Research Article

Comparative efficacy and tolerability of platelet-rich plasma and injectable platelet-rich fibrin in male androgenetic alopecia: A prospective split-scalp interventional study

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Background: Androgenetic alopecia (AGA) is characterized by progressive follicular miniaturization. Platelet-rich plasma (PRP) is used as an autologous regenerative treatment, whereas direct comparative evidence for injectable platelet-rich fibrin (PRF) remains limited.

Methods: In this prospective split-scalp interventional study, 35 men with Hamilton-Norwood Grade II-IV AGA received PRP on the right scalp half and PRF on the left; allocation was fixed, and no formal blinding was documented. Three sessions were administered four weeks apart, with final assessment one month after the third session. Trichoscopically measured hair density, Hamilton-Norwood grade, and adverse effects were compared using paired tests.

Results: Baseline trichoscopy showed hair-diameter variability in 31 (88.57%), single-hair follicular units in 29 (82.86%), peripilar sign in 24 (68.57%), and yellow dots in 14 (40.00%) participants. Baseline hair density was comparable between PRP and PRF sides (132.91 ± 12.02 vs 133.00 ± 11.87 hairs/cm²; $p = 0.727$). Mean gain was 19.06 ± 2.11 hairs/cm² with PRP and 25.77 ± 2.53 hairs/cm² with PRF; the paired difference was 6.71 hairs/cm² (95% CI, 6.39-7.04; $p < 0.001$). One-grade improvement occurred in 11 (31.43%) PRP-treated and 26 (74.29%) PRF-treated halves. Adverse effects occurred on 8 (22.86%) PRP-treated and 1 (2.86%) PRF-treated half ($p = 0.039$).

Conclusion: Both preparations improved short-term outcomes; under the fixed-side split-scalp protocol, PRF was associated with greater hair-density gain and fewer minor adverse effects.

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Introduction

Androgenetic alopecia (AGA) is the most common patterned hair-loss disorder in men and frequently prompts treatment during early adulthood.[1,2] Standard therapies can slow progression, but responses are variable and generally require continued use.[3] Platelet-rich plasma (PRP), prepared from anticoagulated blood, delivers a liquid platelet concentrate whose mediators may support dermal papilla survival, angiogenesis, and anagen induction.[4,5] Injectable platelet-rich fibrin (PRF) is prepared without anticoagulant using a low-speed protocol and can polymerize after injection into a fibrin-rich matrix that retains cellular elements and may prolong local mediator release.[6,7] These formulation differences could influence residence time, extracellular-matrix support, perifollicular signaling, and hair-follicle regeneration. Although comparative studies have reported favorable outcomes with injectable PRF, within-patient head-to-head evidence remains limited. The present study therefore compared the short-term efficacy and tolerability of PRP and PRF using a split-scalp design, which reduces inter-individual biological variability by exposing both treatments to the same participant-level characteristics.[8]

Material and Methods

Study Design

A prospective, longitudinal, split-scalp comparative interventional study was conducted over one year in the Department of Dermatology, Venereology and Leprosy,

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Participants

Consecutive men aged >18 years with clinically diagnosed AGA, visible scalp hair loss, and willingness to undergo platelet-concentrate therapy were screened. Patients with other causes of alopecia, Hamilton-Norwood Grade V or VI disease, current topical minoxidil or topical/oral finasteride use, diabetes mellitus, collagen vascular disease, local scalp infection, platelet dysfunction, critical thrombocytopenia, malignancy, HIV, hepatitis B or C, keloidal tendency, chronic smoking, or unrealistic treatment expectations were excluded.

Baseline evaluation included demographic and clinical history, general and dermatologic examination, standardized scalp photography, Hamilton-Norwood grading,[9,10] and trichoscopy.[11] Trichoscopy was performed on both scalp halves at baseline and at final follow-up to quantify hair density in hairs/cm². Hair-diameter variability, single-hair follicular units, peripilar sign, and yellow dots were recorded at baseline for phenotypic characterization. Complete blood count, bleeding time, clotting time, and HIV tri-dot testing were performed according to protocol.

Sample Size and Recruitment

The current study used consecutive, time-bound recruitment during the one-year study period, with a minimum target of 30 and an expected enrollment of 30-35 participants. The primary outcome was the paired change in trichoscopically measured hair density. Recruitment continued till the study time period and consequently 35 eligible participants were enrolled, and all 35 completed follow-up. To characterize the detectable effect without retrospectively presenting it as an a priori justification, a paired t-test sensitivity calculation was performed. Using the normal-approximation framework $n \approx [(Z(1-\alpha/2) + Z(1-\beta))/d_z]^2$, 35 complete pairs provide approximately 80% power at a two-sided α of 0.05 to detect a standardized paired mean difference (Cohen d_z) of about 0.49.

Intervention

Each participant served as his own control. PRP was administered to the right scalp half and PRF to the left scalp half at each of three sessions separated by four weeks. Side allocation was fixed for all participants in accordance with the approved protocol and was not randomized or crossed over. Both scalp halves were treated during the same visit, and standardized high-resolution photographs were obtained at each visit.

Allocation and Blinding

The study was unblinded due to feasibility. Injector handedness, preferred sleeping side, differential sun exposure, and scalp-side dominance were not recorded; consequently, residual side-related bias cannot be excluded.

For PRP preparation, 10 mL of venous blood was collected using a 21-gauge needle into a sterile tube containing 1-mL acid citrate dextrose. The sample was centrifuged at 1,500 rpm for 15 minutes at room temperature. Plasma and buffy coat were transferred to a plain tube and centrifuged at 3,000 rpm for 10 minutes. Platelet-poor plasma was discarded, and approximately 2 mL of PRP was injected intradermally into the right scalp half per session using a 30-gauge needle.

For injectable PRF preparation, 10 mL of peripheral blood was transferred immediately into a plain tube without anticoagulant and centrifuged in a swing-out rotor at 700 rpm for four minutes. Approximately 1-mL of the upper yellow-reddish liquid PRF layer was collected and injected intradermally into the left scalp half per session. Rotor radius and the corresponding relative centrifugal force were not recorded. Post-preparation platelet concentration, leukocyte composition, and growth-factor concentrations were not measured and are therefore not reported.

Participants were advised to wash the scalp the next day with a mild shampoo and avoid scalp products for four weeks. Adverse effects were assessed 72 hours after each session. For this report, an event was described as mild when it was localized and self-limited, did not interrupt the scheduled treatment course, and required no medication or additional intervention.

Outcomes

The primary outcome was change in trichoscopically measured hair density from baseline to the final assessment, performed one month after the third session. Secondary outcomes were within-side and between-side change in Hamilton-Norwood grade and treatment-emergent adverse effects. The qualitative trichoscopic features were used for baseline phenotyping and were not prespecified as longitudinal efficacy endpoints. All 35 participants had complete final outcome data.

Statistical Analysis

Data were analyzed using SPSS version 23.0. Continuous variables are summarized as mean ± standard deviation (SD), and categorical variables as n (%). Paired Student t tests were used for within-participant hair-density comparisons, with mean paired differences and 95%

confidence intervals (CIs). Hamilton-Norwood grade changes were analyzed using the Wilcoxon signed-rank test, and overall adverse-event occurrence (any event vs none) with the exact McNemar test. Tests were two-sided; $p < 0.05$ was considered statistically significant. *P* values are reported to three decimal places, with values below 0.001 shown as $p < 0.001$.

Ethical considerations

Approval was obtained from the Institutional Ethics Committee (IEC Ref. No. PG/DERMATOLOGY/19/2024; May 9, 2024). Written informed consent was obtained before enrollment, participation was voluntary, and confidentiality was maintained.

Results

All 35 enrolled participants completed the three treatment sessions and final follow-up. Mean age was 31.80 ± 6.85 years (range, 20-44 years), mean age at onset was 27.83 ± 5.21 years, and mean disease duration was 47.23 ± 21.22 months. A family history of AGA was present in 23 (65.71%) participants. Vertex involvement was most frequent [17 (48.57%)], and Grade III was the most common baseline Hamilton-Norwood grade [18 (51.43%)].

Trichoscopic Assessment

At baseline, hair-diameter variability was present in 31 (88.57%) participants, single-hair follicular units in 29 (82.86%), peripilar sign in 24 (68.57%), and yellow dots in 14 (40.00%) (Table 1). Hair density was quantified trichoscopically on each scalp half at baseline and final follow-up; these longitudinal outcomes are reported in Table 2.

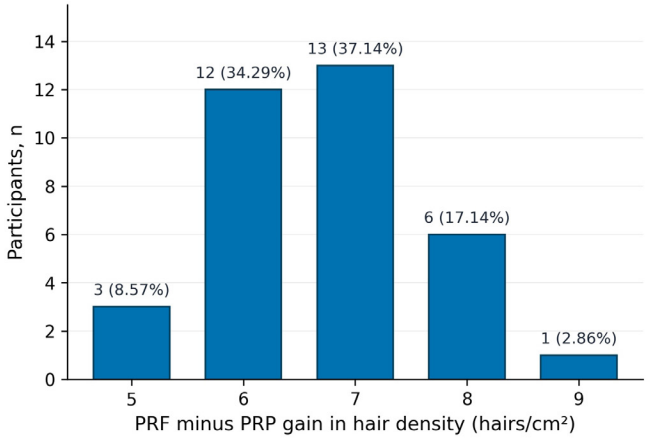

Figure 1: Distribution of the participant-level difference in hair-density gain between PRF- and PRP-treated scalp halves. Positive values favor PRF; labels show n (%). All 35 participants had greater gain with PRF (paired Student t test, $P < 0.001$).

Table 1: Baseline demographic, clinical, and trichoscopic characteristics of participants (N = 35)

Characteristic	*Category*	*n (%)*
Age group	18-25 years	7 (20.00)
	26-35 years	17 (48.57)
	36-45 years	11 (31.43)
Age at onset	≤20 years	4 (11.43)
	21-30 years	19 (54.29)
	>30 years	12 (34.29)
Duration of hair loss	≤36 months	13 (37.14)
	37-72 months	18 (51.43)
	>72 months	4 (11.43)
Family history of AGA	Present	23 (65.71)
	Absent	12 (34.29)
Associated symptoms	None	29 (82.86)
	Itching	6 (17.14)
Hypertension	Present	8 (22.86)
	Absent	27 (77.14)
Site of alopecia	Vertex	17 (48.57)
	Bitemporal	9 (25.71)
	Frontoparietal	9 (25.71)
Baseline Hamilton-Norwood grade	Grade II	9 (25.71)
	Grade III	18 (51.43)
	Grade IV	8 (22.86)
Trichoscopic finding*	Hair-diameter variability	31 (88.57)
	Single-hair follicular units	29 (82.86)
	Peripilar sign	24 (68.57)
	Yellow dots	14 (40.00)

*Trichoscopic findings were not mutually exclusive. AGA, androgenetic alopecia.

Trichoscopic Hair-Density Outcomes

Baseline mean hair density was 132.91 ± 12.02 hairs/cm² on the PRP-treated side and 133.00 ± 11.87 hairs/cm² on the PRF-treated side. The paired difference was 0.09 hairs/cm² (95% CI, -0.41 to 0.58; $p = 0.727$).

On the PRP-treated side, mean hair density increased to 151.97 ± 13.57 hairs/cm², corresponding to a mean gain of 19.06 hairs/cm² (95% CI, 18.33-19.78; $p < 0.001$). On the PRF-treated side, mean hair density increased to 158.77 ± 13.53 hairs/cm², with a mean gain of 25.77 hairs/cm² (95% CI, 24.90-26.64; $p < 0.001$). The mean gain was 6.71 hairs/cm² greater with PRF than with PRP (95% CI, 6.39-7.04; $p < 0.001$). At final follow-up, the paired mean difference in hair density was 6.80 hairs/cm² (95% CI, 6.35-7.25; $p <$

Table 2: Hair-density outcomes on the PRP- and PRF-treated scalp halves (N = 35)

Outcome	*PRP-treated right scalp, mean ± SD*	*PRF-treated left scalp, mean ± SD*	*Paired difference, PRF-PRP (95% CI)*	*p-value*
Baseline hair density (hairs/cm²)	132.91 ± 12.02	133.00 ± 11.87	0.09 (-0.41 to 0.58)	0.727
Final hair density (hairs/cm²)	151.97 ± 13.57	158.77 ± 13.53	6.80 (6.35 to 7.25)	<0.001
Change from baseline (hairs/cm²)	19.06 ± 2.11	25.77 ± 2.53	6.71 (6.39 to 7.04)	<0.001

Positive paired differences favor PRF. *P* values were obtained using paired Student t tests. Values below 0.001 are shown as $P < 0.001$. CI, confidence interval; PRF, platelet-rich fibrin; PRP, platelet-rich plasma; SD, standard deviation.

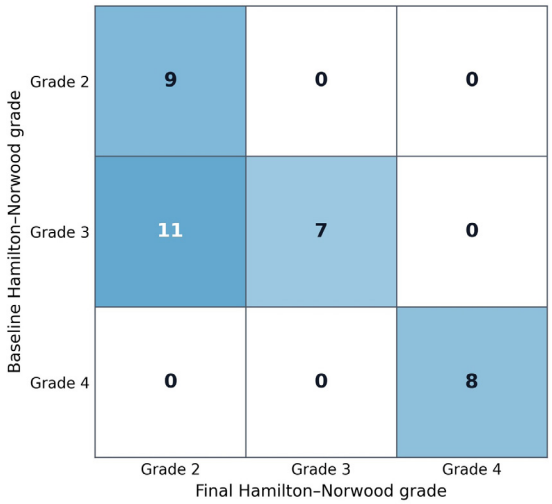

Figure 2: Transition in Hamilton-Norwood grade from baseline to final follow-up on the PRP-treated scalp. Values are participant counts; 11 improved by one grade and 24 remained unchanged (Wilcoxon signed-rank test, $P < 0.001$)

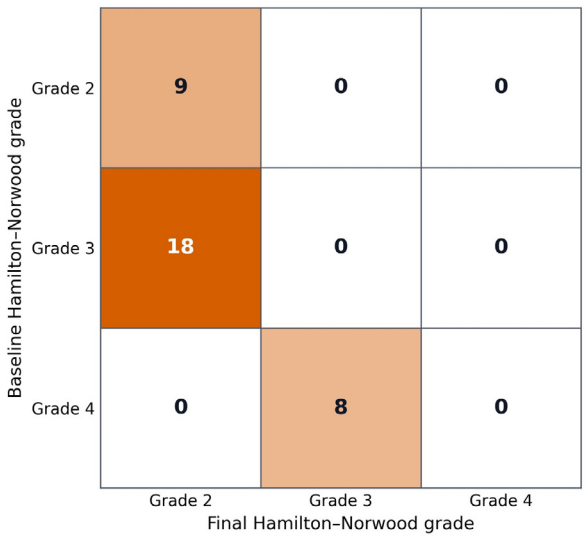

Figure 3: Transition in Hamilton-Norwood grade from baseline to final follow-up on the PRF-treated scalp. Values are participant counts; 26 improved by one grade and 9 remained unchanged (Wilcoxon signed-rank test, $P < 0.001$)

Table 3: Adverse effects on the PRP- and PRF-treated scalp halves (N = 35)

Adverse effect	*PRP-treated right scalp, n (%)*	*PRF-treated left scalp, n (%)*
None	27 (77.14)	34 (97.14)
Transient erythema	5 (14.29)	1 (2.86)
Mild procedural pain	3 (8.57)	0 (0.00)
Total	35 (100.00)	35 (100.00)

Exact McNemar test for any adverse effect versus none: P = 0.039. PRF, platelet-rich fibrin; PRP, platelet-rich plasma.

0.001) (Table 2). All 35 participants had a greater hair-density gain on the PRF-treated side; the participant-level advantage ranged from 5 to 9 hairs/cm² (Figure 1).

Hamilton-Norwood Grade

On the PRP-treated side, 11 (31.43%) participants improved by one grade and 24 (68.57%) remained unchanged; none worsened ($p < 0.001$). On the PRF-treated side, 26 (74.29%) improved by one grade and 9 (25.71%) remained unchanged; none worsened ($p < 0.001$). At final follow-up, the PRF-treated side had a lower grade than the PRP-treated side in 15 (42.86%) participants and the same grade in 20 (57.14%); it was not worse in any participant ($p < 0.001$). Grade transitions are shown in Figures 2 and 3.

Safety

An adverse effect occurred on 8 (22.86%) PRP-treated scalp halves and 1 (2.86%) PRF-treated scalp half ($p = 0.039$). Transient erythema occurred on 5 (14.29%) PRP-treated sides and 1 (2.86%) PRF-treated side; mild procedural pain occurred on 3 (8.57%) PRP-treated sides and on no PRF-treated side (Table 3). All events were localized, self-limited, did not interrupt treatment, and resolved without medication or other specific intervention; they therefore met the reporting definition of mild.

Discussion

This within-patient comparison showed that both platelet preparations improved hair density and Hamilton-Norwood grade after three monthly sessions, but PRF

consistently produced the better short-term response. Baseline hair density was nearly identical between scalp halves, and every participant had a greater density gain with PRF. The clinical grade findings supported the quantitative result: one-grade improvement occurred in almost three-quarters of PRF-treated halves compared with approximately one-third of PRP-treated halves. PRF was also associated with fewer minor adverse effects.

The improvement observed with PRP is consistent with randomized half-head studies by Gentile *et al*. and Alves and Grimalt, which demonstrated objective gains after serial PRP treatment.[12,13] Shapiro *et al*. also evaluated PRP in a randomized split-scalp design and highlighted the heterogeneity of individual response despite controlled treatment.[14] Systematic reviews and meta-analyses have generally found a positive effect of PRP on hair density, while emphasizing variation in preparation methods, treatment schedules, and outcome measurement.[15,16] The mean gain of 19.06 hairs/cm² on the PRP-treated side therefore lies within the direction and magnitude of benefit reported in the existing evidence base.

Evidence for injectable PRF in AGA is less mature but increasingly supportive. Schiavone *et al*. reported clinical improvement with an injectable platelet-leukocyte-fibrin preparation, while Bhoite *et al*. documented visible and dermoscopic improvement in an Indian case series.[17,18] A prospective study by Yao *et al*. also reported improvement after serial injectable PRF sessions.[19] Rani *et al*., in a larger 100-patient randomized parallel-group comparison, reported improvement with both PRP and injectable PRF, with greater efficacy, higher satisfaction, and fewer adverse effects in the injectable PRF group.[20] The present study does not supersede that trial; rather, it adds complementary within-patient evidence by applying both preparations simultaneously to opposite scalp halves. This design reduces between-person variation in genetic susceptibility, age, disease duration, baseline systemic milieu, and treatment responsiveness, although its fixed side allocation introduces a different source of bias. The concordant findings across these distinct designs strengthen the signal favoring injectable PRF while still requiring cautious interpretation.

The relative advantage of PRF is biologically plausible but should not be treated as a proven mechanism. PRP is produced from anticoagulated blood and remains a liquid platelet concentrate, whereas injectable PRF is prepared without anticoagulant and subsequently polymerizes into a fibrin network in situ.[6,7] This matrix can retain platelets, leukocytes, and signaling molecules and may extend their local residence and release compared with a more rapidly dispersing preparation. Experimental work indicates that lower centrifugal force can increase growth-factor release from PRF matrices,[21] liquid injectable PRF can form a provisional scaffold after administration,[22] and different platelet-rich formulations produce distinct growth-factor-release and cell-migration profiles.[23] Prolonged signaling to dermal papilla cells, perifollicular vasculature, and extracellular matrix could therefore contribute to the stronger short-term response observed with PRF. However, platelet dose, leukocyte composition, fibrin architecture, and growth-factor concentrations were not measured in this study, so the mechanism remains inferential.

Both interventions were well tolerated. The observed erythema and procedural pain were mild and self-limited, consistent with the safety profile in PRP trials and injectable PRF series.[12,18,24] The lower adverse-event frequency with PRF may improve acceptability when repeated sessions are required, but the small number of events warrants cautious interpretation.

A major strength was the split-scalp design, which controlled for genetic susceptibility, age, disease duration, systemic factors, and individual treatment responsiveness. Objective trichoscopic hair-density assessment, ordinal clinical grading, complete follow-up, and comparable baseline density further supported internal consistency. Nevertheless, right-left allocation was fixed rather than randomized, and formal blinding of participants and assessors was not documented. Injector handedness, sleeping preference, differential sun exposure, and scalp-side dominance were not recorded. These factors could introduce systematic side-related bias. A crossover was not part of the approved protocol and would also be difficult to interpret because needling, local diffusion, and potentially persistent biologic effects may create carryover between periods or scalp halves.[14] The within-patient design therefore improves control of participant-level confounding but does not eliminate allocation or measurement bias.

Limitations

The study was limited by a feasibility sample of 35 participants and the absence of an a priori effect-size-based sample-size calculation. It was conducted at a single center and included only men with Grade II-IV AGA; women, advanced disease, and patients receiving standard pharmacologic therapy were not represented.

Side allocation was fixed, formal participant or assessor blinding was not documented, and potential side-related influences were not measured. Rotor radius and relative centrifugal force were not recorded, and platelet concentration, leukocyte composition, and growth-factor concentrations were not characterized.[25] Qualitative trichoscopic features were recorded for baseline phenotyping but were not analysed as serial efficacy endpoints. Most importantly, final assessment occurred only one month after the third session, permitting evaluation of short-term response but not durability, maintenance requirements, late adverse effects, or long-term comparative effectiveness.

Conclusion

Three monthly sessions of both PRP and injectable PRF improved short-term trichoscopic hair density and Hamilton-Norwood grade in men with mild-to-moderate AGA. Under the fixed-side, non-randomized split-scalp protocol, PRF was associated with a greater mean density gain, more frequent one-grade improvement, and fewer minor adverse effects than PRP. These findings provide complementary within-patient evidence but should not be generalized as definitive superiority. Larger studies with randomized side allocation, blinded assessment, standardized product characterization, and longer follow-up are required to establish durability and comparative effectiveness.

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