Acta Derm Venereol (Stockh) 1985; Suppl. 114: 157–158

Treatment of Atopic Dermatitis with Steroids

S. MARGHESCU

Hautklinik Linden der Medizinischen Hochschule und der Landeshauptstadt Hannover

The pharmacological properties of corticosteroids, i.e. the antiinflammatory activity, the suppression of specific immunity by cytolysis, the inhibition of division of premature lymphoid cells and the depression of epidermal cell turnover, justify the treatment of atopic dermatitis with this drug. However, it is necessary to separate the wanted from unwanted effects of corticosteroids. This can be attempted in two ways: first by adjustment of dose and frequency of corticosteroid administration; secondly, by delivery of the drug directly to the site of disease.

Relative to the dose, we can distinguish three factors of the topical intensity of steroid effects: the topical availability of the drug, the phenomenon of tachyphylaxis and the circadian biorhythm of the skin and of the cortisol production by the body. The most important factors of the topical bioavailability of the corticosteroids are the conditions of percutaneous absorption, the binding intensity of the drug to cell receptors and the rate of decomposition of steroids in the tissue.

The absorption of corticosteroids through the skin is dependent firstly on the properties of the vehicle: fatty ointments, even under polyethylene occlusion, increase the percutaneous absorption ten times (6). Secondly, the thickness of the horny layer, but above all, the architecture of this layer (compact horny mass or loose horny cells) influences the skin permeability. For example, the absorption on the forearm is ten times higher than on the sole of the foot (1). An intact skin barrier hinders the absorption more than a barrier of psoriatic or eczematous skin.

Two very important factors of the topical effect of steroids are the binding intensity to cell receptors and the rate of decomposition in the tissue. The intensity of binding of steroids to cell receptors can be increased by esterification of the steroid molecule at the position 16, 17 or 21, and by halogenisation at the position 9 or 16 (2). On the other part, the retardation of the decomposition from steroids in the tissue can increase the topical potency of the drug by introduction of methyl-groups at the position 2 or 16, of halogens at position 9, of a hydroxyl-group at position 11 or a double bond between C1 and C2 (4).

By the modification of the steroid molecule, the half-life of the drug can be increased by more than 50% (4). However, the equivalent doses for these steroids tested in different systems is not the same at topical application of the drug. For example, the anti-inflammatory potency of prednisolone in test systems is 4 times higher and these of dexamethasone 30 times higher, than cortisol. In the topical efficiency, the difference is smaller, namely one to two to ten (4). These data suggest that we use less potent steroids in atopic dermatitis, and only on the affected skin surfaces without the facial area and the buttocks of babies.

Tachyphylaxis is the rapid diminution of a pharmacological response to repeated administration of the drug, probably due to occupancy or saturation of drug receptors thus preventing further effects of the drug. Du Vivier & Stoughton (7) showed that the vasoconstrictive response diminishes with succeeding applications, and, the stronger the steroid the faster the onset of tachyphylaxis. On the other hand, animal studies showed, that after 30 hours one application of steroid inhibits DNA synthesis in the skin as profoundly as three applications and, after 54 hours, one application is as effective as 5

applications during the same time. However, the systemic effect after one application is less at 30 hours and non-existent at 54 hours, unlike the effect of three of five applications.

Finally, the circadian biorhythm of the cortisol production by the body with maximal values in serum and tissue in the morning, and the circadian biorhythm of the epidermal proliferation with a maximum also in the morning (5) suggest the administration of steroids in the evening in order to economize steroids and to decrease the antiproliferative effect of the drug.

In atopic dermatitis it is necessary to find a dosage with a maximum of benefit at a minimum of risks. Therefore, the following rules of treatment should be considered:

1. Apply steroids topically in order to have the highest drug concentration at the target tissue. Along with an appropriate vehicle, the dry skin can be improved at the same time.
2. Avoid the "forbidden areas" for steroids, such as the buttocks of babies and the facial area in all age groups.
3. Only the most affected skin surfaces should be treated with strong steroids.
4. Adapt the steroid concentration to the severity of skin changes.
5. Decrease the rate of applications parallel to the actual stage of the skin lesions (3).
6. Apply topical steroids preferably in the evening, in order to diminish the antiproliferative effect of the drug.
7. Economize steroids by using antipruritic agents, restriction of wash proceedings, use of bath-oils and grease on the dry skin, and by consideration of the spontaneous improvement of the skin lesions in summer and in climatically favorable regions.

REFERENCES

1. Feldmann R, Maibach H. Regional variation in percutaneous penetration of ^{14}C-cortisol in man. J Invest Dermatol 1967; 48: 181.
2. Hornstein OP, Schell H. Berücksichtigung rhythmischer Proliferationsschwankungen der Epidermis bei der topischen Cortikoid-Therapie. Eudermie 1981; 1: 34.
3. Marghescu S. Externe Kortikoidtherapie: Kontinuierliche versus diskontinuierliche Anwendung. Hautarzt 1983; 34: 114.
4. Meyers FH, Jawetz E, Goldfien A. Lehrbuch der Pharmakologie. Berlin, Heidelberg, New York: Springer, 1975.
5. Schell H, Hornstein OP. Endogener Kortisolrhythmus und Epidermisproliferation. Aktuel Dermatol 1980; 6: 27.
6. Stüttgen G, Schaefer H. Funktionelle Dermatologie. Berlin, Heidelberg, New York: Springer, 1974: 367.
7. Vivier du A, Stoughton RB. Acute tolerance to the effects of topical glucocorticosteroids. Br J Dermatol 1976; (Suppl.) 12: 25.

S. Marghescu, Hautklinik Linden, Ricklingerstr. 5, D-3000 Hannover 91, F.R.G.