Topical cyclosporine in male pattern alopecia

Amos Gilhar, MD,[a] Thomas Pillar, MD,[a] and Amos Etzioni, MD[b] *Haifa, Israel*

We previously demonstrated a systemic and topical effect of cyclosporine on hair growth in an experimental model composed of human scalp skin transplanted onto nude mice. The aim of this study was to determine whether topical cyclosporine affects male pattern alopecia. For 4 months in a double-blind study, 10 subjects were treated with cyclosporine and three were treated with olive oil. Hair growth was evaluated by photographs and hair counts. Significant hair growth was observed in two of the eight patients who completed the study. In one the hair growth was cosmetically satisfactory. No systemic or cutaneous side effects were noted. (J AM ACAD DERMATOL 1990;22:251-3.)

Numerous side effects, especially nephrotoxicity, have been reported with the systemic use of cyclosporine,[1,2] and its topical use is therefore being investigated. Aldridge et al.[3] found that topical 1% and 2% cyclosporine inhibited contact sensitivity to dinitrofluorobenzene in guinea pigs without evidence of systemic absorption. Recently we found that topical cyclosporine (5%) was of no benefit in psoriasis[4] and alopecia areata,[5] in which no traces of cyclosporine were detected systemically. Previously we observed a direct effect of cyclosporine on human hair in scalp grafted onto nude mice and rats.[6,7] Hypertrichosis has been reported as a side effect of systemic cyclosporine administration.[8] These facts, together with a lack of adverse effects of topical cyclosporine, encouraged us to conduct a pilot study on the effect of topical cyclosporine on human baldness.

PATIENTS AND METHODS

Thirteen patients with male baldness were entered into this study. The age of the patients ranged from 23 to 44 years (mean 33 ± 6.4 years). Duration of baldness ranged from 3 to 20 years (mean 7.82 ± 5.17 years). Patients with hypertension, renal failure, or liver failure were excluded, as well as those who were being treated with immunosuppressants, cytotoxic agents, or peripheral vasodilating medications. All subjects were in good general health. On acceptance into the study, each patient had routine laboratory examinations before treatment, once weekly during the first month of the treatment and twice monthly thereafter. Blood cyclosporine levels were monitored once weekly during the first month and biweekly thereafter. Informed consent was obtained from each patient.

Hair count was performed as described previously.[9] The diameter of the pretreatment bald area was recorded, and photographs were taken. The patients were given 5% cyclosporine in syringes of 2.5 ml. Each patient received 7 ml once weekly. The placebo group received syringes containing olive oil. Medication was applied to the scalp twice daily. The total dose for each application was 0.3 ml. Three subjects received only olive oil for the first 4 months. Ten patients received cyclosporine for the entire 12-month study period. The results in the groups were compared by nonparametric Mann-Whitney *U* test.

RESULTS

Table I summarizes the mean hair count of new hair in the treated area of the eight patients who completed the 12-month study. We considered successful treatment to be an increase in hair count of at least 50% after 4 months and 100% after 12 months. Only two subjects were in this category and are referred to in Table I as "responders." All remaining subjects did not demonstrate such an increased hair count and are referred to in Table I as "nonresponders." The results in the placebo group are also shown in Table I.

After 4 months an increased hair count in the responders was noted, although the increase did not reach statistical significance. After 12 months, however, the responders had a statistically significant increase in number of hairs. An example of a patient who responded is shown in Fig. 1 (before treatment) and Fig. 2 (after treatment).

There were no local side effects, abnormal physical findings, or laboratory abnormalities during the study. All patients failed to show evidence of sys-

From the Laboratory for Skin Research,[a] and the Department of Clinical Immunology,[b] Faculty of Medicine, Technion-Israel Institute of Technology.

Reprint requests: A. Gilhar, MD, Laboratory for Skin Research, Technion Faculty of Medicine, P.O. Box 9649, Haifa 31096, Israel.

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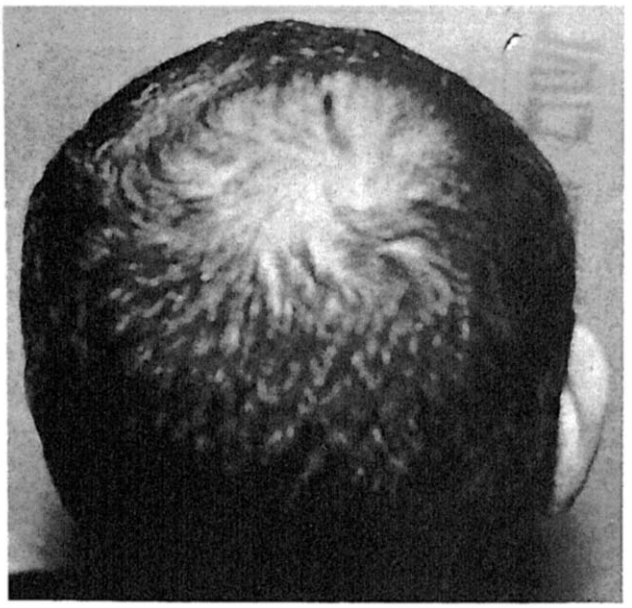

Fig. 1. Patient before start of treatment.

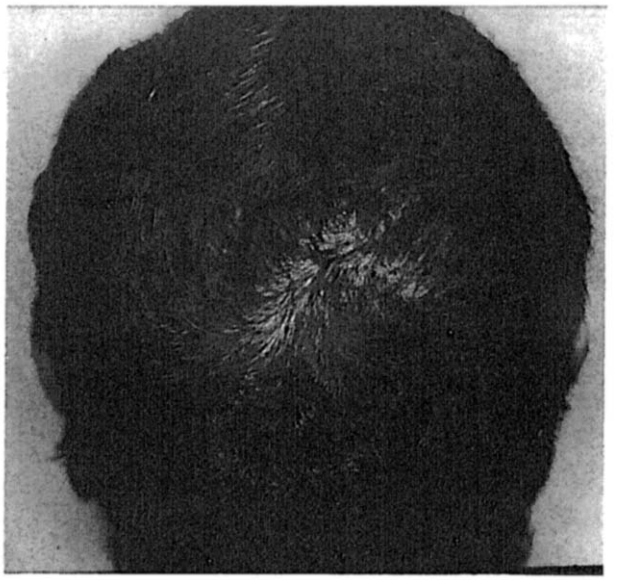

Fig. 2. Patient shows cosmetic improvement after 12 months of treatment.

Table I. Mean change in number of total hairs from baseline hair counts

Treatment	Subjects	Baseline hair count	No. of new hairs (mean ± SD)	
			4 mo	12 mo
Cyclosporine	Responding ($n = 2$)	250.00 ± 50.11	149.0 ± 42.3	381.5 ± 12.0*
Cyclosporine	Nonresponding ($n = 6$)	171.5 ± 109.9	52.07 ± 48.06	71.07 ± 23.90
Olive oil	Control ($n = 3$)	268.00 ± 99.93	73.00 ± 40.22	—

*$p < 0.03$ when responding and nonresponding subjects were compared according to Mann-Whitney U test.

temic absorption of cyclosporine by high-performance liquid chromatography, which is highly specific. The less specific radioimmunoassay techniques, however, detected traces of cyclosporine in samples from the two patients demonstrating hair growth.

DISCUSSION

The use of topical cyclosporine in this 12-month study resulted in a significant hair regrowth in two of eight patients. In one the hair growth response was cosmetically satisfactory.

An initial increase in hair count was also found in the placebo group. This has also been observed in several other studies.[9-11] We considered this increase to be a vehicle effect or related to the application process,[9,11] but it may be the result of a natural variation in the hair density of men with male pattern alopecia.[9,11] The mechanism for regrowth of hair with cyclosporine is still unknown. In the responding subjects, some of the serum samples showed trace amounts of cyclosporine. Thus the possibility of a systemic effect cannnot be excluded, although Aldridge et al.[12] deny such a possibility.

Topical treatment with cyclosporine probably has a direct effect at the cellular level of the hair follicle and may cause a conversion of vellus to terminal hairs. This preliminary study shows that topical application of cyclosporine may be of benefit to some patients with male pattern alopecia.

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Topical erythromycin and zinc therapy for acne

Lawrence Schachner, MD,[a,b] William Eaglstein, MD,[a] Carol Kittles,[a] and Patricia Mertz[a]
Miami, Florida

A double-blind, 12-week study was undertaken to determine the safety and efficacy of a formulation of 4% erythromycin plus 1.2% zinc acetate compared with its vehicle. The study was continued for 40 weeks after the 12-week double-blind phase by switching vehicle-treated patients to active treatment and continuing to give patients treated with active drug the same treatment. Seventy-three female patients started the study; 39 completed 1 full year of study. In the first 12 weeks statistically significant differences were noted in the efficacy of the erythromycin-zinc compared with vehicle for acne severity grades (global assessment) and for papule, pustule, and comedo counts. After crossover, the vehicle-treated group receiving active therapy duplicated the improvement of the group initially treated with erythromycin-zinc. No clinical problems with superinfection or secondary infection occurred during 1 year of treatment in 39 patients. (J AM ACAD DERMATOL 1990;22:253-60.)

Although systemic antibiotic agents have been shown to be effective and relatively safe for the treatment of pustular, papular, and cystic acne, similar effectiveness for the treatment of comedonal acne has not been shown.[1] In addition, the long-term administration of systemic antibiotics (tetracycline and erythromycin) can be associated with gastrointestinal side effects, vaginitis, and photosensitivity.[1] Topical antibiotics have been used in acne treatment for two decades, but significant clinical problems with superinfection or secondary infection have not been reported.[2,3]

Feucht et al.[4] found that a topical preparation of 4% erythromycin plus zinc was significantly better statistically than its vehicle and as effective as 500 mg/day oral tetracycline in reducing overall acne severity and papule lesion counts. The investigators' analysis of comedo grades showed the erythromycin-zinc solution to be statistically better than its vehicle after 8 weeks of therapy.[4]

Although experience with topical zinc preparations in the treatment of acne has been limited, its role as a skin protectant and as an aid to wound

From the Department of Dermatology and Cutaneous Surgery[a] and the Department of Pediatrics,[b] University of Miami School of Medicine.

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Reprint requests: Lawrence Schachner, MD, Department of Dermatology and Cutaneous Surgery, Department of Pediatrics, University of Miami School of Medicine, P.O. Box 016250 (R-250), Miami, FL 33101.

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