

# Five-year follow-up of men with androgenetic alopecia treated with topical minoxidil

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Thirty-one men with androgenetic alopecia completed 4½ to 5 years of therapy with 2% and 3% topical minoxidil. Hair regrowth with topical minoxidil tended to peak at 1 year with a slow decline in regrowth over subsequent years. However, at 4½ to 5 years, maintenance of nonvellus hairs beyond that seen at baseline was still evident. Topical minoxidil appears to be effective in helping to maintain nonvellus hair growth in men with androgenetic alopecia. (*J AM ACAD DERMATOL* 1990;22:643-6.)

Topical minoxidil (Rogaine) has been shown to be an effective agent in the treatment of androgenetic alopecia. In a 4-month, placebo-controlled trial, patients treated with 2% and 3% topical minoxidil twice daily showed a statistically significant increase in target area terminal hair counts versus placebo.<sup>1</sup> During the entire 12-month controlled trial, there was almost a twofold increase in target area terminal hairs in those receiving active drug<sup>1</sup> and 24% to 56% of patients had moderate to dense regrowth.<sup>1-3</sup>

What happens with continued use of topical minoxidil for many years? We reported that hair regrowth tended to plateau after approximately 1 year of treatment with topical minoxidil with maintenance of this growth after 2 years and 9 months of application twice a day. The purpose of this article is to extend the follow-up in those men who have continued to use topical minoxidil for 4½ to 5 years.

## METHOD

**Protocol.** One hundred twenty-six men with androgenetic alopecia completed the first year of a placebo-controlled trial of 2% and 3% topical minoxidil (Fig. 1). At 4 months the placebo-treated group and at 12 months the

**Table I.** Study population at baseline

	Subjects who completed 1 yr but not 4.5-5 yr (n = 95)	Subjects who continued topical minoxidil 4.5-5 yr (n = 31)
Age (yr) (range)	36.0 (20-48)	37.7 (27-48)
Duration (yr) (range)	10.5 (2-30)	9.9 (2-21)
Pattern (%)		
III (vertex)	33	32
IV	30	36
V	28	19
V <sub>A</sub>	7	13
VI	2	0

2% minoxidil group were crossed over to 3% topical minoxidil. Patients applied the study medication twice daily for the entire 4½ to 5 years of long-term follow-up with the exception of a 9- to 12-month period beginning at 2 years when half of the patients were randomized to once-daily application. Because of perceived superior efficacy by patient and investigator alike of the twice-daily application, all patients using topical minoxidil once daily returned to twice-daily dosing by 3 years.

**Subjects.** Thirty-one of the 126 men who completed the first study year continued to use topical minoxidil for 4½ to 5 years. Hair counts were done in the midvertex region as previously described<sup>5</sup> and by the same experienced counter. Hair counts were performed monthly during the first year, at 2 years 9 months, 3 years, and at 4½ to 5 years. Standardized photographs were also taken and evaluated.

**Statistical analysis.** Statistical testing was performed with the  $\chi^2$  statistic for categorical data and linear regression analysis for continuous data.

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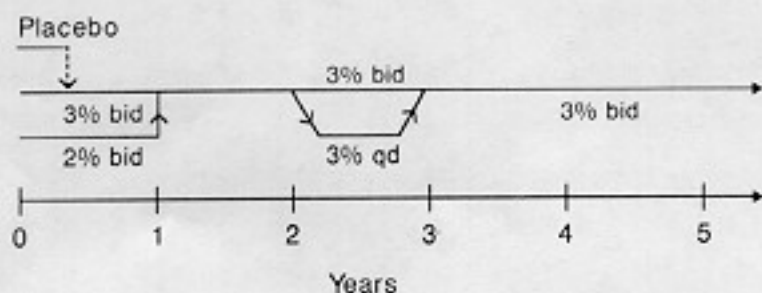


Fig. 1. Topical minoxidil in the treatment of androgenetic alopecia.

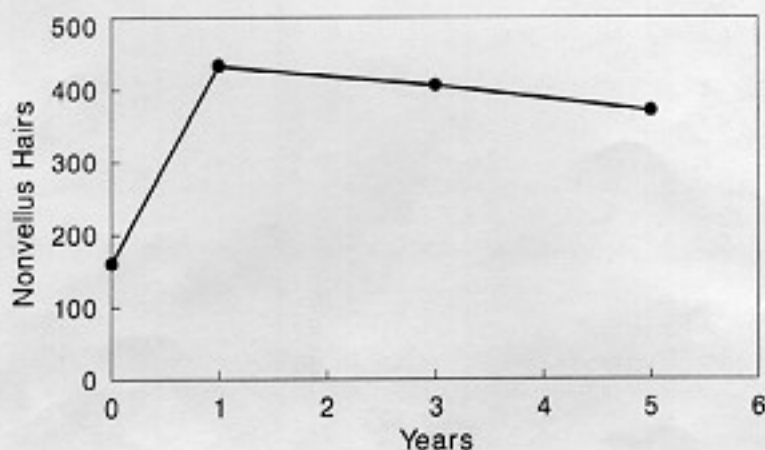


Fig. 2. Longitudinal nonvellus target area hair counts in patients with androgenetic alopecia treated with topical minoxidil.

Table II. Longitudinal nonvellus target area hair counts

Change from baseline nonvellus hairs	Time receiving treatment		
	1 yr	3 yr	4.5-5 yr
Mean	273.4	246.2	211.0
SD	157.1	171.8	164.2
Min/max	4/577	-45/728	-97/570

Min/max, Minimum/maximum; SD, standard deviation.

## RESULTS

A comparison of the age, duration, and pattern of hair loss of those who completed the original 12-month study versus those who continued topical minoxidil for 4½ to 5 years is given in Table I. Patients who completed the long-range follow-up were not statistically different in terms of baseline age, duration, or pattern of baldness from the larger initial group ( $p > 0.15$ ). The patients who continued with

topical minoxidil for 4½ to 5 years tended to have lower baseline nonvellus hair counts ( $p = 0.076$ ) than the short-term group but had a similar amount of hair growth during the initial 12 months ( $p = 0.360$ ).

Hair regrowth with topical minoxidil peaked at approximately 1 year of treatment with a slight but not statistically significant decrease in 1-year counts seen at the 3-year visit ( $p = 0.16$ , Fig. 2). At 1 year there was a mean increase in nonvellus hairs compared with the baseline count of 273.4 ( $\pm 157.1$ ) and that at 3 years, 246.2 ( $\pm 171.8$ ). At 4½ to 5 years a further decrease was noted in the mean nonvellus hair counts (Table II), which was a statistically significant decrease from the 1-year nonvellus hair counts ( $p = 0.012$ ) but was still a significant ( $p < 0.001$ ) increase over the baseline count ( $206.6 \pm 163.3$ ). However, some patients receiving long-term treatment with topical minoxidil continued to have an increase in nonvellus target area counts at 4½ to 5 years beyond their 1-year counts ( $n = 9$ ). Similarly, a few subjects, despite continued

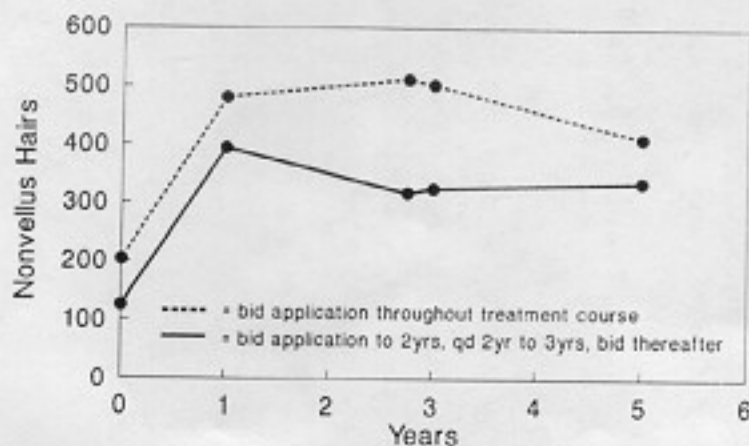


Fig. 3. Longitudinal analysis of target area hair counts in patients using topical minoxidil for androgenetic alopecia: comparison of frequency of application.



Fig. 4. Patient at baseline and 3 years 4 months with topical minoxidil.

treatment with topical minoxidil, had nonvellus target area hair counts decrease below baseline ( $n = 4$ ,  $-36 \pm 40.5$ ).

We attempted to identify whether patients who were treated with topical minoxidil once daily ( $n = 17$ ) for 9 to 12 months had a different subsequent course of hair growth or loss compared with those who continuously used twice-daily topical minoxidil throughout the study ( $n = 14$ , Fig. 3). The once-daily group had a notable decline in target area nonvellus counts between 1 and 3 years ( $-68.2 \pm 90.9$ ,  $p = 0.015$ ) compared with the twice-daily group, who continued to have a slight increase in counts ( $22.6 \pm 104.3$ ). After transfer back to twice-daily treatment, the hair loss stabilized in the daily dose

treatment group. At 4½ to 5 years the change from the 1-year nonvellus hair counts in both treatment groups was not statistically different ( $p = 0.87$ ). The statistical results of the comparison of daily regimens were unaltered by a covariate adjustment for age, duration of baldness, and baldness pattern.

Photographs of patients seen at 3 years 4 months and 4 years 2 months of follow-up are shown in Figs. 4 and 5, respectively.

#### DISCUSSION

In androgenetic alopecia, topical minoxidil produces regrowth of a certain percentage of miniaturized hairs in affected areas. Discontinuation of the medication results in a prompt fall-out in 4 to 6



Fig. 5. Patient at 5 months and 4 years 2 months with topical minoxidil.

months of the hair gained during treatment.<sup>6</sup> A reduced maintenance schedule has not been thoroughly evaluated, but preliminary evidence supports the need to continue indefinitely with a twice-daily regimen to maintain hair growth.<sup>4</sup>

Like Koperski et al.,<sup>7</sup> we<sup>4</sup> found that hair regrowth with topical minoxidil tends to plateau at about 12 months of treatment with a slight decline in this new growth by 2½ to 2¾ years. With follow-up now to 4½ to 5 years, we have found that continued use of topical minoxidil is associated with a slow decline in the 12-month hair counts but continued maintenance of nonvellus hair regrowth well beyond that at baseline. Rietschel and Robertson<sup>8</sup> reported a 45-month follow-up of patients who used topical minoxidil under a similar study protocol and found that there was a continued increase in target hair counts with time. The reason for the disparity is not clear.

We have reported on the equivalency of 2% and 3% topical minoxidil so the results here can probably be extrapolated to the commercially available form of 2% topical minoxidil (Rogaine).<sup>1,9</sup> There are several explanations as to why topical minoxidil could be less effective at 5 years than at 1 year. Perhaps this is secondary to tachyphylaxis or an obligatory cycling in hair growth. Topical minoxidil stimulates the growth of epidermal cells in culture<sup>10,11</sup> and presumably stimulates hair growth by initiating and promoting the anagen phase of these epidermally derived structures. The average duration of anagen in scalp hair is 3 years.<sup>12</sup> Whether

topical minoxidil or any other hair growth promoter can prolong anagen or the way in which it affects the anagen/telogen cycling process is unknown.

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