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Chronic Eczematous Dermatitis of the Hands: A Comparison of PUVA and UVB Treatment

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The efficacy of PUVA and UVB treatment in chronic eczematous dermatitis of the hands was compared in a randomised controlled study including 35 patients who were randomly allocated to PUVA or UVB treatment. One hand was exposed to light and the other served as an untreated control. The dermatitis cleared on the treated hand in all PUVA patients, but in 9 out of 14 there was a relapse within three months. In the UVB group clearing of the skin lesions was not achieved, but compared with the "untreated" hands a statistically significant improvement was found at 12 weeks of treatment. A statistically significant improvement of "untreated" hands was found in both groups. PUVA and UVB treatments are alternative treatment modalities in patients with recalcitrant chronic eczematous dermatitis of the hands. PUVA is superior to UVB. *Key words: Photochemotherapy (PUVA); Short-wave ultraviolet light (UVB) therapy; Contact dermatitis.* (Received June 6, 1986.)

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Eczematous dermatitis of the hands is one of the most common skin disorders. Topical corticosteroids are the treatment of choice, and will clear the dermatitis in most cases, provided causative and exacerbating factors can be avoided. It is not always possible to avoid all provoking factors in the daily environment, however, and some patients will develop a chronic hand dermatitis in spite of treatment including potent topical steroids, tar, and, exceptionally, oral steroids.

Photochemotherapy with oral psoralen (PUVA) is effective in some types of hand dermatoses, particularly psoriasis and pustulosis palmoplantaris (1). There are also a few positive reports of PUVA treatment of allergic and irritant contact dermatitis, idiopathic vesicular palmar dermatitis (dyshidrotic eczema) and chronic hyperkeratotic dermatitis of the palms (thylotic eczema) (1, 2, 3, 4, 5). These reports are, however, based on uncontrolled observations or results from small groups of patients, except one study of 7 patients with dyshidrotic eczema (6).

Shortwave ultraviolet light (UVB) treatment is frequently used in the treatment of psoriasis and some forms of endogenous dermatitis. Its value in contact dermatitis has not been established. An uncontrolled study from 1983, however, showed excellent effect of UVB treatment in 7 out of 10 patients with allergic contact dermatitis (7).

The aims of this study were to evaluate the efficacy of PUVA and UVB treatment in chronic eczematous dermatitis of the hands, utilizing a randomised, controlled trial design, and to compare the two treatments.

PATIENTS AND METHODS

Patients

To be included in the study, the patients were required to fulfil the following criteria: (1) Bilateral hand dermatitis with symmetric distribution and severity. (2) A duration of at least 6 months. (3)

Previous treatment, including topical corticosteroids, without benefit. (4) Dermatitis interfering with daily life.

Reasons for exclusion were: previous or present psoriasis, ongoing fungal infection on the feet, pregnancy, impaired liver or renal function, alcohol abuse or inability to cooperate.

All patients had reduced their exposure to chemicals, water, soil and wear as much as possible. An epicutaneous patch test was performed in all patients, utilizing the standard European allergen series (the International Contact Dermatitis Research Group (ICDRG). The patches were removed after 48 hours and the results read 24 hours later (Table I). Patients with contact allergy were instructed to avoid the allergens.

Thirty-five patients, 31 women and 4 men, entered the study. Verbal informed consent was obtained from all patients. Characteristics of the patients are presented in Table II. The palms were affected in all patients and 27 also had lesions on the backs of their hands and fingers. Twenty-six patients had dermatitis with macroscopic vesiculation. The hand dermatitis was classified as allergic contact dermatitis (22 subjects; 63%), irritant contact dermatitis (6 subjects; 17%), hyperkeratotic dermatitis of the palms (6 subjects; 17%), or idiopathic vesicular palmar dermatitis (1 subject; 3%). In some cases, however, the contact allergy to allergens such as perfumes, lanolin and rubber might be secondary to an irritant contact dermatitis.

Study design

The patients were randomly allocated to either UVB or PUVA treatment. Those born in even years received PUVA treatment and those born in odd years UVB treatment. Patients born on even dates were treated on their right hand and patients with uneven birth dates on their left hand. The other hand was unexposed ("untreated hand"). All patients were treated three times a week for a maximum

Table I. *Contact allergens in 22 patients with positive patch tests*

PUVA-group, $n=13$		UVB-group, $n=9$	
Nickel	3	Nickel	3
Chromium	1	Nickel, cobolt, rubber chemicals	1
Nickel, cobolt	1	Nickel, chromium, contact urticaria (onion)	1
Nickel, chromium	1	Nickel, exposy resin, perfume mixture	1
Nickel, chromium, cobolt	1	Rubber chemicals	2
Perfume mixture, balsam of Peru	1	Lanolin, contact urticaria (mustard)	1
Balsam of Peru	1		
Rubber chemicals	3		
Formaldehyde	1		

Table II. *Characteristics of patients entering the study*

	PUVA ($n=18$)	UVB ($n=17$)
Mean age, years (range)	47 (19–70)	52 (24–62)
Sex (M/F)	3/15	1/16
Mean duration, years (range)	10 (0.5–48)	7 (1–48)
Mean combined severity score (range)		
Treated hand	10.3 (6–18)	10.5 (7–18)
Untreated hand	10.4 (7–18)	10.2 (5–18)
Allergic contact dermatitis	13	9
Irritant contact dermatitis	3	3
Hyperkeratotic (thylotic) dermatitis of the hand	2	4
Idiopathic vesicular palmar dermatitis	–	1
Personal history of		
Atopic dermatitis	3	2
Asthma, conjunctivitis, rhinitis	4	5

of 3 months. However, when the treated hand had cleared (slight to moderate residual erythema was allowed) the treatment was terminated.

During the treatment and the preceding month, topical corticosteroids or tar preparations were not allowed. The patients were encouraged to use emollients such as salicylic acid (2%) in petrolatum or urea (10%) in an emollient base. The patients rubbed in white petrolatum on their hands immediately before each light treatment.

The trial was approved by the Ethics Committee of the Faculty of Medicine of the University of Gothenburg.

Clinical assessments

Clinical assessments were made by the same investigator (K. R.) every three weeks. The following factors were evaluated: desquamation, erythema, vesiculation, infiltration and fissures. The patients' opinion about itching and pain was also registered. Each variable was assessed on a four-point scale: none (0), slight (1), moderate (2) and severe (3). The maximum combined severity score was thus 21. Colour photos were taken before treatment and at three-week intervals. When the treatment was completed, a global evaluation was made independently by the investigator and the patient using a four-point scale: cleared, much improved, somewhat improved, and unchanged/worse. "Cleared" meant no desquamation, vesiculation, infiltration, fissures or subjective symptoms. Some residual erythema was allowed, however. "Much improved" meant and excellent response but some thickening or desquamation persisted. "Somewhat improved" meant a substantial, easily recognised improvement.

PUVA

The PUVA treatment was carried out with a Waldmann PUVA 180+200 unit. One and a half hours before irradiation, the patient ingested 8-methoxy-psoralen (Puvamet®, Draco, Lund, Sweden) in a dose of 0.6 mg/kg bodyweight. The initial UVA dose was 2 Joules/cm^2, and the dose was increased at each treatment session by 1 Joule/cm^2 , except between 4 and 6 Joules, where the light dose was increased by 0.5 Joules/cm^2. The maximum UVA dose was 15 Joules/cm^2. If erythema, oedema or severe itching developed, the dose was kept at the same level or decreased.

Before treatment and after 1 week of PUVA treatment, serum levels of haemoglobin, white blood cells, platelets, creatinine, ASAT and ALAT were determined. Special sunglasses, opaque to UVA, were born during the treatment day.

UVB

The UVB source was a lamp with 6 Philips TL12 tubes of 60 cm length. The irradiation was about 1 milliwatt/cm^2 at a distance of 25 cm (Radiometer IL 1350, Dexter Industrial Green, Newburyport MA, USA). The lamp was placed horizontally 25 cm above the hands. The palms were irradiated in all patients, and those patients who had lesions on the backs of their hands were treated on this side also. The light dose was increased at each treatment session. The following treatment times were used: 30 sec, 45 sec, 60 sec, 1 ½, 2 min, 2 ½, 3 min, 4 min, 5 min, 6 ½, 8 ½, 11 min and 14 min. One second corresponds to 1 mJ/cm^2. If erythema developed, the dose was kept unchanged, or decreased in cases of severe erythema or oedema.

Statistical methods

The PUVA effect was evaluated by comparing the combined severity score of the light-treated hand with the "untreated" hand at 3, 6, 9 and 12 weeks using the paired *t*-test.

The UVB effect was evaluated in the same way.

When comparing PUVA treatment with UVB treatment the combined severity score for the PUVA treated and UVB treated hand was compared with the two sample *t*-test at 3 weeks, 6 weeks, 9 weeks and 12 weeks. In the PUVA group, where the dermatitis cleared in all patients and they therefore discontinued the treatment before 12 weeks, the last observed score was substituted for the missing value.

The results of the global evaluations were compared with the chi-square test.

RESULTS

Thirty-five patients entered the study, 18 in the PUVA group and 17 in the UVB group. Five patients discontinued the treatment prematurely—four in the PUVA group and one in the UVB group. Two patients did not tolerate the Puvamet tablets because of nausea,

lassitude and headache. The other two PUVA patients had to leave the study for personal reasons not related to the treatment. One UVB-treated dermatitis deteriorated at six weeks after *Staph. aureus* infection.

The investigators' and the patients' global evaluation of the results of treatment coincided. The results are shown in Table III.

PUVA treatment

Treated hand. The mean reduction of the combined severity score was 92%. The treated hand cleared in all fourteen patients who completed the study. The treatment time was 3 weeks in 4 patients, 6 weeks in 5 patients and 9 weeks in the remaining 5 patients. The mean number of treatments and total UVA dose are shown in Table III. The maximum single UVA dose varied between 5 and 15 J/cm^2 (mean 8.6 J/cm^2).

Untreated hand. The skin lesions improved, with a mean reduction of the total score of 49%. At the end of the study, the treated hand had a significantly smaller mean severity score than the untreated hand (mean difference 4.6±0.7 (SEM); $p<0.001$). All PUVA-treated hands cleared, compared to only one of the untreated hands ($p<0.001$).

Side effects. Side effects developed in 7 out of 14 patients (50%). Four patients experienced severe nausea from the 8-methoxypsoralen tablets, which led to a dose reduction in one patient. Three patients developed severe oedema, pain and itching in the treated hand, resulting in temporary interruption of the treatment for 1–3 weeks. Another patient developed hyperpigmented spots on the backs of the fingers, which disappeared after treatment. Two patients reported soreness and stiffness in the fingertips of the treated hand during the treatment which disappeared a few weeks after the treatment was completed. In three patients with allergic contact dermatitis, the dermatitis spread to the arms and face, which had not occurred earlier. However, the treated hand did not deteriorate. This happened after three, six and nine weeks and was easily controlled with topical steroids.

The results of routine blood tests were essentially normal.

Table III. *Clinical results at termination of the treatment*

	PUVA (n=14)		UVB (n=16)	
	Treated hand	Untreated hand	Treated hand	Untreated hand
Combined severity score (mean ± SEM)				
Before treatment	10.6±0.8	10.6±0.8	10.3±0.7	10.1±0.8
After treatment	0.8±0.2	5.4±0.7	5.0±0.8	6.4±0.9
Doctor's evaluation				
Cleared	14	1	–	–
Much improved	–	4	7	4
Somewhat improved	–	6	8	8
Unchanged/worse	–	3	1	4
Number of treatments (mean, range)	16 (8–31)		35 (26–44)	
Duration of treatment (days), (mean, range)	44 (16–96)		93 (69–117)	
Total PUVA/UVB dose (mean, range)	100 J/cm^2 (21–329)		11 J/cm^2 (2–27)	

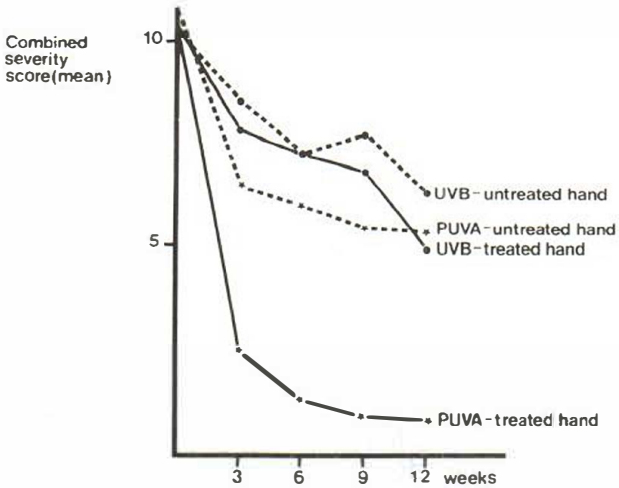

Fig. 1. Changes in combined severity score during the treatment.

UVB Treatment

Treated hand. Fifteen patients improved much or somewhat but in no case had the dermatitis cleared. The mean reduction of the total score was 51%. The maximum single dose was 0.7 J/cm^2 (range 0.2–0.9 J/cm^2).

Untreated hand. After twelve weeks of treatment, this hand had also improved. The mean reduction of the total score was 37%. Overall, no hand was cleared but the dermatitis was much or somewhat improved in 12 patients.

The mean severity score after treatment was significantly smaller in the treated hand than in the untreated hand (mean difference 1.4±0.6 (SEM); $0.01<p<0.05$). However, there was no significant difference in the proportion of much improved or cleared hands between treated and untreated hands ($p<0.1$).

Side effects. Adverse reactions occurred in 2 out of 16 patients (13%). Two patients developed bullae in the treated palm, probably due to the irradiation. Another patient was treated twice with flucloxacillin by mouth due to *Staph. aureus* infection of the dermatitis.

Comparison between PUVA and UVB treatment

The pre-treatment mean total score did not differ between the PUVA- and UVB-treated hands. At the end of the study, the mean total score was significantly lower in the PUVA-treated group ($p<0.001$). The improvement of the PUVA-treated hands over UVB-treated hands was already evident at 3 weeks ($p<0.01$). All 14 PUVA-treated hands cleared, but none of the 16 UVB-treated hands ($p<0.001$).

The untreated hand improved in both groups, somewhat more in the PUVA-treated group but this difference is not statistically significant.

Fig. 1 shows the improvement over time for both treatments. The improvement in the PUVA-treated group was rapid and the score reduced to 2.5 after three weeks. In the UVB-treated group, the score decreased gradually over 12 weeks but was considerably higher than with PUVA. The untreated hand in both groups also improved somewhat during the treatment.

There was no difference in the number of dropouts due to treatment between the UVB and PUVA groups. The number of patients with side effects was greater in the PUVA than in the UVB group ($p<0.001$).

Follow-up

The treated hand cleared in all fourteen PUVA-patients. In nine of them the dermatitis recurred after 1–8 months (mean 3 months). The deterioration came slowly. The dermatitis in five patients were still cleared after a follow-up period of 3 weeks (2 patients) and 2, 8, and 16 months.

Ten patients who did not respond satisfactorily to UVB treatment were later treated with PUVA on both hands. Two patients discontinued the treatment: one owing to a trip abroad and one 50-year-old woman with contact allergic dermatitis (nickel) who developed swollen lips and a feeling of thickness in her throat and nose within 30 min after intake of 8-methoxypsoralen. Provocation with 10 mg 8-MOP was positive. Both hands cleared after 12–37 treatments (mean 21) in 6 of the remaining 8 patients. The mean total light dose was 143 J/cm^2. One of the other patients was much improved and the other somewhat improved.

DISCUSSION

This study demonstrates the efficacy of PUVA treatment of chronic recalcitrant eczematous dermatitis of the hands, since the dermatitis cleared in all 14 patients who completed the treatment. In previous uncontrolled studies, it was found that PUVA cleared the dermatitis in 6 of 9 patients with allergic contact dermatitis (3), in all five patients with hyperkeratotic dermatitis of the palms (4) and in 20 of 36 patients with chronic eczematous dermatitis of the palms and soles (5). The present study clearly shows the importance of an untreated control site when evaluating different treatments for skin diseases with variable disease intensity. The reduction in combined severity score of the untreated hand was 49% in the PUVA group and 37% in the UVB group. The reason for this is unclear. The regular contacts with the medical team might have encouraged the patients to take more care of their hands, including utilizing the keratolytic and hydrating preparations, and a few patients were on sick-leave during the treatment period. In addition, a systematic effect of PUVA or UVB cannot be excluded. We are only aware of two previous controlled studies, both with a small sample of cases: in one trial, the treated hand cleared in all five patients with endogenous eczema but not the control hand (1), and in the other the treated hand cleared in all seven patients with dyshidrotic eczema, whereas the untreated hand did not heal completely (6).

The excellent results of the initial PUVA treatment contrasted with the outcome during the follow-up period. The dermatitis recurred in 9 of 14 patients after a mean period of 3 months. In the study of Tegner & Thelin (5), the remission time was 8 months after one course of treatment, and 14 months for patients who received both initial and maintenance treatment. Other studies have shown that maintenance treatment must be performed regularly, from twice weekly to every second week, to be effective (1, 3). To reduce the number of treatments and the total UVA dose, our policy has been to discontinue the treatment, when the dermatitis has cleared. The reponse to topical steroids was frequently better after relapse. Some patients, however, received another course of PUVA with as good results as in the first treatment period. Thus, it is obvious that PUVA therapy induces a non-specific time-limited suppression of the pathogenetic mechanism(s) resulting in the hand dermatitis. In many patients, continued treatment will be required to maintain the improvement. The potential side-effects of phototherapy therefore have to be considered. Short-term adverse reactions to PUVA are frequent, though usually manageable. Headache, nausea and local reactions such as burning, itching and pigmentation occur (1). The pathogenesis of the dissemination of the dermatitis which occurred in three of our cases is unknown but it was also observed in 2 of 5 cases of palmoplantar dermatitis (1).

The long-term side-effects of PUVA are not yet fully known (8). It is therefore essential that patients on continuous or intermittent PUVA therapy are carefully monitored by dermatologists experienced in phototherapy.

The results of UVB, though better than on the untreated hand, were hardly satisfactory considering the efforts required by the patient and the treatment team. However, in another study, longstanding allergic contact dermatitis of the hands cleared in 7 of 10 patients after UVB twice weekly for five months (7). The intensity of the UVB irradiation was similar. The divergent results may be explained by the lack of controls and a longer treatment period. It is possible that the efficacy of UVB can be improved by daily irradiation, prolonged treatment periods and adjuvant therapy with topical preparations, e.g. steroids and tar. The mechanisms of action of PUVA and UVB in contact dermatitis are not fully known. PUVA and UVB are known to interfere with Langerhans' cells and antigen presentation and may also modulate the inflammatory response (9). There was no difference in therapeutic efficacy between patients with allergic and non-allergic contact dermatitis.

In conclusion, this study has shown that PUVA and UVB can improve chronic eczematous hand dermatitis, that PUVA is superior to UVB, that maintenance treatment is important and that a randomised controlled trial is necessary for proper evaluation of response to therapy.

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