



A STUDY TO COMPARE THE CLINICAL EFFICACY OF PLATELET-RICH PLASMA (PRP) AND PLATELET RICH PLASMA (PRP) WITH MINOXIDIL IN PATIENTS WITH ANDROGENETIC ALOPECIA (AGA)

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KEYWORDS :

Introduction

Pattern or androgenetic alopecia is a genetically defined condition caused by an overreaction to androgens that affects up to 50% of boys and girls. It is distinguished by gradual loss of terminal hair on the scalp at any point after puberty, with a distinct pattern in both men and girls. Hair loss is most noticeable in the vertex and frontotemporal areas of men, although the frontal hairline is usually spared in women, with diffuse apical hair loss seen as a broader anterior section of the hair.^{1,2} With age, the extent of hair loss becomes obvious.

Individuals with a higher genetic propensity to hair loss lose their hair sooner and to a larger extent than those with a lower predisposition. By the age of 25, around 20% of men will exhibit indications of hair loss, which jumps to 75% by the age of 60. Around half of the 75 percent of males will have substantial hair loss in the frontal and vertex regions. Up to 80% of males and 40% of women are affected by AGA.³ Hair loss in women normally happens after menopause, and it is caused by the genetic programming of the hair follicle.

Hair loss may cause significant psychological and emotional anguish, as well as a decline in quality of life. As a result, creating a safe and effective treatment technique in a dermatological practice context may considerably benefit patients. Minoxidil, finasteride, spironolactone, nutritional supplements, and hair transplant surgery are currently available treatments.

Though topical minoxidil and oral finasteride are FDA-approved, they have limitations, including a limited degree of clinical improvement in certain individuals. The effectiveness of existing FDA-approved medications for new hair growth might be disappointing, and considerable improvement is not usually noticed.⁴

Minoxidil topical lotion and finasteride oral pills are FDA-approved conservative treatments for hair loss.⁵ Minoxidil seems to extend anagen, while finasteride is a 5 α reductase type II inhibitor that lowers testosterone conversion to dihydrotestosterone (DHT).⁶ Minoxidil was initially created as an antihypertensive drug, but it piqued people's curiosity when it caused widespread hypertrichosis when taken orally. It is an over-the-counter treatment that stimulates the survival of dermal papillary cells and boosts hair follicle growth by increasing the anagen phase.^{6,7}

It reduces blood and scalp DHT levels and is administered at a daily dosage of 1 mg. Common adverse effects include reduced libido, erectile dysfunction, and decreased ejaculate

volume.⁸ Dutasteride is a type I and II 5 α reductase inhibitor with more efficiency than finasteride.⁹ Other types of conservative treatments—low level laser treatment and prostaglandin analogs are two examples.

Most present treatment approaches are somewhat slow to work and transient, hence there has been a constant quest for better treatment modalities, with platelet-rich plasma (PRP) therapy showing promising outcomes.

Platelet-rich plasma, also known as platelet-rich growth factors or platelet concentrate, is a protein concentrate obtained from whole blood that has been spun to remove red blood cells. In addition to the primary component, which comprises large concentrations of platelets, there are additional components utilized to differentiate various kinds of PRP, such as the presence or absence of leucocytes and platelet-activating chemicals. The efficacy of encouraging tissue regeneration is dependent on the quantity of platelets in the plasma; various studies have demonstrated that concentrations two to six times greater than normal platelet count are necessary for best results.⁹ PRP is extracted from the patient. It comprises about 20 growth factors (GF), the most significant of which are platelet-derived GFs, transforming GF- β , vascular endothelial GF, and insulin-like GF-1, as well as their 10 isoforms. As a result, these growth factors aid in the restoration of hair cell dynamics.¹⁰ PRP stimulates stem cell differentiation, prolongs dermal papilla cell survival, prolongs the anagen phase of the hair cycle, and enhances perifollicular vascular plexus in AGA through several processes mediated by various GFs.^{11,12} Growth factors found in platelet alpha granules work on stem cells in the bulge region of hair follicles, stimulating the formation of new follicles as well as neovascularization. PRP has emerged as a viable therapy option for AGA.

As part of the wound healing process, activated platelets are thought to release a variety of growth factors and cytokines from their alpha granules. When platelets in PRP are injected into the scalp, they get activated and release a variety of growth factors that encourage hair growth. These growth factors are involved in fibroblast activation, collagen formation, extracellular matrix stimulation, and endogenous growth factor overexpression. Platelet-derived growth factor (PDGF), transforming growth factor beta (TGF- β), vascular endothelial growth factor (VEGF), epidermal growth factor (EGF), and insulinlike growth factor-1 (IGF-1) are growth factors released by activated platelets in PRP and are thought to promote cell proliferation, differentiation, angiogenesis, and chemotaxis, all of which are required for new hair

regrowth.¹³ The anagen phase of the hair growth cycle has been demonstrated to be induced and prolonged by IGF-1. Platelets also include thick granules with bioactive substances that promote membrane permeability and control inflammation. Serotonin, histamine, dopamine, calcium, and adenosine are found in dense granules and promote membrane permeability and control inflammation.¹⁴

The specific mechanism of action of PRP in the enhancement of hair growth remains unknown.¹¹ Used in vivo and in vitro models to investigate the effects of PRP on hair development. Activated PRP has been shown to stimulate the proliferation of dermal papilla (DP) cells by activating ERK and protein kinase B (Akt, an anti-apoptotic signaling molecule).¹⁴

PRP EGF and PDGF upregulate the ERK pathway, increasing the transcription of genes involved in cellular proliferation and differentiation. Furthermore, in vitro human DP cells grown with PRP showed enhanced expression of B-cell lymphoma-2 (an antiapoptotic protein).¹¹ Thus, activated PRP is thought to alter the hair cycle by extending the anagen phase and avoiding apoptosis and the catagen phase. When compared to control mice, the telogen-to-anagen transition was likewise sped up.

The anagen phase is assumed to begin with angiogenesis and enhanced vascularization of the follicle. AGA, on the other hand, has been associated with decreased blood flow and oxygen pressure. PRP growth factors operate on stem cells in the bulge region of follicles, causing neovascularization and folliculogenesis. Increased -catenin expression was also reported, which is thought to improve DP cell proliferation, survival, and angiogenesis.¹¹

Despite the fact that multiple clinical studies have shown that PRP treatment is effective in AGA, there is no standard technique for PRP preparation and delivery, nor is there a mechanism to assess outcomes. PRP therapy for AGA patients has been attempted to be standardized. Stevens et al proposed a standard PRP procedure that included using a single spin centrifugation method to produce pure PRP with a platelet enrichment of 3 to 6 times the mean concentration of whole blood and adding a platelet activator such as calcium chloride or calcium gluconate before administering PRP as subdermal injections. Treatment intervals should be monthly for the first three months, then every three months for the next one year.¹⁵

This research compares the clinical effectiveness of PRP therapy with minoxidil therapy, which may help us determine which kind of therapy is more successful, acceptable, and safe in the treatment of AGA.

Aim and Objectives

- (1) To study the efficacy of intradermal PRP alone.
- (2) To study the efficacy of intradermal PRP with topical Minoxidil 5%.
- (3) To compare the efficacy of the above-mentioned regimens.

Materials and Methods

Type of Study: Prospective, Age-matched, Randomized, Comparative, Interventional study.

Place of study: Department of Dermatology Venereology and Leprology, Pacific Medical College & Hospital, Udaipur.

Period of study: 1st December 2020 to 30th November 2022

Source of data: Patient attending OPD of Dermatology, Venereology & Leprology department at Pacific Medical College & Hospital, Udaipur - 313001.

Sample size: Sixty male patients (60) attending the outpatient

clinic of the Department of Dermatology, Pacific Medical College & Hospital were taken who satisfy the above criteria during the study period.

Statistical methods

The data was entered in Microsoft Office Excel 2020 for Windows. All the data analysis was performed using IBM SPSS ver. 20 software. Frequency distribution and cross-tabulation were used to prepare the tables. Quantitative variables were expressed as the mean and standard deviation. Categorical data were expressed as a percentage. PRISM and Microsoft office was used to prepare the graphs. Independent sample t-test and ANOVA (using the simple mean) were used to compare the means. The chi-Square test was used to compare the categorical data. P value of <0.05 is considered as significant.

Methodology

Institute Ethics Committee Clearance was obtained before starting the study.

Written and informed consent was obtained from all the patients (Attached as Appendix- A)

The patients will be randomly divided into two groups:

1. Group A- 30 cases of AGA receiving only intradermal PRP as a treatment modality.
2. Group B- 30 cases of AGA receiving intradermal PRP with 5% topical minoxidil.

A total of 18 ml of fresh whole blood was collected and mixed with 2 ml of 3.8% sodium citrate solution into an autoclaved Falcon tube under proper aseptic precautions. The tube was rotated in a centrifugation machine at 2200 revolutions per minute for 12 min. The "first spin" allows blood separation into three layers, namely, the bottom red blood cell layer, the topmost acellular plasma layer called platelet-poor plasma (PPP), and an intermediate PRP layer called the "buffy coat." The buffy coat along with plasma was collected with the help of Finn pipette into another Falcon tube. The "second spin" was done at 3000 revolutions per minute for 6 min. This allowed the platelets (PRP) to settle at the bottom of the tube. The upper two-third containing PPP was discarded, and the lower one-third of PRP was loaded in 1 mL BD syringe containing calcium gluconate (one part of calcium gluconate 10% and nine parts of PRP) as an activator. By this method, we obtained 3–3.5 mL of PRP having a platelet concentration of 4.2-fold when compared with the whole blood.

Topical anaesthetic cream was applied over the target area 1 h before administration of PRP. Areas to be treated (frontal, parietal, and vertex) were cleaned with 70% alcohol. PRP (0.05–0.1 mL/cm²) was injected intradermally by 1 mL Beckton Dickinson syringe in a retrograde fashion from deep to superficial, at a distance of 1 cm. Injection of PRP was given four times in each patient at intervals of 1 month. NS (placebo) was injected in a similar method. Vital signs and adverse events reported by the patient or elicited by the clinician were assessed at each follow up.

INCLUSION CRITERIA

- (1) Males with Androgenetic alopecia
- (2) Not taking any treatment for AGA for last six months
- (3) Patients of age group 18 years and above

EXCLUSION CRITERIA

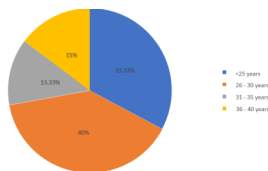
- (1) Alopecia patient other than Androgenetic alopecia
- (2) Patients with chronic liver disease
- (3) Patient with history of bleeding disorder, thrombocytopenia and on Anticoagulant therapy (aspirin, warfarin, heparin)
- (4) Patient on any kind of therapy for AGA for last 6 months.

RESULTS

Age

Out of 60 male subjects included in this study, majority of them (40%) were in the age group of 26 – 30 years, 33.33% of subjects belonged to the age group of <25 years of age, 15% belonged to the age group of 36 – 40 years whereas 13.33% belonged to the age group of 31 – 35 years of age.

Graph 1: Distribution of patients according to age.



Age distribution between groups

PR.P group majority of the patients 14 (46.66%) in age group of 26-30 years followed by <25 years 33.3% (n=7).

PR.P + Minoxidil group, majority of the patients were in the age group of <25 years (43.33%), followed by 26-30 years (33.33%)

The distribution of ages in both the groups was not statistically significant as revealed by the insignificant p value of 0.245.

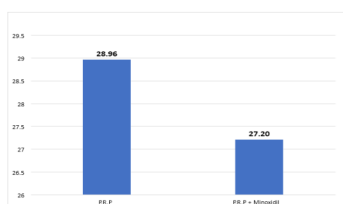
Table 2: Distribution of patients according to age between groups.

Age group	Group		Total	P Value
	PR.P	PR.P + Minoxidil		
<25 years	7 (23.33%)	13 (43.33%)	21 (35%)	
26 – 30 years	14 (46.66%)	10 (33.33%)	24 (40%)	
31 – 35 years	5 (16.66%)	3 (10%)	8 (13.33%)	
36 – 40	4 (13.33%)	4 (13.33%)	8 (13.33%)	

Mean Age Comparison between groups

Mean age in PR.P group was 28.96 years whereas mean age of patients in PR.P + Minoxidil group was 27.20 years. However, the difference between mean age of both the groups was not statistically significant as revealed by the insignificant p value of 0.217.

Graph 3: Mean Age Comparison between groups.



Comparison of age at disease onset between the two groups

Mean disease onset in PR.P group was 24.16 years whereas mean disease onset in PR.P + Minoxidil group was 24.96 years. However, the mean disease onset in both the groups was comparable as revealed by the insignificant p value of 0.696.

Table 4: Age at disease onset comparison between the two groups.

Age at disease onset	Group		Mean	Std Deviation	P value
	PR.P	PR.P + Minoxidil			
	30	30	24.16	3.322	0.696 t = 0.3925
	30	30	24.96	10.659	

Comparison between Mean hair density at baseline and at the end of 4 months in PR.P group.

Mean hair density in PR.P group at baseline was 5.26 ± 1.362 . Mean hair density at end of 4 months was 5.50 ± 1.548 .

This shows an improvement but it is not statistically significant as p value > 0.05.

Table 5: Comparison between Mean hair density at baseline and at the end of 4 months in PR.P group.

Hair density	Mean	Number	Std Deviation	P value
Baseline	5.26	30	1.362	0.526 t = 0.6375
4 months	5.50	30	1.548	

Comparison between Mean hair density at baseline and at the end of 4 months in PR.P with Minoxidil group.

Mean hair density in PR.P + Minoxidil group at baseline was 5.10 ± 1.561 . Mean hair density at end of 4 month was 5.96 ± 1.847 .

In this group, the onset of response compared to PR.P group was earlier at 3 months and with subsequent injections majority of patients showed significant improvement which was appreciated as decrease in hair shedding, improvement in hair texture and volume.

So, there was a significant change in hair density after treatment with PR.P with Minoxidil at the end of 4 months as revealed by the highly significant p value of 0.056.

Table 6: Comparison between Mean hair density at baseline and at the end of 4 months in PR.P with Minoxidil group.

Hair density	Mean	Number	Std Deviation	P value
Baseline	5.10	30	1.561	0.056 t = 1.9478
4 months	5.96	30	1.847	

Intra group comparison of hair density at baseline and at the end of 4 months At the end of 4 months when we compare two groups (Group – A & Group - B) for improvement in hair density. We compared baseline levels with that of hair density levels at the end of 4 months.

In Group – A though the mean hair density levels look to be improved from 5.26 ± 1.362 to 5.50 ± 1.548 but the improvement is not statistically significant as p value > 0.05.

In Group – B hair density level at baseline was 5.10 ± 1.561 improved to 5.96 ± 1.847 at the end of 4 months and the improvement is statistically significant as p value = 0.056.

Side Effects

In our study patients on PR.P group, all of them developed pain and it subsided on its own within 2-3 weeks.

In Patients on PR.P + Minoxidil, out of 30 patients, majority of patients 80% (n=24) complained of heaviness on the day of injection. 6 Patients (20%) complained of forehead swelling which resolved in 2-3 days without any treatment. In 2 patients (6.66%) bruise was noticed.

Table no 7: Side Effects among study subjects.

Side effects	PR.P (Group - A)	PR.P + Minoxidil (Group - B)
Pain	30 (100%)	30 (100%)
Heaviness	-	24 (80%)
Forehead swelling	-	6 (20%)

Bruise	-	2 (6.6%)
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Discussion

Males who have androgenetic alopecia experience pattern hair loss that is progressive. A dermatological disorder that is androgen dependent is defined by the conversion of terminal hair follicles to vellus hair. To stop the spread of the disease, early intervention is necessary.

There are numerous therapy options, including Minoxidil, Finasteride, etc. Hair growth from minoxidil alone is only moderate, necessitating a long- term maintenance regimen. Later, concentrated platelets extracted from the patient's own blood, known as platelet rich plasma (PRP), were added. It is intradermally injected. Once injected, PRP induces local inflammation and damage that release a number of growth factors, including VEGF, PDGF, FGF, and many more that promote hair growth.

Various modalities of treatment have been proposed and used for androgenetic alopecia. No treatment modality is curative. Only after receiving long-term care using a variety of medical therapy methods is hair growth observed; it does not persist after treatment is stopped.

The efficacy of any modality of treatment varies depending on the age of the patient, grade of hair loss, and compliance with treatment.

In this study we decided to research the effects of PRP and Minoxidil in males who have progressive androgenetic alopecia pattern hair loss. It is carried out in Department of Skin and Venerology, PMCH, Udaipur. Androgenic alopecia patients were divided into two group - A, they received PR.P alone as a treatment modality and group - B, they received PR.P + minoxidil as a treatment modality.

Age Distribution

In our study, we included 60 patients of Androgenetic alopecia, the age of patients ranged from 20 to 40 years with mean age of 28.08 ± 5.497 . Majority of patients belonged to the age group of 26-30 years. Our results are consistent with Hajheydari et al.,¹⁶ Dhurat R et al¹⁷ and Kumar MK et al¹⁸ study, mean age of patients was 22.8, 28.6 years and 26.04 years respectively. Although there is high variation in the age groups was noted in previously done studies. In a study done by Shah KB et al.,¹⁹ average age of patients with male pattern baldness were 30.6 years.

Mean Age Comparison between groups

In our study Mean age for group - A was 28.96 and group - B it was 27.20. However, the difference in Mean age in both the groups was statistically insignificant as p value found to be 0.510. Which was similar to the Singh SK et al²⁰ study, th mean age of the patients in "PR.P plus topical minoxidil" group and "PR.P alone" group was 25.6 and 26.5 years, respectively.

Comparison of age of onset between groups

In our study Mean age at disease onset of group A & B were 24.16 & 24.96 years respectively. However, the Mean age of disease onset in both the groups was comparable as revealed by the insignificant p value of 0.696. Similar result was found in the Singh SK et al²⁰ study, they documented the mean age of the patients in "PRP plus topical minoxidil" group and "PRP alone" group was 20.6 and 21.9 years, respectively.

Hair Density Assessment in Group A (PR.P Group)

Mean hair density in PR.P group at baseline was 5.26 ± 1.362 and at end of 4 months Mean hair density was 5.50 ± 1.548 . In this group, younger patients and those with short duration alopecia showed better results. Although there is a difference in the hair density at the end of 4 months when compared to baseline level but this is not statistically significant as

revealed by ($p=0.526$). Similarly, Rodrigues et al²¹ also documented the mean increase in hair count at the end of 12 week was not statistically significant in "PR.P alone" group [$P < 0.955$].

Hair Density Assessment in Group B (PR.P + Minoxidil Group)

Mean hair density in PR.P with Minoxidil group at baseline was 5.10 ± 1.561 and Mean hair density at the end of 4 month was 5.96 ± 1.847 . This group in particular 12 out of 15 patients, the onset of response compared to PR.P group, was earlier at 3 months which was appreciated as decrease in hair shedding, improvement in hair texture, volume and with subsequent injections patients showed marked increase in hair density which was revealed by significant p value of 0.056. Similarly, Singh SK et al²⁰, Pakhomova EE et al²² showed that a combination of PRP and minoxidil was superior to the PRP alone and topical minoxidil alone groups in promoting hair growth in men with AGA and this observation is statistically significant. Greco and Brandt²³, Kang et al²⁴, Park et al.²⁵ and Lopez et al.²⁶ have shown that interfollicular injections of PRP (mesotherapy) produce significant increase in hair shaft diameter, growth rate, and hair density. Greco and Brandt²³ found that traumatizing scalp and infusing PRP into the scalp reversed miniaturization over an 8- month period when compared with control and significant increase of 9.7% in average hair shaft diameter at 4 months and then 6.1% at 8 months in the treatment group was noted.

It is unknown what precise platelet concentration (in PRP) is needed to induce hair regeneration. The "more is better" philosophy may seem to apply in all situations, but Anitua et al.²⁷ argue that this is not always the case. Supporting this opinion are the reports that high concentrations of growth factors transforming growth factor-beta, epidermal growth factor, and platelet-derived growth factor may contribute to impaired wound healing and increased scarring.

Side Effects

In our study, pain was the only complaint encountered by all cases after PRP treatment which subsided on its own in 2-3 weeks, there were no major adverse effects reported in other studies also.

In Patients on PR.P + Minoxidil majority of patients 80% ($n=24$) complained of heaviness on the day of injection. 6 Patients (20%) complained of forehead swelling which resolved in 2-3 days without any treatment. In 2 patient (6.66%) bruise was noticed. These findings were consistent with the Verma K et al²⁸ study.

Patients in PRP + Minoxidil group were mainly pain at injection site because of which four patients left the treatment and were excluded. No significant side effects were observed in Group B patients (PR.P only group) except for mild scaling.

Limitation:

This study included a small number of patients, which was a major drawback given the brief research period.

Conclusion

· In the present study, 60 androgenic alopecia patients were allocated into two groups (30 patients in each group); one received PR.P alone as a therapy (group-A). another group received PR.P with topical minoxidil as a combination therapy.
· Age of the study subjects ranged from 20 to 40 years while most of them were in 26 – 30 years age group.

· Mean age of group-A & group - B were 28.96 and 27.20 respectively. This difference in age between two groups is not statistically significant.

The difference of mean disease onset duration between two

groups is not statistically significant. The difference of mean hair density levels when basal levels were compared to the levels at the end of 4 months were not statistically significant in group – A who received PRP alone as a therapy.

The difference of mean hair density levels when basal levels were compared to the levels at the end of 4 months were statistically significant in group – B who received PRP + topical minoxidil as a combination therapy.

Patients developed certain side effects such as headache, heaviness, forehead swelling, bruise after undergoing treatment for androgenetic alopecia.

The results obtained in the present study allows us to suggest that PRP and topical minoxidil potentiate each other's action when used together and their complex application seems promising for the treatment of androgenetic alopecia.

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