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Topical Cyclosporin A in Alopecia Areata

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We conducted a trial of topical application of 10% cyclosporin A in an oil preparation in 10 patients with alopecia areata and alopecia universalis. After 12 months of therapy, no beneficial response was observed in any of the 10 patients.

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Because of the immunosuppressive effect of CS, combined with its hair growth promotion (1), several studies have been performed in order to investigate a possible beneficial effect of the drug in alopecia areata (AA) and alopecia universalis (AU) (2, 3). Parodi & Rehora (2) and others (3) described a significant hair growth in patients with AA and AU following topical CS application, whereas Manduit et al. (4) deny any benefit from the drug in AA. Because of these conflicting reports we conducted a study focused on patients with severe AA and AU.

MATERIALS AND METHODS

Ten patients with severe AA and AU were enrolled into this study. They were 6 male and 4 female patients, ranging in age from 20 to 54 years. The duration of their disease ranged from 2 to 18 years. Six patients demonstrated AU and 4, AA. One patient had associated autoimmune thyroiditis. All subjects were in good health, as documented by history, physical examination and laboratory evaluation.

Each patient had the following laboratory examinations performed prior to treatment, and again once a week in the first month of treatment; thereafter, twice a month: complete blood cell count, urinalysis, serum urea nitrogen, uric acid, alkaline phosphatase, SGOT, bilirubin, creatine kinase, calcium, phosphorus, lactic dehydrogenase. The CS blood levels of each patient were monitored by both the radio-immunoassay (RIA) and high pressure liquid chromatography (HPLC) method (5) once a week in the first month and once a fortnight thereafter. Scalp biopsy specimens were obtained from each patient prior to treatment and at the completion of the study. Photographs were taken before and monthly during the treatment phase. Response to treatment was defined as growth of terminal hair. All evaluations of hair growth were performed by the same observer (A.G.). The solution contained 10% CS in an oily preparation. The solution (0.5cc) was applied twice a day. Informed consent was obtained from each patient prior to treatment.

RESULTS

After 12 months of treatment, as well as during the follow-up, no significant response was observed in any of the treated patients. Growth of vellus hair was noted in 3 patients with AU. Scalp hair loss was observed in one patient with AA. The histological finding confirmed the clinical observations of unresponsiveness. All patients failed to show any signs of systemic absorption of CS by the HPLC technique, which is highly specific for unchanged drug. The less specific RIA technique detected traces of CS in samples from 2 patients. Laboratory studies did not show any change in the various tests reported before.

DISCUSSION

In animal studies, we were able to show that both systemic and topical CS caused hair growth in nude mice engrafted with normal human scalp and then with skin obtained from patients with AA and AU (6, 7). Moreover, we have conducted a study of topical CS in patients with male pattern alopecia and found a significant hair growth in 2 out of 8 patients (8). In contrast to the animal study, we were unable to show any effect of CS in any of the 10 patients treated.

The lack of effect of topical CS in our severe AA patients, contrary to hair growth observed following

systemic therapy (9) could support the notion of systemic immunologic mechanisms of the disease. Alternatively, the minimal absorption of the drug through the skin may not be sufficient to achieve a response. The undetectable levels of CS in the blood may confirm such an assumption.

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Prostaglandin E_1 and Prostaglandin $F_{2\alpha}$ in Exudate in Nickel Allergy

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Ten nickel-allergic patients and 5 healthy control subjects participated in a study of the kinetics of the flux and concentration of migrated leukocytes and extracellular PGE_1 and $PGF_{2\alpha}$ during a 48 h period, using a skin chamber technique. The patients were provided with two skin chambers, one with and one without nickel challenge. A higher flux of leukocytes, PGE_1 and $PGF_{2\alpha}$ was observed during the second day of allergen exposure, while the concentrations probably due to dilution were unchanged or diminished, indicating an unspecific role of the prostaglandins during the contact allergic reaction. No correlations were found within the groups between the migration of leukocytes and the prostaglandin content. *Key words: Leukocyte migrations; PGE_1; $PGF_{2\alpha}$;* Skin window technique.

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The main alterations of the arachidonate metabolism in delayed hypersensitivity consist of (*a*) inhibition of PGD_2 synthesis, (*b*) a switch from predominantly PGD_2 to a predominance of PGE, (*c*) an increased lipoxygenase activity (1), (*d*) an inhibitory effect of the immune response of PGE by inhibition T-lymphocyte activation (2). Furthermore, PGE inhibits the leukocyte inhibitory factor (LIF) production (3), exhibits a negative inhibitory chemotactic activity and $PGF_{2\alpha}$ exhibits a positive chemotactic activity (4). The purpose of the present study was to measure the release of PGE_1 and $PGF_{2\alpha}$ and leukocyte migration in exudate during the evolution of a delayed hypersensitivity reaction (DHR) in human skin, when using a skin chamber technique.

METHODS

Subjects

The control group consisted of 5 healthy controls (all females, mean age 28 years, age range 23–32), with no eczema or history of allergic contact dermatitis.

The patients studied (8 females, 2 males, mean age 37 years, age range 20–65) all had allergic contact dermatitis to nickel, verified by anamnesis and by patch testing (5). At the time of investigation the eczema was inactive or mildly active and the patients were without medication. All participants had normal blood values. Informed consent was obtained from all subjects, in accordance with the principle of the Helsinki Declaration.

Skin chamber technique, chamber media and collection procedure

A dermabrasion was made with surgical scalpel on the inner surface of both forearms of patients with nickel hypersensitivity and on the right forearm of controls, as previously described (5). A sterile chamber of epoxy material was sealed over the skin window. The chamber applied to the right