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Calcipotriol ointment in nail psoriasis: a controlled double-blind comparison with betamethasone dipropionate and salicylic acid

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Summary This double-blind randomized study was designed to compare the efficacy and safety of calcipotriol ointment (50 μg/g) with betamethasone dipropionate (64 mg/g) and salicylic acid (0·03 g/g) ointment in the treatment of nail bed psoriasis. Fifty-eight patients applied the given drug to the affected nails twice a day for 3–5 months, depending on clinical response. Efficacy was assessed monthly on the basis of nail thickness, measured in millimetres. Photographs of the treated nails were taken at baseline, and after 3 and 5 months. Tolerability was assessed at 3 and 5 months. In patients with fingernail psoriasis, after 3 months of treatment subungual hyperkeratosis was reduced from 2·3 ± 0·1 mm (mean ± SEM) to 1·5 ± 0·1 mm (−26·5%) in the calcipotriol group and from 2·3 ± 0·1 mm to 1·6 ± 0·1 mm (−30·4%) in the betamethasone dipropionate and salicylic acid group [not significant (NS) between treatments, analysis of variance (ANOVA)]. After 5 months, responders showed a 49·2% reduction in hyperkeratosis in the calcipotriol group (from 2·8 ± 0·1 mm to 1·4 ± 0·2 mm) and 51·7% (from 2·1 ± 0·1 mm to 1·0 ± 0·1 mm) in the betamethasone dipropionate and salicylic acid group ($P < 0·001$ from baseline, NS between treatments, ANOVA). In patients with toenail psoriasis, after 3 months of treatment there was an overall reduction in hyperkeratosis from 2·6 ± 0·1 mm to 2·1 ± 0·1 mm (−20·1%) in the calcipotriol group and from 3·0 ± 0·1 mm to 2·3 ± 0·1 mm (−22·9%) in the betamethasone dipropionate and salicylic acid group ($P < 0·001$ from baseline, NS between treatments, ANOVA). By the end of the fifth month there was a 40·7% reduction in hyperkeratosis in the calcipotriol group (from 2·1 ± 0·1 mm to 1·2 ± 0·1 mm) and 51·9% in the betamethasone dipropionate and salicylic acid group (from 2·7 ± 0·1 mm to 1·3 ± 0·1 mm; $P < 0·0001$ from baseline, NS between treatments, ANOVA). The results of the study show that calcipotriol is as effective as a combination of a topical steroid with salicylic acid in the treatment of nail psoriasis and represents a safe alternative in the topical treatment of nail psoriasis.

Patients with psoriasis frequently present nail abnormalities which, in some cases, produce severe functional limitations. This is especially true when psoriasis produces massive hyperkeratosis of the nail bed and hyponychium, resulting in severe nail thickening. Besides cosmetic problems, nail psoriasis may considerably impair manual dexterity and foot biomechanics. Although several new drugs have recently been introduced for the treatment of skin psoriasis, treatment of nail psoriasis still remains a challenge. When nail psoriasis is not associated with widespread disease or psoriatic arthritis, a systemic treatment is not normally recommended.[1,2] Most dermatologists treat nail psoriasis with intralesional or topical steroids, which usually improve the nail symptoms, but require continuous application and may cause significant side-effects.[3–6]

Topical calcipotriol therapy has been successfully used for chronic plaque psoriasis[7] and, according to our recent experience, may considerably improve nail bed psoriasis.[8,9] This drug has also been utilized for treating pustular psoriasis and Hallopeau's chronic acrodermatitis continua.[10,11] The aim of this study

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was to evaluate the efficacy and safety of calcipotriol ointment (50 μg/g) in the treatment of nail bed psoriasis. For this purpose we performed a multicentre double-blind randomized study that compared calcipotriol ointment with betamethasone dipropionate (64 mg/g) and salicylic acid (0·03 g/g) ointment, which is an effective and widely utilized topical treatment for nail psoriasis.

Patients and methods

Patients were eligible if over 18 years of age, of either sex, with a clinical diagnosis of nail bed psoriasis with severe subungual hyperkeratosis (>1 mm for fingernails, >2·5 mm for toenails). Onychomycosis was excluded by direct microscopy and cultures. Pregnant or breast-feeding women were excluded, as were patients with severe renal or hepatic insufficiency, known hypersensitivity to the study molecule, and those receiving vitamin D based therapies (>400 IU/day) or other topical or systemic treatments for psoriasis.

This double-blind controlled trial compared calcipotriol with betamethasone dipropionate and salicylic acid. The trial was conducted in accordance with the principles of the Declaration of Helsinki and amendments. Each patient was asked to give his/her consent to participation.

Patients were treated with calcipotriol ointment (50 μg/g) or betamethasone dipropionate (64 mg/g) and salicylic acid (0·03 g/g) ointment. Patients were instructed to rub the given ointment gently on the nail plate and on the hyperkeratotic nail bed and hyponychium twice daily. The same treatment was given for skin lesions, if present. Treatment was planned to last 3 months for all patients. Patients who showed a 50% or more reduction in the baseline hyperkeratotic thickness at least in one nail (responders) were offered continuation of treatment for 2 further months. Patients who completed the 5-month treatment were then followed for 1 month after discontinuation.

The efficacy of therapy was assessed monthly on the basis of nail thickness (nail plate + hyperkeratotic nail bed), measured in millimetres using a micrometer calliper. At baseline, and after 3 and 5 months (for responders), photographs of the treated nails were taken, using a Nikkor Medical 1·4 lens (Nikkon). At months 3 and 5 patients were asked to express an overall opinion on the acceptability of treatment, using a five-point rating scale: 0, nil; 1, poor; 2, fair; 3, good; 4, excellent. For each nail the difference (delta) and percentage reduction from baseline thickness (mm ± SEM) at each visit were calculated. These findings were analysed by analysis of variance (ANOVA) for independent groups and ANOVA for repeated measures. The χ^2-test was used for acceptability ratings.

Results

A total of 58 patients was enrolled (35 men, 23 women), mean (± SD) age 51·8 ± 14·8 years. Twenty-nine patients (16 men and 13 women, mean age 50·7 years) received topical calcipotriol. The mean duration of nail psoriasis in these patients was 8·3 years. Twenty-nine patients (19 men and 10 women, mean age 53 years) received topical betamethasone dipropionate and salicylic acid. The mean duration of nail psoriasis in these patients was 7·1 years. Two patients assigned to receive calcipotriol presented exclusion criteria and were not considered in the assessment of efficacy; 12 (four with calcipotriol and eight with betamethasone dipropionate and salicylic acid) failed to attend the visits during the trial and were considered as drop outs. The results of treatment are summarized in Fig. 1.

Fingernails

Twenty-nine patients had psoriasis of the fingernails. Thirteen (47 nails) were treated with calcipotriol and 16 (82 nails) with betamethasone dipropionate and salicylic acid. After 3 months of treatment subungual hyperkeratosis was reduced from 2·3 ± 0·1 mm (mean ± SEM) to 1·5 ± 0·1 mm (−26·5%) in the calcipotriol group and from 2·3 ± 0·1 mm to 1·6 ± 0·1 mm (−30·4%) in the betamethasone dipropionate and salicylic acid group [not significant (NS) between treatments, ANOVA]. Eight patients given calcipotriol (28 nails) and 10 with betamethasone dipropionate and salicylic acid (38 nails) showed >50% reduction in their subungual hyperkeratosis in at least one nail (responders). Baseline subungual hyperkeratotic thickness was not homogeneous in these two subgroups (2·8 ± 0·1 mm for calcipotriol and 2·1 ± 0·1 mm for betamethasone dipropionate and salicylic acid).

After 5 months, responders showed a 49·2% reduction in hyperkeratosis in the calcipotriol group (Fig. 2) (from 2·8 ± 0·1 mm to 1·4 ± 0·2 mm) and 51·7% (from 2·1 ± 0·1 mm to 1·0 ± 0·1 mm) in the betamethasone dipropionate and salicylic acid group ($P < 0·001$ from baseline, ANOVA). This improvement persisted at the 6 months visit.

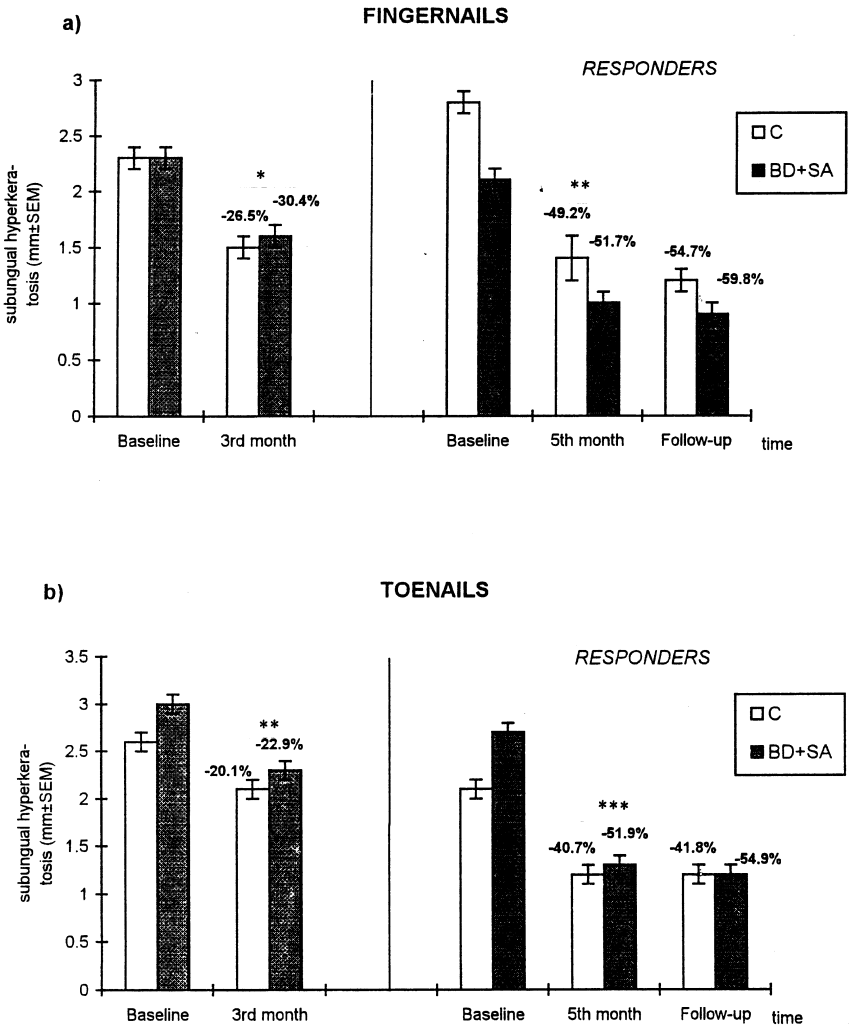

Figure 1. Thickness (mm ± SEM) of subungual hyperkeratosis during treatment of fingernails (a) and toenails (b). The percentages indicate reductions in nail thickness from baseline. The left side of each graphic considers all treated patients. The right side details values for nails of patients who used the treatment for 5 months (responders). Statistical analysis (analysis of variance): *not significant (NS) between treatments; **$P < 0{\cdot}001$ from baseline, NS between treatments; ***$P < 0{\cdot}0001$ from baseline, NS between treatments. C, calcipotriol; BD + SA, betamethasone dipropionate and salicylic acid.

Toenails

Forty-four patients had toenail psoriasis. Twenty of these (109 nails) were treated with calcipotriol and 24 (161 nails) with betamethasone dipropionate and salicylic acid. Baseline nail thickness was 2·6 ± 0·1 mm in the calcipotriol group and 3·0 ± 0·1 mm in the betamethasone dipropionate and salicylic acid group. The two groups were homogeneous. After 3 months of treatment there was an overall reduction in hyperkeratosis to 2·1 ± 0·1 mm (−20·1%) in the calcipotriol group and 2·3 ± 0·1 mm (−22·9%) in the betamethasone dipropionate and salicylic acid group ($P < 0{\cdot}001$ from baseline, NS between treatments, ANOVA). There were seven responders (51 nails) in the calcipotriol group and 12 (58 nails) in the betamethasone dipropionate and salicylic acid group. These two groups were not homogeneous as regards baseline hyperkeratosis: 2·1 ± 0·1 mm in the calcipotriol group and 2·7 ± 0·1 mm in the betamethasone dipropionate and salicylic acid group.

By the end of the fifth month there was a further reduction in hyperkeratosis both in the calcipotriol (1·2 ± 0·1 mm; −40·7%) (Fig. 3) and in the betamethasone dipropionate and salicylic acid group (1·3 ± 0·1 mm; −51·9%) ($P < 0{\cdot}0001$ from baseline, ANOVA). This result persisted at the visit performed 1 month after the end of treatment. At baseline 22 patients (38%) had signs of skin psoriasis, 14 of them (24%) in the group given calcipotriol [Psoriasis Area and Severity Index (PASI) mean baseline score ± SD 4·4 ± 3·3] and eight (14%) in the betamethasone dipropionate and salicylic acid group (PASI score 3·4 ± 2·7). The therapy assigned for nail psoriasis led to significant improvement from baseline in both groups ($P < 0{\cdot}05$ for independent groups, ANOVA).

Assessment of treatment acceptability at the third

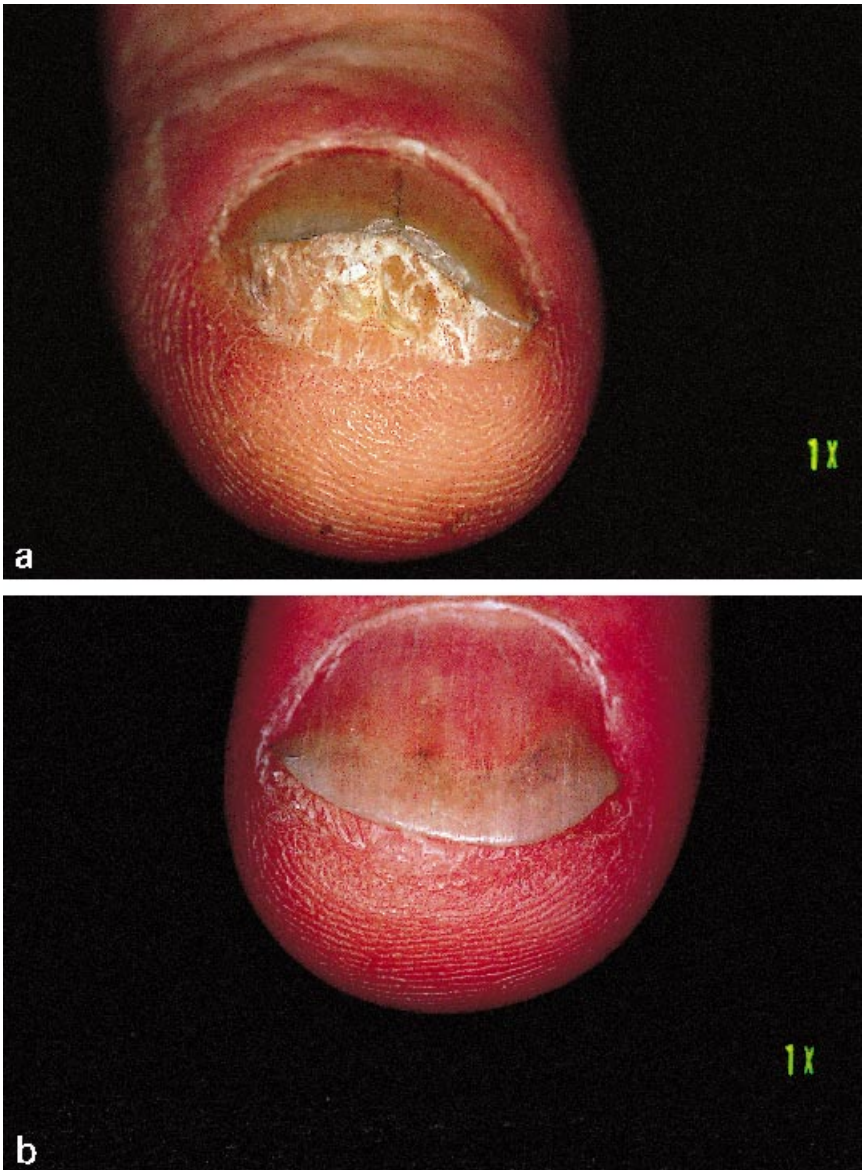

Figure 2. (a) Fingernail psoriasis before treatment. (b) Marked improvement in the subungual hyperkeratosis after 5 months of treatment with topical calcipotriol twice daily.

month gave the following results: calcipotriol group: nil 4%, poor 12%, fair 24%, good 44%, excellent 16%; betamethasone dipropionate and salicylic acid group: fair 23%, good 58%, excellent 19% (NS, χ^2 between treatments). The assessment of treatment acceptability for responders at the fifth month was as follows: calcipotriol group: fair 28%, good 50%, excellent 22%; betamethasone dipropionate and salicylic acid group: fair 19%, good 57%, excellent 24% (NS, χ^2 between treatments). Four adverse reactions arose in three patients given calcipotriol and three in three patients using betamethasone dipropionate and salicylic acid. In the calcipotriol group erythema was reported in one case, periungual irritation in one, burning at the application site in one, and diffuse urticaria in one; in the betamethasone dipropionate and salicylic acid group there were three cases of erythema.

Discussion

The results of our study indicate that topical calcipotriol significantly reduces subungual hyperkeratosis due to nail psoriasis in about half of the patients after 3 months of treatment. In these patients prolongation of treatment for 2 months produced a further improvement in the nail symptoms. There were no significant differences between the results obtained with calcipotriol and the results obtained with betamethasone

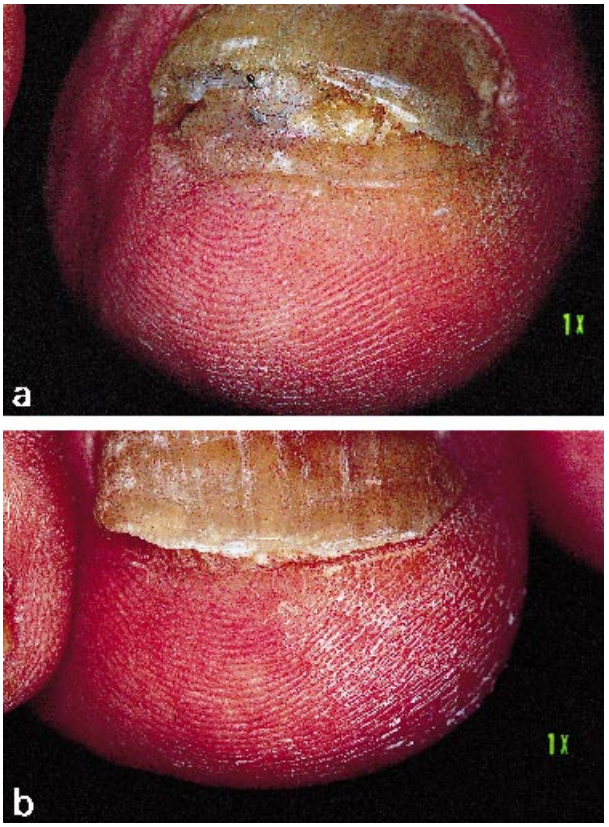

Figure 3. (a) Toenail psoriasis before treatment. (b) Marked improvement in the subungual hyperkeratosis after 5 months of treatment with topical calcipotriol twice daily.

dipropionate and salicylic acid, which produced significant improvement in subungual hyperkeratosis in 58% of patients.

Treatment with calcipotriol was well tolerated and 72% of the patients evaluated this treatment as good or excellent. Side-effects were mild and never required interruption of treatment. Patients with fingernail psoriasis responded better to calcipotriol treatment than patients with toenail psoriasis: a marked improvement was observed in eight of 13 patients with fingernail psoriasis compared with seven of 20 patients with toenail psoriasis. This may be because toenail lesions require a more prolonged treatment than fingernail lesions due to the slow growth rate of toenails. This possibility is also suggested by the fact that toenails that did not respond to treatment had a more severe hyperkeratosis than those that responded to calcipotriol. Similar results were documented in the toenails of patients treated with betamethasone dipropionate and salicylic acid.

Calcipotriol, therefore, is as effective as a combination of a topical steroid with salicylic acid in the treatment of nail psoriasis. However, as nail psoriasis is a chronic condition that requires long-term treatment, topical steroids in this condition may not be a safe treatment, as long-term topical application of these drugs may possibly result in atrophy of the digits or even in focal bone resorption.[4–6] We therefore believe that topical calcipotriol is a safe alternative in the topical treatment of nail bed psoriasis.

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