Topical Minoxidil for Extended Areate Alopecia

GERDA FRENTZ

Department of Dermatology, The Finsen Institute, Copenhagen

Frentz G. Topical minoxidil for extended areate alopecia. Acta Derm Venereol (Stockh) 1985; 65: 172–175.

A double-blind cross over study on the effect of 3 months' treatment with 1% topical minoxidil on 23 individuals with alopecia areata was performed. Thirteen of the patients showed some increase in terminal hair growth, the difference between the number of responders to placebo and minoxidil lotion being significant ($p<0.005$). However, in one case only, the result was cosmetically satisfying. In two male patients the blood pressure increased coinciding with the withdrawal of the minoxidil lotion. *Key words: Alopecia totalis; Alopecia universalis; Topical treatment; Withdrawal hypertension.* (Received May 29, 1984.)

G. Frentz, Department of Dermatology, the Finsen Institute, 49 Strandboulevarden, DK-2100 Copenhagen Ø, Denmark.

Minoxidil (2.4-diamino-6 piperidinopyrimidine-3 oxide) is a potent antihypertensive drug. It is a peripheral vasodilator, especially enhancing the cutaneous blood flow. It does not reduce the blood pressure of normotensive individuals (1). Side effects of systemic minoxidil are hypertrichosis, fluid retention, reflex cardiac stimulation, ECG-changes, angina pectoris, tachycardia, nausea, fatigue, dyspnoea and gynecomastia (2, 3). The hypertrichosis which occurs over the forehead, periorbital area, ears, face, extremities and lower back in at least 80% of the patients slowly diminishes after discontinuation of the drug (4). The cutaneous side effects are generalized papular eruption (2), pigmentation changes (3), coarsening of the skin, flushing, prickling of the skin, bullous eruptions and pseudoporphyria. Besides hypertrichosis colour changes of the hair and alopecia have been reported associated with minoxidil treatment (5). Stimulated by case reports on regrowth of hair in baldness during systemic minoxidil treatment (6, 7), topical application of minoxidil has been introduced for treatment of alopecia (1, 8).

The present report concerns a double-blind cross over study on the effect of 1% minoxidil lotion in extended alopecia of areate type in 23 patients.

MATERIAL AND METHODS

23 out-patients—10 women and 13 men, aged 12–57 years, median 29—with extended alopecia of areate type (areata 4, subotalis 5, totalis 2, subuniversalis 5, universalis 7) with hair disease duration from ½–23 years, median 4,5 years, were studied. Each patient was provided with either 1% minoxidil lotion (ground minoxidil tablet 1%, propylene glycol 10%, aqua purificata 20%, spiritus fortis onto 100%) or placebo lotion (microsized cellulose 11.7%, maize starch 5%, propylene glycol 10%, aqua purificata 20%, spiritus fortis onto 100%). The patients were instructed, on having shaken the minoxidil lotion to applicate 0.5 ml (corresponding 5 mg ground minoxidil) to the scalp in a thin layer every morning and evening for three months. After the night application a thin layer of petrolatum was applied for occlusive purposes according to Weiss et al. (1). Subsequent to 1-month wash-out period the alternative test/placebo lotion was used for the next three months. After a final 1-month wash-out period the trial was finished (Fig. 1).

The patient was seen with 1 month's intervals. At the start of the trial, by the end of month 3, 4, 7, and 8 increase in general hair growth was evaluated by clinical estimation combined with photographic registration. On these occasions also blood sedimentation rate, Hb, leucocytes, differential count, aspartate-aminotransferases, alkaline phospatases, blood potassium and sodium and creatinine and urinalysis as well as ECG were checked. At every visit the blood pressure was measured three times with no less than 1 min interval after resting in horizontal position for at least 15 min. Changes in the

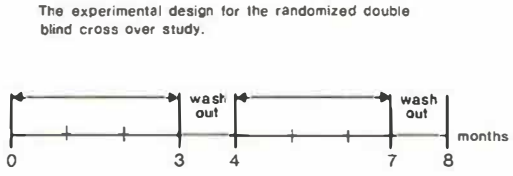

Fig. 1. The experimental design: (↔) placebo or minoxidil lotion. Blood pressure control and clinical follow-up once monthly. (I) Blood pressure control, clinical follow-up, laboratory screening, ECG, evaluation of changes in terminal hair growth on the scalp.

parameters were recorded as significant when exceeding the limits for normal values. All subjective complaints were noted.

For each patient personal atopy, organ specific autoimmune features and thyroid diseases as well as the modality of previous therapeutical approaches were recorded.

The final statistical evaluation of the therapeutical effect on hair growth was performed by the X^2 test with Yates' correction (MacNemar's test).

RESULTS

By the parameter increase in terminal hair growth on the scalp by clinical evaluation combined with photographic registration 13—7 women and 6 men out of the 23 patients—responded positively to the minoxidil lotion. In one patient regrowth occurred in the placebo period as well as in the minoxidil period. None responded to the placebo lotion exclusively. Ten patients showed increase in terminal hair growth only during the minoxidil period. The positive response to the minoxidil lotion versus placebo was highly significant ($p<0.005$).

However, clinically the quality and amount of the regrowing hair was not very impressing and one patient only—with areate affection—achieved cosmetically acceptable regrowth.

As a rule the limited regrowth occurred after 1 to 2 months' treatment. After withdrawal of the active lotion hair loss was seen in 4/13, complete stop of progression in hair growth in 5/13, and reduced progression in hair growth in 4/13, all after 1–2 months. A tendency towards better response in the less extended cases was noted (Fig. 2). The responders were of the same age as the non-responders (median ages 29 versus 27½ years), but the responders had a longer disease duration than the non-responders (median durations 6½ versus 3 1/3 years).

Blood pressure. One female and one male had from the start labile blood pressure at the upper limit of the normal value (170 systolic, 115 diastolic, and 150 systolic, 100 diastolic). In the female—an atopic, aged 36—the blood pressure normalized gradually over some months apparently independent of the phase of the trial. In the male, aged 45, the blood

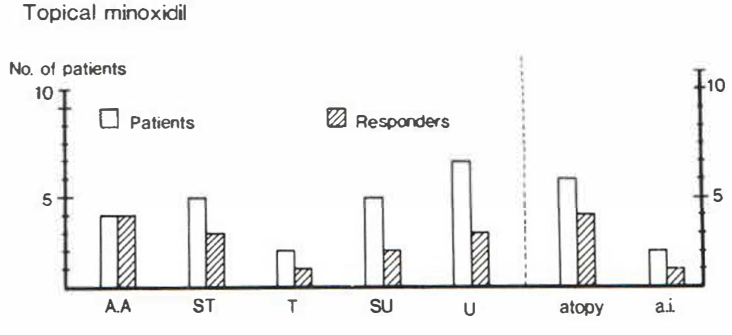

Fig. 2. The distribution of responders to topical minoxidil according to the degree of baldness: areate (AA), subtotal (ST), total (T), subuniversal (SU), and universal (U) alopecia, and to the occurrence of personal atopy or autoimmune conditions (a.i.).

pressure further increased (systolic 160–180, diastolic 105–115) after the minoxidil lotion was discontinued.

At the start of the trial one male, aged 43, who had had a heart attack 3 years before, showed a slightly elevated aspartate aminotransferase value (47 units/litre: normal values 10–40). One month after the minoxidil phase his blood pressure had increased from the previous normal value (140/90) to 180/120, and his aspartate aminotransferase level showed temporarily a further increase (asparate aminotransferase 91 U/l). Five months after the withdrawal of the minoxidil his blood pressure remained increased.

Laboratory screening. No significant changes in the values were seen in any patient except those mentioned above.

ECG. From the start the ECG of all the patients was normal and no significant changes were observed.

Topical side effects. Four patients experienced temporarily scaling and slight itching with or without occurrence of accuminate papules or follicles, but in one patient only this occurred in the minoxidil period.

CONCLUSION AND DISCUSSION

The present study confirms that topical minoxidil as a 1% lotion is capable of producing some terminal hair regrowth in the areate type of alopecia even in long-standing and extended cases. However, within the observation period cosmetically acceptable hair growth was an exceptional event among these severely affected individuals. In 1981 Weiss et al. (1) experienced positive response to topical minoxidil on hair growth in alopecia areata and recently Fenton & Wilkinson (9) in a modified double-blind cross over study reported response to topical minoxidil in about 80% of their patients who were less severely affected than those here studied. Cosmetically acceptable regrowth was seen in 16 of 30 patients in their study.

Hitherto no serious side effects of topical minoxidil have been reported.

Blood pressure elevation has been reported to occur as a rebound phenomenon following withdrawal of systemic minoxidil tretament (10). The amount of minoxidil topically applied in the present study and in the study of Fenton & Wilkinson (9) approximates 5 mg twice a day. However, it cannot be excluded that small amounts of minoxidil can be measured in the blood second to such topical application (8).

The development of the increase in the blood pressure in two males in the present study after the withdrawal of topical minoxidil might very well be coincidental. Concerning the patient with a marginally increased aspartate aminotransferase perhaps indicating decreased ability in the liver to metabolize minoxidil, it cannot be completely disregarded that the withdrawal of topical minoxidil might have played a causative role.

REFERENCES

1. Weiss VC, West DP, Mueller CE. Topical minoxidil in alopecia areta. J Am Acad Dermatol 1981; 5: 224–226.
2. Nawar T, Nolin L, Plante GE, Caron C, Montambault P. Longterm treatment of severe hypertension with minoxidil. Can Med Assoc 1977; 117: 1178–1182.
3. Jacomb RG, Brunnberg FJ. The use of minoxidil in the treatment of severe essential hypertension. A report on 100 patients. Clin Sci Mol Med 1976; 51: 579–581.
4. Burton JL, Marshall A. Hypertrichosis due to minoxidil. Br J Dematol 1979; 101: 593–595.
5. Ingles RM, Kahn T. Unusual hair changes with minoxidil therapy. Int J Dermatol 1983; 22: 120–122.
6. Zappacosta AR. Reversal of baldness in a patient receiving minoxidil for hypertension. N Engl J Med 1980; 303: 1480–1481.

7. Seidman M, Westfried M, Maxey R, Rao TKS, Friedman EA. Reversal of male pattern baldness by minoxidil. A case report. Cutis 1981; 28: 551–553.
8. Editorial. Blood pressure drug aids areata baldness. Medical World News 1982; 31–32.
9. Fenton DA, Wilkinson JD. Topical minoxidil in the treatment of alopecia areata. Br Med J 1983; 287: 1015–1017.
10. Makker SP, Moorthy B. Rebound hypertension following minoxidil withdrawal. J Pediatr 1980; 96: 762–766.