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Therapeutic implications of topical cetirizine 1% in treatment of male androgenetic alopecia: A case-controlled study

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Abstract

Background: Androgenetic alopecia (AGA) is the most common form of alopecia in men. Cetirizine, a second-generation H1 blocker, is known for its anti-inflammatory properties and its ability to decrease prostaglandin D2 (PGD2) production.

Aim: To evaluate the efficacy and tolerability of topical cetirizine in male patients with AGA.

Methods: Two groups of 30 patients each (healthy males aged between 22 and 55 years) with different grades of AGA classified according to the Hamilton-Norwood classification were recruited for this study. Group A subjects applied 1 mL of 1% topical cetirizine daily, while group B subjects served as controls and were instructed to apply 1 mL of a placebo solution for 6 months.

Results: Dermoscopic assessment revealed significantly higher hair regrowth among the cetirizine-treated group ($P < .001$). The patients' satisfaction was significantly higher among the cetirizine-treated group ($P < .001$).

Conclusion: The current study highlights a potential role cetirizine might have in treating AGA. It should be noted that studies are lacking in this regard and more randomized and controlled trials are warranted in order to confirm or refute such early findings.

KEYWORDS

androgenetic alopecia, cetirizine, prostaglandin

1 | INTRODUCTION

Androgenetic alopecia (AGA), also known male pattern baldness, is the most common type of progressive hair loss encountered in males. It is a polygenetic condition with variable degree of severity, age of onset, and location of hair loss.[1]

Classification of AGA by the Hamilton-Norwood scale involves 7 grades (I-VII) in order of increasing severity. Male AGA (MAGA) is clearly an androgen-dependent condition in contrast to female AGA (FAGA) where androgen role remains to be not fully understood.[1] A polygenetic mode of inheritance is observed in both conditions with a number of associated genetic polymorphisms.[2]

Cetirizine is a selective second-generation H1 antagonist with proved anti-inflammatory properties and ability to reduce the expression of, and release of, PGD2 from mast cells.[3] Moreover, in vitro studies showed that cetirizine is able to increase the release of PGE2 in a dose-dependent manner.[4]

Only one report in literature had shown that topical use of cetirizine 1% induced hair growth in mild and moderate cases of AGA and reduced densities of vellus hair.[5]

On the basis of the above evidence and lacking studies that confirm the effectiveness of cetirizine in AGA treatment, the aim of this study was to evaluate the efficacy and tolerability of topical cetirizine in male patients with AGA.

2 | PATIENTS AND METHODS

A sample of 60 patients (males aged between 22 and 55 years) with different grades of AGA classified according to the Hamilton-Norwood classification were recruited for this study. All subjects were explained the nature of the procedure and consented to participate in the study. Ethics and research committee approvals were obtained before the onset of the study.

Of the 60 subjects, Group A comprised of 30 patients was used to assess the efficacy and safety of 1 mL daily application of 1% topical cetirizine (galenic lotion composed of cetirizine 1%, 16% cyclo-silicone-pentamer, 96°C of ethyl alcohol) for the treatment of AGA and another group of 30 patients served as controls who received 1 mL of placebo lotion (16% cyclo-silicone-pentamer, 96 C of ethyl alcohol). The patients were randomly assigned to each group and were given the treatments in identical nonlabeled bottles with a code that both the patient and the dispensing doctor were blinded to. All subjects were instructed to use 10 puffs per day (equivalent to 1 mL) and for 6 months. Patients with systemic diseases, suffering from chronic scalp conditions, using any medications that can potentially induce hair loss (eg, Depo-Testosterone, haloperidol, methotrexate, methylprednisolone, prednisone, testosterone, divalproex sodium) within the last 3 months, were all excluded from the study.

Dermoscopic evaluation was carried out by a blinded dermatologist at baseline and by the end of the 6 months. The number of regrowing hairs per cm^2 was reported. Photographic assessment was carried out by two blinded dermatologists at baseline and at the end of treatment using a 4-grade scale (no improvement, mild improvement, moderate improvement, and good improvement) based on the Hamilton-Norwood (HN) classification. Subjective assessment for the degree of improvement in hair quality was carried out using a numeric scale (−1 means worse, 0 means no change, 1 means mild improvement, 2 means moderate improvement, 3 means good improvement, and 4 means excellent improvement). Any side effects or adverse events were recorded.

Statistical analysis was processed through IBM SPSS software version 20.0, and data were analyzed qualitatively and quantitatively. Significance of the obtained results was judged at the 5% level.

3 | RESULTS

Thirty (30) male patients with different grades of androgenetic alopecia were treated by a 1% topical cetirizine lotion, and another thirty (30) male patients who served as controls were treated by a placebo lotion. Ages insignificantly ranged between 22 and 43 years (mean 31.83 ± 6.18) among cases and between 23 and 45 years among controls (mean 32.97 ± 6.26) ($P = .483$) (Table 1; Figure 1).

No significant difference was observed between cases and controls regarding AGA severity ($P = .853$). Among the cases, 10 (33.3%) presented with HN type III AGA and 10 (33.3%) cases presented with HN type IV AGA. Likewise, the majority of control cases complained of type III AGA (n = 9, 30%) and type IV AGA (n = 8, 26.7%). Five cases (16.7%) and 7 controls (23.3%) were diagnosed with type V hair loss, and no subjects were identified with type I AGA (Table 2).

TABLE 1 Age, grade, and family history comparison among both groups

Age (years)	Cases (n = 30)		Control (n = 30)		*t*	*P*
Min. – Max.	22.0–43.0		23.0–45.0		0.706	.483
Mean ± SD.	31.83 ± 6.18		32.97 ± 6.26			
Median (IQR)	30.0(27.0–37.0)		33.0(28.0–38.0)			
	Cases (n = 30)		Control (n = 30)			
Grade	No.	%	No.	%	χ^2	^{MC}p
I	0	0.0	0	0.0	1.580	0.853
II	2	6.7	4	13.3		
III	10	33.3	9	30.0		
IV	10	33.3	8	26.7		
V	5	16.7	7	23.3		
VI	3	10.0	2	6.7		
	Cases (n = 30)		Control (n = 30)			
Family history	No.	%	No.	%	χ^2	*P*
Negative	10	33.3	11	36.7	0.073	.787
Positive	20	66.7	19	63.3		

Abbreviations: χ^2, Chi-square test; MC, Monte Carlo; *t*, Student's t test; *P*, *P* value for comparison between the two studied groups.

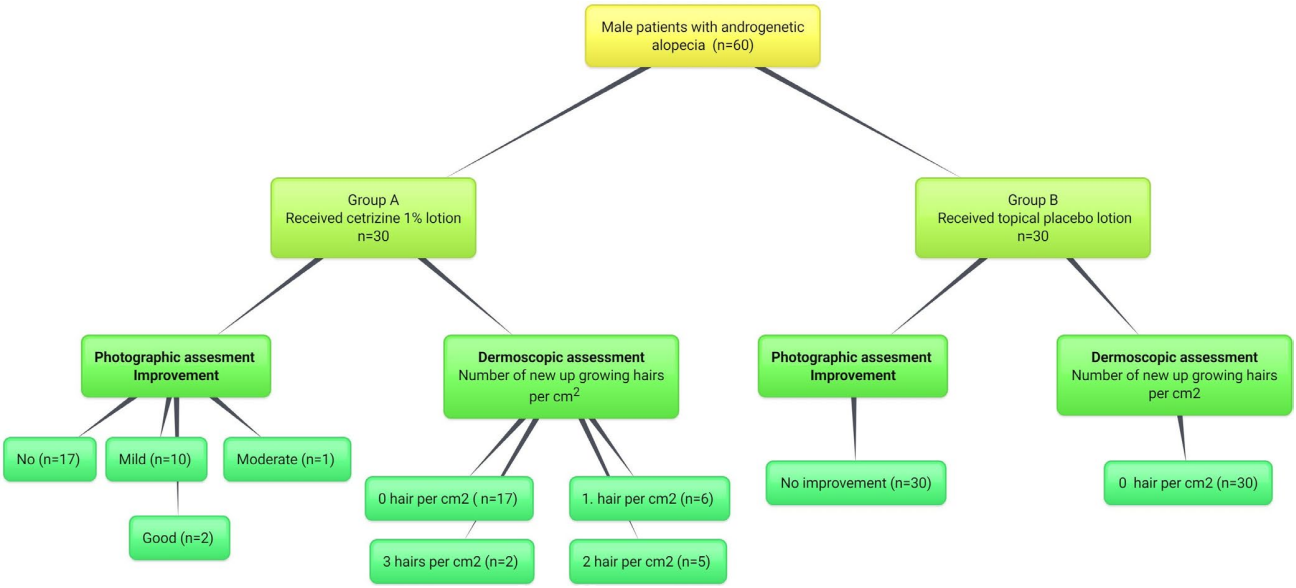

FIGURE 1 Diagrammatic flowchart of study design

TABLE 2 Hair regrowth comparison between both groups

Number of new up growing hairs	Cases (n = 30)		Control (n = 30)			
	No.	%	No.	%	χ^2	^{MC}p
0	17	56.7	30	100.0	16.140	<0.001*
1	6	20.0	0	0.0		
2	5	16.7	0	0.0		
3	2	6.7	0	0.0		

Abbreviations: χ^2, Chi-square test; MC, Monte Carlo; *P*, *P* value for comparison between the two studied groups.
*Statistically significant at $P \leq .05$.

The majority of cases and controls (66.7% and 63.3%, respectively) had a positive family history of AGA ($P < .05$). Both groups showed no significant difference in familial prevalence of AGA ($P = .787$) (Table 3).

Photographic assessment of the control group revealed no improvement among all subjects, while only 17 (56.7%) of the cases demonstrated no improvement. Mild improvement was observed in 10 (33.3%) of the cases, while good improvement was observed in 2 (6.7%) of the cases. The difference in observed improvement among both groups was statistically significant ($P < .001$) (Table 3).

Dermoscopic assessment of regrowing hairs revealed a significant difference between both groups ($P < .001$). Of the 30 cases, 17 (56.7%) demonstrated no new hair growth as per dermoscopy, while 6 (20%) of the cases demonstrated 1 new growing hair per dermoscopic field, 5 (16.7%) of the cases showed 2 growing hair per field, and 2 (6.7%) cases showed 3 growing hairs per field. None of the controls demonstrated any growing hair per dermoscopic evaluation (Figure 2).

Improvement based on self-assessment was significantly higher among cases compared with controls ($P < .001$). Among controls, 26 (86.7%) of the subjects reported no improvement and 4 (13.3%) reported worsening of their condition. In the cases group, 17 (56.7%) of the subjects reported no improvement, 7 (23.3%) reported mild improvement, 5 (16.7%) reported moderate improvement, and only 1 (3.3%) case reported a good improvement (Table 3).

4 | DISCUSSION

The full reason beyond the development of AGA remains to be fully elucidated. A cardinal feature of AGA includes prolongation of the telogen phase and shortening of anagen phase which induces miniaturization of hairs and dysregulation of hair growth cycles.[6]

Treatment of AGA remains to be very challenging with only minoxidil and finasteride being the only approved medications by the United States Food and Drug Administration (US-FDA) and European Medicines Agency (EMA).[7]

Finasteride is a type 2 5α-reductase inhibitor that prevents the conversion of testosterone to dihydrotestosterone (DHT), which is responsible for the miniaturization of the hair follicle seen in MAGA. Finasteride had been associated with decrease in libido, impotence, and post–finasteride syndrome.[8]

TABLE 3 Photographic and self-assessment in both groups

	Cases (n = 30)		Control (n = 30)			
	No.	%	No.	%	χ^2	^{MC}p
Photographic assessment						
No improvement	17	56.7	30	100.0	17.238*	<0.001*
Mild	10	33.3	0	0.0		
Moderate	1	3.3	0	0.0		
Good	2	6.7	0	0.0		
Self-assessment						
No improvement	17	56.7	26	86.7	18.676*	<0.001*
Worse	0	0.0	4	13.3		
Mild	7	23.3	0	0.0		
Moderate	5	16.7	0	0.0		
Good	1	3.3	0	0.0		

Abbreviations: χ^2, Chi-square test; MC, Monte Carlo; *P*, *P* value for comparing between the two studied groups.
*Statistically significant at $P \leq .05$.

Minoxidil is a potassium channel opener drug that results in arteriolar vasodilatation. Minoxidil 2% solution was approved in 1988, while the 5% solution was approved in 1991, and the 5% foam in 2016 for MAGA. Minoxidil use had been adversely associated with irritant contact dermatitis, headache, and hypotension, as well as unwanted body hair growth.[9]

Cetirizine is a selective second-generation H1 antagonist with proved anti-inflammatory properties and ability to reduce the expression and release of PGD2 besides its ability to increase expression and release of PGE2.[3,4]

Only one study in literature assessed the effect of cetirizine on hair density in patients with AGA.[5] It was evident that cetirizine

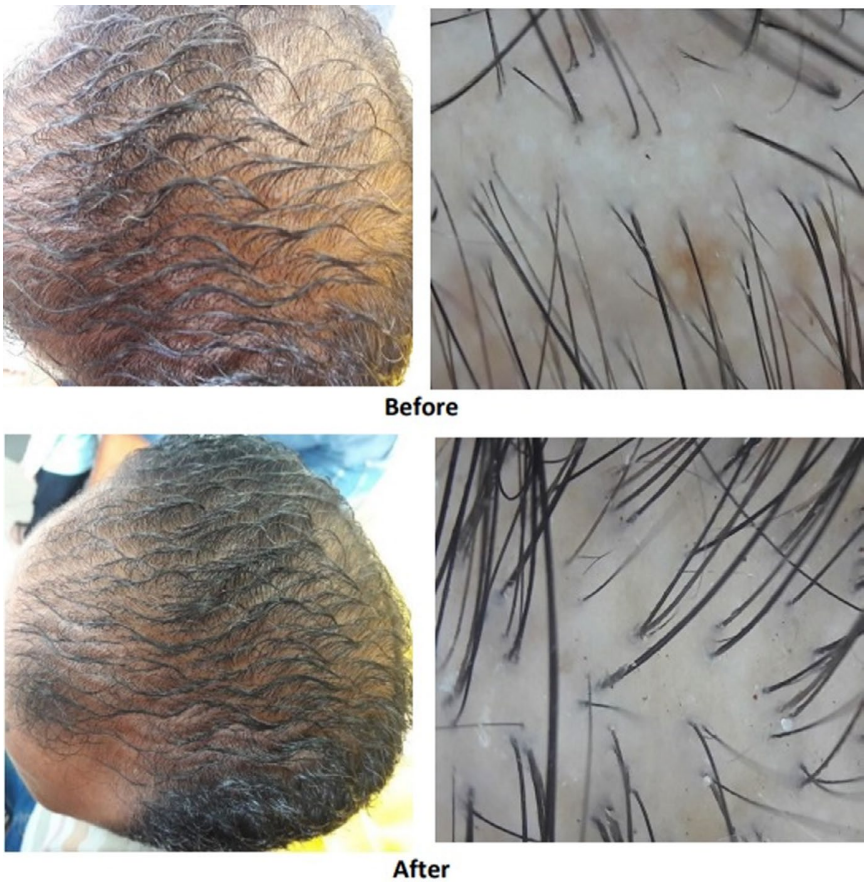

FIGURE 2 Photographic and dermoscopic comparison of a cetirizine 1%–treated patient before and after treatment

increased terminal hair density and diameter besides decreasing vellus hair density. Moreover, a 70-year-old woman with chemotherapy-induced alopecia was treated with a 0.5% cetirizine topical lotion and showed a progressive improvement in her hair density.[10]

Levocetirizine hydrochloride is another H1 receptor antagonist and is the R-enantiomer of cetirizine that is used in many allergic body conditions.[11] It was shown to inhibit the production of PGD2 through binding to cyclooxygenase 2 (COX-2) receptors.[12] In vitro studies reported levocetirizine hydrochloride to inhibit the PGD2-GPR44 pathway and activate the AKT signaling pathway, resulting in proliferation and growth of hDPCs.[13]

Prostaglandins (PG) are reported to play a role in the pathogenesis of AGA. They represent a group of unsaturated fatty acids distributed through various body tissues and are involved in a number of cellular functions including proliferation, differentiation, and apoptosis.[14]

A number of active PG subtypes (prostacyclin, PGD2, PGE2, PGF2α, etc) are derived from the conversion of arachidonic acid under the influence of cyclooxygenase (COX). They exert a number of different functions; however in the follicular unit, PGE2 and PGF2α were found to stimulate hair growth and elongation, while PGD2 was found to limit hair growth and induce miniaturization.[15]

PGD2 was found to activate androgen receptors in the human dermal papilla cells (hDPC) via the protein kinase B (AKT) pathways leading to the release of multiple cytokines that induce follicular apoptosis.[16] Moreover, PGD2 through its effects on G protein–coupled receptor 44 (GR44) found in the outer root sheath of hair follicles and dermal papillae was found to inhibit hair growth cycles and lead to miniaturization of hair follicles.[17] Notably, GR44 receptors, PGD2 mRNA, and protein expression were all found increased in patient complaining of AGA.[18] Of interest, a GR44 receptor antagonist (setipiprant) has shown potentially good results in male AGA when used in doses of up to 4000mgs daily.[19] It is anticipated that it inhibits PGD2 levels inside the outer root sheath of hair follicles.[20]

Topical use of PGD2 was associated with hair loss and inhibition of hair growth cycles in mice treated with hair transplantation.[21] On the contrary, the use of PGE2 was found to induce hair growth in mice models with radiation-induced hair loss. Moreover, PGF2α analogues were approved for the use in improving eyebrow and hair lash growths via improving the local blood circulation.[22]

Limitations to the study include the relatively small sample size and the limited representation of AGA grades among study subjects. Bioavailability of cetirizine in follicular hair sheath and dose-dependent hair growth in comparison with other FDA-approved medications is mandated before judging the appropriateness and safety of the treatment.

The current study highlights a potential role cetirizine might have in treatment of AGA. It should be noted that studies are lacking in this regard and more randomized and controlled trials are warranted in order to confirm or refute such early findings.

CONFLICT OF INTEREST

No conflict of interest.

AUTHOR CONTRIBUTION

All authors contributed equally in producing this work.

DATA AVAILABILITY STATEMENT

Data would be provided upon request.

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REFERENCES

1. Hagenaars SP, Hill WD, Harris SE, et al. Genetic prediction of male pattern baldness. *PLoS Genet*. 2017;13(2):e1006594.
2. Ellis JA, Stebbing M, Harrap SB. Polymorphism of the androgen receptor gene is associated with male pattern baldness. *J Invest Dermatol*. 2001;116:452-455.
3. Charlesworth EN, Kagey-Sobotka A, Norman PS, Lichtenstein LM. Effect of cetirizine on mast cell-mediator release and cellular traffic during the cutaneous late-phase reaction. *J Allergy Clin Immunol*. 1989;83(5):905-912.
4. Roch-Arveiller M, Tissot M, Idohou N, Sarfati G, Giroud JP, Raichvarg D. In vitro effect of cetirizine on PGE2 release by rat peritoneal macrophages and human monocytes. *Agents Actions*. 1994;43(1–2):13-16.
5. Rossi A, Campo D, Fortuna MC, et al. A preliminary study on topical cetirizine in the therapeutic management of androgenetic alopecia. *J Dermatolog Treat*. 2018;29(2):149-151.
6. Danesh-Shakiba M, Poorolajal J, Alirezaei P. Androgenetic alopecia: relationship to anthropometric indices, blood pressure and lifestyle habits. *Clin Cosmet Investig Dermatol*. 2020;13:137-143.
7. Verma K, Tegta GR, Verma G, Gupta M, Negi A, Sharma R. A study to compare the efficacy of platelet-rich plasma and minoxidil therapy for the treatment of androgenetic alopecia. *Int J Trichology*. 2019;11(2):68-79.
8. Zhou Z, Song S, Gao Z, Wu J, Ma J, Cui Y. The efficacy and safety of dutasteride compared with finasteride in treating men with androgenetic alopecia: a systematic review and meta-analysis. *Clin Interv Aging*. 2019;14:399-406.
9. Suchonwanit P, Thammarucha S, Leerunyakul K. Minoxidil and its use in hair disorders: a review. *Drug Des Devel Ther*. 2019;13:2777-2786.
10. Caro G, Fortuna MC, Magri F, Federico A, Carlesimo M. A new treatment of alopecia induced by palbociclib: Topical cetirizine. *J Oncol Pharm Pract*. 2020:1078155220930334. [Epub ahead of print]
11. Kanei A, Asano K, Kanai K, Furuta A, Sasaki K, Suzaki H. Inhibitory action of levocetirizine on the production of eosinophil chemoattractants RANTES and eotaxin in vitro and in vivo. *Vivo*. 2014;28(4):657-666.
12. Abo Dena AS, Abdel Gaber SA. In vitro drug interaction of levocetirizine and diclofenac: Theoretical and spectroscopic studies. *Spectrochim Acta A Mol Biomol Spectrosc*. 2017;181:239-248.
13. Wen S, Wei J, Bao J, et al. Effect of levocetirizine hydrochloride on the growth of human dermal papilla cells: a preliminary study. *Ann Palliat Med*. 2020;9(2):308-317.
14. York K, Meah N, Bhoyrul B, Sinclair R. A review of the treatment of male pattern hair loss. *Expert Opin Pharmacother*. 2020;21(5):603-612.