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Case Series

The efficacy of tretinoin gel 0.1% followed by topical minoxidil-5% in individuals with androgenetic alopecia

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ABSTRACT

Androgenetic alopecia (AGA) is a progressive hair loss condition, with a higher prevalence among males aged 30-50 years in the Indian population. Minoxidil, a topical treatment, is commonly used but shows variable efficacy, particularly in non-responders. Recent studies suggest that combining minoxidil with tretinoin may enhance its effectiveness by increasing scalp absorption and improving hair follicle activity. This case series included 20 patients with AGA (male Norwood-Hamilton grades II-V and female Ludwig grades I-II), clinically diagnosed as non-responders to minoxidil. Participants received a combination therapy of 0.1% tretinoin gel and 5% minoxidil solution over 90 days. Improvements were observed in trichoscopic parameters where 32.9% increase in hair count and density, 3.5% rise in anagen-phase hairs, and 4.8% increase in hair thickness. Investigator global photography assessments revealed 20% of participants showed 51-75% improvement. Advanced AGA grades showed partial reversal. Patient self-assessments indicated 50% improvement in hair quality, 70% in hair coverage, and 75% in overall appearance. Most participants reported new hair growth (80%) and satisfaction with treatment. The combination of 0.1% tretinoin gel and 5% minoxidil demonstrated efficacy in improving hair growth and patient satisfaction in AGA patients who are non- responder to minoxidil.

Keywords: Androgenetic Alopecia, Minoxidil, Tretinoin, Hair growth, Combination therapy

INTRODUCTION

Androgenetic alopecia (AGA) is a common progressive hair loss condition influenced by genetic, hormonal, and environmental factors. It affects individuals across various demographics, with a particularly high prevalence among males aged 30-50 years in the Indian population, reported at 58%.[1] AGA is characterized by the gradual miniaturization of hair follicles, resulting in the transformation of terminal hairs into vellus hairs. While the condition predominantly affects Caucasians, its prevalence is relatively lower among African Americans, Chinese, and Japanese populations.[2] Minoxidil, a topical vasodilator, remains the cornerstone of FDA-approved treatment for AGA, primarily due to its ability to prolong the anagen phase and stimulate hair growth. Despite its widespread use, the response to minoxidil therapy is highly variable, with efficacy limited to 30-40% of patients.[3] This variability has been attributed to differences in sulfotransferase enzyme (SULT1A1) activity in hair follicles, which is necessary for converting minoxidil into its active form, minoxidil sulfate.[4,5]

To improve minoxidil response, topical retinoids such as tretinoin (all-trans-retinoic acid), have been investigated for their ability to enhance minoxidil's efficacy by facilitating its sulfonation, thereby increasing its

bioavailability. When combined with minoxidil, tretinoin may improve treatment outcomes in patients categorized as limited or non-responders.[6,7] Against this background, the present study aimed to evaluate the safety and efficacy of a novel formulation ST-Rich Duo™, which comprising topical tretinoin gel (0.1% w/v) (ST-Rich Booster) and topical minoxidil 5% w/v (ST-Rich M Solution) for managing AGA in patients with limited or no response to minoxidil monotherapy. This prospective analytical study was conducted over 90 days in 20 patients with male and female pattern hair loss attending the Trichology OPD at Cutis Hospital, Bengaluru.

Eligible participants, aged 18-45 years, included males with Norwood-Hamilton grades II-V and females with Ludwig grades I-II, clinically diagnosed as minoxidil non-responders based on global photography assessment. Patients were excluded if they had used isotretinoin, scalp radiation, or chemotherapy within one year; other AGA treatments or botanicals/nutraceuticals for hair regrowth in the previous six months, had uncontrolled hypertension or hypotension, active scalp conditions, a history of scalp reduction, hair weave, pregnancy or lactation. The treatment protocol involved nightly application of 1 mL tretinoin gel followed by 1 mL minoxidil solution after 30 minutes, with an additional morning application of minoxidil. Participants were instructed to maintain proper scalp hygiene and adhere to application guidelines.

CASE SERIES

Among 20 participants enrolled, 17 were males and 3 were females, ranging from 22 and 42 years of age, with an average AGA duration of 3.05 years. At baseline, the AGA grades ranged from grade II to V for male participants and grade L-1 to L-2 for female participants. Post-treatment, showed varying degrees of clinical improvement. Among males with grade V AGA, three showed improvements to grade IV or III, while the others remained unchanged. Of the four participants with grade IV, one improved to grade III. Participants with grade III and grade II AGA maintained their baseline grades. Among female participants, two with grade L-1 remained stable, while one with grade L-2 improved to grade L-1 (Table 1 and Figure 1-5).

The investigator global photography assessment, which rated visual improvement on a scale of 0 to 4 (0-no improvement to 4-76-100% improvement). The highest score of 4 was observed in one participant with improvement from grade V to III. Most other improvements fell within the 1-3 range as mentioned in Table 1.

The trichoscopic evaluation revealed improvements in hair parameters after treatment. Hair count and hair density increased by 32.9%, while the total number of follicular units increased by 24.3%. Although the proportion of anagen-phase hairs improved by 3.5% and telogen-phase hairs decreased by 9.0%. Mean hair thickness increased by 4.8%, reflecting improved hair quality. Terminal and vellus hair percentages showed minor changes, and noted in Table 2.

The subject self-assessment showed a predominantly positive response to the treatment. HGI scoring revealed 50% improvement in hair quality, 70% increase in hair coverage, and 65% reduction in thinning scalp area. HGSS assessment showed 65% satisfaction with hair coverage, 75% improvement in overall appearance, and 80% reporting new hair growth. A minority reported no change, and very few noted a decrease in hair-related parameters, indicating an overall favourable outcome (Table 3).

Table 1: Demography and investigator global photography assessment.

Parameters	Category	N	Percentage (%)
Gender	Male	17	85
	Female	3	15
Age distribution (in years)	≤25	3	15
	26-35	13	65
	>35	4	20
Disease duration (in years)	≤2	7	35
	2.1-4	12	60
	>4	1	5
Baseline AGA grade (males)	Grade II	1	5
	Grade III	6	30
	Grade IV	3	15
	Grade V	7	35
Baseline AGA grade (females)	L-1	2	10
	L-2	1	5
Post-treatment AGA grade (males)	Grade II	1	5
	Grade III	8	40
	Grade IV	3	15
	Grade V	5	25
Post-treatment AGA grade (females)	L-1	3	15

Continued.

Parameters	Category	N	Percentage (%)
Investigator global assessment score*	1	7	35
	2	7	35
	3	5	25
	4	1	5

*0: No improvement; 1: 1-25% improvement; 2: 26-50% improvement; 3: 51-75% improvement; 4: 76-100% improvement

Table 2: Trichoscopy assessment.

Parameters in average	Before	After	% Change in improvement
Hair count	147.1	195.5	32.9
Hair density (/cm^2)	162.9	216.5	32.9
Anagen (%	71.7	74.2	3.5
Telogen (%)	28.3	25.8	-9.0
Terminal (%)	55.2	54.7	-0.9
Vellus (%)	45.0	45.3	0.7
Mean thickness (mm)	0.047	0.049	4.8
Total follicular units	89.3	110.9	24.3

"–" denotes decrease in improvement.

Table 3: Patient satisfaction assessment.

Assessment	Questionnaires	Grade	Total	%
Hair growth index (HGI) scoring	The hair quality -terms of thickness and hair shaft appearance	Increase	10	50
		No change	8	40
		Decrease	2	10
	The thinning scalp area	Increase	1	5
		No change	6	30
		Decrease	13	65
	The amount of hair covering the scalp	Increase	14	70
		No change	6	30
		Decrease	0	0
Hair growth satisfaction scale (HGSS)	The appearance of hair covering the scalp	Increase	13	65
		No change	6	30
		Decrease	1	5
	Overall appearance	Increase	15	75
		No change	4	20
		Decrease	1	5
	New hair growth	Increase	16	80
		No change	4	20
		Decrease	0	0

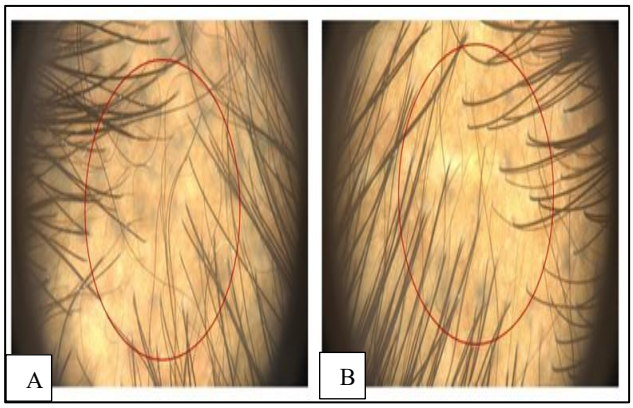

Figure 1 (A and B): Dermoscopic images at baseline (left side) and end of the treatment (right side).

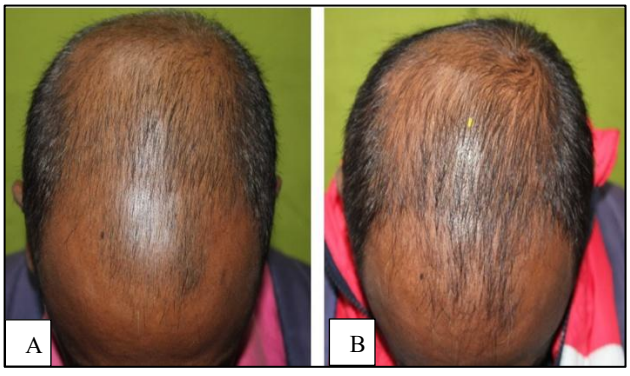

Figure 2 (A and B): Global photographs of AGA patient at baseline (left side) and at treatment endpoint (right side).

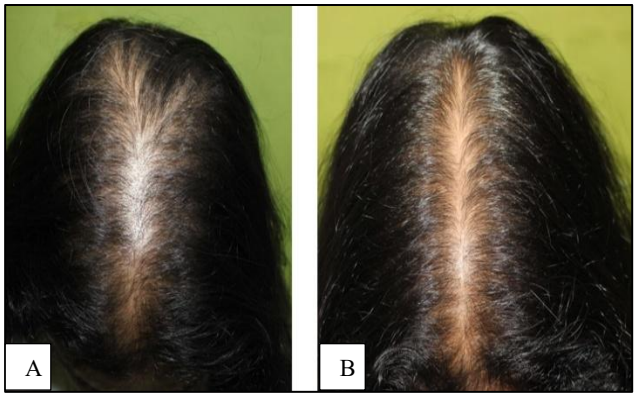

Figure 3 (A and B): Global photographs of FPHL patient at baseline (left side) and at treatment endpoint (right side).

Figure 4 (A and B): Global photographs of AGA patient at baseline (left side) and at treatment endpoint (right side).

DISCUSSION

The combination of minoxidil and tretinoin has shown efficacy in the management of AGA.[8] Tretinoin enhances the absorption of minoxidil by increasing skin permeability and modulating follicular sulfotransferase expression, thereby amplifying its effects on hair growth. It also prolongs the anagen phase, activates critical signaling pathways like Erk and Akt, and prevents apoptosis, resulting in improved hair density and shaft elongation.[7,9] Furthermore, the combination influences the reduction of the stratum corneum barrier and enhances systemic absorption of minoxidil, contributing to its overall effectiveness.[10,11]

In this study, participants exhibited improvements in hair parameters, including hair count, density, and anagen-to-telogen ratios, indicating positive effects on hair regrowth and follicular health. Advanced AGA grades showed partial reversal, while stabilization in lower grades underscored the treatment's preventive potential. The observed efficacy aligns with previous studies, emphasizing the synergistic action of minoxidil and tretinoin in enhancing hair follicle activity and overall outcomes.[7,12]

Importantly, the absence of adverse effects highlights the safety of this combination. Simplified regimens, such as once-daily application of Tretinoin, have demonstrated comparable efficacy to conventional twice-daily treatments, supporting their feasibility and convenience.[13]

Emerging delivery systems, including liposomal formulations, show promise for improving bioavailability and treatment outcomes. While this study utilized a topical solution, future research on advanced delivery technologies could further enhance therapeutic efficacy.[14]

Limitations

The study limitation includes small sample size and relatively short follow-up duration. Larger, multicenter trials with diverse populations are needed to validate these findings. Additionally, exploring long-term efficacy and safety, as well as patient adherence to simplified regimens, would provide deeper insights.

CONCLUSION

This study adds to the growing evidence supporting combination therapies for AGA. The minoxidil-tretinoin combination effectively addressed AGA by enhancing hair regrowth and stabilizing disease progression, with a favourable safety profile. Advances in formulation and application regimens could expand its clinical utility further.

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