety percent of acne scars demonstrate associated loss of collagen (atrophic scars) whereas the remainder demonstrate a gain of collagen (keloidal or hypertrophic scars). Atrophic scars present as depressions secondary to fibrous contractions. Atrophic acne scars are classified into boxcar, icepick, and rolling (3).

The pathogenesis of atrophic acne scarring is not completely understood but is most likely related to inflammatory mediators and enzymatic degradation of collagen fibers and subcutaneous fat. It is not clear why some acne patients develop scars while others do not, as the degree of acne does not always correlate with the incidence or severity of scars. The scarring process can occur at any stage of acne. Early intervention in inflammatory and nodulocystic acne is the most effective way of preventing post-acne scarring but once scarring has occurred, it is usually permanent (3).

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Hypertrophic scars and keloids can be described as variations of typical wound healing. In a typical wound, anabolic and catabolic processes achieve equilibrium approximately 6-8 weeks after the original injury. At this stage, the strength of the wound is approximately 30-40% that of healthy skin. As the scar matures, the tensile strength of the scar improves as a result of progressive cross-linking of collagen fibers. At this point, the scar is usually hyperemic, and it may be thickened, but it tends to subside gradually over months until a flat, white, pliable, possibly stretched, mature scar has developed. When an imbalance occurs between the anabolic and catabolic phases of the healing process, more collagen is produced than is degraded, and the scar grows in all directions. The scar is elevated above the skin and remains hyperemic. Excessive fibrous tissue is classified as either a keloid or a hypertrophic scar (5).

Platelet-Rich Plasma (PRP)

Platelet-Rich Plasma has been defined as the portion of the plasma (fraction of blood), having a platelet concentration above the baseline value. In a healthy individual normal platelet count in whole blood is between $1.5-4.5 \times 10^5 /\mu\text{L}$ (6). Platelet count in PRP has not been yet optimized, but for therapeutic effectiveness, platelet count of 4-5 times

above the baseline should be present in the concentrate (7). Platelet concentrations consequently are increasing more than 1,000,000 platelets/ μ l (8).

PRP has been used with variable success for the treatment in specialties of dermatology, plastic surgery and aesthetics, ear-nose-throat surgery, orthopedics, sports medicine, gynecology and ophthalmology (9).

Mechanism of Action:

PRP is defined as an “autologous concentration of platelets in a small volume of plasma” and is considered to be a rich source of autologous growth factors (10). The membrane bound α -granules are an important intracellular storage pool of growth factors including platelet-derived growth factor (PDGF), transforming growth factor (TGF- β) and insulin-like growth factor (IGF-I) that are needed for wound healing (11).

On activation, these α -granules fuse with the platelet cell membrane and activate secretory growth factors and proteins to a bio-active state. These secreted growth factors (GF) and proteins bind to their trans-membrane receptors on the target cells like epidermal cells, mesenchymal stem cells, fibroblasts inducing an internal signal transduction pathway, thereby increasing expression of various gene sequences in cells like cell proliferation, collagen synthesis, anti-apoptosis (12).

Table (1): Growth factors present in PRP (9),

h Factor	ion
Transforming GF β (TGF-β)	Proliferation of undifferentiated mesenchymal cells; inhibition of lymphocyte and macrophage proliferation; Regulate: Endothelial, fibroblastic and osteoblastic mitogenesis; Collagen synthesis and secretion of collagenases; Mitogenous effect on other GF; Endothelial chemotaxis and angiogenesis
Fibroblast GF (FGF-β)	Stimulates mitogenesis, growth & differentiation of mesenchymal cell mitogenesis
Platelet derived GF (PDGF)	Stimulates mitogenesis of mesenchymal cells; mitogenesis & chemotaxis of fibroblastic, glial, smooth muscle lineage cells;

	regulates collagenase secretion and stimulates epithelial mesenchymal mitogenesis
Vascular endothelial GF (VEGF)	Increases angiogenesis, vascular permeability & endothelial cell mitogenesis
Connective tissue GF (CTGF)	Promotes angiogenesis, chondral regeneration, fibrosis & platelet adhesion
Epidermal GF (EGF)	Stimulates endothelial chemotaxis & angiogenesis; regulates secretion of collagenases; stimulates mitogenesis of mesenchymal & epithelial cells

Preparation of PRP:

After the proper consent & with all aseptic precautions, venous blood is collected in a tube containing an anticoagulant solution sodium citrate. This is followed by soft spin centrifugation at 1200 g for 15 minutes to separate PRP from whole blood at the top of the test tube and then via heavy-spin centrifugation at 1800 g for 10 minutes to obtain a platelet concentrate with a platelet count 4-5 times higher than the baseline (13).

PRP can be used either in non-activated form or as activated PRP. Thrombin, calcium chloride or mechanical trauma leads to activation of the PRP before coming in contact with collagen of the tissues (extrinsic activation) while non activated form gets activated after coming in contact with collagen of the tissues (intrinsic activation) (6). Collagen is a natural activator of PRP, thus when PRP is used in soft tissue, it does not need to be exogenously activated (14).

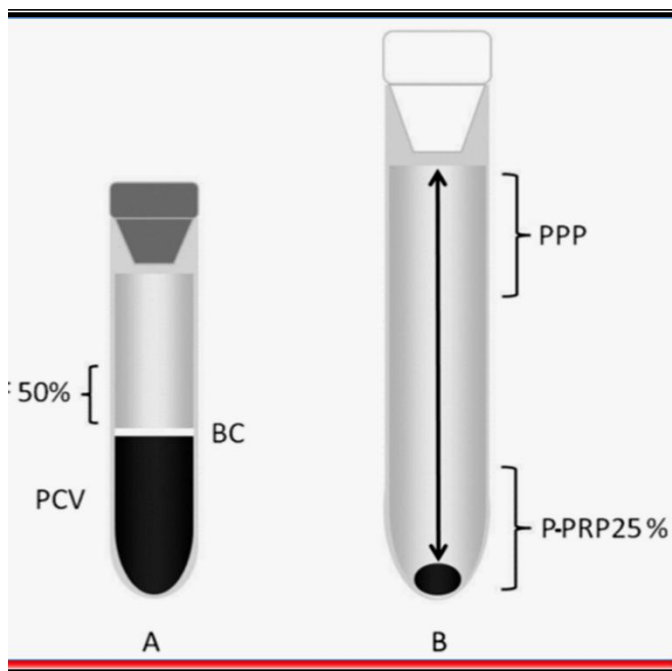


Figure (1):

Left tube (A) containing the first plasma fraction (50%) (FPF) obtained by the single centrifugation tube.

Right tube (B) containing platelet-rich plasma (PRP) obtained by the double centrifugation tube. BC: buffy coat. PCV: packed cell volume. PPP: Platelet poor plasma. P-PRP: Pure Platelet-Rich Plasma,

(Giral(15)).

Classification:

According to the classification proposed by **Ehrenfest et al. (7)**, four main families of preparations can be defined, depending on their cell content and fibrin architecture.

- 1. Pure Platelet-Rich Plasma (P-PRP)** or leucocyte poor PRP products are preparations without leucocytes and with a low-density fibrin network after activation.
- 2. Leucocyte and PRP (L-PRP)** products are preparations with leucocytes and with a low-density fibrin network after activation. It is in this family that is the largest number of commercial or experimental systems exists.
- 3. Pure platelet-rich fibrin (P-PRF)** or leucocyte poor platelet-rich fibrin preparations are without leucocytes and with a high-density fibrin network. These products only exist in a strongly activated gel form and cannot be injected or used like traditional fibrin glues.
- 4. Leucocyte- and platelet-rich fibrin (L-PRF)** or second-generation PRP products are preparations with leucocytes and with a high-density fibrin network.

Methods of Application:

A. Intra dermal injection.

Platelet rich plasma (PRP) is used for stimulation of both superficial and deep dermis layer. For superficial stimulation, injection must be done in the superficial dermis. The PRP must be injected into the deep dermis or sub dermal tissue when using as filler. The superficial injection might be done just like mesotherapy technique in order to improve the skin texture, volume and hydration. Side effects might appear from mild bruising and occasional swelling to rarely infection (16).

B. Topical after microneedling

The procedure is performed under topical anesthesia containing mixture of lignocaine and prilocaine/ tetracaine for 45 minutes to 1 hour. After preparation of the area with antiseptic and saline, the PRP is applied followed by needling which is done in the horizontal, vertical, and oblique directions. The treatment endpoint is identified as uniform pin-point bleeding which is easily controllable.

C. Dermatological Indications: The major uses of PRP in the field of dermatology are:

◆ Androgenetic Alopecia (AGA)

Androgenetic Alopecia (AGA) is the most common form of hair loss but treatment options are limited and moderately effective. The mitogenic & antiapoptotic effects of PRP prolong survival of dermal papillae. PRP modulates angiogenesis and enhance blood flow around hair follicles, thus improving cutaneous ischemic conditions. The use of PRP mesotherapy either alone or as an adjunct to surgical procedures in the patients of androgenic alopecia thus holds promising results (16).

PRP also used as an adjunct to hair transplantation to increase the survival rate after implantation. The pretreatment of follicular units with PRP before transplantation has resulted in improved hair growth and density (17).

◆ **Skin Rejuvenation**

Skin aging is an unpreventable, irreversible process that is influenced by both intrinsic and extrinsic factors. The intrinsic factors like the reactive oxygen species along with matrix metalloproteinases (MMP) reflect different physiological and pathological processes involved in skin aging. There is accumulation of fragmented collagen fibrils that prevents neocollagenesis and causes further degradation of the extra cellular matrix (ECM). Conventional anti-aging strategies are including lasers and topical treatments, increase ECM synthesis through the activation of fibroblast (18).

Different GFs present in PRP stimulates human dermal fibroblasts (HDF). There is an overall increase in collagen type1 levels after PRP with increase in expression of MMP1 & MMP-3 protein. MMP-1 induction in photo aged skin leads to removal of damaged collagen fragments, thus facilitating deposition of new collagen (19).

Topical application of PRP or its direct injection into the skin produces ECM remodelling and induces the synthesis of new collagen by fibroblasts. More recently microneedles and lasers have been tried for increasing skin remodelling by inducing mild inflammatory reactions. However, results of PRP are better on the face and neck revitalization (20).

◆ **Scars and Contour Defects**

The presence of facial scars has both cosmetic as well as psychological effects. Techniques like dermabrasion, chemical peeling, lasers, fat grafting and fillers have been tried but with limited success. PRP effectiveness in treatment of depressed facial scars and use of fractional laser or light-emitting diode phototherapy along with PRP has led to substantial improvement with good cosmetic results and skin rejuvenation (20).

Growth factors present in PRP promotes recovery of laser-damaged skin & accelerates tissue remodelling with increase synthesis of collagen (21).

◆ **Acute and Chronic Ulcers**

The treatment of diabetic foot ulcer is a big challenge. PRP is used either as topical or perilesional injections. Platelet-rich fibrin matrix and a viscous fibrin meshwork rich in GFs, resulted in faster healing and re-epithelization (22).

◆ **Striae Distensae**

Striae distensae are dermal scars with linear atrophic depression. It acts as a challenging cosmetic problem for which present treatment modalities have limited results (8).

Histologically, in the early stage of striae distensae, there are dermal edema and perivascular lymphocytic cuffing and in the later stage, atrophy and loss of rete ridges occur. There is loss of normal random collagen distribution to the level of the mid

dermis or deeper. Elastin stains reveal absent elastin fibers and reduced fibril in the papillary and reticular dermis within affected areas (10, 23).

Injected PRP along with higher energy fluencies using radiofrequency device directly to the dermis have been shown to contain mitogenic and chemo-tactic growth factors important in wound healing. The thermal energy generated by bipolar radiofrequency, denatures the elastic fibers and collagen bundles while PRP stimulates wound healing, thus providing synergistic benefits and good cosmetic results. Histological sections showed the increase of both collagen and elastic fibers was found in the papillary and reticular dermis as well as in sub-epidermal basal zones (24).

Side effect of PRP:

Because PRP involves injecting a substance into the skin, there are potential side effects. PRP is autologous, this reduces the risks for an allergic reaction that can occur from injecting other medications, such as cortisone or hyaluronic acid. It lacks action on nucleus, so is devoid of any mutagenic effects (7, 6). However, there are risks from the injection itself, including:

- Infection
- Nerve injuries
- Pain at the injection site
- Tissue damage (14).

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