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ORIGINAL RESEARCH

ENHANCING TREATMENT OUTCOMES IN ANDROGENETIC ALOPECIA: A PROSPECTIVE COMPARATIVE EVALUATION OF PLATELET-RICH PLASMA AND MINOXIDIL THERAPY

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ABSTRACT

Androgenetic alopecia (AGA) is the most common form of progressive hair loss in adult men. Topical minoxidil is an established first-line therapy, but its onset is slow and adherence to long-term application is variable. Autologous platelet-rich plasma (PRP) has emerged as a promising adjunctive treatment. Objective of the present study was to compare the clinical efficacy, safety and tolerability of intradermal PRP therapy with topical minoxidil 5% solution in male patients with AGA. Methods. In this single-centre prospective comparative study, 60 male patients with clinically diagnosed AGA were randomly allocated using sealed opaque envelopes containing computer-generated random numbers to receive either intradermal PRP once monthly for four sessions (Group A; n = 30) or topical minoxidil 5% applied twice daily for six months (Group B; n = 30). Treatment response was evaluated at six months using global photography, the hair pull test, a validated patient hair- growth questionnaire and a 10-point patient satisfaction score. Platelet counts in whole blood and in the prepared PRP were also recorded. Fifty-one patients (25 in Group A and 26 in Group B) completed the protocol. A negative hair pull test at six months was significantly more frequent in the PRP group than in the minoxidil group (72.0% vs. 38.5%; p = 0.0336). Self- reported moderate increase in hair growth (40.0% vs. 7.7%; p = 0.006), perceived effectiveness in slowing hair loss (60.0% vs. 19.2%; p = 0.0042) and satisfaction with vertex hair appearance (60.0% vs. 19.2%; p = 0.004) were all significantly greater with PRP. Mean overall satisfaction score (1–10) was 7.55 ± 1.02 in the PRP group versus 5.05 ± 1.45 in the minoxidil group (p < 0.001). The mean platelet concentration in PRP rose from 3.07 ± 0.5 × 10^5/mm^3 in whole bloodto 12.4 ± 1.7 × 10^5/mm^3, an approximately fourfold enrichment. Five patients in Group A discontinued because of procedural pain, and four patients in Group B discontinued because of perceived lack of efficacy. Intradermal PRP therapy produced significantly better clinical and patient-reported outcomes than topical minoxidil 5% over six months in male patients with AGA, with a favourable safety profile. PRP appears to be a useful adjunct to standard therapy and may be particularly valuable in patients with limited adherence to topical regimens.

Keywords. Androgenetic alopecia; Platelet-rich plasma; Minoxidil; Hair loss; Growth factors; Comparative effectiveness.

INTRODUCTION

Androgenetic alopecia (AGA) is a chronic, progressive disorder of the hair follicle that is hormonally driven and genetically determined, and represents the most common cause of hair loss in adults [1,2]. The condition is characterised by progressive miniaturisation of terminal scalp hair follicles in a characteristic pattern, with conversion of large pigmented terminal hairs into shorter, finer, less-pigmented vellus-like hairs and shortening of the anagen phase of the hair cycle [1,3]. AGA affects approximately half of men by the age of 50 and a substantial proportion of women, with prevalence increasing further with age [4]. Although not associated with systemic morbidity, AGA carries a recognised psychosocial burden, with documented impact on self-esteem, body image and quality of life [4].

Two pharmacological agents topical minoxidil and oral finasteride are currently approved by the United States Food and Drug Administration for the treatment of AGA. Both have demonstrated efficacy in randomised trials [5,6]; however, neither is curative, both require indefinite use to maintain benefit, and onset of clinically perceptible improvement is

typically slow [6]. Minoxidil application is associated with cosmetic inconvenience and occasional scalp irritation, while finasteride raises concerns regarding sexual side effects in a minority of users [2,6]. These limitations have driven sustained interest in alternative and adjunctive treatments.

Platelet-rich plasma (PRP) is an autologous concentrate of platelets in a small volume of plasma, obtained by centrifugation of anticoagulated whole blood [7]. Activation of the concentrated platelets results in the release of more than twenty bioactive growth factors, including platelet-derived growth factor (PDGF), transforming growth factor-β (TGF-β), vascular endothelial growth factor (VEGF), insulin-like growth factor-1 (IGF-1), epidermal growth factor (EGF) and fibroblast growth factors [7,8]. Experimental and clinical work suggests that these factors stimulate dermal papilla cell proliferation, activate stem-cell niches in the bulge region of the hair follicle, prolong the anagen phase, increase perifollicular vascularisation and promote the conversion of vellus to terminal hairs [8,9].

On the basis of this biological rationale, a growing body of clinical evidence has shown that PRP injections improve hair density and reduce hair shedding in AGA [9-12], and contemporary systematic reviews and meta-analyses have endorsed PRP as a clinically beneficial therapy in this indication [13,14]. Comparative evidence against established therapies, however, remains comparatively limited. The present study was therefore undertaken to compare the clinical efficacy, safety and tolerability of intradermal PRP therapy with topical minoxidil 5% in patients with AGA in a real-world tertiary care setting.

MATERIALS AND METHODS

Study design and setting

This was a single-centre, prospective, open-label, randomised comparative study conducted between January and December 2024 in the outpatient services of a tertiary care institution. The study was performed in accordance with the principles of the Declaration of Helsinki [15] and was approved by the Institutional Ethics Committee. Written informed consent was obtained from every participant after a full explanation of the alternative therapies, their expected benefits, possible adverse effects and limitations.

Participants

Consecutive male patients aged 20-49 years presenting with clinically diagnosed AGA were screened for eligibility. The diagnosis was established on the basis of history and scalp examination, with grading according to the Modified Norwood–Hamilton classification [16]; the Ludwig classification [17] was applied as the corresponding grading scheme in the protocol for female patients, although in the final enrolment only male participants were included. Other causes of hair loss including telogen effluvium, drug-induced alopecia, alopecia areata and systemic illness were excluded clinically. Family history of AGA and lifestyle factors potentially relevant to hair loss (smoking, sun exposure) were recorded for all participants.

Inclusion and exclusion criteria

Inclusion criteria for both treatment arms were: men aged 20-49 years; clinically diagnosed AGA of grade I-V on the Modified Norwood–Hamilton scale; no prior treatment for AGA, or treatment received for less than six months; and a baseline platelet count of $\geq 1.5 \times 10^5/\mu L$.

Exclusion criteria for PRP allocation were the presence of dermatological disorders of the scalp, a personal history of keloid formation, platelet function disorders, current use of anticoagulant or antiplatelet therapy, and concurrent use of finasteride for AGA. Patients deemed unsuitable for PRP for any of these reasons could be allocated only to the minoxidil arm. Exclusion criteria for the minoxidil arm were current use of finasteride or other systemic AGA therapy, coexisting dermatological disease of the scalp, and previous treatment with PRP. Pregnancy and lactation were exclusion criteria specified in the protocol although not applicable to the final enrolled cohort, which consisted entirely of men.

Randomisation and allocation

Eligible patients were allocated to one of two treatment groups using sealed opaque envelopes containing computer-generated random numbers: Group A received intradermal PRP therapy and Group B received topical minoxidil 5%. The study was open-label; treating clinicians and participants were aware of the allocated intervention, but global photographs at baseline and at six months were assessed independently by an evaluator blinded to treatment assignment.

Preparation of platelet-rich plasma

PRP was prepared from autologous whole blood using a standard double-spin technique [11,18]. Approximately 35 mL of venous blood was collected in tubes containing 3.2% sodium citrate as anticoagulant to prevent premature platelet activation and degranulation. The first centrifugation (soft spin) was performed at approximately 1,500 rpm for 15 minutes, separating the sample into three layers: a lower red blood cell layer (approximately 55% of the volume), an upper acellular platelet-poor plasma (PPP; approximately 40%) and a thin intermediate buffy coat (~5%) containing the platelet-rich fraction. The PPP and buffy coat were transferred under sterile conditions into a second tube without anticoagulant. The second centrifugation (hard spin) was performed at approximately 3,000 rpm for 10 minutes, sedimenting the platelets at the bottom of the tube with minimal red cell contamination. Approximately 80% of the supernatant PPP was discarded, and the residual fraction was gently agitated to ensure uniform platelet distribution before counting on an automated haematology analyser.

The prepared PRP was drawn into insulin syringes preloaded with 10% calcium gluconate as an activator at a calcium gluconate-to-PRP ratio of 1:9 [18]. Activated PRP was injected intradermally in 0.1-0.2 mL aliquots at approximately 1cm intervals across the affected interfollicular scalp regions. Four sessions were administered at four-weekly intervals.

Topical minoxidil therapy

Patients allocated to Group B were prescribed topical minoxidil 5% solution and instructed to apply 1 mL to the affected scalp areas twice daily for six months, in accordance with established guidance for use of this preparation in male AGA [5].

Follow-up and outcome measures

Group A patients were reviewed monthly for six months; Group B patients were reviewed at three and six months over the same observation period. Outcomes were assessed using four complementary measures.

Standardised photographs of the vertex, mid-scalp, frontal and temporal regions were obtained at baseline and at six months under identical lighting and positioning conditions, and were reviewed by an independent evaluator blinded to treatment allocation [5].

Hair pull test. The hair pull test was performed at baseline and at six months, with patients instructed not to shampoo for 24 hours before the test. Approximately 60 hairs were grasped between thumb, index and middle finger and gently pulled. Extraction of more than six hairs (> 10% of those grasped) was considered a positive test, and six or fewer (< 10%) a negative test, in keeping with standard methodology [19].

Patient hair-growth questionnaire:Participants completed a validated self-administered hair-growth questionnaire originally developed by Barber et al. [20]. Six of the seven original items were used; the second item was excluded because patients in the pilot phase found it difficult to interpret, with a high risk of response error.

Patient satisfaction score: At the end of the six-month follow-up, patients rated their overall satisfaction with therapy on a 10-point Likert scale, with higher scores indicating greater satisfaction.

In Group A, platelet counts were measured in the prepared PRP before each injection, and the mean across the four sessions was calculated for correlation with clinical outcome.

Statistical analysis

Quantitative variables are expressed as mean ± standard deviation, and categorical variables as frequencies and percentages. Between-group comparisons of continuous variables were performed using the unpaired t-test, and categorical variables were compared using the chi-square or Fisher's exact test as appropriate. Analyses were carried out using Epi Info version 7. A two-sided p-value of less than 0.05 was considered statistically significant.

RESULTS

Participant flow

A total of 60 male patients with AGA were enrolled, with 30 patients allocated to each treatment group. Five patients in Group A discontinued treatment owing to injection-site pain during the procedure, and four patients in Group B discontinued because of perceived lack of improvement at three to four months. Accordingly, 25 patients in Group A and 26 patients in Group B (a total of 51) completed the six-month protocol and were included in the final analysis.

Baseline characteristics

Baseline demographic characteristics and the pattern of hair loss were comparable between the two groups, with no statistically significant differences in mean age, age at onset of AGA, family history of AGA, or distribution of disease severity (Tables 1& 2). Most participants in both groups had Grade II or Grade IV AGA on the Modified Norwood–Hamilton scale.

Table 1. Baseline characteristics of participants who completed the study.

Variable	Group A (PRP)	Group B (Minoxidil)
Number of patients analysed	25	26
Age, years (mean ± SD)	23.7 ± 2.8	24.1 ± 4.5
Age at onset of AGA, years (mean ± SD)	21.1 ± 1.8	21.2 ± 3.1
Family history of AGA, n	18	16

Table 2. Distribution of androgenetic alopecia severity (Modified Norwood–Hamilton classification).

Grade	Group A (PRP), n	Group B (Minoxidil), n
Grade I	0	0
Grade II	9	10
Grade III	7	7
Grade IV	9	8
Grade V	0	1
Total	25	26

Hair pull test

At six months, a negative hair pull test was recorded in 18 of 25 patients in Group A (72.0%), compared with 10 of 26 patients in Group B (38.5%); the difference was statistically significant (p = 0.0336) (Table 3).

Table 3. Hair pull test outcomes at six months.

Outcome at 6 months	Group A (PRP), n (%)	Group B (Minoxidil), n (%)	p-value
Negative hair pull test	18 (72.0)	10 (38.5)	0.0336

Patient hair-growth questionnaire

Self-reported outcomes consistently favoured PRP therapy (Table 4). Significantly more patients in Group A than in Group B reported a moderate increase in hair growth (40.0% vs. 7.7%; p = 0.006) and perceived their treatment to be very effective in slowing hair loss (60.0% vs. 19.2%; p = 0.0042). Satisfaction with the appearance of hair at the vertex was

significantly higher in the PRP group (60.0% vs. 19.2%; p = 0.004), although differences in satisfaction with the frontal scalp and with overall hair appearance did not reach statistical significance. Patients who reported visible reduction in size of the bald spot were more numerous in Group A, but this difference was also not statistically significant.

Table 4. Patient-reported outcomes on the standardised hair-growth questionnaire at six months.

Self-reported outcome	Group A n (%)	Group B, n (%)	p-value
Bald spot getting smaller	12 (48)	8 (30.8)	0.258
Moderate increase in hair growth	10 (40)	2 (7.7)	0.006
Treatment very effective in slowing hair loss	15 (60)	5 (19.2)	0.0042
Satisfied with appearance frontal scalp	6 (24)	4 (15.4)	NS
Satisfied with appearance vertex	15 (60)	5 (19.2)	0.004
Satisfied with overall hair appearance	12 (48)	8 (30.8)	NS

Overall patient satisfaction

The mean overall satisfaction score on the 10-point Likert scale was 7.55 ± 1.02 in Group A and 5.05 ± 1.45 in Group B. The between-group difference was highly statistically significant (p < 0.001), favouring PRP therapy.

Platelet concentration in PRP

In Group A, the mean baseline whole-blood platelet count was 3.07 ± 0.5 × 10^5/mm^3, while the mean platelet count in the prepared PRP was 12.4 ± 1.7 × 10^5/mm^3, representing an approximately fourfold enrichment over baseline (Table 5). This degree of platelet concentration is consistent with values regarded as optimal for therapeutic PRP in published protocols [10,18].

Table 5. Platelet count in whole blood and in prepared PRP (Group A).

Parameter	Mean ± SD (×10^5/mm^3)
Baseline whole-blood platelet count	3.07 ± 0.5
Platelet count in prepared PRP	12.4 ± 1.7

Safety and tolerability

PRP therapy was generally well tolerated. The principal adverse effect was pain at the injection site, which led to discontinuation in five patients. No infections, persistent erythema, paraesthesia or systemic adverse events were observed. In the minoxidil group, mild scalp scaling was reported in a small number of patients but was not severe enough to prompt discontinuation; the four discontinuations in this arm were attributable to perceived lack of efficacy rather than to adverse effects.

Representative imaging

Representative pre- and post-treatment global photographs of patients in Group A and Group B are shown in Figures 1 and 2, respectively, illustrating the clinical improvements observed.

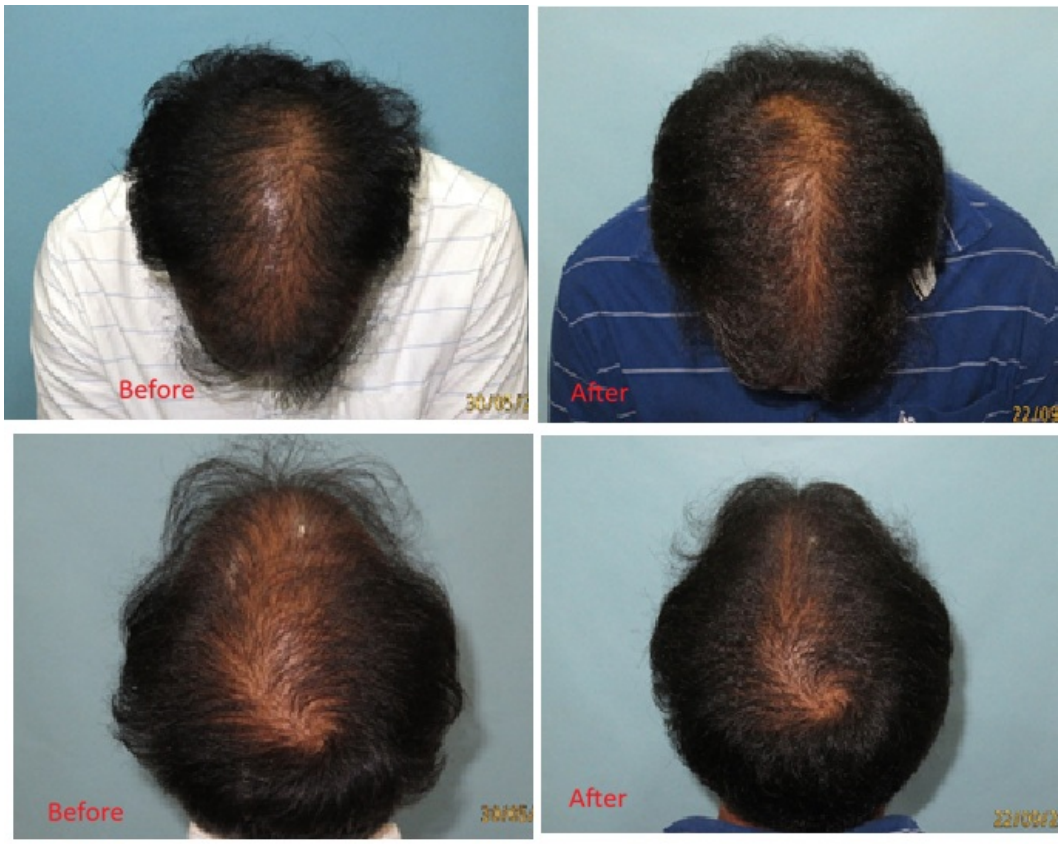

Figure 1. *Representative pre-treatment (before) and post-treatment (after) of Group A (PRP therapy)*

Note: showing improvement in hair density at the vertex.

Figure 2. *Representative pre-treatment (before) and post-treatment (after) of Group B (topical minoxidil 5%).*

DISCUSSION

In this prospective comparative study of 51 men with AGA, intradermal PRP therapy produced significantly greater improvements than topical minoxidil 5% across multiple endpoints including the hair pull test, several items of the validated hair-growth questionnaire and the overall patient satisfaction score over a six-month period. Both therapies were generally well tolerated, with no serious adverse events recorded. To our knowledge, this is one of relatively few prospective comparative studies of these two widely used treatments performed in a real-world Indian tertiary care setting.

The mean platelet concentration in the prepared PRP was approximately fourfold higher than that in whole blood ($12.4 \pm 1.7 \times 10^5/mm^3$ vs. $3.07 \pm 0.5 \times 10^5/mm^3$). This is in close agreement with the four- to sixfold enrichment described by Uebel et al. [21] and within the range reported by Cervelli et al. ($14.84 \times 10^5/mm^3$) [9] and Gkini et al. ($11.02 \times 10^5/mm^3$) [11]. A platelet concentration of approximately three to five times the baseline value is generally regarded as the target for therapeutic PRP in dermatology and aesthetic medicine [22]. Some published studies, including those of Greco and Brandt [23], Betsi et al. [24] and Khatu et al. [10], have not reported the achieved platelet concentration in PRP, which limits cross-study comparison and underscores the value of routine reporting of this parameter.

A persistent challenge in the PRP literature is the absence of a uniformly accepted protocol regarding number of sessions, inter-session interval, activation method and injection technique. The four-session monthly schedule used in the present study is comparable to the three- to four-session protocols employed in earlier reports [9,11], and the volume and spacing of injections were broadly consistent with previously published methods. Standardisation of these variables remains an important research priority and has been highlighted in recent systematic reviews [13,14].

Our findings are concordant with the wider clinical literature on PRP in AGA. Betsi et al. reported that all patients had a negative hair pull test after three PRP sessions, with a mean satisfaction score of 7 on a 10-point scale [24]; the corresponding figures in our cohort were 72.0% and 7.55, respectively. Khatu et al. reported an 81.8% negative hair pull test rate at three months [10], slightly higher than our six-month figure, although patient satisfaction scores were comparable. Cervelli et al., using a three-session protocol, demonstrated significant increases in hair density and anagen-to-telogen ratio in PRP-treated areas relative to control [9]. Gkini et al. similarly described sustained improvements in hair density over a 12-month observation period [11]. The aggregate weight of these reports, together with the results of recent systematic reviews and meta-analyses [13,14], supports a real biological effect of PRP on the AGA phenotype rather than a purely placebo response.

The efficacy of topical minoxidil in AGA has been well established. The pivotal trial of Olsen et al. demonstrated the superiority of the 5% formulation over both 2% minoxidil and placebo, with greater increases in non-vellus hair count at 48 weeks [5]. Tsuboi et al. corroborated this finding in Japanese men, with significantly greater hair-count improvement at 18 weeks for 5% compared with 1% formulations [25]. In our cohort, although topical minoxidil produced modest improvement, the magnitude and patient-reported salience of that improvement were lower than with PRP. The comparative report by Navarro et al., using plasma rich in growth factors versus topical minoxidil in a retrospective analysis, similarly observed greater increases in anagen hair and decreases in telogen hair in the platelet-derived therapy group [26]. Our prospective data extend these observations to a comparison of conventional double-spin PRP with topical 5% minoxidil in a real-world cohort.

Several factors plausibly contribute to the patient-perceived advantage of PRP observed here. The intervention is administered by a clinician at discrete intervals, which sidesteps the daily adherence burden of topical minoxidil and removes the cosmetic inconvenience associated with twice-daily scalp application. The local injection of activated PRP delivers a high concentration of bioactive growth factors directly to the follicular niche, plausibly accelerating clinically apparent improvement [7,8]. By contrast, the slow onset of action of topical minoxidil often three to six months before perceptible change is a recognised reason for discontinuation, and accounted for all four dropouts in the minoxidil arm of the present study [6]. The principal limitation of PRP encountered in our cohort was procedural pain, which led to discontinuation in five of 30 patients; this is consistent with previous reports and is a recognised limitation of intradermal scalp injection therapy [10,11].

CONCLUSION

The intradermal PRP therapy produced significantly better clinical and patient-reported outcomes than topical minoxidil 5% in male patients with AGA over a six-month period, with an acceptable safety profile and procedural pain as the principal limitation. PRP is therefore best viewed as a valuable adjunct to, rather than a replacement for, established pharmacological treatment, with particular value in patients who are dissatisfied with or unable to comply with long-term topical or oral therapy. A combination approach using both modalities may offer the most consistent improvement in clinical outcomes and adherence. Larger, longer and adequately blinded studies, with standardised PRP preparation and objective trichoscopic outcome measures, will be needed to define the optimal place of PRP in the contemporary management of AGA.

Limitations

Limitations include the modest sample size, the single-centre setting, and the relatively short six-month follow-up, which precludes assessment of durability of effect. The study was open-label, which raises the possibility of performance and detection bias in patient-reported outcomes, although global photographs were assessed by a blinded evaluator. Objective trichoscopic measures of hair density per unit area were not used; the addition of such measures, ideally combined with phototrichogram or computer-assisted hair-count techniques, would have strengthened the anatomical evidence. The protocol allowed for enrolment of female patients in principle, but in practice the final cohort consisted entirely of men, limiting generalisability to female pattern hair loss. Larger, multicentre, double-blind randomised trials with longer follow-up and standardised PRP preparation parameters are needed to confirm and extend these findings.

DECLARATIONS

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Author contributions. Both authors contributed to the conception and design of the study, data collection, analysis and interpretation. The first draft was prepared by the corresponding author and critically revised by the co-author. Both authors approved the final version of the manuscript.

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