Use Of Platelet Rich Plasma and Plasma Gel in Management of Post Acne Scars

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Abstract

Background: Acne is a chronic inflammatory skin condition of the pilosebaceous glands that typically begins at puberty and may continue through adulthood, with flares often coinciding with increases of serum androgens. Over 85% of adolescents and 40% of adults develop late onset acne. It is one of the most common dermatological disorders in the world with its incidence and severity influenced by genetics and environment. The concept of using a patient’s own blood or components to enhance the physiological process of healing has been taken place for many years. Platelets can be used locally as a source of growth factors that play an essential role in wound healing. Autologous PRP is obtained from whole blood sample that is drawn and processed in a centrifuge and the red blood cells removed, leaving a high concentration of platelets and growth factors. PRP is then activated by thrombin or calcium chloride, resulting in the cascade and release of growth factors from the platelets. Plasma gel is one PRP formulation having desirable biological or medical properties, deriving from an initial blood composition that comprises proteins in a gelled state as a result of thermal heating and cooling treatment. Plasma gel is highly suitable for use as a filling agent as it is softly and naturally injected into the dermis and subcutaneous fat layer.

Keywords: Platelet Rich Plasma, Post Acne Scars

Background

Acne vulgaris is a common chronic inflammatory disorder of the pilosebaceous unit among adolescents and young adults. It affects about 27% of early adolescents and up to 93% of late adolescents. Typical sites for acne include the face, chest and upper back with the appearance of comedones. Inflamed lesions are characterized by red papules, pustules and often by a subcutaneous abscess (1). Holland et al., (2) found that the inflammatory reaction at the pilosebaceous gland was stronger and had a longer duration in patients with scars versus those without; also, the inflammatory reaction was slower in patients with scars versus those without. They showed a strong relationship between severity and duration of inflammation and the development of scarring; suggesting that treating early inflammation in acne lesions may be the best approach to prevent acne scarring. In the granulation tissue formation phase that follows, damaged tissues are repaired and new capillaries are formed. Neutrophils are replaced by monocytes that-- change into macrophages and release several growth factors which stimulate the migration and proliferation of fibroblasts. New production of collagen by fibroblasts begins approximately 3 to 5 days after the wound is created. Early on, the new skin composition is dominated by type III collagen, with a small percentage (20%) of type I collagen. However, the balance of collagen types shifts in mature scars to be similar to that of unwounded skin, with approximately 80% of type I collagen (3).
Matrix metalloproteinases are extracellular matrix (ECM) degrading enzymes that interact and form a lytic cascade for ECM remodeling. As a consequence, an imbalance in the ratio of MMPs to tissue inhibitors of MMPs results in the development of atrophic or hypertrophic scars. Inadequate response leading to diminished deposition of collagen factors and formation of an atrophic scar while, if the healing response is too exuberant, a raised nodule of fibrotic tissue forms hypertrophic scars (4).

**Platelet rich plasma & plasma gel**

**Definition:**
Platelet-rich plasma is a volume of autologous plasma that contains a platelet concentration above baseline concentration (150,000-350,000/uL) (5).
Platelet concentrates (PC) are defined as autologous or allogeneic platelet derivatives with a platelet concentration higher than baseline. In human blood, normal platelet counts range between 150×10⁹/L and 350×10⁹/L, with an average of approximately 200×10⁹/L. There is still lack of consensus over the correct terminology to define, classify and describe the different PC. PC are widely used in different areas of regenerative medicine in order to enhance wound healing processes; they include platelet-rich plasma (PRP), Platelet gel, platelet-rich fibrin, serum eye drops and PRP eye drops (6).

**Mechanism of action:**
PRP consists of the patient's own plasma that is enriched with a concentration of platelets that exceeds normal levels. It also contains various growth factors, including platelet-derived growth factor (PDGF), transforming growth factor (TGF), vascular endothelial growth factor (VEGF), and insulin-like growth factor (IGF). These growth factors stimulate tissue remodeling and are associated with enhanced healing through the attraction of macrophages, upregulation of collagen synthesis, and promotion of tissue regeneration PRP consists of the patient's own plasma that is enriched with a concentration of platelets that exceeds normal levels. It also contains various growth factors, including platelet-derived growth factor (PDGF), transforming growth factor (TGF), vascular endothelial growth factor (VEGF), and insulin-like growth factor (IGF). These growth factors stimulate tissue remodeling and are associated with enhanced healing through the attraction of macrophages, upregulation of collagen synthesis, and promotion of tissue regeneration platelet-rich plasma consists of the patient's own plasma that is enriched with a concentration of platelets that exceeds normal levels. It also contains various growth factors, including platelet-derived growth factor (PDGF), transforming growth factor (TGF) β, vascular endothelial growth factor (VEGF), Epidermal growth factor (EGF), Connective tissue growth factor (CTGF) and insulin-like growth factor (IGF). These growth factors stimulate tissue remodeling and are associated with enhanced healing through the attraction of macrophages, upregulation of collagen synthesis, and promotion of tissue regeneration (7).
Table 1: List of the most important platelet-derived growth factors and their relevant functions (6).

<table>
<thead>
<tr>
<th>Platelet-derived growth factor</th>
<th>Most representative functions</th>
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<tbody>
<tr>
<td>PDGF</td>
<td>Promotes chemotaxis of macrophages and neutrophils; epithelialization, matrix formation and remodeling</td>
</tr>
<tr>
<td>TGF- β</td>
<td>Inhibition of macrophages and lymphocyte proliferation, mesenchymal stem cells proliferation, neutrophil and monocyte chemotaxis, matrix formation</td>
</tr>
<tr>
<td>FGF</td>
<td>Mitogenic effect on fibroblasts, endothelial cells, mesenchymal stem cells chondroblasts, osteoblasts; it promotes angiogenesis</td>
</tr>
<tr>
<td>EGF</td>
<td>Promotes fibroblast migration and proliferation</td>
</tr>
<tr>
<td>VEGF</td>
<td>Promotes angiogenesis and increases vessel permeability</td>
</tr>
<tr>
<td>CTGF</td>
<td>Promotes platelet adhesion, white blood cell migration and angiogenesis; it also regulates collagen synthesis</td>
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The secreted growth factors immediately bind to the external surface of cell membranes of cells in the graft, flap, or wound via transmembrane receptors. Adult mesenchymal stem cells, osteoblasts, fibroblasts, endothelial cells, and epidermal cells express the cell membrane receptors to the growth factors in PRP. These transmembrane receptors in turn induce an activation of an endogenous internal signal protein, which causes the expression of a normal gene sequence of the cell such as cellular proliferation, matrix formation, osteoid production, collagen synthesis, etc. After the initial burst of PRP-related growth factors, the platelets synthesize and secrete additional growth factors for the remaining 7 days of their life span (8).

It is important to know that the PRP growth factors never enter the cell or its nucleus, so they are not mutagenic, and they act through the stimulation of normal healing, just much faster. Therefore, PRP has no ability to induce tumor formation (9).

Preparation of platelet rich plasma:
There are different methods used for centrifugation. The methods vary according to the duration, speeds, and number of centrifuge steps. Low centrifugation speeds are recommended to avoid fragmentation of platelets and the early release of the secreted proteins.
When the anticoagulated blood is centrifuged, three layers separate out according to their density: the lower layer, consists of red blood cells; the middle layer, consists of white blood cells and platelets; and the upper layer consists of plasma.
According to the number of platelets present in plasma, the plasma phase can be subdivided into three fractions. These fractions are, from most to least abundant: the platelet-poor fraction, the intermediate fraction and the platelet-rich fraction (Figure 9) (10).
The method involves centrifugation of the whole blood by single spin or double spins method. The single spin method separates the whole blood into three basic components: red blood cells (bottom of the tube), platelet rich plasma (middle of the tube) and platelet poor plasma (top of the tube). (11)
The first spin will separate the red blood cells from the plasma, which contains the platelets, the white blood cells, and the clotting factors. The second spin finely separates the platelets and white blood cells together with a few red blood cells from the plasma. This second spin produces the PRP and separates it from the platelet poor plasma (PPP). Platelet rich plasma can be activated by adding thrombin or 10% calcium chloride to stimulate growth factor release (12).

**Figure (1):** Different fractions obtained after centrifugation of anticoagulated blood (10).

**Safety of application of platelet – rich plasma:** Because it is an autologous preparation, PRP is inherently safe and therefore free from transmissible diseases such as HIV and hepatitis. Some have empirically suggested that PRP may promote infections due to the logic that it is a blood clot and that blood agar is used in microbiology laboratories to culture bacteria. However, PRP is not different in substrate than the blood clot that forms in every wound and therefore could not support bacterial growth any more than any other blood clot. In fact, PRP has a pH of 6.5 to 6.7 compared with a mature blood clot of 7.0 to 7.2. It has thus been counter suggested that PRP actually inhibits bacterial growth but no clear studies or data in this subject are confirmed (8).

In case of using commercial kits, the manufacturer instructions should be followed (10). In fact, we need to ensure the feasibility of these kits, concentration and activation of platelet gained. Any patients to undergo the PRP injection should stop any anti-platelet drugs such as aspirin and non-steroidal anti-inflammatory drugs for at least 2 weeks before injection (13).
PRP Indications:
Platelet-rich plasma has actually been used for many years in a wide range of indications. (Figure 10) shows a timeline for the application of PRP in different fields of medicine (14).

Figure (2): Temporal sequence of application of PRP in different fields of medicine (14)

Platelet rich plasma in dermatology:
1- Androgenic alopecia: Improved pull test results and improved hair volume and quality (15).
2- Acne scar: leukocyte- and platelet-rich plasma(L-PRP) administered topically and intradermally post fractional ablative CO₂ laser treatments both showed significant improvement in clinical appearance or acne scars. The duration of erythema and edema was also reduced (16).
3- Facial rhytides: PRP has been noted to significantly improve wrinkles and skin tone through stimulated neocollagenesis and angiogenesis (17).
4- Combination Therapies:
   - Hyaluronic acid fillers and dermal augmentation agents serve as scaffolds to which PRP binds, enhancing skin rejuvenation, soft tissue augmentation, and overall aesthetic appearance (18).
   - Administering PRP after fractional laser resurfacing improves skin elasticity, induces fibroblasts, and increases collagen density (19).
Plasma gel

Tissue engineering is a newly emerging biomedical technology and methodology based on a smart and unique combination of cells and growth factors to assist and accelerate regenerating and repairing of defective and damaged tissues (20).

Plasma gel (PG) is a semi-solid material derived from human autologous plasma, as a result of thermal treatment (heating then cooling) and contains numerous growth factors and cytokines. It is definitely rich in fibrin and coagulated proteins. It is really appropriate for use as inert biofiller as it can be smoothly and accurately injected into the dermal and subcutaneous layers (21).

In a randomized controlled study, (PRP) gel has been used at the surgical field in superficial parotidectomy to reduce post-operative complications, with a particular focus on preserving facial nerve functionality and improving cosmetic results. PRP and PRP gel have been used in several conditions to enhance wound healing processes. During wound healing, platelet-derived growth factors can stimulate tissue repair and cell proliferation, influence extracellular matrix deposition, and support cell proliferation and differentiation (22).

Uses of the plasma gel:

1. Repairing meniscus tears:
   Meniscus tears are very common injuries which occurred in athletes and aging populations. Currently, the injured menisci are treated surgically by partial or total meniscectomy. Both procedures have shown poor long-term clinical results as evidenced by articular cartilage degeneration, articular surface flattening, sub-chondral bone sclerosis, and the early onset of osteoarthritis (20). Liu et al, (20) has made a study on 15 white rabbits by injecting PRP gel and bone marrow derived stem cells (BMSCs) into the defect area in the meniscus and found that this combination enhance formation of cartilage-like tissue.

2. Plasma gel in wound healing:
   Chronic wounds, such as diabetic foot ulcers, represent a serious clinical problem for patients and clinicians. Management of these wounds has a strong economic impact worldwide (6). Promising indications for topical PG applications might be for treatment of chronic non-healing wounds and supportive healing after incisional wounds that occur, for example, in diabetic patients who are at risk of impaired wound healing. PG has been used successfully in wound care patients to close chronic non-healing (diabetic) ulcers (23). Another interesting finding in one study was the effect of PG on the reduction of pain, an effect which is still not understood (24).

3. Healing of experimentally induced critical-sized radial bone defects in rats:
   Alidadiet et al, (25) investigated the role of human platelet gel embedded within gelatin (Gel) scaffold on healing of critical sized radial bone defects in rats.

4. Treatment of surgical site infection with Methicillin-resistant Staphylococcus aureus:
   PRP gel has also become a promising agent for treating surgical site infections. In this study, the researchers investigated the antibacterial activity and wound healing effectiveness of PRP in an animal model of Methicillin-resistant Staphylococcus aureus subsp. (MRSA N315)-contaminated superficial soft tissue wounds (26).

5. Skin Flap Surgeries and has a large effect on its survival:
   Skin flap grafting is one of the most common tissue transplantations for wound repair and organ reconstruction. Thus, improving the survival rate of the transplanted skin flap is important. the PRP gel increased the survival rate of the skin flap. In addition, it reduces the inflammation response in skin flap
transplantation and has better effects in terms of generating new soft tissue (27). superficial parotidectomy:
The use of PRP gel seems to have positive effects on clinical outcomes in superficial parotidectomy for benign tumours. Moreover, it represents an efficient and low-cost procedure that reduce complications. (22).

6. Severe hidradenitis suppurativa (HS) treatment:
   Fabio Nicoli et al, (28) has experienced the surgical excision and closure using (PRP) gel and Hyalomatrix in a patient with severe HS involving most of the body surface. Severe HS can be safely and effectively managed with wide excision, PRP gel and Hyalomatrix to achieve a successful outcome.

8. Plasma gel as a new modality in treatment of atrophic acne scars:
Platelet-rich plasma has obtained worldwide attention in acne scar treatment. Plasma gel is one PRP formulation having desirable biological or medical properties, deriving from an initial blood composition that comprises proteins in a gelled state as a result of thermal heating and cooling treatment. It is highly suitable for use as a filling agent as it is softly and naturally injected into the dermis and subcutaneous fat layer (29).

The reduction in complications and adverse effects from immune response is the potential advantage of using a self-derived product (30).

Plasma gel showed a remarkable improvement for most patients after one session, providing a quick and easy solution for acne scars (29).

9. Infraorbital rejuvenation:
Plasma gel could be considered as promising autologous dermal filler for infraorbital rejuvenation. It is simply accomplished without any financial problem or probability of immunological or inflammatory responses (31).

References


