



Original Research Article

Platelet rich plasma therapy- Myth vs Reality

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ARTICLE INFO

Article history:

Received 03-02-2024

Accepted 21-05-2024

Available online 01-06-2024

Keywords:

PlateletRich Plasma

PlateletDerived Growth Factor

Patterned hair loss

Vancouver scar scale

Goodman & Baron's quantitative scar

scale

ABSTRACT

Background: The transformative journey of Platelet-rich plasma, fueled by discovery of Platelet-Derived Growth Factor (PDGF), underscores its regenerative potential. This comprehensive exploration delves into fundamental characteristics and applications with a focus on its growing prominence in dermatology and aesthetics.

Materials and Methods: An open labelled interventional study was conducted at a tertiary health care centre in Western India to assess the efficacy and safety of PRP in various indications that mainly included patterned hair loss, post traumatic scars, acne scars, melasma and striae distensae. Patients were included in the study based on pre-determined inclusion and exclusion criteria. 6 sessions of PRP were conducted and response to therapy was evaluated using standard objective and subjective scores.

Results: The study included 60% female cases with most patients in the age group of 31-40 years (51.2%). For patterned hair loss, the mean change in hair count at end of therapy was significantly greater for baseline to final ($P < 0.005$). For post-traumatic scars, the mean change in Vancouver scar score at end of 6th sitting was significantly greater for first visit to last visit ($P < 0.001$). For melasma, the mean change in Modified MASI score at end of treatment was significantly greater for first visit to last visit ($P < 0.001$). For acne scars and striae distensae, the mean change in objective assessment scores was significantly greater when compared to baseline ($p < 0.001$). Side effects were predominantly early, with 13.8% reporting pain and 10% a burning sensation, while late side effects were minimal at 3.8%. Subjective improvement was reported by 76.25% of cases, ranging from 51% to 75%.

Conclusion: The study's results, while acknowledging certain limitations, emphasize PRP's potential efficacy in diverse dermatological conditions. The study underscores the correlation between dermatological conditions and treatment outcomes, highlighting the positive impact of PRP therapy.

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1. Introduction

1.1. Unlocking the potential of platelet-rich plasma (PRP) therapy: A journey through evolution and innovation

In regenerative medicine, Platelet-Rich Plasma (PRP) therapy has emerged as a transformative and versatile

therapy. Originating in the 1980s, PRP's evolutionary journey from its initial applications in oral surgery to its widespread use in dermatology and aesthetics represents a remarkable progression. This article embarks on a comprehensive review of PRP, describing its evolution, fundamental characteristics, applications, and the role of automated devices, with an emphasis on its emerging presence in dermatology and aesthetics.¹

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1.2. Evolution and origin

The roots of PRP therapy trace back to the 1980s when it first found utility in oral surgery. What began as a treatment has evolved into a versatile therapeutic approach with applications spanning various medical fields. The hallmark of PRP lies in its concentrated platelets within a limited plasma volume.

Therapeutic Potential of PDGF: The key moment in PRP's evolution came with the discovery of Platelet-Derived Growth Factor (PDGF). Initially recognized for its efficacy in dentistry and surgical procedures, PDGF's discovery as a key player in hair restoration opened new ways for PRP applications in dermatology.

1.3. Understanding PRP

At its core, PRP stands as an effective concentration of multiple growth factors primarily derived from platelets and plasma proteins. Fibrin, fibronectin, vitronectin, and other proteins are present in a potent cocktail of growth factors useful for modulating tissue repair and regeneration. The activation of platelets, triggered by contact with coagulation triggers, initiates the degranulation of pre-packaged growth factors. This cascade, in turn, activates transmembrane receptors on various cells, inducing internal signal-transduction pathways that amplify the body's innate wound-healing processes.

1.4. PRP composition and significance.²

PRP is a regenerative therapy that involves the extraction and concentration of platelets from a patient's blood.

Growth factors in PRP and their biological functions:

Platelet derived growth factor (PDGF): Enhances collagen synthesis, proliferation of bone cells, fibroblast chemotaxis and proliferative activity, macrophage activation.

Transforming growth factor β (TGF- β): Enhances synthesis of type I collagen, promotes angiogenesis, stimulates chemotaxis of immune cells, inhibits osteoclast formation and bone resorption.

Vascular endothelial growth fact (VEGF): Stimulates angiogenesis, migration and mitosis of endothelial cells, increases permeability of the vessels, stimulates chemotaxis of macrophages and neutrophils.

Epidermal growth factor (EGF): Stimulates cellular proliferation, differentiation of epithelial cells, promotes cytokine secretion by mesenchymal and epithelial cells.

Insulin-like growth factor (IGF): Promotes cell growth, differentiation, recruitment in bone, blood vessel, skin and other tissues, stimulates collagen synthesis together with PDGF.

Fibroblast growth factor (FGF): Promotes proliferation of mesenchymal cells, chondrocytes and osteoblasts, stimulates the growth and differentiation of chondrocytes

and osteoblasts.

1.5. Classification of platelet concentrates²

The classification categorizes platelet concentrates into four types based on leucocyte and fibrin content:

1. P-PRP (Pure Platelet-Rich Plasma): Contains a large number of platelets, and only the superficial buffy coat layer is used.
2. L-PRP (Leucocyte- and Platelet-Rich Plasma): Contains most platelets, leucocytes, and some residual red blood cells. The entire buffy coat layer and a superficial layer of RBCs are used.
3. P-PRF (Pure Platelet-Rich Fibrin): PRP mixed with an activator to form a stable fibrin matrix.
4. L-PRF (Leucocyte- and Platelet-Rich Fibrin): Blood is collected without anticoagulant, and a natural coagulation process forms a clot that includes platelets and leucocytes.

1.6. In vitro studies and growth factors

In vitro studies have demonstrated that activated PRP releases growth factors like platelet-derived growth factor-AB (PDGF-AB) and transforming growth factor- β 1 (TGF- β 1). The release of these growth factors is associated with heightened proliferation of stem cells and fibroblasts. However, the optimal dosing of activated PRP varies by cell type, and the clinical benefits of higher platelet dosages remain unclear.

1.7. Safety and contraindications

While PRP is generally considered a safe and non-invasive intervention, there are contraindications- platelet dysfunction, critical thrombocytopenia, anticoagulation, hemodynamic instability, sepsis or infection, and chronic liver disease.

1.8. Possible adverse events^{3,4}

LOCAL-Injection site pain, Erythema, Oedema, Bruising, Scalp pruritus, transient hair shedding.

OTHER-Cervical Lymphadenopathy, Serum sickness, Allergic reaction to calcium citrate preparation ,Cutaneous sarcoidal lesions, Irreversible monocular blindness after glabellar injection.

1.9. PRP in dermatology:^{5,6}

The application of PRP in dermatology has seen popularity in addressing various indications such as hair restoration and chronic ulcers. The concentration of growth factors and plasma proteins in PRP makes it a promising therapeutic modality for tissue repair and regeneration in dermatological conditions like alopecia,⁴ skin rejuvenation,

scar revision,⁵ pigmentary disorders and wound healing.

1.10. Preparation of activated PRP:²

PRP is prepared manually or using automated devices in a day care setting just before the procedure. The process involves strict aseptic conditions and temperature regulations. The double spin method, involving both light-spin and heavy-spin centrifugation, is preferred for manual preparation. Automated devices, though time-saving, vary in standards, leading to different PRP products.

1.11. Concentration of PRP

Achieving an effective therapeutic concentration of platelets in PRP is crucial. While the mean blood platelet level is approximately 200,000/dL, a concentration of more than 1 million/dL (about four to seven times the mean levels) is generally regarded as therapeutically effective. The concentration of PRP platelets can impact its angiogenic potential, and studies have shown both inhibitory and stimulatory effects at lower and higher concentrations.

1.12. Fallacies in PRP therapy⁷

There is a gross lack of standardisation in PRP procedures parameters like-time and speed of rotation, specific gravity, platelet concentration.

Commercially available automated devices have unknown efficacy and biological dissimilarities between the final processed product, need for platelet activation, interval between sessions and the total number of sessions required for advertised benefit remains unclear.

2. Materials and Methods

The present study is an Open labelled Interventional Prospective study conducted at a tertiary health care centre in Western India over a period of 2 years. A total of 100 patients were enrolled in study fulfilling the inclusion criteria out of which 80 patients have completed treatment and 20 patients were lost in follow up (Out of which 2 patients were of AGA, 7 patients were of FPHL, 5 patients were of TE, 2 patients were of acne scar, 3 patients were of post traumatic scar and 5 patients were of melasma and 5 patients were of striae).

2.1. Inclusion criteria

Both genders, Age, >18 years and <50 years, Both naive and previously treated patients, who had stopped therapy for 1 month or more for the dermatological conditions included, Patient giving consent for follow-up and photographs.

2.1.1. Dermatological conditions included in this study

Hair – Chronic Telogen Effluvium, Patterned hair loss, Androgenic alopecia, Female Patterned hair Loss.

Skin – Scars (Acne scars, Post-traumatic scars), Melasma, Striae (striae Rubrae, Striae alba).

2.2. Exclusion criteria

Pregnant and lactating mothers, Platelet dysfunction, atient on Anticoagulant therapy,Local infection at the site of PRP administration, Nonsteroidal anti-inflammatory drugs use within 48 hours, Glucocorticoid injection at the site of PRP within 1 month, Systemic glucocorticoid use within 2 weeks, Heavy smokers, Anemia –Hb less than 11.5 gm/dl, Thrombocytopenia (platelet less than 1.5 lac/ μ l), Acute or chronic illness, Metabolic and systemic disorders, Patient with Positive viral markers (HIV, HBsAg, HCV),Patient with Unrealistic expectations.

2.3. Pre-procedure considerations

A brief and relevant medical history and physical examination was done at screening to ensure relevant eligibility criteria, Appropriate patient education and discussion was done about PRP therapy, Benefits of therapy, possible side effects and prognosis of treatment.

Informed and written consent was signed and digital photographs were taken prior to the initiation of the procedure.

Patient evaluation with appropriate grading of condition requiring PRP.

2.4. PRP preparation:⁸

Principle of PRP preparation- “Differential centrifugation”. In differential centrifugation, acceleration force was adjusted to sediment certain cellular constituents based on different specific gravity.

Step: 1 - A 30-cc venous blood draw will yield 3-5 cc of PRP depending on the baseline platelet count of an individual, the device used, and the technique employed. So according to need in the treatment approximately 10-30cc of Patient’s blood was taken in a anticoagulant containing vaccute (blue vaccute containing sodium citrate).

Step: 2 - Put blood vaccute in centrifuge machine with maintaining balance on each side.

1st Spin (Soft spin) – 3000 RPM for 4 minutes.

Transfer the supernatant plasma containing platelets into Plain vaccute (Red vaccute) with the use of pink needle (18G) to fasten the process with 2ml syringes.

2nd Spin (Hard spin) -4000 RPM for 3minutes.

The lower 1/3rd is PRP and upper 2/3rd is platelet-poor plasma. Remove.

Platelet poor plasma with 2ml syringe.

Lower 1/3rd PRP is collected after gently shaking the tube to suspend the platelet pellets (Present at the bottom of the tube) in a minimum quantity of plasma and draw it in insulin syringes to inject. The Prepared PRP should be used maximum within 7-10 minutes after preparation.

2.5. PRP injections

The patient was placed in an appropriate and comfortable position that allows for sterility and access to the site of injection.

All necessary materials for the injection (PRP, needles (18G,22G), syringes (Insulin syringes, 2ml Syringes), cotton swab, gauze piece, spirit, betadine, gloves) planned and placed on a sterile table.

Clean the area of treatment first with betadine-soaked gauze piece and then after with spirit-soaked gauze piece to enhance penetration.

Use of topical anesthetic ointments (45 minutes prior to injections or lignocaine injections) according to need of patient.

Intradermal injection should be made at approximately 0.1 ml/cm² in selected area using the nappage technique (multiple small injection in a linear pattern 1 cm apart to a depth of 1.5 – 2.5 mm).

Put cap or dressing material at the site of Injection.

2.6. Post-procedure considerations

Monitor for post-procedure complications.

Patient was given post-procedure instructions and precautions to be taken after procedure

Follow-up:6 sittings done within a 6-month of time frame, 4 weeks apart.

Re-examine the patient for pain, any reaction at injection site, Patient's response will be recorded.

2.7. Objective assessment

Chronic Telogen effluvium- Hair pull test.

Androgenic alopecia-Norwood Hamilton's score.

Female pattern hair loss- Ludwig's score.

Acne scars-Goodman and baron's quantitative scar scale.

Post traumatic scars- Vancouver scar scale.⁹

Melasma – Modified MASI Score.¹⁰

Striae distensae – Surface area before and after.

Subjective assessment was done using self-assessment questionnaire.

At the end of 6th sitting grading was done, photographs were taken with informed consent and compared, Monthly analysis of outcome was done at every sitting.

3. Results

The study focused on dermatological conditions, assessing age, gender, marital status, education, duration, treatment history, diagnoses, and side effects. Key findings include a predominant 51.2% occurrence in the 31-40 age group, 60% female cases, and 67.5% married individuals. Significant improvements post-PRP therapy were observed in hair count, MMS, VSS, GBQSS, and SA, underscoring the treatment's efficacy in various dermatological conditions.

Amongst patients with patterned hair loss, the mean change in hair count at end of 6th sitting was significantly greater for baseline to final (137.32 ± 12.56 vs. 163.14 ± 11.89 respectively, $P < 0.005$ as per student's paired t test with 95% CI).

11.3% of total patients are of melasma patient, out of them 1(1.2%) patient had MMS 5 score, 1(1.2%) patient had MMS 10 score, 1 (1.2%) patient had MMS 11 score, 3(3.7%) patient had MMS 12 score, 2 (2.5%) patient had MMS 16 score and 1(1.2%) patient had MMS 6 score. The mean change in MMS score at end of 6th sitting was significantly greater for first visit to last visit (6.7 ± 1.6 vs. 3.5 ± 1.1 respectively, $P < 0.001$ as per student's paired t test with 95% CI).

7.5% of total are of PTS, out of them 2 (2.5%)patients had VSS3 score, 1(1.2%) patient had VSS4 score, 1(1.2%) patient had VSS 5 score, 1 (1.2%)patient had VSS 7 score and 1 (1.2%)patient had VSS 8 score. The mean change in VSS score at end of 6th sitting was significantly greater for first visit to last visit (5.0 ± 2.1 vs. 3.2 ± 1.8 respectively, $P < 0.001$ as per student's paired t test with 95% CI).

For patients with acne scars, the mean change in GBQSS score at end of 6th sitting was significantly greater for first visit to last visit (4.2 ± 2.3 vs. 2.0 ± 1.6 respectively, $P < 0.001$ as per student's paired t test with 95% CI).

Amongst patients with striae, 1(1.2%) patient had SA of largest striae was $3.7*0.2$ cm,1(1.2%) patient had SA of largest striae $4.2*0.3$ cm, 1(1.2%) patient had SA of largest striae $4.7*0.8$ cm, 1(1.2%) patient had SA of largest striae $4*0.8$ cm and 1(1.2%) patient had SA of largest striae $5*1$ cm. The mean change in SA at end of 6th sitting was significantly greater for first visit to last visit (1.23 ± 0.20 vs. 0.15 ± 0.05 respectively, $P < 0.001$ as per student's paired t test with 95% CI).

76.2% of cases have no any early side effects, 13.8%of cases have pain and 10.0% of cases have burning sensation. 96.2% of cases have no any late side effects, while only 3.8% of cases have headache.

4. Discussion

Platelet Rich Plasma, a bioactive agent that has been used in recent decades as a new therapeutic option in various dermatological conditions. Used as a sole treatment and in other cases as an adjuvant tool, showing positive effects on tissue repair at the structural and functional level. Though PRP has spanned various fields of dermatology, it is evident that factors such as the strength and number of centrifugations and the method used to activate platelets influences the quality of PRP, which may be related to the variety of results obtained. Additionally, the high cost of commercially available PRP kits, precludes its use over a larger population. It has been observed in various studies that the two-step procedure renders the highest output. 500xg or 900xg for a total period of 8-10 min was optimal

when performing a procedure that involved two spins.⁶

Autologous PRP is quite safe. The mitogenic effect of PRP is limited to the normal healing process. PRP is not mutagenic as whatever growth factors it delivers, act through signal transduction only.¹¹ These growth factors do not enter the cells or nucleus. There may be local injection site reactions like transient erythema or pain. Secondary infection is rare when the procedure is carried out under strict septic precautions. Since PRP is Autologous, there is no risk of transmission of Hepatitis B, C or HIV.

PRP has already attracted attention in plastic surgery, orthopaedics surgery and cardiac surgery because of its potential use in rejuvenating effects, rapid healing, reduced chance of infection, decreased chance of hypertrophic keloids and scars.¹²

Growth factors are known to activate the proliferative phase and trans-differentiation of hair and stem cells and produce new follicular units. bFGF is reported to promote the in vitro proliferation of papilla cells, and thereby plays a key role in elongating hair shaft. In addition to growth factors (GFs), platelets release numerous other substances (e.g., fibronectin, vitronectin, sphingosine 1-phosphate, etc.) that are important in wound healing. An advantage of PRP over the use of single recombinant human growth factor delivery is the release of multiple growth factors and differentiation factors upon platelet activation. Several studies demonstrate the potential role of PRP in the field of dermatology.¹¹

Bendinelli et al.¹¹ reported an anti-inflammatory effect by reducing the expression of the COX 2 and CXCR4 genes. All these mechanisms explain the effectiveness of PRP in indications such as acne, scars, chronic ulcers, alopecia.

In present study, majority (51.2%) of cases were 31 to 40 years of age group followed by 42.5% of cases 21 to 30 years, 3.8% of cases below 21 years and 2.5% of cases were above 40 years of age group. Three fifth (60.0%) of cases were female and 40.0% of cases were male. Majority (67.5%) of cases was married and 32.5% of cases were unmarried in present study. Three fourth (76.2%) of cases had previously taken some or the other form of treatment in the past (mostly topical Minoxidil and less commonly systemic Finasteride) and 23.8% of cases have no history of treatment in this study. Majority (76.2%) of case have no any early side effects, 13.8% of cases have pain and 10.0% of case have burning sensation. 96.2% of case have no any late side effects, only 3.8% of cases have headache in present study. Mistry et al. found that the most common side effect in PRP group was pain in 7.14% patients followed by pruritus in 3.57% patient and irritation in 3.57% patient.³ The mean change in hair count at end of therapy was significantly greater for baseline to final visit (137.32 ± 12.56 vs. 163.14 ± 11.89 respectively) mean changes from baseline was 25.81. Mistry et al. found that mean change in hair count was 24.29 ± 5.91 . Similar

results were observed in a study conducted by Khatu et al.¹³

The mean change in MMS score at end of 6th sitting was greater for first visit to last visit (6.7 ± 1.6 vs. 3.5 ± 1.1 respectively, $P < 0.001$ as per student's paired t test with 95% CI). Found modified Melasma Area and Severity Index (mMASI) score decreased by 20.42 ± 7.979 to 12.253 ± 7.37 (95% CI 0.89-1.47; $p = 0.02$).

The mean change in VSS score at end of 6th sitting was significantly greater for first visit to last visit (5.0 ± 2.1 vs. 3.2 ± 1.8 respectively, $P < 0.001$ as per student's paired t test with 95% CI). Mohamed H et al.¹⁴ found improvement as VSS change from 7.8 ± 2.8 vs. $3.8 \pm$ with P value < 0.002 . The mean change in GBQSS score at end of 6th sitting was significantly greater for first visit to last visit (4.2 ± 2.3 vs. 2.0 ± 1.6 respectively, $P < 0.001$ as per student's paired t test with 95% CI) found reduction in GBQSS score as 3.2 ± 0.7 to 1.8 ± 0.6 , $P = 0.01$.¹⁴ The mean change in SA at the end of therapy was significantly greater for first visit to last visit (1.23 ± 0.20 vs. 0.15 ± 0.05 respectively, $P < 0.001$ as per student's paired t test with 95% CI). Found change in the surface area 2.3 ± 0.03 vs. 1.2 ± 0.05 respectively, $P < 0.03$.

In present study majority (73.8%) of cases have objective improvement 51% to 75% followed by 17.4% of cases have 76% to 100% and 8.8% of cases were 26% to 50% objective improvement. In present study majority (76.25%) of cases have subjective improvement 51% to 75% followed by 12.5% of cases have 76% to 100% and 11.25% of cases have 26% to 50% subjective improvement.

5. Limitations of the Study

Our study has not compared PRP with other traditional methods used to treat different dermatological condition.

Mean follow up of patients is also short to draw conclusion regarding the long-term effectiveness of treatment.

6. Conclusion

In summary, Platelet Rich Plasma (PRP) therapy, despite being erroneously perceived as a novel and experimental technique, has a historical foundation dating back to the 1970s. Contrary to myths, PRP injections for hair and skin conditions are established as simple and feasible, constituting valuable adjuvant modalities. While theoretical support exists for various dermatological applications, the current evidence base is limited, lacking robust randomized controlled trials.¹⁵ Notwithstanding its favorable safety profile and outpatient convenience, caution is warranted. The evolving frontier of PRP in dermatology and aesthetic medicine holds promise, demanding comprehensive research for substantiated long-term efficacy and safety assessments.

7. Source of Funding

None.

8. Conflict of Interest

None.

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Cite this article: Karia UK, Bhabhor M, Doshi YJ, Rajwadi AA, Shah BJ. Platelet rich plasma therapy- Myth vs Reality. *IP Indian J Clin Exp Dermatol* 2024;10(2):218–223.