

## Does Topical Minoxidil Increase Skin Blood Flow?

### A Laser Doppler Flowmetry Study

E. M. DE BOER,<sup>1</sup> P. D. BEZEMER,<sup>2</sup> D. P. BRUYNZEEL<sup>1</sup> and C. NIEBOER<sup>1</sup>

<sup>1</sup>Department of Dermatology and <sup>2</sup>Department of Medical Statistics, the Free University of Amsterdam, The Netherlands

de Boer EM, Bezemer PD, Bruynzeel DP, Nieboer C. Does topical minoxidil increase skin blood flow? A laser Doppler flowmetry study. *Acta Derm Venereol (Stockh)* 1988; 68:271-274.

Cutaneous blood flow was measured by Laser Doppler Flowmetry after topical application of minoxidil lotion, in 9 healthy males with androgenetic alopecia, and other volunteers. No reaction in the cutaneous blood flow was seen after application of 2%, 5%, or placebo minoxidil lotion. *Key words:* Cutaneous blood flow; Androgenetic alopecia. (Received October 10, 1987.)

E. M. de Boer, Department of Dermatology, Free University Academic Hospital, De Boelelaan 1117, 1081 HV Amsterdam, The Netherlands.

In patients with severe hypertension, orally administered minoxidil (2,4-pyrimidinediamine, 6-(1-piperidinyl)-3-oxide) has been shown to be a potent vasodilator. In normotensive persons, however, oral minoxidil does not lower the blood pressure [1]. The topical application of minoxidil has been introduced for alopecia areata and androgenetic alopecia. The mechanism of action is uncertain. Biopsies taken from the scalp before and during this treatment showed a decrease of the perifollicular infiltrate in alopecia areata [4]. In both types of alopecia, normalization of the size and form of the withered hair follicle and reopening of previously closed dermal vessels have been reported [1, 2, 3].

The purpose of the present investigation was to study whether topical minoxidil influences cutaneous blood flow. And, if so, is there a difference in the effect of minoxidil on the skin blood flow between patients with regrowth of hair and those without. The blood flow was recorded by Laser Doppler Flowmetry (LDF).

## MATERIALS AND METHODS

### Laser Doppler Flowmetry

Cutaneous blood flow was measured by LDF (Periflux PF2, Perimed, Stockholm, Sweden). The blood flow is recorded linearly as the product of the encountered red blood cells and their mean velocity [4, 5]. The radiation penetrates the skin to a depth of 1-1.5 mm, measuring the dermal capillaries and arteriovenous shunts [4].

With a newly designed plexiglass probeholder, adhesive tape for fixation was at least 1.5 cm away from the measuring point. In this probeholder the probe was placed 4 mm above the skin surface, thus enlarging the measured area from about 3 mm<sup>2</sup> to 20 mm<sup>2</sup>.

### Study subjects

Group I consisted of 50 healthy males with early stage androgenetic alopecia who had been treated with 2% minoxidil lotion or a placebo for 6 months. At random, 5 persons were chosen (group Ia), who showed regrowth of hair on the vertex and 5 persons (group Ib) who did not (age range 28-43 years). One person in group Ia dropped out because of illness. The volunteers stopped the minoxidil treatment 3 days before the tests.

Group II consisted of 12 healthy females (age range 19-56 years). In the literature, no sex difference with regard to hypertrichosis due to minoxidil therapy has been observed.

### Study design

In group I, 1 ml of a 2% minoxidil lotion was applied on 50 cm<sup>2</sup> of the balding vertex. In group II, minoxidil lotion was applied to the volar aspects of a forearm in two concentrations (5% and 2%).

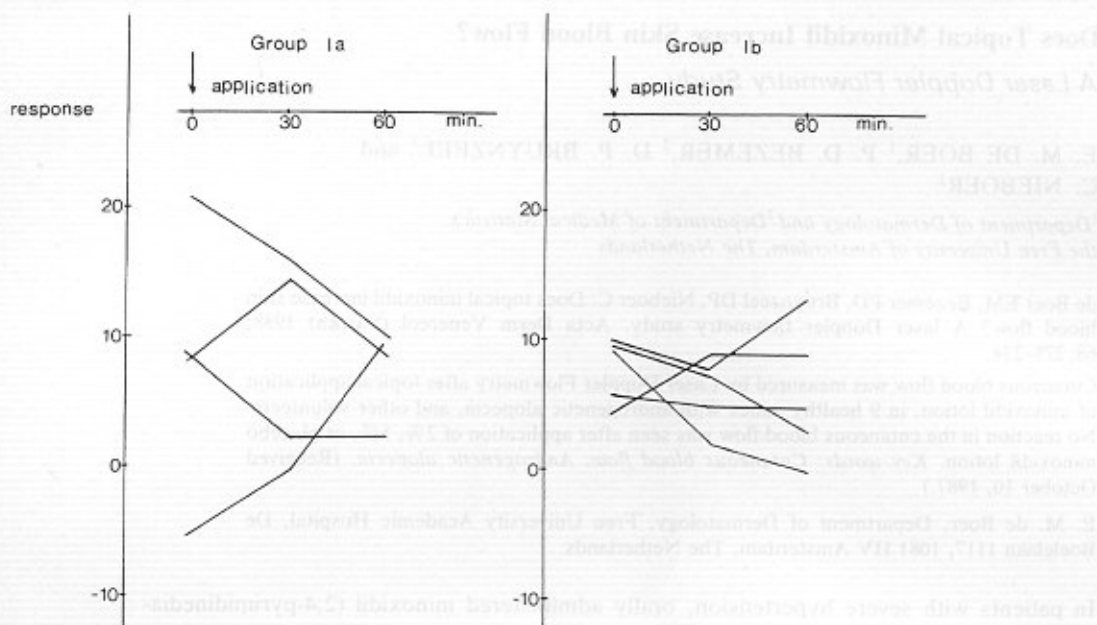


Fig. 1. Results in group I: responses prior to, 30 and 60 min after application of 2% minoxidil lotion for each person. Mean values are indicated; no significant difference was observed between the 3 consecutive days.

Testing on forearms is our standard procedure in LDF. The lotion without the drug served as a blank control. LDF was done prior to application of the solutions and 30 respectively 60 min afterwards, on 3 consecutive days.

Non-treated skin control sites were measured in order to overcome variation in normal blood flow.

#### Minoxidil lotion

Group I was investigated with Regaine (2% minoxidil lotion) and group II with minoxidil lotion prepared by the hospital pharmacy.

#### Statistical methods

The relevant response is defined as the difference between the LDF measurement at the site of application and the corresponding untreated control value. This term 'response' will be considered in the interpretation of the results.

With standard analysis of variance methods it was tested, at a two-sided significance level of 5%:

- 1) For group Ia and Ib: whether the response systematically differs between three occasions, namely prior to, 30 and 60 min after application, and between the 3 days (analysis of variance with 3 factors: persons, days and occasions).
- 2) For group II: as in 1), but in addition differences between the three concentrations were tested (analysis of variance with 4 factors: persons, days, occasions and concentrations).

## RESULTS

In group I, cutaneous blood flow did not increase after application of 2% minoxidil lotion, nor was there an increase over days. The variation in skin blood flow in the minoxidil-treated test sites was similar to that in the control sites (Fig. 1). One person complained on the third day of itching on the scalp which was due to a flare-up of seborrheic eczema. The recorded value was not reliable and therefore excluded.

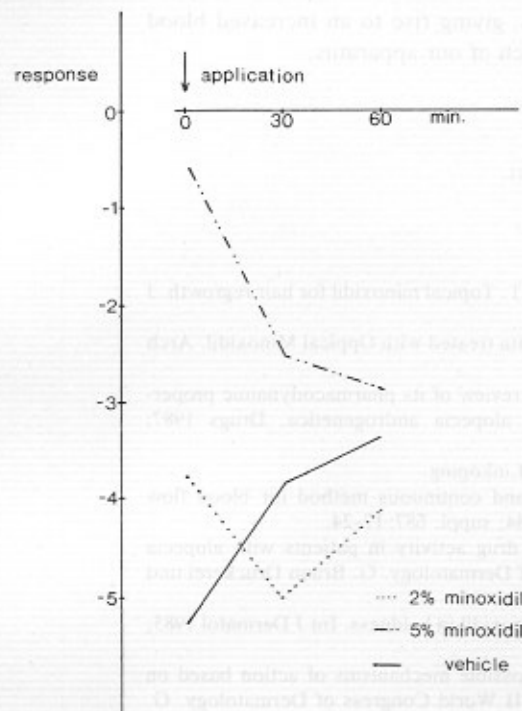


Fig. 2. Results in group II: response prior to, 30 and 60 min after application of the lotion. The measurements on 3 consecutive days in the 12 persons have been averaged as no significant difference was observed.

In group II, no significant difference could be detected in the response on three different occasions, nor at 3 consecutive days nor for three different concentrations. Minoxidil-treated sites did not differ from the vehicle-treated or untreated control sites (Fig. 2).

## DISCUSSION

No significant increase of blood flow on the balding scalp after application of 2% minoxidil lotion has been observed in this study. There was no difference in subjects who showed regrowth of hair on treatment with this solution and persons without regrowth. Application of 2% and 5% minoxidil lotion on the forearms also did not increase the skin blood flow in the other group of volunteers. In this group the importance of including a daily untreated control site was demonstrated. Changes in the temperature did influence the recorded values of the treated and untreated skin sites equally, and therefore did not influence the end results.

The working mechanism of topical minoxidil is uncertain, but it has been suggested that the induced hair growth may be related to increased cutaneous blood flow. Minoxidil, as a potent vasodilator, might thus stimulate the microcirculation in the surroundings of the hair follicle [6, 7, 8]. Wester et al. [9] used LDF and photopulse plethysmography to measure scalp flow in 16 balding subjects in a study with 1%, 3% and 5% minoxidil lotion. Only the 5% solution caused a statistically significant increase in blood flow. These observations contrast with our results and those of Bunker & Dowd [10], who did not observe an increase in scalp blood flow after application of a 3% minoxidil solution. Our findings support the hypothesis of Bunker & Dowd [10] that topical minoxidil induces hair growth in androgenetic alopecia by other mechanisms than by virtue of peripheral vasodilatation. However, the possibility cannot be excluded that percutaneous resorption of

minoxidil occurs, especially through the hair follicles, giving rise to an increased blood flow in the perifollicular plexus that is beyond the reach of our apparatus.

#### ACKNOWLEDGEMENT

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