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Topical calcipotriol in the treatment of intertriginous psoriasis

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Summary The purpose of this study was to examine the effectiveness and side-effects of the vitamin D analogue calcipotriol, applied topically to psoriatic skin lesions in intertriginous areas, in an open and uncontrolled trial. Twelve patients with psoriasis vulgaris who presented with psoriatic lesions in the axilla, and inguinal and anal folds, were treated with calcipotriol ointment (50 μg/g) twice daily for 6 weeks. Examination and photographic documentation were performed before treatment, at 3 weeks of treatment, and at 6 weeks of treatment. The mean improvement in the extent and severity of the psoriatic plaques was determined with a semiquantitative grading system closely related to the psoriasis area and severity index (M-PASI). Two of 12 patients showed insufficient response to therapy. Five of 12 patients showed a quick response within 3 weeks or less, and five of 12 patients showed a slow response which could be seen only after 6 weeks of treatment. Minimal burning was reported in one patient, slight lesional and/or perilesional irritation in five patients, and, in the remaining, no side-effects occurred. Topical calcipotriol is an effective and safe treatment for intertriginous psoriasis.

Calcipotriol is a synthetic 1,25-dihydroxyvitamin D analogue which has been shown to produce a statistically significant decrease in erythema, thickness and scaling in psoriatic lesions.[1–9] However, the use of calcipotriol in intertriginous psoriasis has not previously been studied because of the concern that treatment with calcipotriol in skin folds could cause skin irritation. Irritation occurs in about 5–10% of patients treated with calcipotriol ointment.[1,5] There are at least three clinical types of skin irritation: (i) lesional and/or perilesional irritation;[10] (ii) a head and neck dermatitis;[10] and (iii) a burning and itching sensation with no visible reaction.[11] The face and skin folds are thought to be particularly sensitive to calcipotriol ointment.[1,12] For this reason, it has been recommended that calcipotriol be used with care for the treatment of psoriatic lesions in the skin folds.[1,3,11,13]

Therapy of chronic intertriginous psoriasis may be difficult because of the side-effects associated with the long-term use of topical steroids, and the lack of alternative treatments. Occasional clinical observations, in which patients applied calcipotriol to skin folds, suggested that calcipotriol might be of particular benefit in intertriginous psoriasis, and prompted the present study.

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Methods

Study design

Twelve patients suffering from intertriginous psoriasis were treated with calcipotriol ointment (50 μg/g) for 6 weeks. After a wash-out period of 2 weeks (no treatment), the ointment was applied twice daily to the psoriatic lesions, followed by hand washing. No other topical treatment in the intertriginous localizations was permitted during the observation period. The treatment of psoriatic plaques in non-intertriginous localizations included calcipotriol ($n = 1$), calcipotriol and topical steroids ($n = 5$), ultraviolet B (UVB) radiation ($n = 2$), calcipotriol and UVB radiation ($n = 2$), and no treatment ($n = 2$). During UVB radiation, the intertriginous areas were covered.

Patients

Patients were included in the trial if they presented with psoriasis of one or more of the following regions: axillae, anal fold, inguinal folds, perianal region and scrotum. Excluded were acute guttate or pustular psoriasis, and

Table 1. Modified psoriasis area and severity index (M-PASI)

Score	0	1	2	3	4	5	6
Erythema, infiltration desquamation	None	Slight	Moderate	Severe	Very severe	—	—
Involved area in % of maximum	0	1–9	10–29	30–49	50–69	70–89	90–100 (maximum)

Calculation: M-PASI = [$score_{erythema} + score_{infiltration} + score_{desquamation}$] × modified area (range: 0–72).

patients who had received systemic antipsoriatic treatment within a 2-month period. Most subjects were outpatients, and were 18 years of age or older. Men and women were studied, but women of childbearing potential had to use contraception. The duration of the intertriginous psoriasis varied from 1 month to 45 years. Former treatments for intertriginous psoriasis included topical steroids in four patients; salicylic acid in two patients; calcipotriol, UVB radiation and tar in one patient respectively; and no therapy in six patients.

Clinical assessment

Examination and photographic documentation were performed before treatment, at 3 weeks of treatment, and at 6 weeks of treatment. At each visit, the investigator assessed the extent and the severity of the psoriasis with a modified psoriasis area and severity index (M-PASI). The M-PASI is the result of a modified area score in which the maximum of involved skin is taken as 100%. It was calculated by multiplying the modified area score with the severity score, which is equivalent to the severity score of the PASI (Table 1).

Any adverse events reported by the patient, or any skin reactions noted by the investigator, were recorded. At the end of therapy, the patient assessed semiquantitatively the change in his or her psoriasis and side-effects. Statistical analysis was performed using the Wilcoxon sign rank test.

Results

The psoriatic lesions showed improvement in all patients, with the exception of two. After 3 weeks, the clinical response was significant, with a reduction of the M-PASI from 31·7 to 19·7 ($P = 0·041$). After 6 weeks, improvement continued (M-PASI: 6·2; $P = 0·002$). Infiltration and desquamation improved after 3 weeks of treatment ($P = 0·031$, $P = 0·0039$), whereas erythema and involved area were only reduced after 6 weeks of treatment ($P = 0·0059$, $P = 0·0049$) (Fig. 1).

Three groups of patients could be distinguished according to the speed of the clinical response: (i) fast responders, (ii) slow responders, and (iii) non-responders. Group 1 showed more than 50%, group 2 less than 50%, and group 3 did not show any important

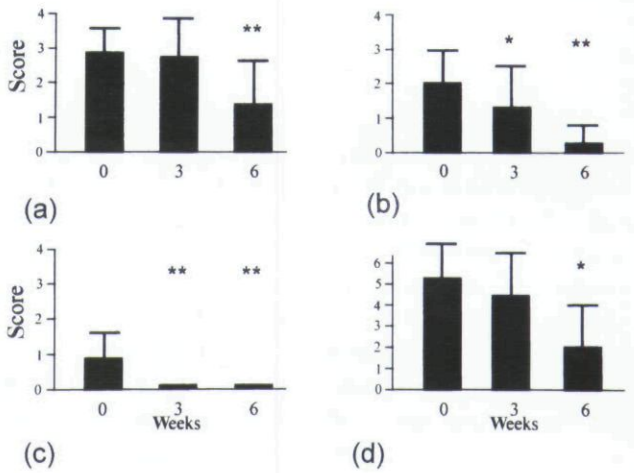

Figure 1. (a) Erythema, (b) infiltration, (c) desquamation and (d) involved area before and during treatment of intertriginous psoriasis with calcipotriol (means ± SD). *, $P < 0·05$; **, $P < 0·01$.

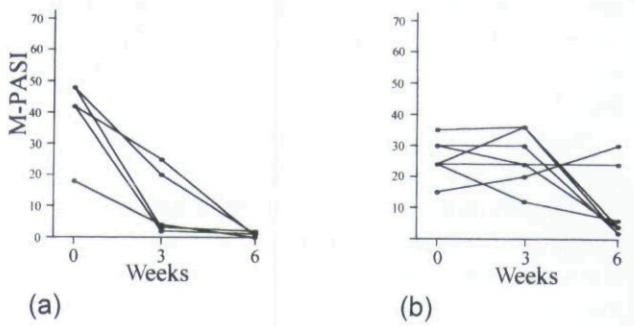

Figure 2. (a) Fast responders ($n = 5$) and (b) slow and non-responders ($n = 7$) to treatment.

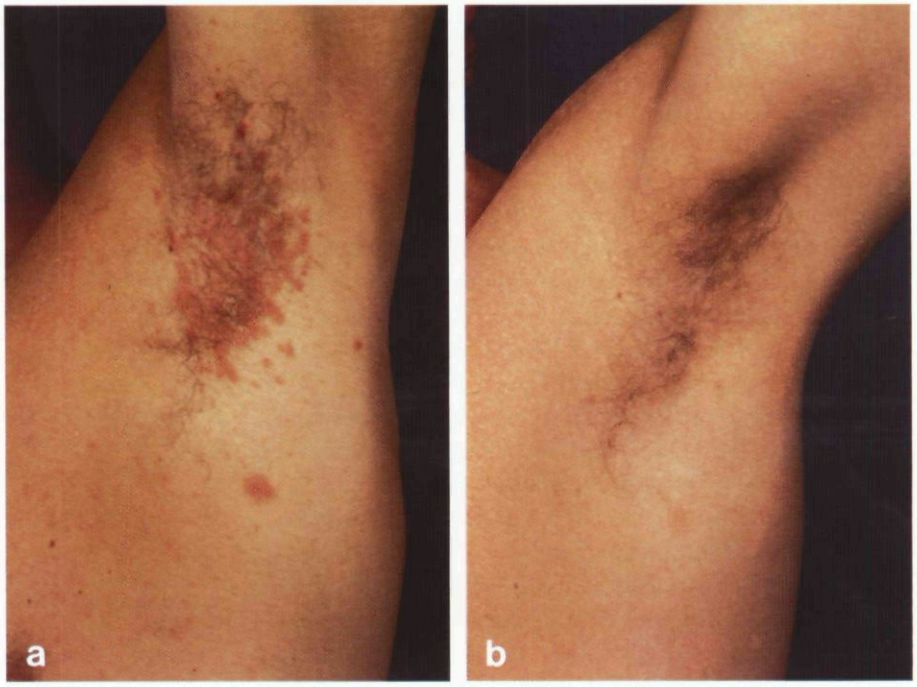

Figure 3. Intertriginous psoriasis in left axilla of patient 4: (a) before treatment, (b) after 6 weeks of treatment.

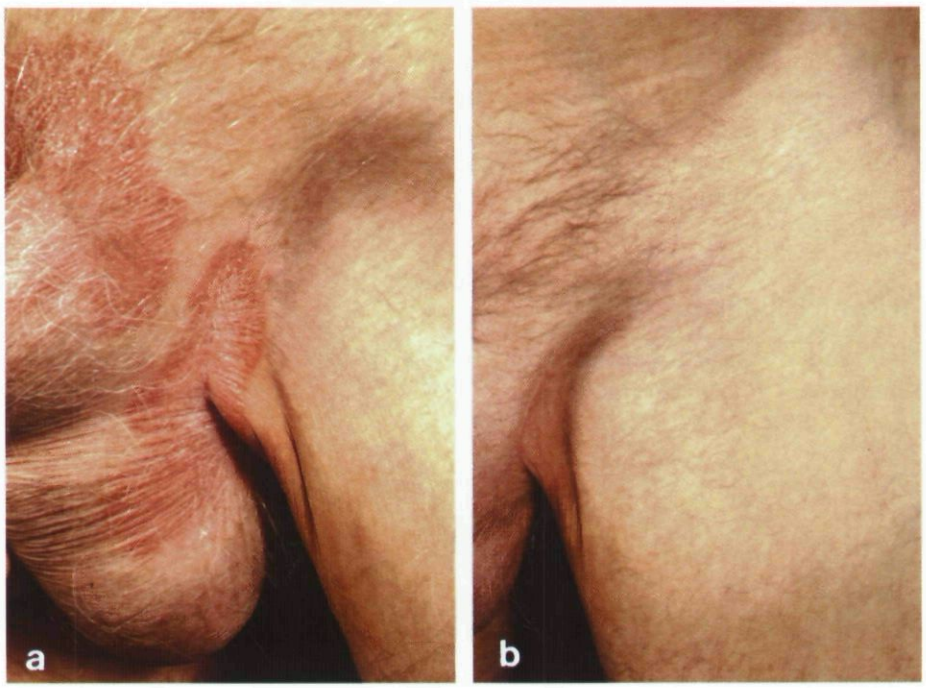

Figure 4. Intertriginous psoriasis in anal fold and perianal region of patient 10: (a) before treatment, (b) after 6 weeks of treatment.

improvement in the M-PASI at 3 weeks of treatment (Fig. 2). Photographic documentation of clinical improvement is shown in Figures 3 and 4.

Adverse events of minimal burning and/or perilesional irritation were recorded in four patients at 3 or at 6 weeks of treatment. Only one patient showed slight irritation during the whole treatment period. No other side-effects occurred. On self-assessment, one patient complained of slight burning, but the rest had no subjective complaints.

Discussion

In the present study, the effectiveness of calcipotriol in intertriginous psoriasis has been demonstrated. A significant improvement in the psoriasis was recorded

after 3 weeks of treatment, with a further reduction in the psoriatic lesions being noted after a further 3 weeks. In particular, infiltration and scaling improved after 3 weeks, whereas erythema and the area of involvement were only reduced after 6 weeks of treatment. It is unlikely that UVB treatment to other body sites led to improvement in intertriginous regions. A striking feature was the apparent lack of serious adverse reactions and subjective complaints. Only five patients had minimal lesional or perilesional irritation. These were so mild that the affected patients did not even mention them in their personal diaries.

The efficacy of calcipotriol in intertriginous sites with a visible effect already being seen after 3 weeks treatment, leads to the question of whether the treatment is as safe as it is in plaque psoriasis. The quicker clearance in intertriginous localizations may be the result of less scaling in these areas and better absorption of calcipotriol through the thinner skin. Some recent investigations suggest that calcipotriol increases the serum calcium level when applied using the recommended guidelines.[14] We conclude that serum calcium should be studied prospectively during calcipotriol treatment of intertriginous psoriasis. This study has not yet been performed, and calcium metabolism should be monitored in these patients. The most sensitive indicator of an alteration in the systemic calcium homeostasis is the 24-h urinary calcium excretion.[14]

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