Efficacy of Platelet-Rich Plasma *versus* 5% Topical Monixidil for the Treatment of Androgenetic Alopecia

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ABSTRACT

Objective: To compare the efficacy of platelet-rich plasma (PRP) *versus* 5% topical minoxidil for the treatment of androgenetic alopecia (AGA).

Study Design: Randomised-controlled trial.

Place and Duration of the Study: Department of Dermatology, PNS Shifa Hospital, Karachi, Pakistan, from 1st November 2021 to 31st July 2022.

Methodology: Seventy AGA patients aged between 18-60 years of either gender were randomly divided into two groups. Group A was given 5% topical minoxidil and Group B was given PRP. Both groups were followed up over a period of 6 months, and the final analysis was done with the help of global photography, hair pull test, and patient satisfaction score.

Results: At the end of 6th month, 27 patients (77%) in Group A had a negative hair pull test as compared to only 14 (40%) in Group B (p = 0.001). In Group A, 32 patients (91.4%) reported improvement in hair scalp from baseline. Whereas, in Group B, 26 patients (74.3%) reported improvement from baseline (p = 1.00). PRP was effective in 26 patients (74.5%) and 5% topical minoxidil in 15 patients (43.7%) (p = 0.007).

Conclusion: PRP therapy can be a useful alternative to topical minoxidil in the treatment of AGA.

Key Words: *Androgenetic alopecia, Global photography, Platelet-rich plasma, 5% Topical minoxidil, Treatment.*

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INTRODUCTION

Pattern baldness is polygenetic, multifactorial, dermatological condition characterised by slowly progressive miniaturisation of scalp hair in a particular pattern, affecting males and females.[1] It affects up to 70% of men and 40% of women.[2] Incidence of androgenetic alopecia (AGA) increases with age, i.e. more than 50% of men over 50 years and 40% of women by the age of 50 years may experience baldness.[3,4] Good hair is an integral part of an attractive personality; progressive thinning and loss of hair significantly affect the quality of life, in terms of resulting in low self-esteem, low self-image, anxiety, and depression.[5]

5% Topical minoxidil and oral finasteride are the medicinal therapies for the management of AGA that have received FDA approval in US. Due to variable efficacy and emerging concern about side effects related to minoxidil and finasteride, more treatment regimens are under trial and are used off the label.[6,7]

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A study reported that 62.5% of AGA patients were satisfied with autologous platelet rich plasma (PRP) as compared to 35.76% with minoxidil.[8] PRP is autologous preparation of platelets in concentrated plasma.[9] It contains more than 20 growth factors of which the most important growth factors include PDGF, TGFβ, VEGF, and IGF-1 along with their isoforms. Apart from various growth factors, PRP contains plasma proteins fibrin, fibronectin, and vitronectin. In AGA, PRP induces differentiation of stem cells, prolongs survival of dermal papilla cells, increases perifollicular vascular plexus by multiple mechanisms, and prolongs anagen phase of hair cycle.[10]

To the best of authors' knowledge, majority of such studies had been done at an international level, but the local data about its significance is insufficient. Paucity of information in this regard exists in Eastern and Southern Asian countries which has different geographical setups, climates, dietary habits, lifestyles, and economical soundness as compared to the western world. Besides, through review of the literature, it was found that only a few studies were available with a large sample size. The aim of this study was to compare the efficacy of PRP *versus* 5% topical minoxidil for the treatment of AGA.

METHODOLOGY

This research was conducted in the Department of Dermatology, PNS Shifa Hospital, Karachi, Pakistan, from 1st November 2021 to 31st July 2022 after the approval of study protocol from

the Ethical Committee of the hospital. This randomised-controlled trial was registered at Iranian Registry of Clinical Trial (IRCT) (Registration number: IRCT20210811052139N1). The sample size was calculated using the Openepi calculator programme, setting alpha error at 5% and power at 80%. Seventy patients clinically diagnosed with AGA for a duration over 6 months, aged between 18 to 60 years, with Hamilton-Norwood Grade ≥2 and ≤5 or Ludwig scale Grade 1-2, platelets count more than 150, 000 /µl to 450,000/ µl who had not used any therapy for AGA in the last three months were included *via* non-probability consecutive sampling technique. Patients with alopecia other than AGA, such as telogen effluvium, alopecia areata, acquired cicatricial alopecia, or anagen effluvium, warfarin, heparin, aspirin, or with any bleeding disorder, any infective disease of the scalp or skin disease, hypersensitivity to minoxidil in past, pregnancy/lactation, and patient with comorbidities such as diabetes, and chronic liver and disease, and thyroid disorder were also excluded.

Male patients were divided from Grade II-V as per the modified Norwood-Hamilton scale and female patients were divided into Grade I-II as per Ludwig scale. A brief history of demographic data (age, gender, duration of AGA, family history of baldness) was taken. The patients were inquired regarding the life style-related factors that can potentially exacerbate AGA, such as smoking and exposure to the sun. The Modified Norwood-Hamilton criteria for males and the Ludwig scale for females were used to determine the grade of AGA. Patients received counselling on the advantages, drawbacks, and restrictions of both management regimens. An informed written consent was acquired when the procedure was explained to the patient. The enrolled patients were randomly divided into two groups using the lottery method, Group A and B, each with 35 participants. Group B received treatment with 5% topical minoxidil therapy given as 1 ml, two times daily for six months, and Group A received monthly injections of PRP.

Group A was advised to not use any oil on the scalp before the procedure. The scalp was cleaned by spirit, and nerve block was done by using the local injection, lignocaine, by insulin syringe at supratrochlear, supraorbital, and occipital region. After all aseptic measures, 30 ml of venous blood was extracted into a citrate phosphate dextrose-filled tube (to prevent platelet activation and degranulation), and blood was then subjected to two spins, a soft spin at 2500 rpm for 10 minutes and a hard spin at 3500 rpm for 15 minutes. Soft spin separated blood in 3 layers, lowermost layer was of red blood cells (RBC), the uppermost layer was platelet-poor plasma (PPP) and the middle layer was PRP (platelet-rich plasma). In another tube, PPP, PRP (using a calcium gluconate to PRP ratio of 1:9), and a few RBC without anticoagulants underwent hard spin. PRP was settled at the bottom and PPP at the uppermost layer. PPP was discarded and the remaining PRP was used for the procedure. This PRP was extracted for the treatment in a sterile insulin syringe enclosing calcium gluconate which could activate platelets. PRP was then administered intradermally in doses of 0.1 to 0.2 ml each, spaced 1 cm apart, in interfollicular areas. A total of six sessions were done, each session was 1 month apart. Participants of Group B were advised to apply 5% topical minoxidil, 1 ml over dry scalp 12 hourly. Participants of both groups were assessed on 0, 3, and 6 months. Serial photographs were taken at each assessment. These photograph were assessed by a consultant dermatologist who did not know the group of the patient (double blinded).

The efficacy of both groups was evaluated using the patient satisfaction scores,[8] global photography, and the hair pull test.

At the end of each period, baseline and post-treatment images in global photography were taken and evaluated by a blinded evaluator. To capture the entire scalp, several images were taken with iPhone 12 ProMax camera. The vertex, mid-pattern, frontal, and temporal pattern were four perspectives that received a lot of attention in particular. Results were interpreted by the investigator 7 point score (- 3 = greatly decreased, -2 = moderately decreased, -1 = slightly decreased, 0 = no change, 1 = slightly increased, 2 = moderately increased, 3 = greatly increased).[14]

At the beginning of treatment and then six months after the treatment, a hair pull test was conducted to determine severity of disease. Prior to the hair pull test, patients were instructed to wait for 24 hours before shampooing.

In the hair pull test,[8] the thumb, index, and middle fingers were used to grip roughly 60 hair. The hair were then pulled firmly yet delicately. A positive result was defined as $\geq$6 hair or 10% of total number of hair acquired, whereas a negative result was defined as <6 hair or 10% of total number of hair collected. Furthermore, patient satisfaction was assessed by self-administered hair growth questionnaire as worsening from baseline, not improving from baseline, and improving from baseline. Finally, efficacy was measured after the 6th month of treatment and was labelled as positive if there was negative pull test, investigation 7 point score was >2 and improvement from the baseline.

SPSS version 26 was used to enter and evaluate the data. Mean and standard deviation were calculated for the quantitative variables like age and the length of baldness. For the categorical factors including gender, grade of baldness, family history of baldness, and efficacy, frequencies, and percentages were determined. The quantitative variables were compared using an independent t-test, while the qualitative outcome variable was compared using a Chi-square/Fisher's exact test. The standard for determining statistical significance was two-sided, $p = 0.05$.

RESULTS

In Group A, the mean age was 28 ± 6.8 years and the mean duration of baldness was 7 ± 5 months, while in Group B, the mean age of the patients was 26.9 ± 5.9 years and mean duration of baldness was 6.9 ± 5.8 months. Twenty-three patients (65.7%) were male and 12 patients (34.2%) were female in Group A while in Group B, 27 patients (77%) were male and 8 patients (33%) were female.

Table I: Demographic details of the patients.

Demographics	Group A (n = 35)	Group B (n = 35)	p-value
Age (Mean ± SD)	28 ± 6.8 years	26.9 ± 5.9 years	0.472
Duration of baldness (Mean ± SD)	7 ± 5 months	6.9 ± 5.8 months	0.938*
Gender, n (%)			
Male	23 (65.7%)	27 (77%)	
Female	12 (34.2%)	08 (33%)	0.289**
Family history of baldness, n (%)			
Yes	22 (62.8%)	23 (65.7%)	
No	13 (37.1%)	12 (34.2%)	0.803**
Grade of baldness (male), n (%)			
Grade II	10 (43.7%)	11 (40.7%)	
Grade III	04 (17.3%)	4 (14.8%)	
Grade IV	08 (34.7%)	10 (37%)	0.96**
Grade V	01 (4.3%)	02 (7.4%)	
Grade of baldness (female), n (%)			
Grade I	09 (75%)	05 (62.5%)	
Grade II	03 (25%)	03 (37.5%)	0.55**
Smokers, n (%)			
Yes	13 (37%)	11 (31.4%)	0.614**
No	22 (63%)	24 (68.5%)	

** Independent t-test, **Chi-square/Fisher's exact test.*

Table II: Patient satisfaction about the growth of hair since the start of the study.

Patient satisfaction	Group A (n = 35)	Group B (n = 35)	p-value
Worsening from baseline	0	0	0.000*
Not improving from baseline	3 (8.5%)	16 (45.7%)	
Improving from baseline	32 (91.4%)	19 (54.2%)	

**Chi-square test.*

Most of the male patients were classified into Grade II and IV in either of the group with no significant difference between the two groups. Similarly, most of the female patients lied in Grade I in either group with no statistically significant difference. Twenty-two patients (62.8%) in Group A and 23 patients (65.7%) in Group B had history of AGA. In Group A, 13 patients (37%) were smokers whereas in Group B, 11 (31.4%) were smokers. Both groups were comparable in terms of demographic details as p-values were not statistically significant, as shown in Table I.

Twenty-seven patients in Group A (77%) had a negative hair pull test as compared to only fourteen patients in Group B (40%) with statistically significant difference (0.001) (Figure 1).

In Group A, 3 patients (8.5%) reported to be not improving from the baseline, and 32 (91.4%) reported improvement from baseline, whereas in Group B, 16 patients (45.7%) reported not improving from the baseline and 19 patients (54.2%) reported improving from the baseline; p-value was statistically significant (p<0.001), as shown in Table II.

PRP was effective in 26 AGA cases (74.5%) and 5% topical minoxidil was effective in 15 cases (43.7%), hence, statistically significant difference was observed (p=0.007) (Figure 2).

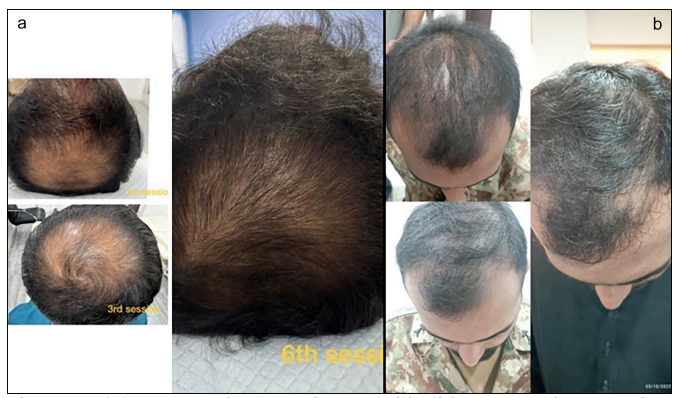

Figure 1: (a) Group B (0, 3, and 6-month); (b) Group B (0, 3, and 6-month).

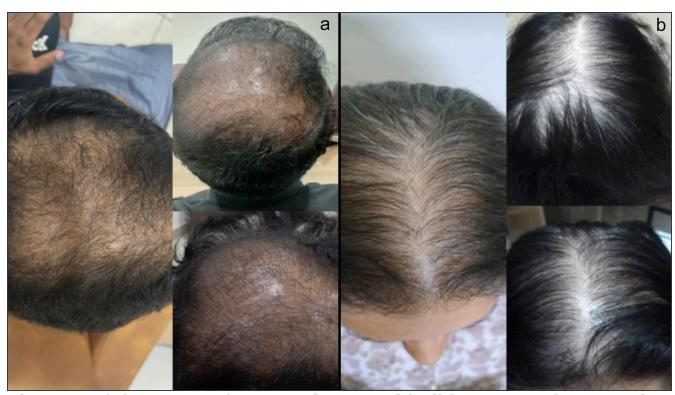

Figure 2: (a) Group A (0, 3, and 6-month); (b) Group A (0, 3, and 6-month).

DISCUSSION

AGA is the most prevalent cause of hair fall in a general practice. There has been continuous search for new treatment options in AGA due to the limited current treatment options. PRP therapy had recently demonstrated some promising outcomes. In this study, PRP therapy was compared with an already well-established minoxidil therapy in order to determine which therapy was more effective for treating AGA.

In the present study, all the patients were between 18 to 60 years of age. Overall, the mean age was 27.75 years which was comparable with the mean age reported by Shruti Gupta *et al.,* i.e. 28.3 years.[11]

Concerning the family history of AGA, 62.8% of patients in Group A and 65.7% of patients in Group B had positive history which was comparable to the study conducted by Łukasik *et al*. which showed 65% prevalence of family history in patients with AGA.[12] This supported the well-known fact that AGA is genetic and inherited from family.

Both the manual double-spin approach and mechanised equipment can be used to prepare PRP. PRP was prepared manually using the double-spin method in the current investigation; Ubel *et al*. and Khatu *et al*. also used comparable techniques to prepare PRP.[13,14] In studies by Betsi *et al*. and Cervelli *et al*., automated equipment was used for PRP preparation.[15,16] On average, automated devices took 5–10 minutes to separate PRP from blood in a single spin at 1100–1500 cycles/minute.

Even though PRP therapy had been used in AGA for more than ten years, there were still no established treatment regimens for PRP therapy that could specify the number of sessions or the time intervals between them. In the present study, PRP therapy was administered monthly for six months - six sessions were administered once monthly - which was similar to Cervelli *et al's*. administration of PRP therapy monthly for six months.[16]

The evaluation methods used in the current study were global photography, hair pull test, and patient and self-structured questionnaire[8,14,15] to assess the patient satisfaction for both Group A and B. Similar evaluation methods were also used by Betsi *et al*. which included a clinical examination, digital images, hair pull test, and patient satisfaction score.[15] In their study, all the patients (100%) had a negative hair pull test after the third treatment, and patient satisfaction score was 7.0 on a scale of 1-10. In this study, negative hair pull test was in 27 patients (77%) in Group A and 14 (40%) in Group B. Khatu *et al*. used global photography, clinical examination, and phototrichogram to evaluate responses to the treatment in PRP patients;[16] and in their study, 81.81% of patients had negative hair pull test at 3 months (four sessions) of treatment which was slightly higher as compared to the present study, that is, 77% at 6 months (six sessions), while patient satisfaction score was 7 on a scale of 1-10 which was almost comparable to the current study.

Olsen *et al*. conducted randomised clinical research in 2002 to compare the effects of 5% topical minoxidil solution, 2% topical minoxidil solution, and placebo on AGA.[17] The assessment techniques included patient self-examination, physician assessment of hair growth utilising hair growth questionnaire, and hair count generated from computer-assisted scans of macrophotographs of clipped hair in 1 cm^2 target evaluation area in balding vertex scalp. In this study, a self-structured questionnaire was employed to assess the patient satisfaction for both treatment modalities as well as other characteristics like global photography and the hair pull test which were not included in the study by Olsen *et al*.

From RCTs that assessed the effectiveness and safety of minoxidil monotherapy, minoxidil+PRP, or PRP monotherapy for males with AGA Hamilton-Norwood Stages I-V,[9,18,19] possibilities were extrapolated. Utilising doctors' ratings based on prospective clinical investigations conducted in 6-month cycles, treatment response and possibilities for various health statuses were calculated. Photographs, dermoscopic analyses, and hair pull tests were utilised to evaluate the therapy responses.[20] Fifty-five percent of participants with minoxidil PRP,[20] 53% of participants with PRP monotherapy,[18] and 51% of participants with minoxidil monotherapy showed improvement during the first cycle.[21] Ninety-nine percent of participants continued minoxidil+PRP, 97% of participants continued PRP monotherapy,[22] and 91% of participants continued minoxidil monotherapy beyond the initial 6-month cycle for those who responded.[8,9] Ninety-eight percent of men who improved over the successive cycles completed the therapy, while 50% of men who did not respond did not continue the treatment.[8,19–22]

Lack of follow-up of the patients and side-effects of both treatments were not encountered in the current research. The effects of treatment on anagen and telogen hair were also not observed. Other limitations included the use of non-probability sampling technique which may limit the generalisability of the results. Further studies with larger sample size along with assessment of side-effects of PRP therapy may provide a better picture regarding the PRP therapy.

CONCLUSION

PRP is an exciting new therapeutic option for hair growth and stimulation in patients of androgenic alopecia. PRP therapy can be a valuable adjuvant to topical minoxidil therapy in the treatment of AGA. Individuals who are dissatisfied with or noncompliant with the frequent use of minoxidil may prefer it in particular.

ETHICAL APPROVAL:
The study was conducted after receiving an approval from the Ethical Committee of the PNS Shifa Hospital, Karachi (ERC/2021/Dermatology 57).

PATIENTS' CONSENT:
Informed consent was obtained before conducting the study.

COMPETING INTEREST:
None of the authors declared any conflict of interest.

AUTHORS' CONTRIBUTION:
GA: Concept, literature review, and writing.
NA: Concept, literature review, and critical review.
FZ: Design, analysis and interpretation, and literature review.
TM: Data collection and drafting.
OF: Interpretation of data and critical revision.
All authors approved the final version of the manuscript to be published.

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