Scholars Journal of Applied Medical Sciences
Abbreviated Key Title: Sch J App Med Sci
ISSN 2347-954X (Print) | ISSN 2320-6691 (Online)
Journal homepage: https://saspublishers.com

OPEN ACCESS

Dermatology

Clinical Efficacy of PRP-Therapy, Minoxidil, and Their Combination in the Treatment of Men with Androgenetic Alopecia

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DOI: https://doi.org/10.36347/sjams.2024.v12i08.027 | **Received:** 02.07.2024 | **Accepted:** 06.08.2024 | **Published:** 28.08.2024

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Abstract **Original Research Article**

Background*:** Platelet-rich plasma (PRP) therapy holds promise as a treatment for androgenetic alopecia (AGA). This study aimed to compare the clinical efficacy of PRP therapy, minoxidil, and their combination in treating men with AGA, and to evaluate PRP's effects on hair follicle (HF) cell proliferation via skin biopsy. ***Materials and Methods*:** This prospective study was carried out at tertiary hospital from June 2021 to June 2022. A total of 69 men were divided into three groups: PRP therapy, minoxidil, and combined therapy. Clinical efficacy was assessed through hair morphometrics, while cell proliferation was evaluated using antibodies against β-catenin, CD34, Ki67, and Dkk-1. ***Results*:** PRP therapy proved more effective than minoxidil ($p = 0.005$). Combined therapy significantly outperformed minoxidil monotherapy ($p < 0.0001$) and PRP monotherapy ($p = 0.007$). Following PRP application, there was a notable increase in the absolute and relative expression areas of β-catenin and CD34, alongside a significant rise in the Ki67+ index. ***Conclusions: PRP represents a viable treatment option for AGA. Combining PRP with minoxidil shows promise in enhancing treatment outcomes for AGA by increasing HF cell proliferative activity and improving hair morphology.
Keywords: platelet-rich plasma (PRP); androgenetic alopecia (AGA); minoxidil; hair morphometry; hair follicle cell proliferation.

INTRODUCTION

Androgenetic alopecia (AGA), commonly known as male pattern baldness, is a prevalent condition affecting a significant proportion of the male population. Characterized by progressive hair thinning and loss, AGA can have profound psychological and social impacts. Over the years, various treatments have been explored to manage and potentially reverse this condition. Among these, Platelet-Rich Plasma (PRP) therapy and Minoxidil stand out due to their distinct mechanisms of action and therapeutic benefits. This introduction aims to delve into the efficacy of PRP therapy, Minoxidil, and their combination in treating men with androgenetic alopecia [1-3].

Platelet-Rich Plasma (PRP) therapy has emerged as a promising treatment for AGA due to its potential to stimulate hair growth through autologous blood-derived growth factors. PRP involves centrifuging a patient's blood to concentrate platelets, which are then injected into the scalp. These platelets release growth factors that can promote hair follicle regeneration and increase hair density. Studies have shown that PRP therapy can significantly improve hair count, hair thickness, and hair root strength, making it a viable option for patients seeking non-surgical interventions for hair loss [4-7].

Minoxidil, a topical medication, has been a cornerstone in AGA treatment for decades. Originally developed as an antihypertensive drug, Minoxidil was found to have the side effect of promoting hair growth. It works by prolonging the anagen phase (growth phase) of the hair cycle, thus preventing hair follicles from shrinking [8-11]. Regular application of Minoxidil has been proven to increase hair density and reduce hair loss. While its exact mechanism is not fully understood, Minoxidil is widely regarded as an effective treatment for male pattern baldness, especially in the early stages of hair loss.

Combining PRP therapy with Minoxidil may offer synergistic benefits, enhancing the efficacy of both treatments. PRP's regenerative properties, coupled with Minoxidil's ability to extend the hair growth phase, could potentially yield superior results compared to either treatment alone. Preliminary studies suggest that

the combination therapy can lead to greater improvements in hair density, thickness, and overall hair health. This integrated approach could be particularly beneficial for patients who have not responded adequately to monotherapy [12-15].

Both PRP therapy and Minoxidil have demonstrated efficacy in treating androgenetic alopecia in men. While PRP therapy leverages the body's natural growth factors to rejuvenate hair follicles, Minoxidil acts by prolonging the hair growth cycle. Their combination could represent a more effective strategy, offering hope to those affected by this common yet distressing condition.

Objective

To assess the clinical Efficacy of PRP-Therapy, Minoxidil, and Their Combination in the Treatment of Men with Androgenetic Alopecia.

METHODOLOGY

This prospective study was carried out at tertiary hospital from June 2021 to June 2022. Sixty-nine men aged 18 to 53 years (mean age 29.7 ± 1.9 years) were observed in the study, with most participants (81.1%) being between 21 and 40 years old. The duration of AGA varied from 11 months to 12 years, averaging 3.3 ± 0.61 years. According to the Norwood-Hamilton scale, 91.3% of the patients had AGA degrees II-IV.

Inclusion criteria required male patients with AGA degrees I-IV on the Norwood-Hamilton scale. Patients were offered treatment options—PRP, Minoxidil, or their combination—along with explanations of each method's advantages and expected clinical effects. The patients were then divided into three groups based on their chosen treatment. Exclusion criteria included AGA degree VI or higher, confirmed hyperandrogenism, inflammatory scalp processes, usage of external hair growth stimulants, medications affecting steroid hormones, endocrinopathies affecting steroid hormones, and hair transplants. Additional exclusion criteria for PRP therapy included medications lowering platelet levels, leukocytosis or thrombocytopenia, treatment side effects, and a tendency to form keloid or hypertrophic scars.

The first group received PRP injections, the second group received PRP combined with 5% Minoxidil solution, and the third group used only 5% Minoxidil solution. Minoxidil was applied twice daily to the dry scalp without rinsing for four months. PRP therapy involved four procedures at one-month intervals. The study was designed as a prospective, controlled, randomized trial with a four-month follow-up period. Pre-treatment observation groups were similar in age, AGA degree, and morphometric parameters. Control measurements were taken before treatment and after four months. Group 3 was assessed after four months of Minoxidil use, while Groups 1 and 2 were evaluated one month after their fourth PRP session. Evaluators were blinded to treatment groups and periods.

For PRP, 18 mL of venous blood was collected, centrifuged twice, and 4 mL of PRP was injected into the scalp. The average platelet count in PRP was 882.5 ± 143.62 × 10^9/L. Clinical efficacy was assessed using hair growth morphometric indicators via a digital video camera and software. Hair density, vellus and telogen hair proportions, and average hair diameter were measured.

Hair density before treatment ranged from 381 to 479/cm^2, lower than the regional average of 540 to 600/cm^2. Vellus hair proportion and average diameter were also below regional averages. Treatment effects were assessed by hair density, diameter, and proportions of vellus and telogen hair. Significant improvements in multiple indicators indicated high therapy effectiveness. Skin biopsies for immunohistochemistry were performed before and after PRP therapy, assessing markers like Ki67, Beta-catenin, CD34, and DKK-1 using digital microscopy and morphometry.

Statistical analysis was performed using the R programming language. Significant results were considered with a p-value of < 0.05.

RESULTS

Complex Therapy (PRP + Minoxidil), PRP alone, and Minoxidil alone. Before treatment, measurements for hair density on 1 cm^2 were 408.4 ± 43.6, 381.5 ± 45.4, and 479.3 ± 51.5, respectively, for each group. After treatment, these values changed to 539.6 ± 52.1, 426.1 ± 50.1, and 554.8 ± 53.5, showing dynamics of change of 131.2, 44.6, and 75.5, respectively, with significant p-values of 0.00004, 0.000067, and 0.00073. The share of vellus hair decreased by 30%, 17%, and 2%, respectively, with p-values of 0.00082, 0.002225, and 0.7647. Average diameter of all hair increased by 26%, 12%, and 2%, respectively, with p-values of 0.00004, 0.001947, and 0.338. The share of telogen hair decreased by 39%, 16%, and 5%, respectively, with p-values of 0.00008, 0.02836, and 0.338.

Table 1: Dynamics of morphometric indicators of hair growth

		Complex Therapy (PRP + Minoxidil)			PRP			Minoxidil		
Variable	**Unit of Measurement**	**Before Treatment**	**After Treatment**	**Dynamics of Change**	**Before Treatment**	**After Treatment**	**Dynamics of Change**	**Before Treatment**	**After Treatment**	**Dynamics of Change**
	Abs.	408.4 ± 43.6	539.6 ± 52.1	131.2	381.5 ± 45.4	426.1 ± 50.1	44.6	479.3 ± 51.5	554.8 ± 53.5	75.5
Hair density on 1 cm^2	Δ(%)			32%			12%			16%
	p-value			0.00004			0.000067			0.00073
	Abs.	51.8 ± 6.3	36.5 ± 7.4	−15.3	49.6 ± 7.3	41.0 ± 7.7	−8.6	34.4 ± 5.3	35.2 ± 6	0.8
Share of vellus hair, %	Δ(%)			−30%			−17%			2%
	p-value			0.00082			0.002225			0.7647
Average	Abs.	38.8 ± 4.2	48.8 ± 5.1	10.0	39.8 ± 3.5	44.4 ± 4.5	4.6	39.3 ± 1.9	40 ± 2.9	0.7
diameter of all	Δ(%)			26%			12%			2%
hair, μm	*p*-value			0.00004			0.001947			0.338
	Abs.	50.4 ± 7.3	30.7 ± 7.4	−19.7	42.0 ± 6.4	35.3 ± 7.0	−6.8	42.8 ± 6.7	44.9 ± 6.9	2.1
Share of telogen hair, %	Δ(%)			−39%			−16%			5%
	p-value			0.00008			0.02836			0.338

The comparative analysis of treatment effectiveness between observation groups 1 (PRP) and 2 (PRP + Minoxidil) revealed significant differences in key indicators of hair growth. Group 2 demonstrated superior outcomes with a notable increase in hair density (131.2 hairs per square centimeter) compared to Group 1 (44.6 hairs per square centimeter), with a highly significant p-value of 0.0001. Additionally, Group 2 exhibited a greater reduction in vellus hair (15.3% decrease) compared to Group 1 (8.6% decrease), though this difference was not statistically significant (p = 0.0715). The average diameter of all hair increased significantly more in Group 2 (10.0 micrometers) than in Group 1 (4.6 micrometers), with a p-value of 0.0071. Moreover, Group 2 showed a substantial decrease in telogen hair (19.7% reduction), significantly more than Group 1 (6.8% reduction), with a p-value of 0.0025.

Table 2: Comparison of the effectiveness of treatment in observation groups 1 and 2

Change in Variable (Abs.)	**Monitoring Groups**		**Comparative Evaluation of Efficacy in Groups 1 and 2**
	1 (PRP)	**2 (PRP + Minoxidil)**	
Hair density on 1 cm^2	44.6	131.2	0.0001
Share of vellus hair, %	−8.6	−15.3	0.0715
Average diameter of all hair, μm	4.6	10.0	0.0071
Share of telogen hair, %	−6.8	−19.7	0.0025

Group 2 showed significantly higher improvements in hair density (131.2 vs. 75.5 hairs/cm^2, p = 0.0347), a notable reduction in vellus hair (−15.3% vs. +0.8%, p = 0.0009), a substantial increase in average hair diameter (10.0 vs. 0.7 μm, p = 0.00001), and a significant decrease in telogen hair (−19.7% vs. +2.1%, p = 0.00003) compared to Group 3. These results underscore the added benefit of PRP alongside minoxidil, highlighting its efficacy in enhancing hair growth metrics and supporting its role as a superior treatment option for androgenetic alopecia compared to minoxidil alone.

Table 3: Comparison of the effectiveness of treatment in observation groups 2 and 3

Change in Variable (Abs.)	Monitoring Groups		Comparative Evaluation of Efficacy in Groups 1 and 2
	1 (PRP)	2 (PRP + Minoxidil)	
Hair density on 1 cm^2	131.2	75.5	$p = 0.0347$
Share of vellus hair, %	−15.3	0.8	$p = 0.0009$
Average diameter of all hair, µm	10.0	0.7	$p = 0.00001$
Share of telogen hair, %	−19.7	2.1	$p = 0.00003$

The results for hair density on 1 cm² ranged from a minimum decrease of 57% to a maximum increase of 127%, with quartiles showing median improvement at 20% and substantial variation between 5% and 44%. Average diameter of all hair ranged from a decrease of 46 µm to an increase of 177 µm, with quartiles demonstrating median growth at 13 µm, ranging from a decrease of 3 µm to an increase of 28 µm.

Table 4: Dynamics of hair growth indicators after treatment by quartiles of growth distribution

Variable	Minimum Value (%)	Q1 %)	Median (%)	Q3 (%)	Maximum Value (%)
Hair density on 1 cm^2	−57	5	20	44	127
Average diameter of all hair, µm	−46	−3	13	28	177
Share of vellus hair, %	230	15	−19	−41	−74
Share of telogen hair, %	960	14	−17	−48	−90

Group 2 (PRP + Minoxidil) showed the highest effectiveness, with 14 cases (64%) categorized as highly efficient and 8 cases (36%) demonstrating a positive clinical effect. Group 1 (PRP) had 9 cases (36%) rated as highly efficient and 7 cases (28%) showing a positive effect. Group 3 (Minoxidil) had 13 cases (59%) with a positive clinical effect but did not achieve high efficiency in any cases. Overall, the combined therapy (Group 2) showed the most favorable outcomes, underscoring its efficacy in treating androgenetic alopecia compared to PRP or minoxidil alone.

Table 5: Assessment of clinical efficacy

	1 (PRP)		2 (PRP + Minoxidil)		3 (Minoxidil)		Total
Effectiveness	Abs.	%	Abs.	%	Abs.	%	
Highly efficient	9	36	14	64	0	0	23
Positive clinical effect	7	28	8	36	13	59	28
Lack of clinical effect	9	36	0	0	9	41	18

DISCUSSION

PRP therapy is a simple, cost-effective, and feasible treatment for hair loss, serving as an alternative for AGA. Our study demonstrated significant improvements in patients receiving PRP injections, with hair density and average diameter increasing by 12%, vellus hair decreasing by 17%, and telogen hair by 16%, aligning with global literature on PRP efficacy. Among 47 patients treated with PRP, only 4 (8.5%) reported injection site pain, which did not necessitate stopping treatment. No other side effects were noted.

In the control group treated with 5% minoxidil solution, hair density increased by 16%. Comparative analysis showed no significant difference between the PRP and minoxidil groups regarding hair density (12% and 16%, respectively). However, PRP outperformed minoxidil in other hair growth indicators: average hair diameter was 6.3 times greater, vellus hair share was 11.8 times lower, and telogen hair share was 3.1 times lower. The superior results of PRP might be due to the short average follow-up, suggesting that longer studies are needed for conclusive results. Minoxidil's effectiveness is better evaluated over 6–12 months. Our data also indicate that PRP has a delayed effect, improving hair growth dynamics over 8–12 months.

One study found greater telogen reduction with PRGF compared to topical minoxidil for AGA treatment. Recently, another study also noted PRP therapy's superiority over minoxidil, suggesting it as a valuable alternative for AGA [17]. The combined use of PRP and minoxidil was notably effective, as shown other study, demonstrating enhanced clinical effects compared to monotherapy with minoxidil or finasteride [18]. Other study found higher patient satisfaction with the combination of minoxidil, PRP, and dermoroller compared to minoxidil alone, assessed after 6 months [19].

Our study confirmed the high clinical efficacy of combined therapy, surpassing PRP monotherapy and minoxidil in hair density by 1.74 times, hair shaft thickness by 14.3 times, telogen hair share by 9.3 times, and vellus hair share by 19.1 times. The combination therapy exceeded PRP monotherapy in hair density by 2.9 times, hair shaft diameter by 2.2 times, and telogen hair share by 2.9 times, although the difference in vellus

hair share (1.8 times) was not statistically significant ($p = 0.0715$).

Minoxidil does not affect testosterone levels or androgen sensitivity in hair follicles but prolongs the anagen phase and enhances dermal papilla cell proliferation. PRP and minoxidil together potentiate each other's actions, promoting hair growth. In 2014, PRP proved effective for AGA patients resistant to minoxidil and finasteride. Minoxidil's active metabolite, minoxidil sulfate, stimulates hair growth, with resistance linked to low sulfotransferase activity. Platelets exhibit minoxidil sulfotransferase activity, suggesting a potential link to PRP's efficacy combined with minoxidil.

CONCLUSION

The enhancement of β-catenin, Ki67, and CD34 protein expression following PRP therapy signifies processes that positively influence hair morphology. PRP's impact on cell proliferation, apoptosis, and prolongation of the anagen phase of the hair follicle cycle is reflected in morphological changes such as reduced telogen and vellus hair, increased hair count, and thicker average hair diameter. Our clinical and immunohistochemical findings align with previous in vitro studies on PRP's molecular and biological effects on hair follicles.

Comparative assessment of treatment outcomes between minoxidil monotherapy and PRP monotherapy showed no differences solely in hair density. However, PRP demonstrated significantly superior efficacy in other metrics ($p \leq 0.0243$), underscoring its promise as an AGA treatment. The benefits of combined therapy exceeded those of PRP alone and minoxidil, making it a viable option for patients with AGA up to Norwood–Hamilton scale stage 5.

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