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# A PROSPECTIVE, COMPARATIVE STUDY OF PLATELET RICH PLASMA (PRP) AS MONOTHERAPY VERSUS COMBINATION THERAPY OF PRP WITH TOPICAL MINOXIDIL AND SYSTEMIC FINASTERIDE IN ANDROGENETIC ALOPECIA

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## ABSTRACT

**BACKGROUND:** Platelet Rich Plasma (PRP) has emerged as a potential therapy for androgenetic alopecia (AGA).
**AIMS AND OBJECTIVES:** To Compare safety and efficacy of PRP monotherapy versus combination therapy [PRP+ topical Minoxidil 5% + systemic finasteride(1mg)] in AGA.
**MATERIAL AND METHODS:** Thirty treatment -naive patients (grade III-VI AGA) were included. Seven PRP sittings were given fortnightly over 3 months. Assessment was based on hair pull test, global photos, patient/ investigator assessment scales. Due to three drop-out patients, final analysis was done on Group A (PRP monotherapy n= 14) and Group B (combination therapy n= 13).
**RESULTS:** Hair pull test was negative at 12 weeks. Maximum response was seen by 5th session, vertex alopecia showed better response compared to temporal areas. Investigator and patient assessment showed better response in Group B.
**CONCLUSION:** PRP showed good efficacy and safety profile. Combination therapy was statistically superior to monotherapy.

**KEYWORDS** : Androgenetic Alopecia, Platelet Rich Plasma, comparative study

## INTRODUCTION

Androgenetic alopecia (AGA) affects up to 80% of men and 50% of women.[1] Hair loss affects self-esteem, personal attractiveness and may lead to depression. [2] Standard treatment modalities include topical minoxidil and systemic finasteride. [3] PRP is defined as volume of plasma fraction of autologous blood with above baseline platelet concentration. [4] Numerous studies have evaluated safety and efficacy of PRP under ideal conditions. [5] This study evaluates the efficacy and safety of PRP as monotherapy or combination therapy to standard treatments.

## METHODS AND MATERIALS

A prospective, comparative interventional study was conducted over a period of 10 months in the outpatient Department of Dermatology. Approval of Ethics committee and informed consent from patients was taken. Thirty patients with AGA (grade III-VI Hamilton-Norwood classification) who had not received any systemic or topical treatment for AGA in last 6 months were included. Patients with other causes of alopecia, keloidal tendency, history of lichen planus, psoriasis, bleeding disorders or on anti-coagulant medications, active infection at the local site were excluded.

The diagnosis of pattern hair loss was established on basis of a detailed medical history and clinical examination. Laboratory tests included complete blood cell count, HIV serology and HbsAg. Two groups of patients included: Group A (n=16), administered PRP as mono therapy and Group B (n=14), treated with PRP along with topical Minoxidil 5% and systemic finasteride 1 mg. Three patients [Group A (n=2), Group B (n=1)] who dropped out were not included in the analysis.

PRP was prepared using an automated refrigerated centrifuge. Patient's blood was collected in a vacutainer with anticoagulant citrate phosphate dextrose (8.5ml blood and 1.5 ml anticoagulant). The centrifuge machine was set at precool mode and vacutainer was kept for 30 minutes. The separation mode was selected (1550 rpm for 13min) and vacutainer was placed in the machine. The supernatant fluid was taken in a sterile tube after separation and subjected to concentration (2200 rpm for 8 mins). The upper 2/3rd part was discarded and 0.5ml of calcium chloride was added to the lower 1/3rd. PRP was injected on the scalp (multiple small injections 1-cm apart) with the help of insulin syringe. Seven PRP sittings were given 15 days apart over 3 months.

Assessment was based on hair pull test, global standardized photos on every visit, patient and investigator assessment scales at 12 weeks. Physician assessed the standardized photographs taken at baseline and at 12weeks on a standard seven-point scale (Table 1) The patients' perception of improvement in the degree of hair fall and hair growth was evaluated at baseline and at 12 weeks on a five-point Likert scale.(Table 1) The results obtained were tabulated using t-Test: Two-Sample Assuming Unequal Variances' and its statistical significance was evaluated.

**Table 1: Investigator and patient assessment scales**

| Investigator assessment (7-point scale) | |
|---|---|
| -3 | Severe worsening |
| -2 | Moderate worsening |
| -1 | Mild worsening |
| 0 | No change |
| 1 | Mild improvement |
| 2 | Moderate improvement |
| 3 | Excellent improvement |
| **Patient assessment scales (5-point scale)** | |
| 0 | No improvement |
| 1 | Mild improvement (0-25%) |
| 2 | Moderate improvement (25-50%) |
| 3 | Good improvement (50-75%) |
| 4 | Excellent improvement (75-!00%) |

## RESULTS

Twenty-seven male patients were evaluated. Mean age of patients was 22.7yrs and duration of disease was 2.26 years. Number of patients with alopecia grades included:- Group A (grades III, IV, V : n=10, 2, 2 ) and Group B (grades III, IV, V ,VI : n=6,2,4, and 1) respectively. In both groups, hair fall reduced in 3 sessions and maximum response was seen in 5th session. Hair pull test which was positive in 14 patients at baseline was negative in all patients at 12 weeks.Vertex alopecia improved better than temporal in Group B.

Investigator assessment on standardized 7-point scale showed that in group A (n=14); 3 patients (21.4%) had no response, 11 patients (78.57%) showed some response +2(n=1) and +1(n=10). In group B (n=13) 100% patients showed some improvement, +3 (n=3), +2 ( n=6), +1 (n=4). P value was 0.02 (< 0.05), difference in observed

values was significant. On patient assessment, two (14%) patients in Group A showed >50% improvement compared to eight (61%) patients in Group B. Two patients in group B showed >75% improvement. P value was 0.01(<0.05), the difference in observed values was significant. The significant improvement was confirmed by a high overall patient satisfaction in Group B compared to Group A (figure 2 and 3). The side effects were minimal pain, redness at the time of injections and pinpoint bleeding.

**Figure 3- Group A (PRP monotherapy): Pre-treatment and 12 weeks Post-treatment; Investigator score +1,Patient score-2**

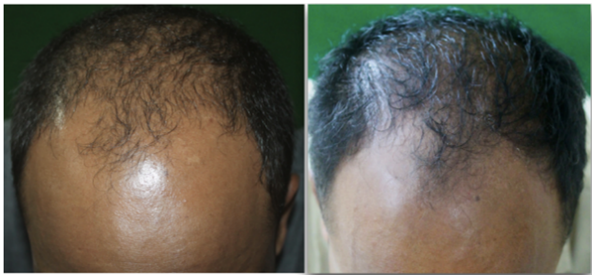
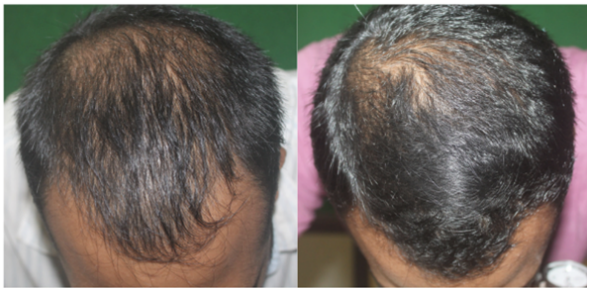


**Figure 4- Group B (PRP +topical 5%minoxidil+ oral finasteride): Pre-treatment and 12 weeks Post-treatment, Investigator score +3, Patient score-3**



## DISCUSSION

Androgenic alopecia is characterized by a shortened anagen phase and miniaturization of terminal to vellus hair, current therapeutic strategies target cellular proliferation and differentiation during the hair cycle.[6]

PRP is being increasingly used in AGA. Activation of alpha granules of platelets releases numerous proteins, including platelet-derived growth factor (PDGF), transforming growth factor (TGF), vascular endothelial growth factor (VEGF), insulin-like growth factor (IGF), epidermal growth factor (EGF) and interleukin (IL)-1.[7, 8] The growth factors act on stem cells in the bulge area of the follicles, stimulating development of new follicles and promoting neovascularisation. [9] Primitive stem cells of ectodermal origin are found in bulge area and germinative cells of mesenchymal origin are found at dermal papilla. Interactions between primitive stem cells and germinative cells along with binding of growth factors activate proliferative phase, giving rise to future follicular unit.[9] Anti-apoptotic effects of activated PRP has also been proposed as one of the factors stimulating hair growth.[10, 11,12] PRP increases proliferation of dermal papillae cells through stimulation of protein kinase B and extracellular regulated kinase (ERK) signaling pathways, which contribute to apoptosis and cell growth regulation. [11,13]

Different study designs and comparative treatment arms have been used to study safety and efficacy of PRP in AGA. There are studies with only PRP as monotherapy [14,15] as well as PRP versus placebo in split head comparison. [16,17,18,19,20,21,22] PRP has been used in combination with medical and procedural modalities of treatment. A comparative study of topical 5% minoxidil alone versus microneedling with PRP plus topical 5% minoxidil has been reported .[23] A randomized, placebo-controlled double blind half-head study with treatment arms (PRP + minoxidil 5% solution or PRP + oral finasteride) and control areas of the scalp (placebo + minoxidil 5% solution or placebo + oral finasteride) has been recently reported.[24] The groups compared in the current study design has not yet been reported in literature.

The sample size in most published studies includes 10–30 subjects.[14,16,17,19,20,21,25,26,27] The duration studies varies from 6 months to 2 years; however interval between the treatment sessions was longer 3 weeks to 3 months .[14,15,19,20,21] The duration in this study was 12 weeks with a 15 day interval between two sessions, similar treatment protocol and duration of study has been reported in numerous studies. [16,25,26,27] Long follow-up duration helps to assess various clinical outcome measures and helps to find out relapse rates.

A standardized treatment protocol for the technique of PRP preparation and application of PRP in AGA is lacking. The centrifugation technique used, addition of activator and final concentration of platelets affects the results of PRP.[13,28] PRP is separated from whole blood first by 'soft-spin' centrifugation and then the platelets are concentrated by 'hard-spin' centrifugation with removal of the supernatant plasma".[29] The double-spin method is preferred over the earlier prevalent single-spin method, as the desired concentration of platelets was not achieved by the latter. [30] Montalava et al compared two methods of obtaining PRP double spin and single spin and found the former better than later in platelet concentration.[31] PRP can be activated by thrombin, calcium chloride or mechanical trauma. Addition of activators has not shown significant differences in platelet yield in a study done by Gentile et al. [32] Recently published systematic review and meta-analysis have concluded that there are no well-defined protocols for centrifugation and addition of activators.[33,34] Temperature during processing is crucial to prevent platelet activation and 21-24 C is recommended.[35] The current study employed automated refrigerated centrifuge to prepare PRP. Dhurat et al had concluded that 900 g for 5 min for first centrifugation and 1,000 g for 10 mins for second centrifugation at 16°C in a refrigerated centrifuge produced the most optimal yield of PRP. [36] Giusti et al determined that $1.5 \times 10^6$ platelets/ µL is the optimal concentration of platelets for induction of angiogenesis in endothelial cells. It was suggested that higher concentrations decreased the angiogenic potential of platelets for follicular and perifollicular angiogenesis. [28] Application of PRP with intradermal injections is commonly used, however few studies have used microneedling with dermaroller prior to PRP application. [23,26]

Assessment parameters to evaluate PRP efficacy vary, these include objective methods like phototrichogram, global photographs, histology, immunohistochemistry, hair pull test, dermoscopy, use of magnifying lens and subjective methods like patient satisfaction and evaluation questionnaires. [5] Negative hair pull test after four sessions of PRP in 12 patients and in all patients after 12 weeks was observed in this study, a finding comparable with the study conducted by Besti et al [37] and Kachhawa.[22] .Vertex alopecia improved better than temporal in this study, probably systemic finasteride was the factor contributing to this response.[38] Both investigator and patient assessment scales showed better improvement in combination group and the results were statistically significant. Patient satisfaction has been evaluated with questionnaires in various studies. [14,16,17,19,27,29,39] Alves et al has used PRP in combination with minoxidil or with finasteride and has found statistically significant improvement in PRP + minoxidil versus PRP + finasteride.[24] No major side effects were noted. Pain during procedure, transient erythema and edema noted in this study has also been reported in other studies.[5,23]

The limitations of this study were small sample size, short follow-up period, objective evaluation methods (trichoscan, dermoscopy, hair thickness) were not performed. Patterned alopecia in males and females manifest differently and may have different mechanisms, hence it may be in-appropriate to extrapolate the results to both sexes in studies evaluating only a single sex. In a recent systematic review and meta-analysis no conclusive evidence could be found for PRP as treatment modality in AGA due to lack of well- designed randomized controlled studies. [33,34] Studies comparing efficacy of

PRP at different concentrations are required to know the exact concentration of platelet required to achieve optimum hair regrowth. Further studies with larger sample size, including both male and female pattern hair loss and with longer follow- up periods should be performed.

## CONCLUSION

PRP is a simple, cost-effective and feasible treatment option for hair loss and can be regarded as a valuable adjuvant treatment modality for AGA. This study found a significant difference between the two groups that used PRP as monotherapy and as an adjuvant to minoxidil and finasteride treatment. PRP as adjuvant therapy to standard treatments had better results than PRP monotherapy on investigator and patient assessment scales. Although PRP has sufficient theoretical scientific basis to support its use in hair restoration, clinical evidence is still weak. PRP is however a promising treatment option for patients with AGA in view of its excellent safety profile and relatively low cost.

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