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Low Dose Versus Medium Dose UV-A1 Treatment in Severe Atopic Eczema

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Twenty-two patients with severe atopic eczema were included in a therapy study with UV-A1 (wavelengths > 340 nm) treatment. The patients were divided into two dose groups, each consisting of 11 patients. One group received 10 J/cm² and the other 50 J/cm² five times a week for 3 consecutive weeks. No topical or systemical steroids or antihistamines were allowed. Using the SCORAD index as a measure of disease activity before onset of therapy and after 10 and 15 treatments, we observed a significant improvement in both dose groups after 15 treatments (10 J/cm²: $p < 0.05$, 50 J/cm²: $p < 0.005$). After 10 treatments only the improvement in the 50 J/cm² group was significant ($p < 0.005$); the difference between the two dose groups was significant ($p < 0.05$). The clinical efficacy of treatment was reflected neither by a decrease of serum IgE nor by a decrease of elevated serum levels of soluble adhesion molecules sICAM-1 and sELAM-1 in the two dose groups. In contrast, a marked but not significant decrease of serum ECP could be observed in the 50 J/cm² group only. We conclude from these and other published data that although 10 J/cm² UV-A1 has a limited effect on patients with severe atopic eczema, higher doses are of higher efficiency in the treatment of this condition. ***Key words: eosinophil cationic protein; adhesion molecules; immunomodulation.***

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Treatment of atopic eczema with ultraviolet radiation is an established method of therapy since many years. Several studies have been published on different treatment regimens with UV-A, UV-B or UV-A + UV-B (1–3). Recently, a study comparing the results of UV-A1 (wavelengths > 340 nm) and UV-A + UV-B in the treatment of atopic eczema has been performed (4). In this study, UV-A1 was administered in extremely high doses of 15 × 130 J/cm² and showed superior effects compared to conventional UV-A + UV-B therapy. The results of a second uncontrolled study of UV-A1 therapy using lower and escalating doses were reported (5). Since both studies used the same scoring system to measure the activity of disease, a comparison of the therapeutic effects revealed that the latter, with lower doses of UV-A1, was weaker. The long term side-effects (e.g. skin aging, carcinogenesis) of higher doses of UV-A1 are not yet known. Therefore, we conducted a study comparing clinical and laboratory effects of low (15 × 10 J/cm²) and medium (15 × 50 J/cm²) dose UV-A1 treatment of severe atopic eczema in order to find out the lowest optimal effective dose of this therapeutic method.

PATIENTS AND METHODS

Patients

Twenty-two patients with severe atopic eczema (12 males and 10 females, mean age 32.0 ± 12.9 years) were included. The severity of skin involvement was measured employing the SCORAD index (6). In brief, this index system includes a maximum of 20 score points for body surface extension of lesions, a maximum of 62 points for representative presence of erythema, infiltration, exsudation, excoriation and lichenification plus total skin dryness, and finally a maximum of 20 points for presence of itching and disturbance of sleep as judged by the patient himself. Only patients with an initial score above 39 points were included. Excluded were patients with prurigo nodularis and atopy, age under 18 years, history of polymorphous light eruption, and patients with viral or bacterial superinfection. Written informed consent was given. The characteristics of the patients in both dose groups are shown in Table I.

Phototesting

Before onset of treatment, all patients underwent a phototesting with the lamp later used for UV-A1 therapy, to determine the minimum erythema and pigmentation doses (MED, MPD). Four areas at the lower back measuring 3 cm in square were exposed to 10, 35, 50 and 90 J/cm², respectively. Erythema and pigmentation were judged 24 and 48 h later.

Phototherapy

The UV-A1 treatment was performed in a Photomed CL 150.000 bed (MTU, Wenningsen, Germany), emitting wavelengths of 340–500 nm only (5). Irradiations were given five times a week for 3 consecutive weeks either with 10 or 50 J/cm², yielding total doses of 150 or 750 J/cm² in the two dose groups. All patients were assigned to a dose group in which a lower dose than their MED in the pretreatment phototesting was administered. UV-A1 treatment was accompanied by topical moisturizing ointments. No topical or systemical steroids or antihistamines were administered during therapy.

Assessment of clinical response

The disease activity was measured by means of the SCORAD index, as explained above, before onset of therapy and after 10 and 15 treatments by the same investigator. Photographs were taken before onset and at the end of the therapy.

Assays for serum parameters

ELISAs for soluble adhesion molecules sICAM-1 and sELAM-1 (E-selectin) were performed as described previously (7, 8). Serum IgE and ECP were measured by fluoroenzyme immunoassays (FEIAs) from Kabi Pharmacia Diagnostics, Uppsala, Sweden, as described (9). Control serum samples were taken from 22 healthy controls (14 males, 8 females, mean age 38.4 ± 11.1 years).

Statistics

The difference of pre- and post-treatment SCORAD values and serum parameter levels and between the different dose groups were tested for significance using paired *t*-tests.

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Table I. *Patients with severe atopic eczema (AE) treated with UV-A1 irradiations: characteristics*

	UV–A1 therapy	
	15 × 10 J/cm²	15 × 50 J/cm²
Age (years; median, range)	27 (22–64)	26 (21–41)
Sex (males/females)	5/6	7/4
SCORAD (points)	64.5 ± 14.8	62.7 ± 12.6
Duration of AE (years)	24.5 ± 15.8	20.4 ± 9.5
Skin type (I/II/III/IV)	1/5/5/0	0/3/7/1
n	11	11

RESULTS

The results of phototesting for MED and MPD of a total of 38 individual patients with severe atopic eczema are shown in Fig. 1. Twenty-two of them were included in the present study. The median MED was 90 J/cm² and the median MPD was 50 J/cm².

The decrease of SCORAD values during therapy in both dose groups is shown in Fig. 2. In the 10 J/cm² group, 5 patients had a good, 3 a moderate and 3 a poor response. In the 50 J/cm² group, 7 patients had a good, 3 a moderate and only 1 a poor response. No patient had a complete healing of his symptoms. The reduction of SCORAD levels was mainly a result of the reduction of the symptoms of itching and sleep disturbance ($p < 0.05$) and of the reduction of infiltrative, exsudative and excoriated lesions. Surface extension, erythema, lichenification and dryness were less affected by the treatment.

The change in serum levels of possible markers for disease activity is shown in Table II. Significantly elevated serum levels of sICAM-1 and sELAM-1 ($p < 0.001$) could be detected before onset of therapy; these did not decrease despite clinical improvement in both dose groups. Serum IgE levels did not show a reduction in either of the two dose groups. In contrast, serum ECP levels markedly decreased following therapy in the 50 J/cm² dose group but not in the 10 J/cm² dose group. However, this effect was not statistically significant.

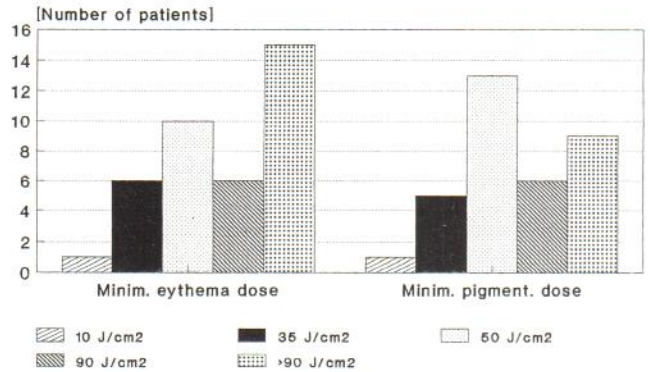

Fig. 1. Minimum erythema dose (MED) and minimum pigmentation dose (MPD) with UV-A1 in 38 patients with severe atopic eczema. MED was juged after 24 h, MPD after 48 h.

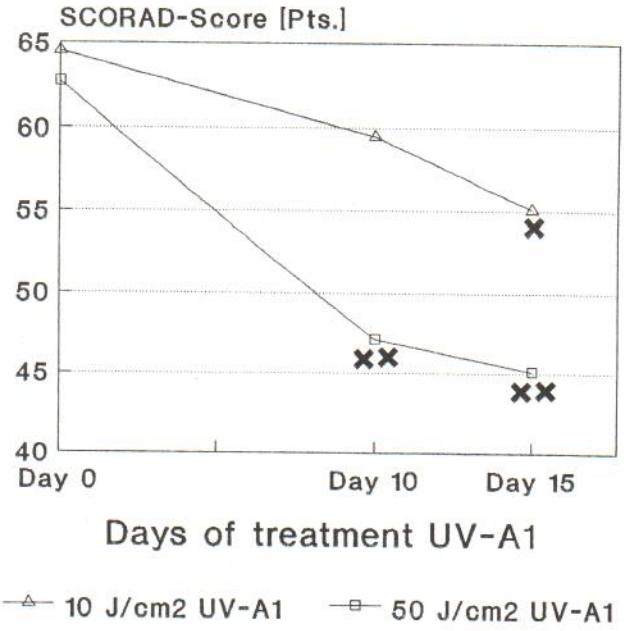

Fig. 2. Clinical status of 22 patients with severe atopic eczema during therapy with UV-A1 assessed by SCORAD score. The improvement during treatment was significant after 10 and 15 irradiations in the group treated with 15 × 50 J/cm² and after 15 irradiations in the 10 J/cm² dose group (xx = $p < 0.005$, x = $p < 0.05$; $n = 11$ in both dose groups).

DISCUSSION

Recently, Krutmann et al. (4) demonstrated the therapeutic effect of high dose UV-A1 treatment in 15 patients with severe atopic eczema. In this study a superior effect ($p < 0.01$) of 15 × 130 J/cm² (total dose 1,950 J/cm²) compared to a combined therapy with 15 × up to 30 mJ/cm² UV-B and 7.5 J/cm² UV-A could be demonstrated. Efficiency was measured using a scoring system developed by Costa et al. (10). During treatment with UV-A1 mean score values decreased from 53 to 14 points after 15 irradiations. In a second open study Meffert et al. (5) treated patients with severe atopic eczema with UV-A1 using a different equipment emitting only wavelengths of 340 to 500 nm ("cold-light-therapy"). Escalating doses starting with 3.3 or 6.6 J/cm²

Table II. *Serum levels of IgE, ECP, sICAM-1 and sELAM-1 before and after 15 treatments either with 10 J/cm² or 50 J/cm² UV-A1 in patients with severe atopic eczema (n = 9 in each dose group)*

Serum parameter	Dose group	Pre-treatment	Post-treatment
IgE (kU/l)	10 J/cm²	5,956 ± 4,089	5,776 ± 4,217
	50 J/cm²	4,778 ± 6,490	4,623 ± 5,797
ECP (µg/l)	10 J/cm²	24.7 ± 16.8	26.8 ± 38.2
	50 J/cm²	27.7 ± 41.0	18.1 ± 13.5
sICAM-1 (ng/ml)	Control	296 ± 46	n.d.
	10 J/cm²	533 ± 64	546 ± 79
	50 J/cm²	596 ± 116	610 ± 154
sELAM-1 (ng/ml)	Control	48.8 ± 22.7	n.d.
	10 J/cm²	91.2 ± 30.2	85.1 ± 24.6
	50 J/cm²	88.8 ± 28.1	94.0 ± 33.1

were administered ten times to 30 patients (total doses 220 or 410 J/cm^2, respectively). Efficiency was measured using the same scoring system, and the mean severity score values decreased from 64 to 37 points after ten treatments. No difference between the two dose groups was seen.

In the present study we used the same UV-A1 equipment as Meffert et al. The final cumulative dose was 150 J/cm^2 in the 10 J/cm^2 group and 750 J/cm^2 in the 50 J/cm^2 dose group. Both groups consisted of 11 patients. We used a different scoring system for the measurement of disease activity which was worked out by the European Task Force on Atopic Dermatitis, the SCORAD index (6). We found a significant ($p < 0.05$) difference of therapeutic efficiency between the two dose groups. In the 50 J/cm^2 group the mean scoring value decreased from 63 to 47 points and in the 10 J/cm^2 group from 65 to 60 points after ten treatments. However, since patients were not randomly allocated to the dose groups in order to avoid erythematous reactions, it could not completely be ruled out that patients with lower MED for UV-A1 intrinsically respond more poorly to this phototherapy.

Serum ECP levels have been proposed as markers for disease activity in atopic eczema (11). Krutmann et al. (4) have shown that there was a significant decrease in serum ECP levels in the group treated with high dose UV-A1 during clinically effective treatment. Only a slight effect was seen in the group treated with combined UV-A + UV-B. In our study there was only a marked decrease of serum ECP in the clinically more effective 50 J/cm^2 dose group, although this effect was not statistically significant. The two studies revealed no effect of UV-A1 treatment on serum IgE levels despite clinical improvement.

We conclude from these data that low doses of 10 J/cm^2 UV-A1 per day are not optimally effective in the treatment of severe atopic eczema and that higher doses should be administered. Further studies are required to clarify the question whether medium doses of approx. 25 to 50 J/cm^2 UV-A1 per single treatment allow therapeutic effects comparable to those of high doses above 100 J/cm^2 when more than fifteen irradiations are applied. In that case it would be possible to administer lower cumulative doses in order to minimize possible long-term side-effects of UV-A1 treatment.

The exact mechanism of action of UV-A1 in atopic eczema is not yet known. High doses of UV-A1 (approx. 140 J/cm^2) have been shown to alter the number and function of Langerhans' cells (12, 13), while medium doses of UV-A1 (50 J/cm^2) failed to have such effects (14). Furthermore, high dose UV-A1 has been shown to reduce mRNA coding for gamma interferon but not for interleukin-4 in lesional skin during treatment (15). Recently it was reported that UV-A1 can suppress late type allergy reaction towards inhalative allergens (atopypatch test) in patients with atopic eczema (16).

The adhesion molecule ICAM-1 is expressed on keratinocytes in lesional skin from atopic eczema and contact dermatitis (17). It was demonstrated that UV-A1 suppresses the expression of this molecule on keratinocytes during sufficient therapy (16). Beside keratinocytes, leukocytes and endothelial cells are possible sources of the soluble form sICAM-1, which was found in increased levels in the sera of our patients with severe atopic eczema. These elevated serum levels of sICAM-1 did not decrease during effective therapy in the two dose groups. The adhesion molecule ELAM-1 is expressed on dermal vascular endothelial cells in lesional skin in atopic eczema (18). We have found increased levels of the soluble form sELAM-1 in the sera of our patients with severe atopic eczema, which did not decrease during UV-A1 therapy. We conclude that the serum levels of these two adhesion molecules are no suitable markers for actual skin involvement in patients with severe atopic eczema.

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