

## LETTERS TO THE EDITOR

**Treatment of Psoriatic Nails with Tazarotene Cream 0.1% vs. Clobetasol Propionate 0.05% Cream: A Double-blind Study**

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Nail psoriasis affects 20–55% of psoriatic patients. It often represents a significant cause of distress because of the visible lesions and the chronic course of the disease. Treatment options include corticosteroids, vitamin D3 analogues, 5-fluorouracil, urea, anthralin, cyclosporine and radiotherapy (1).

Tazarotene is an acetylenic retinoid with documented therapeutic results in skin psoriasis. The therapeutic potential of tazarotene 0.1% gel in nail psoriasis has been evaluated in one open-label study (2) and one placebo-controlled study (3) with promising results.

The objective of this double-blind study was to compare the efficacy of tazarotene 0.1% cream with clobetasol propionate 0.05% cream in nail psoriasis.

**MATERIAL AND METHODS**

A total of 46 psoriatic patients with nail involvement were included in the study. Onychomycosis was excluded through direct microscopy and culture. A 12-week washout period was allowed for topical and systemic medications. Exclusion criteria were: uptake of any systemic agent for psoriasis or other condition that might have an effect on the nail lesions (e.g. retinoids, cyclosporine, methotrexate, systemic corticosteroids, biological agents) and could not be discontinued; pregnancy; and lactation. The patients were randomly assigned by computer to two groups. The first group was instructed to apply tazarotene 0.1% cream (Zorac<sup>®</sup> cream 0.1%, Pierre Fabre, Paris, France) to the affected nail plates, surrounding nail folds and periungual skin under occlusion at bed-time for 12 weeks. The second group was instructed to apply clobetasol propionate 0.05% cream (Butavate<sup>®</sup> cream, Allen, Athens, Greece) in the same way. Occlusion was performed after application of the cream, using common transparent membrane obtained through general stores. Both agents were given to the patients in identical containers by the department's nurse, according to the computer's randomization. Each container initially contained 60 g of the prescribed agent. If the cream was used up, the patients were given further containers by the department's nurse. Outcome measures were assessed at baseline and at weeks 4, 8 and 12 using the nail psoriasis severity index (NAPSI) (4) to grade the following parameters independently: pitting, onycholysis, subungual hyperkeratosis and salmon patches. Although independent scoring for target nails is discouraged by NAPSI designers because it is time-consuming for assessments in daily practice, we decided to take advantage of its increased sensitivity in this comparative study. Splinter haemorrhage improvement was not assessed due to the lesion's low prevalence

in the study population. Follow-up evaluation was performed 12 weeks after the end of therapy. Investigators were blinded regarding the agent applied by each patient.

**RESULTS**

Sixteen out of 23 patients with a total of 46 involved nails in the tazarotene group, and 14 out of 23 patients with a total of 41 involved nails in the clobetasol group completed the study. The major reason (10/14 patients) for drop-out was urgent need for systemic therapy due to deterioration of the patients' cutaneous psoriasis. Four patients repeatedly failed to keep to the follow-up schedule due to business arrangements and were withdrawn from the study.

Five patients asked for a third container before the end of the 12 weeks. All other patients used more than 1.5 containers. Although the contents were not actually weighed, the estimated quantity of the agents used was 8–12 g of the prescribed agent per week.

In order to assess the efficacy of the agents, data were submitted to a double multivariate repeated measures analysis: baseline (week 0), week 4, week 8, end of treatment (week 12), and follow-up (week 24). Although fingernail response was quicker than toe-nail response in both groups, a cumulative analysis was considered more appropriate for statistical validity reasons. The results showed a significant time-effect improvement ( $F=51.81$ ,  $df=16$ ,  $p < 0.001$ ) for all four measures (pitting, onycholysis, hyperkeratosis and salmon patches)

Table I. *Nail psoriasis severity index (NAPSI) scores for all four assessed signs at baseline, end of treatment and follow-up for both agents. Mean and standard deviation*

Sign	Agent	Baseline (week 0)	End of treatment (week 12)	End of follow-up (week 24)
Pitting	Tazarotene	1.13 (0.88)	0.28 (0.45)	0.97 (0.71)
	Clobetasol	1.09 (0.99)	0.36 (0.48)	0.97 (0.85)
Onycholysis	Tazarotene	1.97 (1.27)	0.82 (0.73)	1.54 (1.00)
	Clobetasol	1.90 (1.28)	0.82 (0.62)	1.73 (1.09)
Hyperkeratosis	Tazarotene	1.80 (1.04)	0.36 (0.48)	0.97 (0.80)
	Clobetasol	1.70 (0.95)	0.58 (0.66)	1.56 (0.83)
Salmon patches	Tazarotene	1.15 (0.89)	0.17 (0.38)	0.69 (0.72)
	Clobetasol	1.07 (0.78)	0.19 (0.45)	0.85 (0.61)

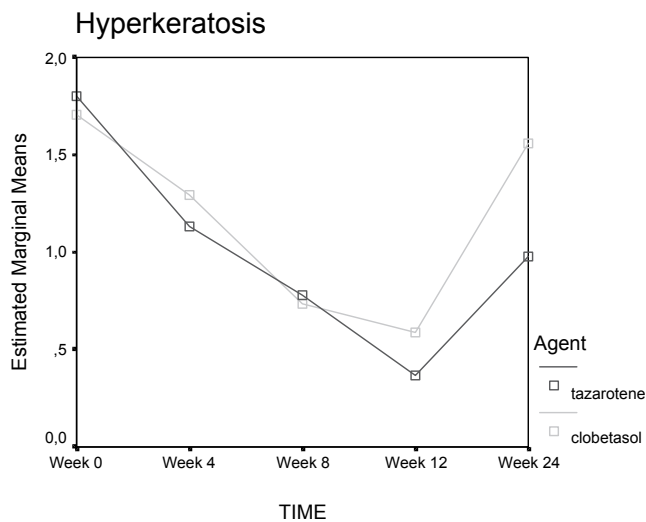


Fig. 1. A significant time effect improvement in hyperkeratosis is shown with both agents. Treatment phase: 0–12 weeks

with both agents (Table I, Fig. 1). Comparison of the improvement between administered agents did not reach statistical significance. Although lacking clinical importance, the multivariate interaction between agent and time was found to be significant ( $F=3.56$ ,  $df=16$ ,  $p < 0.001$ ). This finding means that the clinical improvements produced by the two agents are changing over time, both of them statistically significant, but are changing in different ways. On further univariate investigation, this agent-time interaction statistical significance was attributed only to hyperkeratosis improvement ( $F=6.33$ ,  $df=3.15$ ,  $p < 0.001$ ). *Post hoc* tests indicated that, at the end of the follow-up period, clinical improvement for hyperkeratosis was better with tazarotene treatment ( $t=3.31$ ,  $df=85$ ,  $p < 0.001$ ).

Three out of 16 patients (18.75%) in the tazarotene group reported adverse events, including desquamation and erythema of nail fold skin, periungual irritation, paronychia and irritation of the skin of the toe or finger distanced from the nail area. One out of 14 patients (7.14%) in the clobetasol group reported a sensation of burning on the nail fold skin. All adverse events reported were mild, with the symptoms ameliorating after a few days. All patients in both groups declared satisfaction with the results at the end of the treatment period.

## DISCUSSION

Nail psoriasis shares the chronic course of its skin counterpart with occasional flare-ups and remissions. However, contrary to advances in the treatment of skin psoriasis during the last years, therapy of psoriatic nails remains a challenge.

In the population under study, both tazarotene 0.1% cream and clobetasol 0.05% propionate cream were

found considerably to improve pitting, hyperkeratosis, onycholysis and salmon patches in patients with nail psoriasis after 12 weeks of treatment. Discontinuation of therapy resulted in significant regression of the signs for both groups, with the exception of hyperkeratosis, which seemed to retain significant improvement 12 weeks after the end of treatment for the patients applying tazarotene. These results tend to confirm previous studies reporting good clinical response after treatment with tazarotene gel in both fingernails and toe-nails (2, 3). Although clobetasol cream at a concentration of 0.05% is generally thought to present poor efficacy in the control of nail psoriasis because of limited penetration, our experience suggests that it has encouraging efficacy comparable to that of tazarotene under occlusion. Excellent results in psoriatic nails have also been reported with a nail lacquer formulation containing clobetasol 8% (1, 5).

Following topical application, tazarotene is rapidly hydrolysed in the skin by esterases to its active metabolite, tazarotenic acid, which binds selectively to the retinoic acid receptors beta/gamma. Pharmacologically, tazarotene affects the primary abnormalities associated with psoriasis: it normalizes epidermal differentiation and exhibits a potent anti-proliferative effect (6). Its mode of action in nail psoriasis might be attributed to exertion of these well-documented properties on the nail matrix and nail bed cells.

Adverse effects were mild and transient in both groups, demonstrating good tolerability of both products. These results indicate that tazarotene 0.1% cream is a safe and effective therapy for nail psoriasis, presenting a cosmetically acceptable treatment that satisfies the patients.

## ACKNOWLEDGEMENT

The authors declare no conflicts of interest.

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