ABSTRACT

Calcipotriol Irritation: Mechanism, Diagnosis and Clinical Implication

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Irritant dermatitis of any degree occurs in 15–20% of psoriatics treated with calcipotriene (Calcipotriol INN, MC903) ointment. The onset is typically 2–4 weeks after treatment was started. There are two distinct clinical types, viz. lesional/perilesional and head and neck dermatitis. The dermatitis is both cases directly related to the drug in situ, topically applied to the lesions or transferred by the hand-to-face route with the facial region representing a locus of minor resistance.

Calcipotriene is not cytotoxic *per se* in clinically relevant formulations. The irritation is of the indirect or secondary type, in a way resembling irritation by retinoids. Occlusive patch testing of calcipotriene solution 50, 10, 2, 0.4 μg/ml on untreated controls shows many doubtful and 1+ reactions, while 2+ reactions are umcommon. 1,25-dihydroxy-vitamin D_3 in equimolar application shows the same frequency of irritant reactions. Application of calcipotriene 500 μg/ml results in no more frequent irritancy than 50 μg/ml, and the upper end of the dose irritation curve is not linear as it is with the primary irritant sodium lauryl sulphate (SLS). It is not known whether the irritant and the therapeutic effects of calcipotriene share a common mechanism.

Evaluation of positive patch test reactions to calcipotriene by means of bioengineering techniques shows increased blood flow but minor or no increase in transepidermal water loss (TEWL). The surface may be papular. Ultrasonography shows a subepidermal echolucent band and disturbed pilosebaceous units.

Irritancy to calcipotriene is to some extent vehicle dependent. The ointment vehicle containing propylene glycol 10% probably enhances shunt penetration via the pilosebaceous unit. In the scalp a gel and a cream formulation gave more frequent irritation than an isopropanol solution.

In patients exhibiting a severe dermatitis reaction during therapy, allergic sensitization is a possibility. Nevertheless, it is a clinical experience that calcipotriene is often tolerated again after an interval. Allergy patch testing should not be performed with the ointment, but with a buffered isopropanol solution and probably in 1% dilution.

The non-irritant threshold concentration is not yet known, but Leo studies to solve this problem are proceeding.

There is a high risk of false-positive reactions, particularly +?, and 1+, while 2+ reactions may be indicative of allergy, especially if reproducible after a period.

For the clinical dermatologist it is more simple and conclusive to perform a repeated open application test (ROAT) with the ointment (BID for 7 days, antecubital skin) and decide whether the patient should in the future avoid calcipotriene, or not.

It should be borne in mind that the sensitivity of individuals' skin to irritants is complex, with a number of endogenous and exogenous factors operating at any time, resulting in periods, of higher or lower susceptibility.

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