  ISSN 0954-6634

Topical finasteride in the treatment of androgenic alopecia. Preliminary evaluations after a 16-month therapy course

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The enzyme 5α-reductase (5AR), which catalyzes reduction of testosterone to the more potent metabolite dihydrotestosterone, has been assumed to play a key role in a variety of skin disorders, including acne, seborrhea, hirsutism, and androgenic alopecia (AA). Also, evidences have been provided supporting the pathogenetic relevance of higher rates of testosterone reduction at lesional level. The azasteroid finasteride, a 5AR inhibitor, is widely employed in the treatment of benign prostatic hyperplasia; by contrast, its potential role in other androgen-related conditions have been, so far, only poorly evaluated.

We present herein the results of a single-blind, placebo-controlled, 16-month trial carried out in 52 patients with AA using a 0.005% finasteride solution. The clinical outcome, in terms of both hair regrowth and balding areas reduction, seems to be encouraging, in the absence of either any evidence of percutaneous absorption of finasteride, or local/systemic untoward effects.

We also briefly review the possible pharmacodynamic and pharmacokinetic bases of the use of topically delivered finasteride in AA. (*J Dermatol Treat* (1997) 8: 189–192)

Received 23rd August 1996
Accepted 18th March 1997

Keywords: ***Androgenic alopecia — Androgen-related conditions — Finasteride — 5α-Reductase***

Introduction

Much evidence has been provided to support the hypothesis that disorders of androgen metabolism are important in the pathogenesis of a variety of skin diseases, including acne, seborrhoea, hirsutism, and androgenic alopecia.[1] An amplified response of androgen-sensitive tissues is thought to be involved through either an enhanced capacity of the intracellular receptor to bind the hormones or a higher local conversion of relatively weak androgens into more potent metabolites. In this pathogenic framework the enzyme 5α-reductase (5AR) is likely to play a cornerstone role by catalysing the reduction of testosterone to dihydrotestosterone, whose potency is nearly twice that of testosterone.[2]

On the basis of this evidence, the use of finasteride (*N*-(1,1-dimethylethyl)-3-oxo-4-aza-5α-androst-1-ene-17β-carboxamide),[3] a 5AR inhibitor, may be a rational therapeutic approach to androgen-related diseases. To our knowledge, the oral use of this drug in subjects with androgenic alopecia has been only poorly evaluated.[4–6]

The aim of this study was to assess the tolerability and efficacy of finasteride delivered topically in males and females with androgenic alopecia.

Patients and methods

The study group comprised 52 otherwise healthy subjects with androgenic alopecia (28 males and 24 females; aged 18 to 38 years, mean 28; Table I). No patient had received therapy for alopecia or other cutaneous or noncutaneous diseases for at least 1 month prior to beginning the protocol. Moreover, no female patient had been taking oral contraceptives during the previous year. After informed consent had been obtained, patients were randomly allocated into two study groups: 26 patients received a 0.005% solution of finasteride; the remainder received the vehicle only (consisting of 50% ethyl alcohol, 25% propylene glycol, and 25% distilled water). The identity of the treatment was concealed from the patients, according

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	Age (years)	Disease duration (years)	Disease severity[a]
Males	Mean 24, range 18–35	Mean 3, range 2–5	II (13 patients) III (15 patients)
Females	Mean 32.8, range 23–38	Mean 2, range 1–3	I (11 patients) II (13 patients)
All	Mean 28, range 18–38	Mean 2, range 1–5	

[a]According to the scale of Hamilton[7] and Ludwig[8] for males and females, respectively

Table I
General characteristics of 52 patients with androgenic alopecia.

to a single-blind study design. The trial was conducted over a 16-month period during which each patient applied 1.0 ml of the study medication using a graduated dropper twice daily to the balding area(s) of the scalp. All patients were examined at monthly intervals. At each visit, photographs were taken. During treatment the clinical response was followed by comparing sequential photographs.

At the end of the study, the assessment of the results in terms of hair regrowth was made by the same staff member according to the six-point scale shown in Table II.

The results were also evaluated in terms of hair loss by performing a 'wash test' at 2-month intervals. The wash test was carried out according to the following standardized procedure: patients were asked not to wash their scalp for 1 week, during which they had to comb their hair twice a day (morning and evening). They were instructed to collect all hairs lost during shampooing at the end of this period (this was accomplished by placing a small-mesh net over the drain of the bathtub at home). The bimonthly hair counts of all patients were then recorded and the unpaired Student's *t*-test was used to evaluate the significance of differences observed between the two study groups throughout the treatment course. Furthermore, at the end of treatment the patients' opinions and self-perceived changes in the status of the scalp hair were recorded and categorized according to a four-point scale of effectiveness with 3 indicating high effectiveness and 0 indicating no effect.

5	Complete restoration of hair density
4	Marked reduction of balding area(s)
3	Slight reduction of balding area(s)
2	No change compared to baseline
1	Slight enlargement of balding area(s)
0	Marked enlargement of balding area(s)

Table II
Six-point scale for evaluation of hair regrowth.

Prior to treatment and every 3 months, the following laboratory tests were carried out: complete blood cell count; full serum and urine chemistry panel; and determination of plasma concentration of total testosterone, free testosterone and dihydrotestosterone. The latter investigations were performed only in the group receiving finasteride, in order to detect any possible systemic effect related to percutaneous absorption of finasteride. In females, blood samples were taken on day 21 of the menstrual cycle.

Results

Of the 52 patients enrolled, 36 (69.2%) completed the entire study period. Notably, all dropouts occurred in the placebo group after 1 to 10 months. Moreover, the overall tolerability of the treatment was excellent. No patient experienced any local or systemic untoward effect. In particular, in the finasteride group laboratory data revealed no relevant change in plasma levels of total testosterone, free testosterone or dihydrotestosterone. On the basis of these findings any significant percutaneous absorption of the drug could reasonably be excluded.

Evaluation of hair regrowth

During the first 3 months of the trial, the clinical response was not significant. The scores for hair regrowth ranged from 1 to 2 with no significant difference between the two study groups. By contrast, throughout the subsequent course of the study a significant improvement in the status of the scalp hair was observed among the finasteride-treated patients. At the end of the study, the clinical results were scored 4 in 12 patients and 3 in the remaining 14. Response to treatment was substantiated by both an increase in the hair density at the periphery of balding areas and a progressive, though slow and incomplete retrieval of the hair texture within previously bare sites. Patients initially grew vellus-type hair that tended to change to thicker, pigmented terminal hair as the clinical response progressed. As for the group receiving placebo, only ten patients were evaluable at the end of the study. The high number of dropouts was a result of the lack of any improvement in the status of the scalp hair. These results were scored as follows: 2 in three patients, 1 in three patients and 0 in four patients.

Evaluation of hair loss

As shown in Table III and Figure 1, differences between the two study groups in terms of hair counts after the wash test were not significant at baseline or during the first 4 months of treatment. However, beginning from the 6th month, a progressive decrease in the rate of hair loss was observed in the finasteride group. Differences between the groups showed a gradually higher level of significance ($P > 0.1$ to < 0.0001).

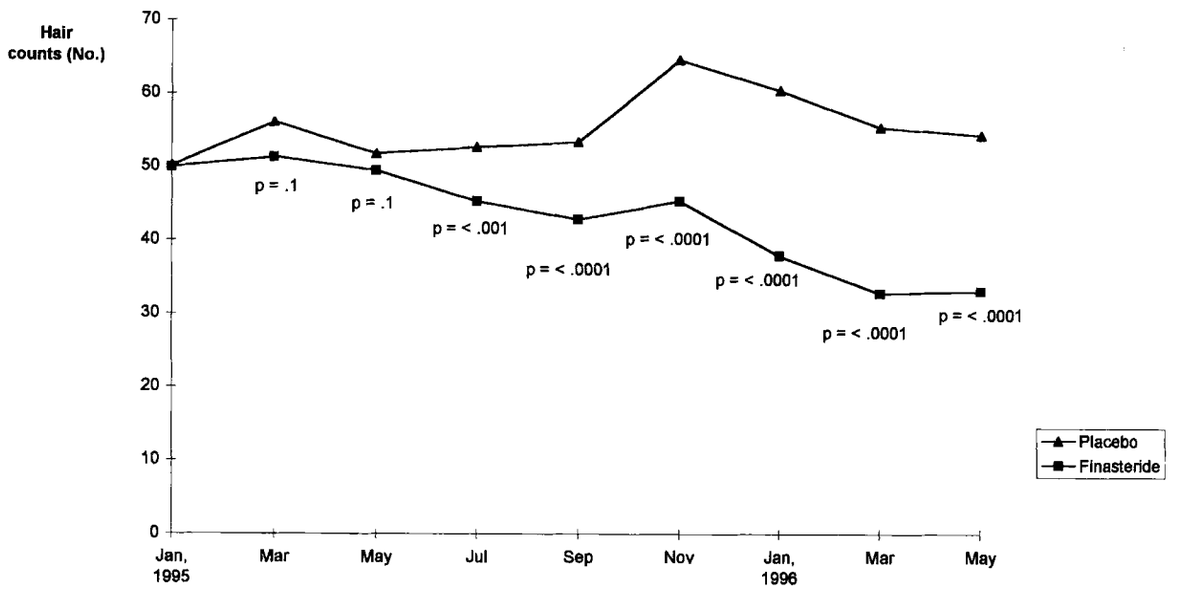

Figure 1
Results of the wash tests in the finasteride-treated and placebo-treated groups.

Treatment time (months)	Hair counts Finasteride	Placebo	P-value
Baseline	49.8±5.9	50.0±8.8	>0.1
2	51.2±10.2	56.0±10.3	0.1
4	49.4±4.9	51.7±5.9	0.1
6	45.2±7.4	52.6±5.5	<0.001
8	42.8±7.4	53.3±5.9	<0.0001
10	45.3±4.6	64.5±4.9	<0.0001
12	37.8±4.5	60.4±4.1	<0.0001
14	32.7±4.3	55.3±8.5	<0.0001
16	36.8±8.1	54.2±6.2	<0.0001

Values are means±SD

Table III
Hair counts from the wash tests.

Patients' opinion on the effectiveness of treatment

Among the finasteride group the overall judgement of cosmetic improvement was positive. Effectiveness was scored 3 by 19 patients (73%) and 2 by the remaining 7. By contrast, among the placebo group the results in the 16 patients who completed the study were scored as follows: 2 in one patient, 1 in three patients and 0 in six patients.

Discussion

The steroid 5AR[9] catalyses the reduction of testosterone to dihydrotestosterone, the hormone implicated in the development of a series of androgen-related disorders ranging from benign prostatic hyperplasia to male-pattern baldness.[1] There are two isozymes of 5AR with different biochemical properties and patterns of distribution in human tissues: in skin and cutaneous appendages type 1 is much more concentrated than type 2 which predominates in organs of the urogenital tract (prostate, seminal vesicle and epididymis).[10] 5AR inhibitors, such as the azasteroid finasteride,[3] are useful in the management of benign prostatic hyperplasia. By contrast, the use of finasteride in androgenic alopecia has been hampered by the fact that it affects quite selectively the activity of the type 2 isozyme whereas it is much less active against the type 1 isozyme,[11] which predominates in the skin. These circumstances are responsible for a type 1-associated residual reduction of testosterone and a consequent persistence of a significant rate of dihydrotestosterone production.

The effects of oral administration of finasteride on the balding scalp and serum levels of dihydrotestosterone in patients with male-pattern alopecia have been recently evaluated by Dallob et al[4] who found a meaningful decrease in the concentration of the hormone after a 4-week course of 5 mg per day. Keeping in view the above mentioned low affinity of finasteride for scalp type 1 isozyme and the low concentrations of finasteride-sensitive type 2 isozyme in hair follicles,[9] the effects of an even longer course of treatment with oral finasteride may be expected to be quite unsatisfactory.

On the basis of these findings, we attempted to evaluate the possibility of overcoming such kinetic disadvantages by delivering high amounts of finasteride just within the balding areas via topical administration of the agent. Considering the results obtained in terms of both hair

regrowth and hair loss reduction, along with the excellent or good patients' self-perceived response to treatment, we believe that the overall outcome of this pilot study encourages further evaluations in which higher concentrations of finasteride may be found to increase the clinical response.

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