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Long-term, intermittent treatment of chronic hand eczema with mometasone furoate

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Summary Chronic hand eczema can be incapacitating, and there is little knowledge of the efficacy and safety of long-term treatment with topical corticosteroids. We compared the efficacy and safety of two different schedules for the treatment of chronic hand eczema with a potent topical corticosteroid, mometasone furoate. In a prospective, open, randomized trial, 120 patients with chronic hand eczema were treated daily with mometasone furoate fatty cream until the dermatitis cleared or for a maximum of 9 weeks. Those who cleared were randomized to treatment for up to 36 weeks with mometasone furoate on Sunday, Tuesday and Thursday (group A), mometasone furoate on Saturday and Sunday (group B) or no further corticosteroid treatment (group C). In the event of relapse, patients were permitted daily treatment with mometasone furoate for 3 weeks on two separate occasions. For 50 of 106 randomized patients, daily treatment for 3 weeks controlled their dermatitis; 29 needed 6 weeks and 27 needed 9 weeks of treatment. During the maintenance phase, 29 of 35 (83%) in group A, 25 of 37 (68%) in group B and nine of 34 (26%) in group C had no recurrences ($P = 0{\cdot}001$, χ^2-test). Side-effects were minimal. It is concluded that long-term, intermittent treatment of chronic hand eczema with mometasone furoate fatty cream is effective and safe.

Key words: hand eczema, intermittent treatment, long-term treatment, prospective randomized trial, skin atrophy

The point prevalence of hand eczema among adults is approximately 5%, with twice as many women as men affected.[1] This dermatitis tends to become chronic[1] and accounts for a high percentage of those who have occupational dermatoses.[2,3] While the ideal treatment for hand eczema is to identify and eliminate its cause, this is not always possible. A wide range of suppressive treatments is available. These include topical corticosteroids, ultraviolet B, Grenz rays, PUVA and chemotherapy.[4–8] There is limited knowledge on the efficacy and safety of the long-term treatment of hand eczema with topical corticosteroids.[4] The current study is an attempt to find an effective and safe treatment by comparing two different treatment schedules using the potent topical corticosteroid mometasone furoate.

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Subjects and methods

Twenty men and 100 women aged 17 years or older were recruited in three centres in Denmark from April 1994 to May 1996. The inclusion criterion was eczematous hand dermatitis which had persisted for more than 6 months in spite of attempts to identify and remove the cause. All the patients had to have been patch tested with the European standard patch test series within 2 years of initiation of the study. Instructions given about contact allergens before the study were not altered or repeated. The exclusion criteria were hand eczema with acute infection, hyperkeratotic hand eczema, hand dermatoses other than eczematous dermatoses, contact allergy to components of the topical remedies used in the study and fungal infections of the hands and/or feet. Pregnant or lactating women and patients in systemic immunosuppressive therapy were also excluded.

The severity of pruritus, erythema, vesicles, scaling and fissures was determined on a scale of 0–3 (0, no symptoms; 1, few symptoms; 2, moderate symptoms; 3, severe symptoms). Scores for area were based on a clinical judgement of the total involved area of both hands: 0, no involvement; 1, $<1/3$; 2, $\geq 1/3 < 2/3$, 3, $\geq 2/3$. A total score of >6 was required for inclusion in the study. The investigation was carried out as an open, prospective, randomized trial. Initially, the dermatitis of all the patients was treated openly for 3 weeks with one daily application of mometasone furoate (Elocon^{R}, Schering Plough, Farum, Denmark) fatty cream. The patients were then examined clinically. If the dermatitis had not subsided, one or two additional 3-week periods of treatment were given, and the patient was seen 3 and possibly 6 weeks later. If the dermatitis had not subsided after 9 weeks of treatment, the patient dropped out of the study.

Patients for whom the initial once-daily treatment controlled the dermatitis to the extent that the clinical judgement was that daily treatment was no longer necessary were randomized into one of three groups: (A) treatment with mometasone furoate fatty cream on Sundays, Tuesdays and Thursdays (B) treatment with mometasone furoate fatty cream on Saturdays and Sundays and (C) treatment with the emollients Essex^{R} cream and Essex^{R} ointment (Schering Plough) but no corticosteroids. Clinical evaluations were carried out after 3, 6, 12, 18, 24 and 30 weeks of maintenance treatment and were based on the above-mentioned features of severity of dermatitis. Atrophy of the skin in the treated areas was evaluated on a scale of 0–3 using the same criteria as described for the other features. If recurrences (defined as a score as high as or higher than the initial score) occurred during the maintenance phase, daily treatment with mometasone furoate was permitted for a maximum of two separate periods of 3 weeks followed by the same maintenance treatment schedule as before the recurrence. If there were more than two recurrences during the maintenance period, the patient dropped out. If obvious bacterial infection occurred during the trial, a course of oral antibiotics and/or potassium permanganate soaks was permitted. All the patients were given Essex^{R} cream and ointment to be used freely, and these were the only emollients permitted.

Statistical analysis and ethics

Demographic data were compared to ensure that patients from the three centres and the randomization groups were comparable. The intention-to-treat principle was used to calculate the effect of the treatments. The primary efficacy variable was the number of recurrences in the three groups during the maintenance phase and the times at which these occurred. Secondary efficacy variables were: (i) the length of time it took to control the dermatitis during the initial treatment period; (ii) the time it took to control the dermatitis of various subgroups of patients; and (iii) the number of recurrences and the time to recurrence in subgroups of patients during the maintenance phase.

The study was planned and carried out in accordance with Helsinki Declaration II and the good clinical practice guidelines of the EU. The protocol was approved by the medical ethics committees in the regions included in the study.

Results

The 120 patients ranged in age from 17 to 70 years (median 31). The duration of dermatitis was from 6 months to 30 years (median 3 years). The dermatitis of 41 patients (34%) was on the dorsal aspect of the hands and/or fingers. Thirty-eight patients (32%) had dermatitis on the palmar aspect of the hands and/or fingers, and 40 patients (33%) had dermatitis at both sites. The site was not listed for one patient. There were no statistically significant differences in the demographic features represented in the three centres or in the three randomization groups.

The initial severity of the hand eczema indicated by the sum of the scores for pruritus, erythema, vesicles, scaling, fissures and one-half of the score for affected area of the dorsal aspects of the hands and one-half for area of the palmar aspects, was $\leq 8{\cdot}9$ for 56 patients, 9–11·9 for 47 patients and ≥ 12 for 14 patients. The initial score was not listed for three patients. Ninety-nine patients (83%) had only hand eczema; the remainder also had dermatitis at various other sites. Fifty (42%) had one or more positive patch tests, most commonly to nickel (22 patients), the perfume-mix (15), cobalt (six) and balsam of Peru (five). The possible relevance of patch test results was determined prior to the study and was not considered as a part of the current investigation.

The diagnoses were allergic contact dermatitis (27), irritant contact dermatitis (31), atopic dermatitis (27), recurrent vesicular hand dermatitis (13), other diagnoses or diagnosis not given (22). Seventy-six of the patients (63%) had occupations considered to be 'dry', such as office work, while 42 (35%) had 'wet' occupations

such as cleaning, patient care and hairdressing. Occupation was not listed for two patients. Fourteen of the 120 patients dropped out during the initial phase, most because of failure to return for follow-up. Three patients dropped out because their dermatitis could not be controlled.

Of the 106 patients who were randomized, 50 (47%) required 3 weeks, 29 (27%) required 6 weeks and 27 (25%) required 9 weeks of treatment to control the dermatitis during the initial phase. Dorsal hand eczema was controlled more rapidly than palmar or dorsal and palmar ($P = 0{\cdot}05$) (Table 1). None of the following factors had a statistically significant influence on the time it took to control the dermatitis during the initial phase: the sex of the patients, whether they had wet or dry occupations, the presence of atopic dermatitis, patch test positivity or negativity and the severity of the individual symptoms pruritus, erythema, vesicles, scaling or fissures or the extent of the dermatitis.

During the maintenance phase, patients treated three times a week had fewer recurrences than patients treated twice a week and than patients who were not treated with topical corticosteroids. The differences among the three groups (A, B and C) were statistically significant (Table 2). A survival analysis of time of recurrence shows similar results (Fig. 1). For the groups given active treatment, there was no difference between the results for wet or dry occupations (Table 3). Patch test positive patients had the same number of recurrences as patch test negative patients. A diagnosis of atopic dermatitis did not increase the risk of recurrence.

One patient in group A, three in group B and four in group C received additional treatment during the maintenance phase, either as potassium permanganate soaks, antibiotics or both. Based on number of recurrences, there was no indication of decreasing effectiveness of the topical steroid during the maintenance phase. For 10 patients, mild skin atrophy was noted at some point during the study. Three (one in group A, two in group B) had atrophy at onset which disappeared during the study. Five (two in group A, three in group B) had mild atrophy at the final visit.

Table 1. Duration of the initial phase needed to control the dermatitis of 106 patients in relation to the location of their hand eczema (prior to randomization). Dorsal hand eczema was controlled more rapidly than palmar eczema or dorsal and palmar eczema ($P = 0{\cdot}05$)

	Duration of initial treatment (weeks)			
Location	3	6	9	Total
Dorsal	23 (66%)	8 (23%)	4 (11%)	35 (100%)
Palmar	11 (32%)	10 (29%)	13 (38%)	34 (100%)
Dorsal + palmar	16 (43%)	11 (30%)	10 (27%)	37 (100%)
Total	50 (47%)	29 (27%)	27 (25%)	106 (100%)

Discussion

This was a two-part study. One hundred and twenty patients with chronic hand eczema were treated once daily with mometasone furoate fatty cream during an initial phase (Table 1). For one-quarter of all the patients, it was necessary to treat daily for 9 weeks to control the dermatitis. Most studies on topical corticosteroid treatment of contact dermatitis have been carried out over periods of 3–6 weeks, and high-potency preparations such as mometasone furoate have proven effective.[9] Thus, it would appear that hand eczema requires a longer treatment period than other types of eczematous dermatoses.

Table 2 and Figure 1 show that long-term maintenance treatment was necessary to control the hand eczema. Only one of 13 patients (8%) with dorsal hand eczema not treated with topical steroids completed the maintenance phase of the current study without recurrences. The effects of maintenance treatment were independent of the occupation of the patient, patch test reactivity and atopy. Dorsal hand eczema was controlled more quickly than palmar eczema during the initial phase (Table 1). During the maintenance phase, those patients using emollients alone and who had dorsal hand eczema, had the greatest number of recurrences (Table 2). This might indicate that palmar eczema tends to run its own course regardless of therapy, while dorsal eczema responds better to treatment and that, in order to prevent recurrence, dorsal eczema requires long-term intermittent treatment.

Table 2. The number and percentage of patients without recurrence during the maintenance phase, according to location and treatment given (106 randomized patients)

Location	Group A	Group B	Group C
Dorsal	9 of 10 (90%)	10 of 12 (83%)	1 of 13 (8%)
Palmar	12 of 14 (86%)	7 of 11 (64%)	4 of 9 (44%)
Dorsal + palmar	8 of 11 (73%)	8 of 14 (57%)	4 of 12 (33%)
Total	29 of 35 (83%)	25 of 37 (68%)	9 of 34 (26%)

$P = 0{\cdot}001$, χ^2 test for the difference between treatments for the total number of patients.

The need for a potent maintenance treatment was also noted by Möller *et al.*[4] In their study, twice weekly maintenance treatment with a very potent topical corticosteroid was more effective than the similar application of a moderate-strength preparation. The design of the current study did not permit the evaluation of whether or not prolonged, intermittent treatment and the long-term remission of hand eczema hastens cure of the dermatitis. Ideally, the maintenance phase should have been double-blind. This would, however, have required a very complicated distribution of the medicaments, with many different tubes for various days of the week. We felt the risks of mistakes by the patients and of poor compliance to be too great.

Intermittent maintenance therapy is desirable in order to reduce the amount of steroid used and thereby the risk of atrophy and of tachyphylaxis. Although tachyphylaxis commonly occurs after short periods of continuous treatment with potent topical steroids,[10,11] we saw no evidence of this phenomenon in terms of an increasing number of recurrences during the maintenance phase in the groups treated with a topical steroid (Fig. 1). Quick recovery may explain why tachyphylaxis was not seen when intermittent treatment schedules were used.[12]

Apart from tachyphylaxis, the major concern in long-term use of potent topical corticosteroids is atrophy of the skin. This may occur with continuous as well as intermittent treatment schedules.[13] Only five of the 106 randomized patients had evidence of mild atrophy of the skin at the completion of the current study. These five patients were in the groups that used a topical steroid during the maintenance phase, suggesting that the atrophy was treatment related. There may be some question of investigator bias on this issue. The study was open to the investigators, and they may have been particularly aware of atrophy in the two groups treated with topical steroids throughout the entire study period. It is interesting to note that three patients had mild or moderate atrophy at the onset of the study. The atrophy in these patients disappeared during the study, even though some received prolonged treatment with a steroid two or three times a week. This indicates that atrophy may be reversible even if intermittent treatment with a topical corticosteroid is continued. This is in contrast to the results of a study in which corticosteroids were applied to normal abdominal skin. In this study decreased collagen synthesis did not return to normal, even after a 2-week corticosteroid-free period.[14]

We conclude that long-term intermittent treatment of chronic hand eczema with mometasone furoate is effective and that the use of emollients alone is insufficient to control, in particular, dorsal hand eczema. The described treatment rarely causes atrophy, and this is mild when present.

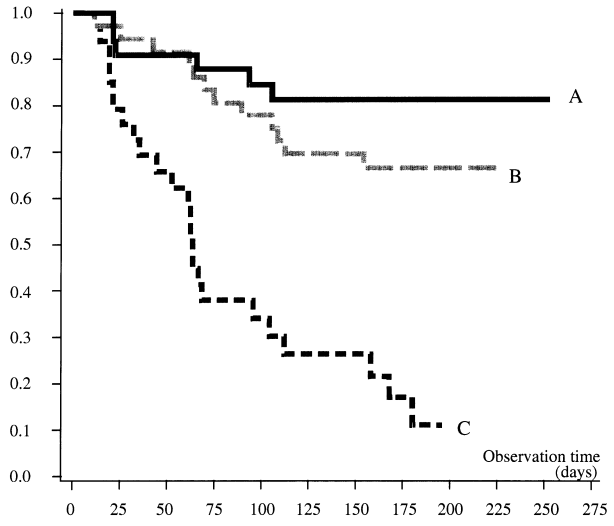

Figure 1. Survival analysis of the time of recurrence during the maintenance phase for 106 randomized patients. (A) Treatment with mometasone furoate fatty cream on Sundays, Tuesdays and Thursdays; (B) treatment with mometasone fatty cream on Saturdays and Sundays; (C) treatment with the emollients Essex^{R} cream and Essex^{R} ointment but no corticosteroids. Treatment A was better than B which was better than C ($P = 0{\cdot}0001$).

Table 3. The number and percentage of patients without recurrence during the maintenance phase, according to wet or dry occupation

Type of occupation	Group A	Group B	Group C
Wet[a]	8 of 9 (89%)	10 of 15 (67%)	1 of 12 (8%)
Dry[b]	21 of 26 (81%)	14 of 21 (67%)	8 of 22 (36%)

Information missing for one patient. [a]$P = 0{\cdot}001$, [b]$P = 0{\cdot}006$, χ^2 test for the differences among treatments A, B and C. $P = 0{\cdot}077$, χ^2 test for the difference between wet and dry occupations in group C.

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