

Topical minoxidil reported hair discoloration: a cross-sectional study

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Abstract

Minoxidil is a widely utilized medication androgenic alopecia. An original investigation on its potential to cause hair darkening

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in treated people is lacking. We conducted an observational study using two face-validated questionnaires that dermatologists altered to assess minoxidil's hair discoloration risk. This Saudi Arabian survey collected data in October and November 2022. One questionnaire targeted the population, while the other targeted dermatologists. Survey 1 included 453 patients, 56.7% of whom were 18-24 and mostly female. It's interesting that 26% (n=118) detected hair greying and 14.8% (n=67) noticed other color changes. With P-values of 0.0001, longer-term minoxidil users and those with a family history of hair greying had higher hair discoloration. Dermatologists completed Survey 2 (57 participants). Nearly 60% of dermatologists have ten years of experience. 42.1% of dermatologists saw grey hair after minoxidil use. 17.5% of doctors blame minoxidil for hair graying. This observational study examined the data of over 400 patients to determine if minoxidil could cause hair discoloration. Based on the data, we hypothesize that this drug may cause hair discoloration with prolonged use and in people with a family history of hair greying.

Introduction

Minoxidil belongs to the vasodilator medication class, and it was first approved in the 1970s as an antihypertensive drug indicated for refractory hypertension.¹ However, due to one of its adverse effects, hypertrichosis, topical formulations were introduced to stimulate and enhance hair growth and slow hair thinning.²

The mechanism of action of minoxidil has yet to be fully understood, but it is thought to work by vasodilatory effects. It activates the vascular endothelial growth factor, increasing cutaneous blood flow, oxygen, and growth factor delivery to the hair follicle.³ It also leads to potassium channel activation in the hair follicles, which prolongs the anagen phase and shortens the telogen phase.⁴

Topical minoxidil is the mainstay treatment for androgenetic alopecia (AGA). However, it is also an off-label treatment for many hair disorders, including alopecia areata, chemotherapy-induced alopecia, frontal fibrosing alopecia, telogen effluvium, and loose anagen hair syndrome.²

While minoxidil has been used for decades to increase the rate of hair growth and prevent hair loss in patients, this study aims to investigate a phenomenon witnessed in practice with limited reports in the literature, which is the effect of minoxidil on hair color changes.

Materials and Methods

Study design

A cross-sectional study was done using two anonymous self-administered questionnaires designed in the Survey Monkey tool

(Survey Monkey Inc.); the first was for the general population, and the second was for dermatologists. It was distributed in the dermatology clinic and on social media platforms such as Twitter, Snap Chat, Instagram, and WhatsApp. Data was collected between October-November 2022.

Table 1. Characteristics of the participants (n=453).

Variables	Number	%
Age under 18 years		
16	3.5	
18-24 years	257	56.7
25-34 years	130	28.7
35-44 years	36	7.9
45-64 years	14	3.1
Above 65 years	0	0.0
Gender		
Male	140	30.9
Female	313	69.1
Nationality		
Saudi	391	86.3
Non-Saudi	62	13.7
Level of education		
High school diploma	68	15.0
Bachelors	321	70.9
Post graduate education	64	14.1
Do you have any type of hair loss?		
Yes	410	90.5
No	43	9.5
What type of hair loss?		
Male pattern hair loss	107	23.6
Female pattern hair loss	63	13.9
Telogen effluvium	30	6.6
Alopecia areata	17	3.8
Traction areata	1	0.2
I don't know	235	51.9
In what form did you use minoxidil?		
Oral	9	2.0
Liquid solution (drops, spray bottle)	447	98.7
Have you noticed any greying of hair with the use of minoxidil?		
Yes	118	26.0
No	335	74.0
If yes, how long after using minoxidil?		
3-5 months	62	13.7
6-8 months	22	4.9
1 year	15	3.3
More than 1 year	33	7.3
Not sure	69	15.2
Have you noticed any other changes in hair color?		
Yes	67	14.8
No	386	85.2
If yes, what color changes did you notice?		
Light brown	52	11.5
Orange	9	2.0
Yellow	4	0.9
Other	38	8.4
Do you use any other medications for hair loss?		
Yes	89	19.6
No	364	80.4
Do you have a history of familial greying of the hair?		
Yes	90	19.9
No	363	80.1

Questionnaires

Survey questions were formulated based on our literature review to include all the reported hair color changes associated with minoxidil use. We also included other greying of hair factors such as age and family history of early greying of hair. It took an average of 2 minutes to complete either of the questionnaires. For validation, a pilot study was conducted on 7 participants to confirm that the questions were well formulated and took an average of 2 minutes to complete. For a full description of the questionnaire, see Appendix.

Ethical consideration

The ethical review board approved the study at Security Forces Hospital, Riyadh, Saudi Arabia. Accreditation number (H-01-R-069). Informed consent was obtained from all participants before filling out the survey.

Statistical analysis

Data were analyzed using Statistical Package for Social Studies (SPSS 22; IBM Corp., New York, NY, USA). Categorical variables were expressed as percentages. chi square test and Fisher exact test were used for categorical variables. A P-value <0.05 was considered statistically significant.

Results

The total number of enrolled patients was 453, most of whom were between 18 and 34 years old. Almost 69.1% were female, and 86.3% were Saudi. Most of the participants have bachelor's or postgraduate education. 90.5% of the participants have a type of hair loss. Androgenic alopecia accounted for 37.5%. Interestingly, the percentage of greying of hair with the use of topical minoxidil was 26% (n=118). While 14.8% (n=67) noticed other hair color changes. Further demographic characteristics are presented in Table 1.

In addition, we analyzed the patients' data to seek the changes in hair color that was induced by topical minoxidil; 51.13% of the

enrolled patients experienced hair changes while they were on topical minoxidil course. The most common color change that was noticed was lightening of hair color to light brown (46.43%). Most of the patients (92.6%) reported that they were using topical minoxidil for 3-5 months; and during this period, they noticed the color changes. Further details are presented in Tables 2 and 3.

We performed correlation analyses and found that the presence of familial greying history and the duration of the course were two significant factors in inducing hair changes by topical minoxidil, P-value of 0.020, 0.046, respectively. Further details are presented in Table 4.

In addition, we analyzed the dermatologists' responses to our questionnaire; the total number of dermatologists was 57. Almost 60% of the physicians have ten years or more experience in Dermatology. 42.1% of the physicians noticed greying of hair on their patients after using minoxidil. 17.5% of the physicians think minoxidil caused hair greying, and 10.5% noticed other hair discoloration with minoxidil use. 7% of the other hair color discoloration noticed they were light brown, and 3.5% was orange. Further details are presented in Tables 5 and 6.

Discussion

This study involved analyzing the data of more than 400 patients utilizing minoxidil to establish a consensus on the effect of an unwanted side-effect of a prevalently used medication to treat hair loss. We aimed this study to find the correlation between minoxidil usage and the long-term greying of hair by utilizing a face-validated questionnaire.

Our analysis revealed that most patients currently on topical minoxidil are female in gender, more than 90% are using it to treat their hair loss, and 26% of these patients experienced hair discoloration that started after using topical minoxidil. Further analysis revealed that those with a previous family history of hair greying were the most affected, and those using the medication for more than one year were significantly more affected by hair greying than the rest of the group.

Table 2. Induced graying of hair of topical minoxidil use by gender (n=453).

		Female		Male		p
		Number	%	Number	%	
Have you noticed any greying of hair with the use of minoxidil?	Yes	84	26.84	34	24.29	0.568
	No	229	73.16	106	75.71	
If yes, how long after using minoxidil?	3-5 months	45	32.61	17	26.98	0.244
	6-8 months	16	11.59	6	9.52	
	1 year	11	7.97	4	6.35	
	More than 1 year	17	12.32	16	25.40	
	Not sure	49	35.51	20	31.75	
Have you noticed any other changes in hair color?	Yes	50	15.97	17	12.14	0.288
	No	263	84.03	123	87.86	
If yes, what color changes did you notice?	Light brown	39	52.00	13	46.43	0.429
	Orange	5	6.67	4	14.29	
	Yellow	2	2.67	2	7.14	
	Other	29	38.67	9	32.14	
Do you use any other medications for hair loss?	Yes	68	21.73	21	15.00	0.096
	No	245	78.27	119	85.00	
Do you have a history of familial greying of the hair?	Yes	58	18.53	32	22.86	0.286
	No	255	81.47	108	77.14	

Topical minoxidil proved its efficacy in AGA and is currently widely used off-label for other hair loss conditions. Furthermore, the side effects of such a widely used medication are currently being investigated; it is well-established that minoxidil causes minoxidil-induced telogen effluvium, skin irritation, and scalp changes in the scalp. However, very few studies reported a correlation between minoxidil usage and hair color changes.⁵⁻⁹ In the literature, few case reports were published reporting a rare side-effect due to the prolonged usage of minoxidil;^{10,11} Lyakhovitsky *et al.* noticed the development of xanthochromia that was mainly attributed to topical minoxidil treatment.¹⁰

In addition, Cranwell *et al.* noticed a marked color change in a patient treated with oral minoxidil for Loose anagen hair syn-

drome; they postulated that the marked color change could be used as an indicator of the disease resolution. However, the mechanism underlying the marked color change remains unclear to the authors.¹¹ On the other hand, Bublin *et al.* reported drug-induced hair color changes should only be considered if the patient has no other causes of such a condition. And that the mechanism behind such side-effect is unknown and require further investigation.¹²

The authors, in their systematic review, classified minoxidil as a drug that requires further confirmatory data to be considered a drug that may induce hair discoloration; Yale *et al.* conducted a systematic review and proved that the most common causes of hair color changes were stimulators of melanogenesis, vitamin supplementations, and anti-inflammatory medications; their com-

Table 3. Induced greying of hair of topical minoxidil use by age (n=453).

Variable		Under 18 years		18-24 years		25-34 years		35-44 years		45-64 years	
		Number	%	Number	%	Number	%	Number	%	Number	%
Have you noticed any greying of hair with the use of minoxidil?	Yes	2	12.50	43	16.73	46	35.38	20	55.56	7	50.000
	No	14	87.50	214	83.27	84	64.62	16	44.44	7	50.000
If yes, how long after using minoxidil?	3-5 months	1	16.67	35	35.00	18	28.13	6	16.67	2	22.222
	6-8 months	0	0.00	13	13.00	7	10.94	2	5.56	0	0.000
	1 year	0	0.00	3	3.00	6	9.38	4	11.11	2	22.222
	More than 1 year	0	0.00	11	11.00	17	26.56	3	8.33	2	22.222
	Not sure	5	83.33	38	38.00	16	25.00	7	19.44	3	33.333
Have you noticed any OTHER changes in hair color?	Yes	3	18.75	37	14.40	17	13.08	7	19.44	3	21.429
	No	13	81.25	220	85.60	113	86.92	29	80.56	11	78.571
If yes, what color changes did you notice?	Light brown	3	50.00	29	54.72	13	41.94	5	13.89	2	40.000
	Orange	0	0.00	5	9.43	4	12.90	1	2.78	0	0.000
	Yellow	0	0.00	2	3.77	1	3.23	0	0.00	0	0.000
	Other	3	50.00	17	32.08	13	41.94	2	5.56	3	60.000
Do you use any other medications for hair loss?	Yes	3	18.75	45	17.51	29	22.31	8	22.22	4	28.571
	No	13	81.25	212	82.49	101	77.69	28	77.78	10	71.429
Do you have a history of familial greying of the hair?	Yes	1	6.25	36	14.01	31	23.85	15	41.67	7	50.000
	No	15	93.75	221	85.99	99	76.15	21	58.33	7	50.000

Table 4. Induced greying of hair of topical minoxidil use by educational level.

Variable		High school diploma		Bachelors		Post graduate education		p
		Number	%	Number	%	Number	%	
Have you noticed any greying of hair with the use of minoxidil?	Yes	10	14.7	85	26.5	23	35.9	0.020*
	No	58	85.3	236	73.5	41	64.1	
If yes, how long after using minoxidil?	3-5 months	10	41.7	46	31.5	6	19.4	0.020*
	6-8 months	1	4.2	19	13.0	2	6.5	
	1 year	2	8.3	9	6.2	4	12.9	
	More than 1 year	1	4.2	21	14.4	11	35.5	
	Not sure	10	41.7	51	34.9	8	25.8	
Have you noticed any OTHER changes in hair color?	Yes	7	10.3	51	15.9	9	14.1	0.491
	No	61	89.7	270	84.1	55	85.9	
If yes, what color changes did you notice?	Light brown	6	42.9	40	51.9	6	50.0	0.610
	Orange	1	7.1	8	10.4	0	0	
	Yellow	0	0	4	5.2	0	0	
	Other	7	50.0	25	32.5	6	50.0	
Do you use any other medications for hair loss?	Yes	12	17.6	66	20.6	11	17.2	0.712
	No	56	82.4	255	79.4	53	82.8	
Do you have a history of familial greying of the hair?	Yes	10	14.7	61	19.0	19	29.7	0.046*
	No	58	85.3	260	81.0	45	70.3	

*Significant p-value.

prehensive systematic review did not report minoxidil as a drug that may induce hair color changes.¹³

We hypothesize that minoxidil could be classified as a drug that potentially induces hair discoloration; however, no original studies, up to our knowledge, provide valuable data to withdraw consensus conclusions. Therefore, we encourage further data to be reported in the literature investigating the ability of minoxidil to

induce hair discoloration. Furthermore, the traits associated with the patients who experience hair discoloration must be reported to withdraw valuable conclusions about the potential of this widely used drug to induce the complication, as mentioned earlier.

This study contains a few limitations that must be addressed. First, this study was cross-sectional, which involves the unavoidable limitations of a study design, such as the probability of bias.

Table 5. Characteristics of the physicians and their opinion about the use of minoxidil (n=57).

	Number	%
Gender		
Male	27	47.4
Female	30	52.6
Professional occupation		
Resident	14	24.6
Assistant consultant	5	8.8
Consultant	38	66.7
How long have you been practicing dermatology?		
1 year	7	12.3
2-3 years	6	10.5
4-5 years	10	17.5
10 years	20	35.1
More than 15 years	14	24.6
Have you noticed greying of hair on your patients after using minoxidil?		
Yes	24	42.1
No	33	57.9
If yes, how long after using minoxidil?		
3-5 months	5	8.8
6-8 months	4	7.0
1 year	4	7.0
More than 1 year	1	1.8
Not sure	8	14.0
Do you think minoxidil caused the greying of hair?		
Yes	10	17.5
No	2	3.5
Not sure	10	17.5
If greying of hair was noted, which formulation was used by the patient?		
Oral	1	1.8
Liquid solution	21	36.8
Did you notice any OTHER hair discoloration with minoxidil use?		
Yes	6	10.5
No	47	82.5
If Yes, what color did you notice?		
Light brown	4	7.0
Orange	2	3.5

Table 6. Opinion of the physicians by their professional occupation.

Variable		Resident		Assistant consultant		Consultant		p
		Number	%	Number	%	Number	%	
Have you noticed greying of hair on your patients after using minoxidil?	Yes	8	57.1	3	60.0	13	34.2	0.231
	No	6	42.9	2	40.0	25	65.8	
If yes, how long after using minoxidil?	3-5 months	3	42.9			2	16.7	0.559
	6-8 months			1	33.3	3	25.0	
	1 year	2	28.6			2	16.7	
	>1 Year					1	8.3	
	Not sure	2	28.6	2	66.7	4	33.3	
Do you think minoxidil caused the greying of hair?	Yes	4	57.1	2	66.7	4	33.3	0.670
	No	1	14.3			1	8.3	
	Not sure	2	28.6	1	33.3	7	58.3	

Second, the questionnaire utilized was only face-validated and was revised by experts in the field of dermatology; yet, not utilizing a validated questionnaire is a limitation of this study. Third, we only surveyed the patients in the kingdom of Saudi Arabia and Middle Eastern in ethnicity; therefore, the results presented could not apply to other ethnicities, including Caucasians, Asians, and Hispanics. Nevertheless, this study may be a stepping stone in encouraging further reported data about the effect of minoxidil in inducing hair discoloration.

Conclusions

In our study, although minoxidil is a safe and well-tolerated medication, undesirable side effect such as change in hair pigmentation have been reported by many patients and dermatologist. Greying of the hair was the most common color noticed by participants, followed by different shades of brown and yellow. Our finding suggests a possible association between changes in hair pigmentation and minoxidil. Therefore, dermatologists should be mindful of this adverse event as to educate patients about it. Nonetheless, more research is required to develop a deeper understanding of such relationship.

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