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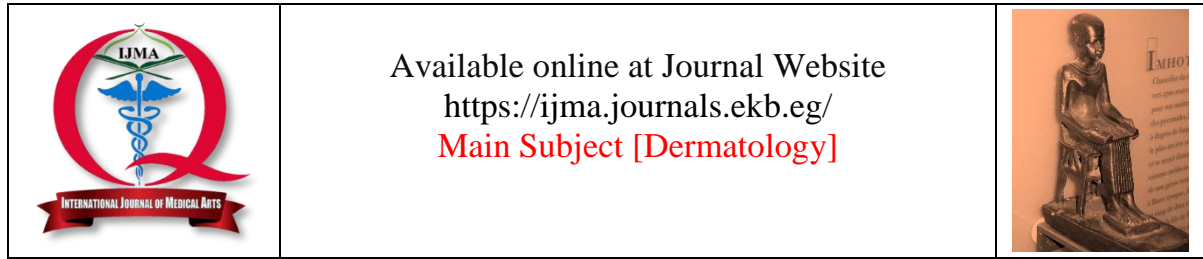


## INTERNATIONAL JOURNAL OF MEDICAL ARTS

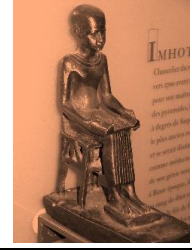
VOLUME 6, ISSUE 6, JUNE 2024

**P- ISSN: 2636-4174**  
**E- ISSN: 2682-3780**





Available online at Journal Website  
<https://ijma.journals.ekb.eg/>  
 Main Subject [Dermatology]



## Original Article

# Efficacy of Topical Latanoprost Versus Topical Minoxidil In the Treatment of Alopecia Areata: Clinical and Dermoscopic Study

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## ABSTRACT

### Article information

Received: 15-05-2024

Accepted: 25-06-2024

DOI: 10.21608/IJMA.2024.289839.1970.

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**Citation:** Abd Allah FM, Atallah RB, Semary SS, Elshahat OM. Efficacy of Topical Latanoprost Versus Topical Minoxidil In the Treatment of Alopecia Areata: Clinical and Dermoscopic Study. IJMA 2024 June; 6 [6]: 4544-4552. doi: 10.21608/IJMA.2024.289839.1970.

**Background:** The non-scarring hair loss caused by alopecia areata is a result of a persistent inflammatory condition of unclear origin. As of right moment, alopecia areata has no suggested course of therapy.

**Aim of the work:** The aim of this research was to assess the efficacy of topical minoxidil and topical latanoprost in managing alopecia areata.

**Patients and Methods:** A total of 40 individuals diagnosed with alopecia areata were randomly divided into two treatment groups. Specifically, Group A comprised 20 patients who were administered topical latanoprost solution at a concentration of 0.1%, whereas twenty patients in Group B received topical 5% minoxidil. Clinical and dermoscopic imaging were utilized to evaluate the response to therapy.

**Results:** Both treatment approaches resulted in a notable enhancement in all dermoscopic observations associated with alopecia areata when analyzing pre- and post-therapy results. The latanoprost group exhibited notably greater effectiveness compared to the minoxidil group. The minor side effects of both treatment plans were erythema and itching and no major side effects.

**Conclusion:** Based on pre- and post-treatment the dermoscopic findings in alopecia areata patients showed dramatically improvement by either 0.1% Latanoprost or topical 5% Minoxidil.

**Keywords:** Alopecia Areata; Minoxidil; Latanoprost; Dermoscopy.



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## INTRODUCTION

Alopecia areata [AA] is a complex autoimmune illness that preserves hair follicles while causing non-scarring hair loss. It could be recurrent or persistent, particularly in cases of significant hair loss. Hair loss can manifest as  $\geq$  one distinct round or oval patches <sup>[1]</sup>.

Alopecia areata [AA] may affect the body or scalp. AA totalis refers to AA that compromises the entire scalp, whereas AA universalis refers to AA that compromises the entire body. Atopic dermatitis, thyroid illness, asthma, allergic rhinitis, and autoimmune disorders like vitiligo and thyroiditis are conditions that are frequently linked to AA <sup>[2]</sup>.

Approximately 2% of the general population globally has AA, and there is no variation in this incidence among sexes, ages, or races. Although AA can impact individuals at any age, the first onset is more common in the third and fourth decades of life <sup>[3]</sup>. Even though the exact pathophysiology of AA is not entirely understood, accumulating data from human AA skin and blood samples as well as AA mice models suggests that immunological privilege collapse is a major player in the AA pathogenesis <sup>[4]</sup>.

The development of AA is largely dependent on the collapse of the hair follicle [HF]-immune-privileged [IP] site. In particular, the downregulation of IP guardians like transforming growth factor- $\beta$ 1 [TGF- $\beta$ 1] and interleukin-10 [IL-10], along with the local upregulation of NKG2D ligands [e.g., MICA and ULBP3/6], cytokines like IL-15, IL-2, and CXCL2, are the reasons behind the loss of the HF-IP site. All of these elements play a part in the HF's loss of immunological tolerance and the subsequent attack of autoantigens produced and released by keratinocytes, melanocytes, and/or dermal papilla fibroblasts during the anagen hair phase <sup>[3, 5]</sup>.

According to recent studies, neuropeptides can cause neurogenic inflammation, activate mast cells around hair follicles, and encourage keratinocyte apoptosis. All of these processes can lead to damage to hair follicles. However, more research is needed to determine the precise etiology of alopecia areata <sup>[6, 7]</sup>.

Compared to other high-burden dermatoses, the clinical practice guidelines for AA are very weak and of low methodological quality, despite the high occurrence of AA in the general population. This makes it difficult for doctors to help patients receive better care <sup>[8]</sup>. In many cases, the diagnosis of AA is made based on clinical observation. Yellow,

black, or "exclamation marks" on dermoscopy indicate active disease, as do tapering and broken hairs. Vellus hair is frequently seen in late or dormant phases of AA <sup>[9]</sup>.

There are many different ways to treat AA, ranging from nonmedical approaches [such stopping treatment altogether, getting microbladed, or using hair prosthesis] to medical approaches [like the more recent immuno-modulating Janus Kinase [JAK] inhibitors]. Lesions with less than 25% total scalp involvement, or smaller AA lesions, often resolve on their own quite well. Rates of spontaneous remission can range from 68% in patients with less than 25% scalp involvement to 8% in those with more than 50% involvement <sup>[10]</sup>.

In AA, topical steroids, intralesional steroids, topical immunotherapies, JAK inhibitors, and systemic corticosteroids are among the therapy modalities with moderate to high treatment success rates. Topical calcineurin inhibitors, topical latanoprost, topical minoxidil, cryotherapy, methyl-aminolevulinic acid photodynamic therapy, excimer lasers, pulsed infrared diode lasers with a wavelength of 904 nm, and antihistamines are other less common but potentially effective treatment options <sup>[11]</sup>.

However, for the treatment of severe cases of AA, neither the European Medicines Agency [EMA] nor the Food and Drug Administration [FDA] have approved the use of contact immunotherapy, glucocorticoids [topical, intralesional, and systemic], or other immunosuppressive drugs [methotrexate, azathioprine, and cyclosporine] <sup>[12]</sup>.

The FDA first authorized the oral vasodilator medication minoxidil in 1979 to treat refractory hypertension. The use of minoxidil in several dermatological problems is representative of its continued on-label indications. However, it is also commonly used in off-label regimens for alopecia areata, scarring alopecia, and abnormalities of the hair shaft. It's also used to enhance the growth of body hair in other places, such the face <sup>[13]</sup>.

Latanoprost is a synthetic analog of prostaglandins [PGF2a]. Topical 0.1% latanoprost could produce significant improvement in hair density as compared to baseline of AA patients <sup>[14]</sup>.

The objective of this study was to assess the effectiveness of topical minoxidil and topical latanoprost in treating alopecia areata using various techniques.

## PATIENTS AND METHODS

Forty patients with alopecia areata were included in a randomized controlled experiment. Patients who participated in the study were selected at random from the dermatological outpatient clinic at Al-Azhar University Hospital Damietta. The study was conducted from March 2021 to December 2022 at the Dermatology Department of the Damietta Faculty of Medicine, Al-Azhar University.

**Ethical considerations:** Protocol for the study was accepted by the medical ethics council of Al-Azhar University's Damietta Faculty of Medicine in Egypt. Before the trial began, all patients were made aware of the hazards involved, and they all provided both written and verbal agreement to be included.

**Inclusion criteria:** Localized alopecia areata [ $<$  three patches], aged between twelve and sixty, who had not taken any AA treatment for at least six weeks before the study.

**Exclusion criteria:** Patients with contraindications for latanoprost or minoxidil therapies, had considerable alopecia areata [more than three patches], were pregnant, had serious medical conditions, or had dermatological problems were eliminated.

### Treatment protocol

**Topical 5% minoxidil gel:** The 5% Minoxidil Forte® topical gel, 60 gm, was acquired from Pharmicare Egypt Co. in Cairo, Egypt. A 5% minoxidil gel was used.

**Topical 0.1% Latanoprost:** Latanoprost 0.1% was made in a solvent solution [ethanol, propylene glycol, and distilled water mixed at a volume ratio of 50%:20%:30%]. The lotion was kept under observation for any indications of deterioration while it was kept in dark glass bottles. Each patient received a newly created formulation every two weeks [15].

### Grouping of the studied patients

Patients were divided randomly into two groups of 20 patients each:

1. Group I: 20 patients with alopecia areata applied topical 0.1% latanoprost lotion twice daily.
2. Group II: 20 patients with alopecia areata applied topical 5% minoxidil gel twice daily.

Prior to applying the drug, patients were asked to disinfect the lesions with hot water. The topical medication was then applied in a thin layer over the entire affected area, with rubbing twice daily for a duration of 12 weeks.

**Demographic, clinical and Dermoscopic examinations:** Through taking the participants' histories, the following clinical and demographic data was obtained: Personal history; past medical history, including trauma, surgery, and chronic illness; family history of AA; present medical history, encompassing the beginning, progression, and length of AA; risk factors; any other skin conditions; related systemic or autoimmune disorders; as well as pharmaceutical history, including any topical or systemic treatments used for the disease's previous or current attacks.

**Dermatological examination:** Localized patchy alopecia areata type and lesion distribution; A dermoscopic examination [Dermlite DL4] is performed both before and during treatment to look for signs of disease activity, such as yellow dots, black dots, broken hairs, exclamation mark hairs, and tapering hairs. Short vellus hairs and terminal hairs are indicators that the illness is improving. Before the start of treatment [baseline], during the three months of the treatment period, and following the three months of treatment, a picture was taken.

**Statistical analysis:** Data are represented using the mean  $\pm$  SE. The data were analyzed using the statistical software SPSS for Windows [Version 21.0; SPSS Inc., Chicago, IL, USA]. A one-way ANOVA was utilized to compare the two groups, with a significance level of  $P < 0.05$  being regarded statistically significant.

## RESULTS

The present study is a clinical trial that included 40 patients with newly diagnosed localized [ $<$ 3 patches] AA, to assess the efficacy and safety of topical 0.1% Latanoprost lotion versus topical 5% minoxidil gel in treatment of localized alopecia areata.

**Socio-demographic changes:** Between the study groups, there was no statistically significant difference in terms of age, sex, family history, or previous therapy [Table 1].

**Clinical evaluation:** The patient with alopecia areata showed remarkable improvement both

before and after receiving either minoxidil [fig. 1a & b] or latanoprost [fig. 1c & d].

**Dermoscopic findings:** There is no statistically significant difference between the studied groups with respect to baseline dermoscopic findings. Between the groups under investigation, there was no discernible variation in the baseline dermoscopic findings [Table 2].

**Dermoscopic findings after six weeks of follow-up:** Comparing the minoxidil group to the latanoprost group after six weeks, there was a substantial increase in the incidence of hair breakage [Table 3].

**Dermoscopic findings after 12 weeks of follow up:** By dermoscopy after 12 weeks, there

was a statistically significant decrease in vellus hair and a statistically significant increase in black dot frequency among the minoxidil group compared to the latanoprost group [20 versus none] [table 4].

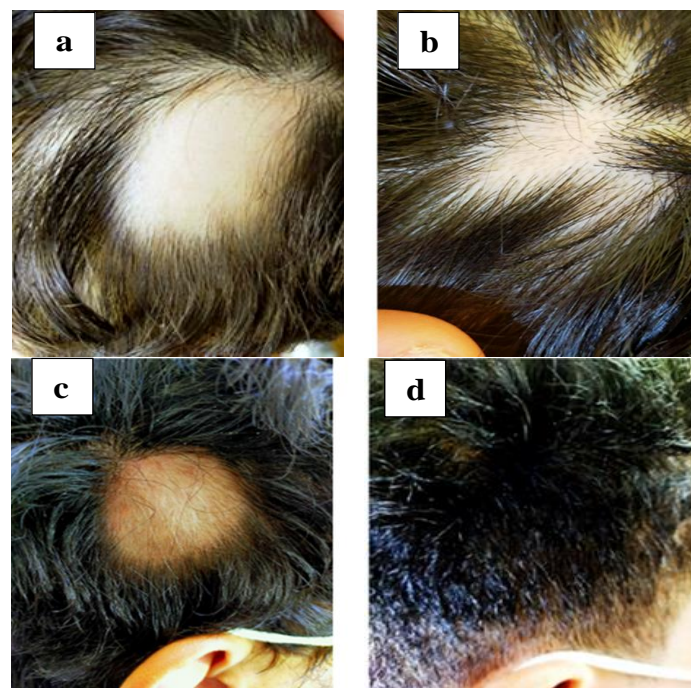
**Adverse effects:** Regarding burning and itching, there is no statistically significant difference between the Latanoprost and Minoxidil groups [table 5].

**Patient assessment:** After 6 weeks of treatment, there is an excellent improvement observed in the minoxidil group compared to the latanoprost group [20% versus 0%]. However, after 12 weeks of treatment, in both groups, there is no statistically significant difference in the degree of improvement [table 6].

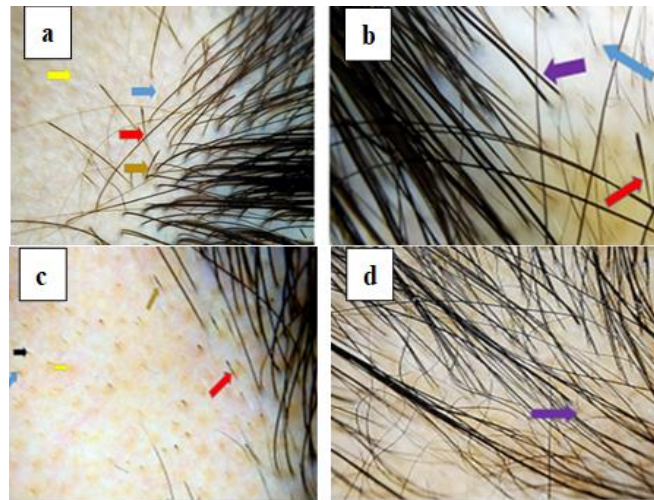
**Table [1]:** Socio-demographic changes in both groups

		Latanoprost group N=20 [%]	Minoxidil group N=20 [%]	Test of significance
<b>Age/years [mean ± SD]</b>		6-55 19 ± 8.78	5-62 29.2 ± 7.47	t=0.715 p=0.1578
<b>Sex</b>	Male	14 [70]	13 [65]	$\chi^2_{FET}=3.25$ P=0.657
	Female	6 [30]	7 [35]	
<b>Family history [-ve]</b>		20 [100]	20 [100]	.....
<b>Stress</b>	-ve	9 [45]	14 [70]	$\chi^2=0.500$ p=0.480
	+ve	13 [55]	6 [30]	
<b>Previous treatment</b>		0	0	

t: Student t test,  $\chi^2_{FET}$ : Fischer exact test



**Figure [1]:** Demonstrating remarkable improvement in alopecia areata patients treated with topical Latanoprost [a: prior to treatment, b: following treatment]; Outstanding progress in a patient suffering from alopecia areata patients treated with topical minoxidil [c: prior to treatment, d: following treatment]



**Figure [2]:** Alopecia areata patients' dermoscopic findings revealed a and c: black arrow [black dots], blue arrow [vellus hair], purple arrow [terminal hair], and red arrow [exclamation mark] prior to treatment. Figures b and d: following treatment, AA activity is completely gone, and short vellus hair [blue arrow] and terminal hair [purple arrow] are seen

**Table [2]:** Comparison of dermoscopic findings at baseline among the studied groups

Dermoscopy at baseline	Latanoprost group N=20 [%]	Minoxidil group N=20 [%]	Test of significance	
Black dot	10 [50]	11 [55]	$\chi^2=2.27$	p=0.354
Yellow dot	15 [75]	12 [60]	$\chi^2=1.39$	p=0.145
Broken hair	5 [25]	7 [35]	$\chi^2=0.35$	p=0.145
Exclamation mark	9 [45]	10 [50]	$\chi^2=1.27$	p=0.327
Vellus hair	9 [45]	8 [40]	$\chi^2=0.841$	p=0.384
Terminal hair	2 [10]	2 [10]	$\chi^{2FET}=0$	p=1.28

$\chi^2$ : Chi-Square test, FET: Fischer exact test

**Table [3]:** Comparison of dermoscopic findings after 6 weeks of follow up among the studied groups

Group	Latanoprost group N=20[%]	Minoxidil group N=20 [%]	Test of significance	
Black dot	6[30]	6 [30]	$\chi^2=1.75$	p=0.185
Yellow dot	9 [45]	10 [50]	$\chi^2=0.739$	p=0.390
Broken hair	0	4 [20]	$\chi^2=8.14$	p=0.004*
Exclamation mark	6 [30]	6 [40]	$\chi^2=0.368$	p=0.544
Vellus hair	12 [60]	15 [75]	$\chi^2=2.08$	p=0.149
Terminal hair	7 [35]	4 [20]	$\chi^2=0.085$	p=0.771

$\chi^2$ : Chi-Square test, \*statistically significant

**Table [4]:** Comparing the study groups' dermoscopic results during a 12-week follow-up and comparing them to the baseline

Group	Latanoprost group N=20[%]	Minoxidil group N=20[%]	Test of significance	
Black dot	0 [0.0]	20 [100]	$\chi^{2FET}=4.35$	p=0.037*
Yellow dot	6 [30]	5 [25]	$\chi^2=0.085$	p=0.771
Broken hair	3 [15]	2 [10]	$\chi^{2FET}=0.758$	p=0.384
Exclamation mark	5 [25]	4 [20]	$\chi^2=1.05$	p=0.306
Vellus hair	20 [100]	12 [16]	$\chi^2=9.52$	p=0.002*
Terminal hair	16 [80]	15 [75]	$\chi^2=2.59$	p=0.107

$\chi^2$ : Chi-Square test, \*statistically significant

**Table [5]:** Comparison between the two studied groups according to adverse effects

Side effects	Latanoprost group N=20[%]	Minoxidil group N=20 [%]	Test of significance	
Erythema	4 [20]	5 [25]	$\chi^2=0.254$	p=0.625
Itching	8 [40]	9 [45]	$\chi^2=0.84$	p=0.281

**Table [6]:** Patient assessment distribution among the studied groups

	Degree of improvement	Latanoprost group N=20 [%]	Minoxidil group N=20 [%]	Test of significance
<b>After 6 weeks</b>	Poor	0 [0.0]	1 [6.6]	$\chi^2_{MC}=11.47$ p=0.005*
	Fair	10 [50]	4 [20]	
	Good	1 [5]	3 [15]	
	Very good	9 [45]	9 [45]	
	Excellent	0 [0]	4 [20]	
<b>After 12 weeks</b>	Poor	0 [0.0]	1 [5]	$\chi^2=5.74$ p=0.062
	Fair	4 [20]	2 [10]	
	Good	3 [15]	5 [15]	
	Very good	6 [30]	4 [20]	
	Excellent	7 [35]	8 [40]	

$\chi^2$ : Chi-Square test MC: Monte Carlo test \*statistically significant

## DISCUSSION

The primary objective of this study was to evaluate and compare the effectiveness of topical 0.1% latanoprost solution with topical 5% minoxidil gel in treating localized alopecia areata. Each study group consisted of 20 matched patients diagnosed with alopecia areata.

Regarding the dermoscopic finding; we found that the main findings are; black dot [50 and 55%], yellow dot [75 and 60%], Broken hair [25 and 35%], Exclamation mark [45 and 50%], Vellus hair [45 and 40%] and Terminal hair [10 each] for latanoprost versus minoxidil groups, with no statistically significant difference between studied groups.

Consistent with findings from a different study that indicated 70.8% of cases had black dots and 79.16% had yellow dots. Short vellus hair [44.44%], broken hair [43.15%], and exclamation mark hair [31.9%] were seen. It was previously believed that one yellow dot per field of vision was the most common result linked to higher severity of AA [21].

Additionally, based on another research, common dermoscopic observations in alopecia areata included yellow spots [84.1%], vellus hairs [62.6%], black dots [48.4%], exclamation marks [30.9%], and broken hair [9.5%] [20].

Guttikonda *et al.* [22] examined the significance of dermoscopy in diagnosing alopecia areata. Their dermoscopic observations comprised black dots [58%], yellow dots [88%], broken hairs [56%], tapering hair [26%], pigtail hair [14%], short vellus hair [66%], and Pohl-Pinkus constrictions [2%].

Previous research and our findings indicate that yellow dots are the most prevalent observation. The exception to this is Inui *et al.*'s study, where

yellow dots were more difficult to discern, likely because the patients' skin was yellow [23].

The difference in results could be attributed to several factors including skin characteristics [since Asian skin tends to have a yellowish hue, identifying yellow spots on dermoscopy might be difficult], hair care routines, and types of dermoscopes used [24].

We used 0.1% lotion latanoprost in the current trial, and after 12 weeks, all results for the latanoprost group demonstrated a statistically significant change in the frequency of dermoscopic findings. We discovered a statistically significant difference in the frequency of dermoscopic findings between baseline and after 6 and 12 weeks in the latanoprost group. After six weeks, a clear enhancement was observed in the appearance of the yellow spot, fragmented hair, and fine vellus hair. Nevertheless, during a 12-week period, four cases of broken hair reappeared, one case of black dot showed a considerable recovery, between six and twelve weeks, there was no observed difference in the yellow spot, and terminal hair showed a significant increase between six and twelve weeks.

After six weeks, 50% reported reasonable improvement, 45% reported very good improvement, and 35% noted significant improvement. Among the side effects, 20% encountered redness while 40% experienced itching.

The growth of hair induced by Latanoprost is believed to result from various processes. These include the transition of follicles from resting phase to growth phase, early stimulation of follicle enlargement in the growth phase, extension of the growth phase leading to longer hair, triggering a growth signal for cell division at the start of the growth phase, and enhancement of molecules promoting cell adhesion and enzymes involved in follicle enlargement, restructuring, and movement [25].



This study showed a notable statistical variance in the dermoscopic observations frequency for all outcomes of topical 5% minoxidil gel from the initial assessment to the 12-week follow-up. After six weeks, vellus hair, broken hair, and yellow spots all showed notable improvement. However, there was a distinct enhancement in fragmented hair after 12 weeks, and there was also a noticeable improvement in fine vellus hair from the 6th to the 12th week. Terminal hair also showed a noticeable improvement between 6 and 12 weeks.

Regarding improvements, 20% and 73.3% of respondents noted erythema and itching, respectively. After six weeks, 45% expressed very good improvement and 40% reported outstanding improvement.

Compared to a placebo, topical 3% minoxidil treatment has been found in numerous randomized controlled trials to somewhat improve hair regeneration. Although there were little to no effects in patients with extensive AA, the treated area demonstrated denser and faster hair growth. There were no indications of systemic effects and very few side effects with minoxidil [26].

Application of minoxidil topically encourages proliferation at the hair bulb's base and differentiation above the dermal papilla. A handful of the many mechanisms of action include potassium channel opening, angiogenesis, vasodilatation, and enhanced cell proliferation. The number of short vellus hair and the amount of upright growing hair were both considerably raised by minoxidil after three months of treatment. Minoxidil was more effective than other AA types such as ophiasis and alopecia totalis in treating patchy alopecia [27].

Furthermore, some research has indicated that increasing the concentration of topical minoxidil could be advantageous in addressing alopecia areata due to its dose-dependent effects. In cases of extensive alopecia areata [involving more than 75% of the scalp], 5% minoxidil showed an 81% increase in fully developed hair growth, in contrast to 38% in the group using 1% minoxidil [28].

A recent study assessing the safety and efficacy of various concentrations of topical minoxidil [5%, 10%, and a placebo] in treating androgenetic alopecia [AGA] highlighted that topical minoxidil treatment is crucial in the management plan. The FDA has approved the use of 5% minoxidil for AGA in patients with realistic expectations and early-stage fine hair, citing good tolerability, minimal side effects, reasonable cost, and satisfactory outcomes. Results from the study suggest that both 5% and

10% concentrations of topical minoxidil are similarly effective for men with AGA. However, increasing the concentration may yield nearly identical results while potentially compromising tolerability and adherence to treatment [29].

Between the two groups, we found that after six weeks, the group using minoxidil exhibited a notably higher occurrence of broken strands and dark patches, a difference that was statistically significant. In contrast, the group treated with latanoprost showed a statistically significant reduction in the incidence of vellus hair after twelve weeks, as assessed through dermoscopy.

Statistically significant variations were observed between minoxidil and latanoprost in terms of the level of progress at six weeks [20% compared to 0%]. By the twelve-week mark, a notable contrast was evident in the rates of substantial improvement for minoxidil and latanoprost [40% and 35%, respectively]. In relation to adverse effects, there were no discernible variations between the minoxidil and latanoprost cohorts.

These findings align with those of **Fiedler and Buys**, who noted that individuals with severe alopecia areata [AA] responding positively to topical 5% minoxidil exhibited a trend towards normalization in hair follicle dimensions, depth, and structure, along with a noticeable migration of T cell populations from the skin to the peripheral blood. Conversely, those who did not respond did not experience these changes [28].

There is a likelihood that the partial enhancement observed in the latanoprost cohort could be attributed to the notion that both latanoprost and minoxidil operate in a similar manner by stimulating the enzyme prostaglandin endoperoxide synthase-1 [PGHS-1] within dermal papilla cells. Because of its cytoprotective characters and ability to stimulate hair growth, prostaglandin E2 [PGE2] is created as a result of the effect [30].

**Limitations of the study:** Limited sample size and brief monitoring period

**Conclusion:** Based on pre- and post-treatment the dermoscopic findings in alopecia areata patients showed dramatically improvement by either 0.1% Latanoprost or topical 5% Minoxidil.

**Conflicts of interest:** None.

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# IJMA



## INTERNATIONAL JOURNAL OF MEDICAL ARTS

VOLUME 6, ISSUE 6, JUNE 2024

**P- ISSN: 2636-4174**  
**E- ISSN: 2682-3780**