Efficacy of UVA1 phototherapy in 230 patients with various skin diseases

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None declared.

Summary

Objective: Investigation of the efficacy of ultraviolet (UV) A1 phototherapy on atopic eczema, scleroderma, granuloma annulare, urticaria pigmentosa, prurigo nodularis, lichen sclerosus et atrophicus, T-cell lymphoma, keratosis lichenoides chronica, chronic urticaria and some rare, sclerosing skin diseases.

Methods: The data of 230 patients treated with low-dose, medium-dose and high-dose UVA1 therapy during 6 years were retrospectively analysed. The mean single dose (J/cm^2), the mean number of irradiations and the mean total dose (J/cm^2) were evaluated. The efficacy of phototherapy was assessed by a grading scale and the number of patients was given in percentage for each group.

Results: Good therapeutic effects of UVA1 therapy were shown in patients with atopic eczema, scleroderma, lichen sclerosus et atrophicus, keratosis lichenoides chronica, prurigo nodularis and with cutaneous T-cell lymphoma. Positive effects in some patients were seen in the urticaria pigmentosa and granuloma annulare group, no change to slight improvement was seen in most of the patients with rare, sclerosing skin diseases and no effect was seen in the chronic urticaria group.

Conclusion: Besides topical and systemic therapy, UVA1 radiation is a good option of treatment in various skin diseases. It is one of the first-line treatments for several sclerotic diseases and it often improves pruritus considerably.

In former years, patients were treated with broad-band ultraviolet (UV) B (280–320 nm), broad-band UVA (320–400 nm) or combination regimens. Broad-band UV phototherapy, however, is more and more replaced by the use of irradiation devices that allow treatment with selected emission spectra. Two such modalities which have their origin in European Photodermatology are narrow-band UVB phototherapy, which uses long-wave UVB radiation above 300 nm, and UVA1 therapy, which selectively uses long-wave UVA radiation above 340 nm (1).

Long-wavelength UVA (340–400 nm; UVA1) therapy has been available since 1981 (2). Depending on the skin disease, high doses of UVA1 (up to 130 J/cm^2), medium doses (40–70 J/cm^2) or low doses of UVA1 (10–30 J/cm^2) radiation are administered during a single treatment session. UVA1 phototherapy is effective in the treatment of inflammatory skin disease such as exacerbated atopic eczema, localized scleroderma and granuloma annulare (2, 3). UVA1 has various effects that may contribute to the suppression or prevention of eczema flares like its ability to induce T-lymphocyte apoptosis and to reduce the number of Langerhans cells and mast cells in the dermis. Moreover, an increased collagenase expression may lead to the improvement of morphea. Another effect is the reduction of pruritus through inhibitory effects on histamine release from basophils and mast cells (2, 4). UVA1 therapy is generally well tolerated. The main acute adverse effects are erythema, hyperpigmentation, polymorphic light eruption, pruritus due to dryness of skin and the major chronic adverse effects include photoaging and skin cancer (2).

Study design and methods

Data were collected in the Department of Dermatology and Allergy from August 1999 to June 2005 (approximately 6 years). Two hundred and thirty patients with various skin diseases were treated and the data were analysed retrospectively: 86 patients with atopic eczema (39 males, 47 females, age 40.22 ± 16.6 years), 54 patients with scleroderma (14 males, 40 females, age 46.17 ± 19.12 years), 20 patients with granuloma annulare (three males, 17 females, age 57.90 ± 10.13 years), 19 patients with urticaria pigmentosa (three males, 16 females, age 41.37 ± 12.1 years), 17 patients with prurigo nodularis (seven males, 10 females, age 59.65 ± 16.89 years), 10 patients with lichen sclerosus et atrophicus (one male, nine females, age 64.4 ± 7.49 years), seven patients with T-cell lymphoma (four males, three females, age 67.0 ± 19.0 years), five patients with keratosis lichenoides

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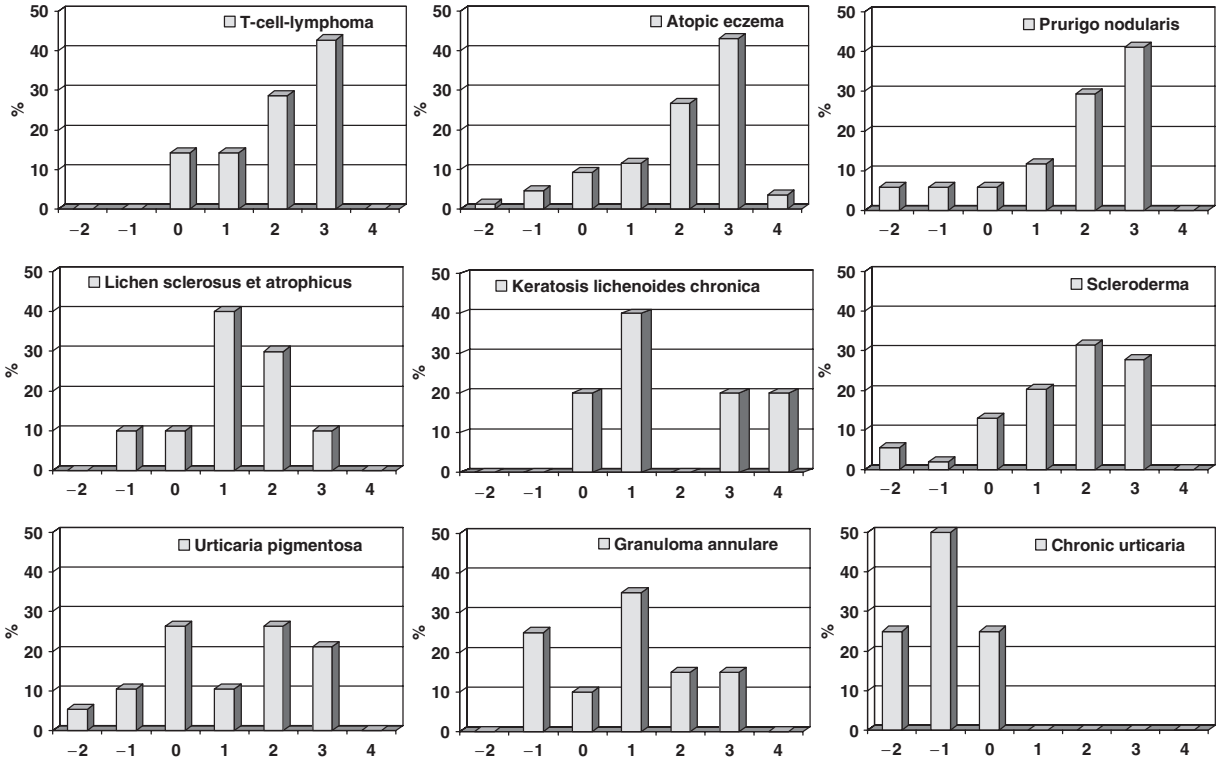

Fig. 1. Evaluation of the efficacy of UVA1 therapy on various skin diseases according to the clinical evaluation of the skin by a physician. Number of patients per group in percentage (axis of ordinates). Assessment of the results by a grading scale (axis of abscissas): (−2) withdrawal after six irradiations; (−1) aggravation; (0) no change; (1) slight improvement; (2) moderate improvement; (3) marked improvement; (4) complete healing.

chronica (one male, four females, age 50.80 ± 15.25 years), four patients with chronic urticaria (one male, three females, age 46.75 ± 11.98 years) and eight patients with a rare sclerosing skin disease that is to say three male patients with scleredema adultorum Buschke (51, 59, 60 years), one male and one female patient with graft-versus-host disease (58 and 5 years), one male patient with nephrogenic fibrosing dermopathy and one female patient each with Werner syndrome and eosinophilic fasciitis. Patients in which treatment was stopped after less than six single irradiations without worsening of skin disease due to other reasons were excluded from the study. Patients whose skin got worse after few treatments due to irradiation were included. Adjuvant treatment during UVA1 therapy was continued.

Clinical evaluation

The skin was clinically evaluated by the physician, pruritus intensity was indicated by the patients. The descriptive documentation was carried out in written records. The efficacy of the phototherapy was assessed by a grading scale [(−2) withdrawal after six irradiations; (−1) aggravation; (0) no change; (1) slight improvement; (2) moderate improvement; (3) marked improvement; (4) complete remission].

Phototherapy

The mean single dose (J/cm^2), the mean number of irradiations and the mean total dose (J/cm^2) were evaluated for each disease group. As irradiation source, we used dermalight ultraA1 (Dr. Hoenle GmbH, Kaufering, Germany). The UV radiation spectrum was between 340 and 440 nm. The intensity of the radiation was 80 mW/cm^2 at a distance of 50 cm.

Results

The results are summarized in Fig. 1 and Table 1. Overall, an improvement of the skin disease (slight improvement to complete remission) was observed for each disease group except for chronic urticaria and some rare sclerosing skin diseases; it ranged from 57.9% in the group of urticaria pigmentosa to 85.7% in the group of patients with cutaneous T-cell lymphoma. In the last group only seven patients were treated, with six of them (85.7%) showing an improvement of their skin disease [with one patient scoring 1 (14.3%), two patients scoring 2 (28.6%), three patients scoring 3 (42.8%)]. The mean single dose used was 48.6 ± 6.9 J/cm^2, the mean number of irradiations was 24.26 ± 12.24 and the mean cumulative dose was 1077.86 ± 524.7 J/cm^2.

Similar good results were shown in 73/86 (84.8%) patients with atopic eczema [with 10 patients scoring 1 (11.6%), 23 patients scoring 2 (26.7%), 37 patients scoring 3 (43.1%) and three patients scoring 4 (3.5%)]. The mean single dose used was 60.23 ± 15.74 J/cm^2, the mean number of sessions was 13.13 ± 4.01 and the mean total dose was 773.08 ± 339.49 J/cm^2.

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Table 1. Summary of the patients' data and the phototherapy (mean ± standard deviation)

Diagnosis	Cases, *n*	Males, *n* (%)	Individual doses (J/cm^2)	Irradiations, *n*	Total doses (J/cm^2)
Atopic eczema	86	39 (45.0)	60.23 ± 15.74	13.13 ± 4.01	773.08 ± 339.49
Scleroderma	54	14 (25.9)	59.81 ± 27.40	21.10 ± 13.10	1203.15 ± 1133.95
Granuloma annulare	20	3 (15.0)	75.50 ± 33.20	16.20 ± 6.00	1352.50 ± 1095.10
Urticaria pigmentosa	19	6 (31.6)	72.11 ± 21.49	13.80 ± 3.68	942.63 ± 400.96
Prurigo nodularis	17	7 (41.2)	47.60 ± 9.70	13.94 ± 6.50	650.00 ± 379.10
Lichen sclerosus et atrophicus	10	1 (10.0)	55.50 ± 23.40	20.70 ± 8.76	1018.00 ± 575.30
Keratosis lichenoides chronica	5	1 (20.0)	70.70 ± 13.60	19.00 ± 6.52	1352.00 ± 584.05
T-cell lymphoma	7	4 (57.0)	48.60 ± 6.90	24.26 ± 12.24	1077.86 ± 524.70
Chronic urticaria	4	1 (25.0)	55.00 ± 17.30	8.25 ± 3.95	477.50 ± 345.87
Scleredema adultorum Buschke	3	3 (100)	57.90	31.60	1620.00
Graft versus host disease	Pat. 1	Female	21.00	72.00	1520.00
	Pat. 2	Male	41.60	19.00	790.00
Nephrogenic fibrosing dermopathy	1	Male	54.00	15.00	810.00
Werner syndrome	1	Female	35.00	10.00	350.00
Eosinophilic fasciitis	1	Female	35.00	10.00	350.00

The UVA1 therapy of patients with prurigo nodularis led to good results as well. An improvement was stated in 14/17 (82.4%) patients [with two patients scoring 1 (11.8%), five patients scoring 2 (29.4%), seven patients scoring 3 (41.1%)]. The mean single dose, the mean number of irradiations and the mean total dose were 47.6 ± 9.7, 13.94 ± 6.5 and 650.0 ± 379.1 J/cm^2, respectively.

Also good results were found in patients with lichen sclerosus et atrophicus with 8/10 (80.0%) patients showing an improvement of their skin disease [with four patients scoring 1 (40%), three patients scoring 2 (30%), one patient scoring 3 (10%)]. The mean single dose used was 55.5 ± 23.4 J/cm^2, the mean number of sessions was 20.7 ± 8.76 and the mean total dose was 1018.0 ± 575.3 J/cm^2.

Skin changes were reduced in 4/5 (80.0%) patients with keratosis lichenoides chronica [with two patients scoring 1 (40%), no patient scoring 2, one patient scoring 3 (20%) and one patient scoring 4 (20%)]. The mean single dose, the mean number of irradiations and the mean total dose were 70.7 ± 13.6, 19.0 ± 6.52 and 1352.0 ± 584.05 J/cm^2, respectively.

Similar good results were shown in scleroderma with 43/54 (79.6%) patients getting smooth skin [11 patients scoring 1 (20.3%), 17 patients scoring 2 (31.5%), 15 patients scoring 3 (27.8%)]. The mean single dose used was 59.81 ± 27.4 J/cm^2, the mean number of irradiations was 21.1 ± 13.1 and the mean total dose was 1203.15 ± 1133.95 J/cm^2.

The efficacy of UVA1 therapy was less pronounced in patients with urticaria pigmentosa and granuloma anulare.

Eleven of 19 (57.9%) patients with urticaria pigmentosa showed an improvement of their skin disease [with two patients scoring 1(10.5%), five patients scoring 2 (26.3%), four patients scoring 3 (21.1%)]. The mean single dose used was 72.11 ± 21.49 J/cm^2, the mean number of irradiations was 13.8 ± 3.68 and the mean total dose was 942.63 ± 400.96 J/cm^2.

Regarding the patients with granuloma annulare, the skin disease ameliorated in 13/20 (65%) patients [with seven patients scoring 1 (35%), three patients scoring 2 (15%), three patients scoring 3 (15%)]. A mean single dose of 75.5 ± 33.2 J/cm^2, a mean number of irradiations of 16.2 ± 6.0 and a mean total dose of 1352.5 ± 1095.1 J/cm^2 were used.

UVA1 therapy showed no effect (mean number of irradiations 8.25 ± 3.95) in the chronic urticaria group. The mean single dose used was 55.0 ± 17.3 J/cm^2 and the mean total dose was 477.5 ± 345.87 J/cm^2.

In the group with rare sclerosing skin diseases, only a small number of patients were treated. One patient with scleredema adultorum Buschke showed a marked improvement whereas the other two patients only showed a slight improvement of their skin (mean dose 57.9 J/cm^2, mean number of irradiations 31.6). One patient with graft-versus-host disease showed a moderate improvement (mean dose 21.0 J/cm^2, number of irradiations 72), in the other patient phototherapy had no effect (mean dose 41.6 J/cm^2, number of irradiations 19). The patient with nephrogenic fibrosing dermopathy showed a slight improvement (mean dose 54.0 J/cm^2, number of irradiations 15.0) whereas the patients with Werner syndrome and eosinophilic fasciitis had no change of their skin disease (mean dose 35.0 J/cm^2, number of irradiations 10.0 in each patient).

Discussion

Mostly we used medium-dose UVA1 therapy for the different skin diseases. In earlier studies, patients were often treated with higher doses comparing with later studies. That is why we started the investigations years ago with higher doses resulting in different individual mean single doses for the different skin diseases.

Medium-dose UVA1 therapy in patients with atopic eczema led to a moderate to marked improvement in most patients as observed in earlier studies (5). In the past years UVA1 phototherapy has been proved to be effective in atopic eczema and to be superior to UVA/UVB or PUVA therapy (6). Krutmann *et al.* (7) showed in their studies that high-dose UVA1 therapy

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showed a significant clinical improvement of severe atopic eczema and Tzaneva *et al.* (8) compared high-dose and medium-dose UVA1 therapy in a half-side comparison study which showed a comparable effect. In contrast, low-dose UVA1 therapy did not lead to significant reduction in severity of atopic eczema (9, 10). Although high- and medium-dose therapy showed good results, relapses are often a problem after 4–12 weeks (5, 8).

Also sclerosing skin diseases improved in our study with medium-dose UVA1 therapy. Stege *et al.* (11) compared high-dose and low-dose UVA1 therapy in patients with scleroderma and could reduce skin thickness and stiffness after high-dose UVA1 therapy significantly. In other studies, low-dose UVA1 (12, 13) and medium-dose UVA1 (14) in scleroderma was effective. Others (15) showed that medium-dose UVA1 therapy in localized scleroderma was significantly more effective than narrow-band UVB treatment.

Medium-dose UVA1 therapy in patients with lichen sclerosus et atrophicus and keratosis lichenoides chronica showed an improvement in most of them. Kreuter *et al.* (16) could reduce clinical score, decrease skin thickness and increase dermal density in 10 patients with lichen sclerosus et atrophicus even by the use of low-dose UVA1 therapy. PUVA therapy is another effective therapeutic option in these patients (17). Polderman *et al.* (18) showed a clearance of 98%, 88%, 82% and 41% in four patients who had medium-dose UVA1 therapy for keratosis lichenoides chronica.

Our quite good results of medium-dose UVA1 therapy in patients with T-cell lymphoma might depend on the few patients treated. The complete clearance of T-cell lymphoma in 11/13 patients in another study (19) may be due to high-dose UVA1 irradiation.

The results in patients with granuloma annulare treated with medium- to high-dose UVA1 therapy were not so good, only about half of the patients improved. This agrees with the results of Schnopp *et al.* (20) where substantial response or near-complete healing occurred in 50% of patients with medium- to high-dose UVA1 therapy. In contrast, the investigations of Muchenberger *et al.* (21) showed that high-dose UVA1 therapy led to complete clearance or considerable improvement in all patients. Like in atopic eczema, relapses after 3 months seem to be a problem. There are even more studies showing the positive effect of PUVA therapy in patients with granuloma annulare (22–24).

Only half of the patients with urticaria pigmentosa improved after medium-dose UVA1 therapy. Stege *et al.* (25) treated four patients with high-dose UVA1 following relief from itch, decrease of histamine and serotonine release. Others (26) showed no difference between high- and medium-dose UVA1. The pruritus and quality of life improved considerably, the number of lesions was not reduced. Hence, UVA1 therapy is worth trying in patients with urticaria pigmentosa, but also oral and bath PUVA therapy is an effective possibility to treat mastocytosis (27).

There are, to our knowledge, no studies published on UVA1 therapy and prurigo nodularis although our results were quite good. As a chronic disease there are limited treatment modalities. An improvement was stated by Ferrandiz (28) with narrow-band UVB phototherapy combined with thalidomide.

We were unable to show an effect of UVA1 therapy on chronic urticaria. Overall there are only few data in the literature about the treatment of chronic urticaria with UV light. Only solar urticaria can be successfully treated with UV hardening. A 'non-specific' chronic urticaria is much more difficult to treat (29).

In our patients with scleredema adultorum Buschke, one showed a marked and two showed a slight improvement of their skin with the medium-dose regimen. Tuchinda *et al.* (30) could show a moderate to good response in 80% of the patients even treated with low-dose UVA1 therapy, similar to another study (31) showing a complete clearance of the skin disease with low-dose UVA1 irradiation. The UVA1 therapy with low-dose regimen and a high number of irradiations in graft-versus-host disease showed a moderate improvement whereas a medium-dose regimen with less number of irradiations showed no effect similar to the results of Tuchinda *et al.* (30). Medium-dose UVA1 therapy in nephrogenic fibrosing dermopathy led to slight improvement similar to another study (32) using high-dose UVA1.

In conclusion, our study showed good therapeutic effects of UVA1 therapy in atopic eczema, scleroderma, lichen sclerosus et atrophicus, keratosis lichenoides chronica, prurigo nodularis and cutaneous T-cell lymphoma. Positive effects in some of our patients were seen in the urticaria pigmentosa, granuloma annulare and the rare sclerosing skin disease group and no effect was seen in the chronic urticaria group.

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