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Research Article

Comparison of the effectiveness of topical Latanoprost and topical Minoxidil in treating Scalp Alopecia Areata in relation to CD8 cell expression: A study using clinical, dermoscopic, and immunohistochemical methods

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ABSTRACT

Background: Non-scarring hair loss on the scalp or any hair-bearing surface is the hallmark of the autoimmune disease Alopecia Areata (AA). Numerous approaches have been used to treat this condition, but the degree and duration of the illness determine how successful the treatments are.
Aim of the Study: We aimed to evaluate the efficacy of topical latanoprost versus topical minoxidil in treating patchy Alopecia Areata.

Patients and Methods: Thirty individuals with Alopecia Areata were randomly divided into two groups: Group A (15 patients) received topical latanoprost 1%, while Group B (15 patients) received topical minoxidil 5%. Dermoscopic imaging and a punch biopsy were taken and processed for histopathological and immunohistochemical studies, as well as to assess patient satisfaction to evaluate therapeutic response.

Results: Both treatment modalities demonstrated significant enhancement in all dermoscopic findings related to Alopecia Areata before and after therapy, with Group B showing much higher efficacy than Group A. In both treatment groups, immunohistochemically stained sections revealed a negative immunoreaction for CD8 T lymphocytes, indicating a reduction in inflammatory lymphocytic infiltration. Erythema and itching were the only insignificant side effects associated with both treatment regimens.

Conclusion: Both topical minoxidil and latanoprost are beneficial in promoting hair regrowth in patients with Alopecia Areata.

Introduction

Alopecia Areata (AA) is an autoimmune disease characterized by non-scarring hair loss on the scalp or any hair-bearing surface that affects about 2% of the general population, including all ethnic groups, genders, and age groups. AA affects the quality of life, and it can lead to psychological illnesses like sadness and anxiety (1).

The critical criteria used to diagnose AA are its characteristic clinical symptoms. For AA patients, trichoscopy and histopathology are clinically significant (2).

The clinical presentation of AA can range from localized, well-defined hair loss patches to widespread scalp or body involvement. Relapsing and remitting episodes are unpredictable for most AA patients. However, they can persist in some people, particularly those with significant hair loss (3).

Clinically, AA manifests as one or more non-scarring alopecic patches on the scalp; however, it can also occasionally progress to refractory AA subsets such as band-like hair loss along the hairline on the temporal and/or occipital region (alopecia ophiasis), total scalp hair loss (alopecia totalis, AT), or whole-body hair loss (alopecia universalis, AU) (4).

Numerous approaches could be used to treat AA, including topical, systemic, or locally injected steroids; topical immunotherapy, minoxidil, or irritants such as anthralin; and systemic immunosuppressants like methotrexate or cyclosporine. Success rates change according to the severity and prognosis of the illness. Latanoprost, a prostaglandin (PG) analog, can cause hypertrichosis of the eyelashes, surrounding adnexal hair, and skin vellus hair (5).

Latanoprost and prostamide analogs may be helpful in the treatment of hair loss, particularly AA. Latanoprost can cause the skin's vellus hair, surrounding adnexal hair, and eyelashes to become hypertrichotic(6).

Furthermore, vasodilating agents like minoxidil, used to treat hypertension, are linked to hair growth and are commonly used to treat disorders that cause hair loss, such as AA. (7).

The exact mechanism by which minoxidil induces hair regeneration remains unclear. It has been demonstrated to enhance cutaneous blood flow to the scalp and, through activating potassium channels, to facilitate the change of hair follicles from the resting telogen phase to the active anagen phase (8).

This study used different procedures to compare the efficacy of topical latanoprost versus topical minoxidil in managing alopecia areata.

Patients and methods

A randomized controlled study was carried out on thirty cases of alopecia areata. Participants were randomly selected from the dermatology outpatient clinic at Al-Azhar University Hospital at Damietta Faculty of Medicine, Al-Azhar University, from April 2022 to October 2022.

Ethical considerations

The medical ethics committee at Damietta Faculty of Medicine, Al -Azhar University, Egypt, approved the study's protocol. All the risks involved were informed to all patients before the study started, and each enrolled patient gave verbal and written consent. Every eligible participant was randomly assigned to one of two groups using a computer-generated randomization process: group A received topical latanoprost, while group B received topical minoxidil.

Inclusion and exclusion criteria

Thirty patients with localized alopecia areata (<3 patches) who were between the ages of 12 and 60 years, not receiving any AA medication at least six weeks before the study, were included in the study. Patients were excluded if they had severe medical disorders or dermatological diseases, pregnant females, those with substantial alopecia areata (less than three patches), and those who were contraindicated for latanoprost or minoxidil treatments.

Treatment protocol

Minoxidil Forte® 5% topical gel 60 gm was purchased (Pharmacare Egypt Co., Cairo, Egypt). Before applying the drug, the lesions were cleaned with hot water. The patients were then instructed to use the topical medication in a thin layer to the entire affected patch, rubbing it twice daily for 12 weeks.

Latanoprost 0.1% was prepared in a solvent solution (a combination of ethanol, propylene glycol, and distilled water at a volume ratio of 50%: 20%: 30%). The lotion was stored in dark glass bottles, and throughout that time, it was monitored for any signs of deterioration. Every two weeks, each patient received a freshly made formulation (6).

Methods

A comprehensive history taking, general, dermatological, and dermoscopic examinations were performed on thirty patients. Following this, they were instructed to use thermal water to clean the lesions before applying the drug and to apply a thin layer of topical medication, rubbing it twice daily for 12 weeks. Cases were randomly assigned to two groups (١٥ patients/each): the first group was treated with topical latanoprost 1% twice daily, and the other group received topical minoxidil 5% lotion twice daily.

After the initial assessment, each patient underwent a clinical evaluation every two weeks. Dermoscopy was used to measure the improvement during the 12-week treatment period and detect any recurrences. Growth was calculated at 6 and 12 weeks using a 5-point semi-quantitative regrowth score (RGS). A photograph was taken twice: the baseline, which was taken before the start of therapy, and the 12-week treatment period. Punch samples (4 mm) were collected from the edge of the most recent patch of AA both before and after treatment. After that, they were prepared for histological examination by staining with hematoxylin and eosin to assess structural changes and CD8 immunohistochemistry to identify T cells. The generated slides were examined using light microscopy (Raywild). The Leica Quin 500 analyzer computer system was utilized as an image analyzer to assess the immunoexpression density.

Statistical analysis

Statistical analysis of the quantitative data (mean and standard deviation) using student t-test in SPSS program (V20). Correlations between two quantitative variables were assessed using the Spearman coefficient. The level of significance was considered at p values <0.05.

Results

Regarding age, sex, family history, and prior therapy, no statistically significant difference exists between the groups under investigation (Table 1).

Table 1. Socio-demographic data of the study groups

		Latanoprost group N=15	Minoxidil group N=15	Test of significance
Age/yearsmean±SD		3–51 18 ± 3.25	3.5-60 32.2 ± 9.36	t=0.807 p=0.424
Sex	Male	10(66.7)	8(53.3)	P=0.490
	Female	5(33.3)	7(46.7)	
Stress	-ve	6(40)	10(66.7)	p=0.480
	+ve	9(60)	5(33.3)	
Previous treatment		0	0	

*Statistically significantly at p <0.05.

Clinical Findings

Following a 12-week course of treatment with either latanoprost or minoxidil, clinical evaluations revealed significant improvements in alopecia areata patients in both groups compared to baseline Figure. 1.

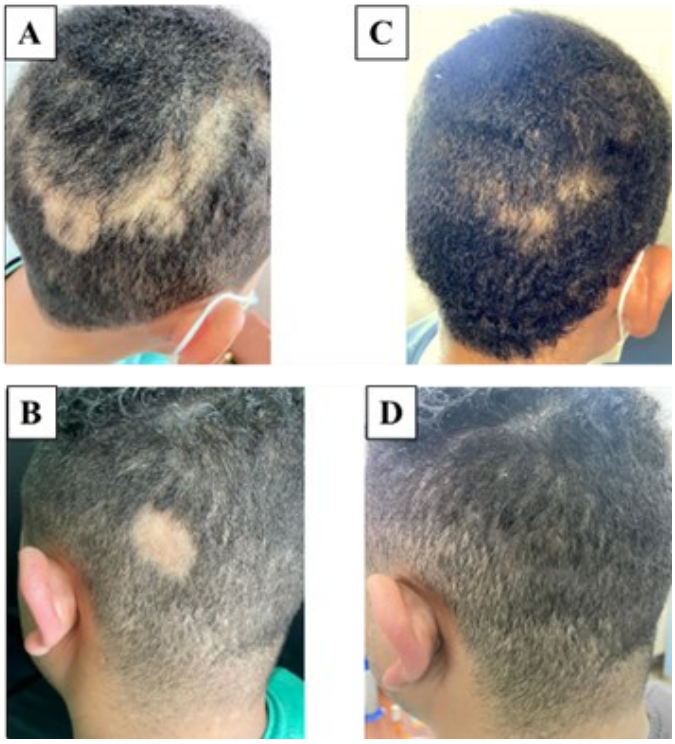


Figure 1. a photograph showing patients with alopecia areata (A) AA patient (<3 patches) before treatment; (C) after treatment with topical latanoprost showed excellent improvement; (B) AA patient (<3 patches) before treatment; (D) after treatment with topical Minoxidil showed excellent improvement;

Dermoscopic findings

Regarding the baseline dermoscopic findings, there is no statistically significant difference between the analyzed groups Table. 2 and Figure 2.

Table 2. Comparing the study groups' baseline dermoscopic findings.

Dermoscopy at baseline	Latanoprost (N=15 group (%))	Minoxidil group ((%) (N=١٥	Significance
Black dot	9 (60)	11 (73.3)	p= 0.239
Yellow dot	13 (86.6)	10 (66.6)	p= 0.088
Broken hair	4 (26.6)	7 (46.6)	p= 0.145
Exclamation mark	8 (53.3)	10 (66.6)	p= 0.248
Vellus hair	7 (46.6)	8 (53.3)	p= 0.396
Terminal hair	1 (6.6)	1 (6.6)	p= 1.0

After six weeks of follow-up, compared to both groups at baseline, there was a substantial decrease in disease activity signals and an increase in improvement signs in both treated groups with either latanoprost or minoxidil. Additionally, after six weeks, the frequency of breaking hair was significantly higher in the minoxidil group compared to the latanoprost group Table 3 and Figure 2.

Table 3. The dermoscopic findings in cases after six weeks of follow-up compared to baseline findings.

Dermoscopy after treatment (6 weeks)	Latanoprost group N=15 (%)		Minoxidil group N=15 (%)	
Time	Baseline	After six weeks	Baseline	After six weeks
Black dot	9(60)	5(33.3) [a]	11(73.3)	3(20) [ab]
Yellow dot	13(86.6)	6(40) [a]	10(66.6)	7(46.6) [ab]
Broken hair	4(26.6)	0 [a]	7(46.6)	4(26.6) [ab]
Exclamation mark	8(53.3)	4(26.6) [a]	10(66.6)	6(40) [ab]
Vellus hair	7(46.6)	15(100) [a]	8(53.3)	14(93.3) [ab]
Terminal hair	1(6.6)	5(33.3) [a]	1(6.6)	0(0) [ab]

[a] Significantly different from the same group at baseline (p <0.05).
[b] Significantly different from the treated group with latanoprost after six weeks (p <0.05).

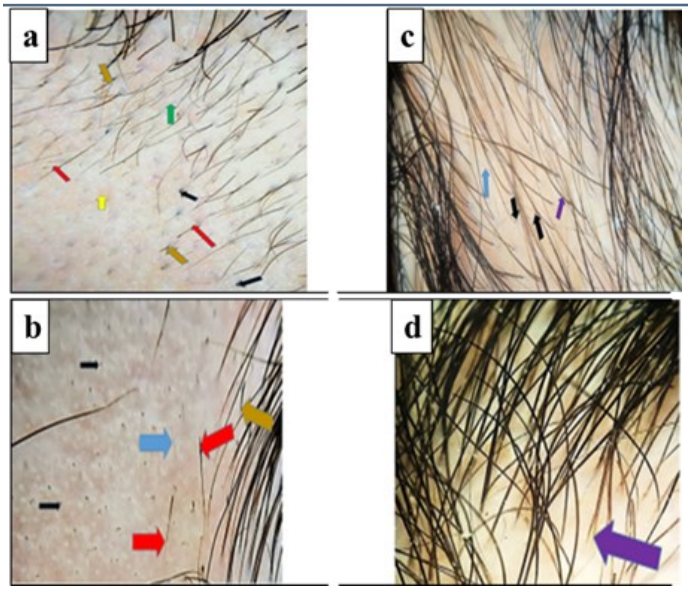


Figure 2. Dermoscopy results (a and b) for patients with A.A. include: red arrow (exclamation mark), black arrow (black dots), blue arrow (vellus hair), and purple arrow (terminal hair); (c and d) following topical latanoprost or minoxidil treatment, exhibiting the elimination of all AA activity features and the appearance of short vellus hair (blue arrow) and terminal hair (purple arrow).

There was a significantly higher incidence of black dots among the group with minoxidil than latanoprost (20 versus none) and a lower frequency of vellus hair among the group with minoxidil than the latanoprost group by dermoscopy after 12 weeks (Table 4).

Table 4. The dermoscopic findings in cases after 12 weeks of follow-up compared to baseline findings.

Findings	Latanoprost group N=15 (%)		Minoxidil group (%) N=١٥	
Time	Baseline	After 12 weeks	Baseline	After 12 weeks
Black dot	9(60)	0(0.0) ٭	11(73.3)	3(20) ٭٭
Yellow dot	13(86.6)	5(33.3)٭	10(66.6)	6(40)٭٭
Broken hair	4(26.6)	2(13.3)٭	7(46.6)	1(6.6)٭٭
Exclamation mark	8(53.3)	4(26.6)٭	10(66.6)	3(20)٭٭
Vellus hair	7(46.6)	25(100)٭	8(53.3)	10(66.6)٭٭
Terminal hair	1(6.6)	10(66.6)٭	1(6.6)	13(86.6)٭٭

Significantly different from the same group at baseline ($p < 0.05$).
Significantly different from the treated group with latanoprost after 12 weeks ($p < 0.05$).

Histopathological and immunohistochemical findings at treatment baseline and 12 weeks later

Before therapy, a light microscopic examination of skin samples at baseline showed a perifollicular inflammatory lymphocytic infiltration. Palisading basaloid cells encircle an instead twisted trichilemma to form the telogen germinal unit. After a 12-week course of topical latanoprost treatment, the hair follicle showed modest inflammatory lymphocytic infiltration; however, the group treated with minoxidil also showed an uneven island of basaloid cells, indicative of the telogen germinal unit (Figure 3).

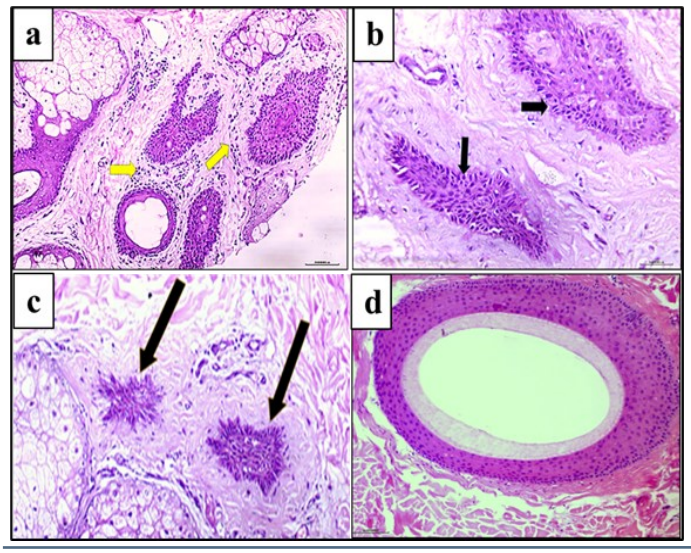


Figure 3. A Photomicrographs of a skin specimen demonstrate that (a, b) both A.A. groups had irregular islands of basaloid cells before treatment at baseline, which represent the telogen germinal unit (short black arrow) and perifollicular infiltration by the inflammatory lymphocytes; (d, g) that both treated groups had increased numbers of telogen hairs (long black arrows) and anagen hair follicles following treatment with either latanoprost or minoxidil (Hx.&E.× 400).

Before receiving either latanoprost or minoxidil, immunohistochemically stained sections in A.A. demonstrated a high positive immunoreaction for CD8+ T lymphocytes, although there was a noticeable decrease in CD8+ immunoexpression following therapy (Figure 4).

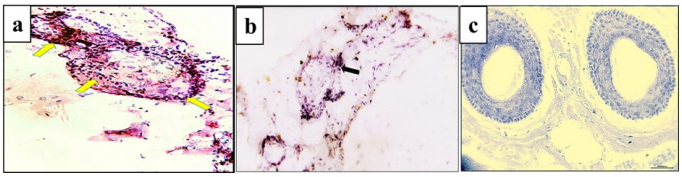


Figure 4. photomicrographs of skin specimens demonstrate a significant rise in CD8-positive immunoexpression in both A.A. groups before therapy at baseline (a). However, there was a noticeable drop in CD8+ immunoexpression following latanoprost (b) or minoxidil (c) treatment. (CD8+T. Immune stain × 400).

Comparison between study groups according to degree of improvement

After six weeks of treatment, there was a statistically significant difference in the degree of improvement between the methotrexate and minoxidil groups. Still, there was no statistically significant difference between the group receiving minoxidil and the group receiving latanoprost. The minoxidil group showed significantly more improvement than those receiving latanoprost (Table 5).

Table 5. Assessments of the degree of improvements by the patients of study groups.

Improvement degree		Latanoprost (N=15 group (%))	Minoxidil group (N=١٥ ((%)	Significance
After six weeks	Poor	0(0.0)	1(6.6)	p=0.005*
	Fair	8(53.3)	2(13.3)	
	Good	0	2(13.3)	
	Very good	7(46.6)	7(46.2)	
	Excellent	0	3(20)	
After 12 weeks	Poor	0	1(6.6)	p=0.074
	Fair	4(26.6)	2(13.3)	
	Good	3(20)	0	
	Very good	3(20)	4(26.6)	
	Excellent	5(33.3)	8(53.3)	

Statistically significantly at $p < 0.05$.

Comparison between study groups according to side effects

There is no apparent difference between the Latanoprost and Minoxidil groups regarding erythema and irritation. (Table 8).

Table 6. Comparison of the side effects among the study groups.

Adverse effects	Latanoprost group N=15	Minoxidil group N=15(%)	Significance
Burning sensation (Erythema)	3(20.0)	3(20)	p=0.733
Itching	9(60.0)	11(73.3)	p=0.225

Discussion

Alopecia Areata (AA) is an autoimmune disease caused by attacking hair follicles with T-cells, leading to quickly growing patches of hair loss on the scalp and beard. Several forms of AA are present (alopecia totalis, or complete scalp hair loss, and alopecia universalis, or loss of eyebrows, eyelashes, and all body hair). Patients with this condition often have psychiatric issues and a decline in their quality of life (9).

Alopecia Areata is diagnosed by physical examination or trichoscopy; however, the diagnosis is unclear in certain circumstances, so a scalp biopsy may also be needed (10).

Histopathological features of acute AA include peribulbar lymphocytic infiltration in hair follicles containing intrafollicular and peri-follicular CD4+ T (11).

Immunosuppressive medications, including cyclosporine, systemic corticosteroids, and contact immunotherapy, demonstrate the autoimmune character of AA by significantly improving patients (12).

The objective of the current study was to evaluate and compare topical minoxidil 5% lotion and topical latanoprost 0.1% lotion for the treatment of localized alopecia areata. We enrolled 15 matched individuals with alopecia areata in each group. To our knowledge, this study compares the immunohistochemical characteristics of the cellular infiltrate in alopecia areata before and after topical use of minoxidil and latanoprost.

Dermoscopy is increasingly used to assess hair loss and whether or not it leaves scars. Dermoscopic observations of various types of hair loss assist medical professionals in their daily work and prevent needless biopsies (13).

According to baseline dermoscopic findings in the current study, the main findings for the latanoprost versus minoxidil groups are black dot (60&73.3%), yellow dot (86.6&66.6%), broken hair (26.6&46.6%), exclamation mark (53.3&66.6%), vitellus hair (46.6&53.3%), and terminal hair (6.6 each). There is no statistically significant difference between the studied groups.

According to our results, another study showed that black dots were found in 70.8% of cases and yellow dots in 79.16%) of cases. There were observations of short vellus hair in (44.44%), broken hair in (43.15%), and exclamation mark hair in (31.9%). The most frequent finding associated with higher severity of AA was thought to be one yellow dot per field of vision. (14).

Furthermore, according to a different study, yellow spots (84.1%), vellus hairs (62.6%), black dots (48.4%), exclamation marks (30.9%), and broken hair (9.5%) were the most frequent dermoscopic findings in AA (13).

Along with similarity, Guttikonda and his colleagues evaluated the clinical significance of dermoscopy in alopecia areata. They found various dermoscopic patterns in AA patients: yellow dots (88%), black dots (58%), broken hairs (56%), tapering hair (26%), pigtail hair (14%), short vellus hair (66%), and Pohl-Pinkus constrictions (2%) were the different dermoscopic patterns seen (15).

In contrary to our results, the yellow dots were challenging to see in Inui *et al.*'s study on AA patients (16).

This discrepancy in results can be ascribed to various factors, such as skin types (the yellowish tone of Asian skin may make it challenging to see the yellow dots on dermoscopy), shampooing practices, and the type of dermoscopy employed (17).

In the current study, we employed 0.1% lotion latanoprost. We discovered that all findings for the latanoprost group showed a statistically significant change in the frequency of the dermoscopic conclusions between baseline and after 6& 12 weeks. After six weeks, there was a noticeable improvement in the yellow dot, broken hair, and vellus hair. But after 12 weeks, there was a reappearance of broken hair in 4 cases, a considerable improvement in the black dot (0 cases), no change in the yellow dot between 6 and 12 weeks, and a significant appearance of terminal hair after 6 and 12 weeks.

As regards the patient evaluation of the degree of improvement in cases treated with latanoprost, after six weeks, 53.3% of patients reported reasonable improvement, 46.6% reported perfect improvement, and 33.3% reported excellent improvement. As regards the side effects, 20% and 60% reported erythema and itching, respectively.

Latanoprost-induced hair growth is thought to be caused by several mechanisms, including follicles transitioning from telogen to anagen, stimulating follicular hypertrophy early in the anagen phase, extending the anagen phase and increasing hair length as a result, inducing a mitogenic stimulus required to start cell division at the beginning of anagen, and upregulating cell adhesion molecules and proteases involved in the enlargement, remodeling, and downward migration of the hair follicle (6).

In this study, we revealed that between the baseline and the 12-week follow-up, there was a statistically significant change in the frequency of dermoscopic findings in all topical minoxidil 5% lotion results. Six weeks later, the vellus hair, damaged hair, and yellow spots significantly improved. However, there was a discernible improvement in broken hair after 12 weeks, and between 6 and 12 weeks, there was also a noticeable improvement in vellus hair. After 6 and 12 weeks, there was a noticeable appearance of terminal hair.

As regards the degree of improvement that patients assessed in cases of latanoprost, 46.2% reported perfect improvement after six weeks, and 53.3% reported outstanding improvement after twelve weeks. 20% and 73.3% of respondents reported erythema and irritation.

In agreement with our study, randomized controlled trials, in comparison to placebo, showed that 3% topical minoxidil treatment somewhat increased hair regrowth. Patients with widespread AA showed little to no effects; however, hair growth was noticed faster and became denser at the treated spot. Minoxidil was shown to have only minimal side effects and no signs of systemic effects (18).

Topical minoxidil promotes differentiation above the dermal papilla and proliferation at the base of the hair bulb. Vasodilatation, angiogenesis, improved cell proliferation, and potassium channel opening are only a few of the numerous modes of action. After three months of treatment, minoxidil significantly increased the amount of short vellus hair and upright developing hair. Regarding patchy alopecia, minoxidil worked better than other forms of AA, like ophiasis and alopecia totalis (19).

Furthermore, due to its dose-response action, other studies have indicated that a higher topical minoxidil concentration was desirable in treating AA. 5% minoxidil showed 81% terminal hair regeneration in significant AA (more than 75% scalp involvement), compared to 38% in the 1% minoxidil group (20). Similar to our results, previous studies examined the efficacy and safety of topical minoxidil at 5%, 10%, and placebo in the treatment of AA; the researchers concluded that topical minoxidil is the cornerstone of the management strategy for AA (21, 22).

The FDA has approved a concentration of 5% for AA, which has good tolerance, no significant side effects, a fair cost, and satisfactory results when given to patients with reasonable expectations and vellus hair present in the early stages. This trial shows that topical minoxidil at 5% and 10% is approximately as effective in males with AGA. Higher concentrations, however, may reduce compliance and tolerance with nearly the same outcome (22).

After comparing the two treatments, by dermoscopy after 12 weeks, we discovered that the minoxidil group had a significantly higher rate of broken hair and black spots after six weeks, and the latanoprost group had a significantly reduced rate of vellus hair.

In terms of enhancement, after six weeks, minoxidil showed a considerably better degree of improvement (20% against 0%), and after 12 weeks, minoxidil and latanoprost showed exceptional enhancement (53.3% and 33.3%, respectively). There was no discernible variance in side effects between the minoxidil and latanoprost groups.

Histologically, AA is characterized at baseline by several degrees of follicle degeneration and a perifollicularly dense infiltration of CD8+ T cells. After 12 weeks of minoxidil treatment, biopsies from AA treated with minoxidil showed reappearance of average hair follicle diameter and structure.

Using immunohistochemical stains, we could determine that the minoxidil group had a statistically significantly lower number of CD8+ T cells than the latanoprost group. These results were consistent with those of Fiedler and Buys, who discovered reappearance of average hair follicle diameter, depth, and structure, as well as an apparent shift in T cell populations from the skin into the peripheral blood, were characteristics of patients with severe AA who responded to topical minoxidil 5%. None of these modifications were seen by nonresponders (20).

Furthermore, a theory stated that latanoprost and minoxidil function similarly by activating the enzyme prostaglandin endoperoxide synthase-1 (PGHS-1) in dermal papilla cells could account for some of the partial improvement observed in the latanoprost group. The process causes prostaglandin E2 (PGE2) to be produced, which is known to have cytoprotective properties and promotes hair growth. (23).

Conclusion

Topical minoxidil 5% and topical latanoprost 0.1% lotion both demonstrated substantial success in treating localized alopecia areata, with no discernible differences between the two treatment regimens, after six weeks of treatment, minoxidil showed statistically significant improvement over latanoprost.

Limitations of the study

small sample size and a short follow-up time.

Declaration of Competing Interests

The authors declare no competing interests

Data sharing plans

Data are available from the corresponding author upon reasonable request

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