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Different low doses of broad-band UVA in the treatment of morphea and systemic sclerosis
A clinico-pathologic study

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Background: **Numerous treatment modalities, some with potentially hazardous side effects, are currently used for morphea (M) and systemic sclerosis (SS) with limited success. Low-dose ultraviolet A (UVA) phototherapy (20 J/cm^2) was found to be highly effective for sclerotic patches, even in patients with advanced and rapidly evolving lesions.**
Objective: **To determine the effectiveness of different low doses of UVA in treating patients with M and SS.**
Methods: **Sixty-three patients complaining of M and 15 patients complaining of SS received 20 sessions of UVA (320–400 nm) each. Patients were divided randomly into three groups that received 5, 10 and 20 J/cm^2, with cumulative UVA doses of 100, 200, and 400 J/cm^2, respectively. The efficacy of therapy was judged clinically (by sequential inspection and palpation) and histopathologically by morphometry in M cases.**
Results: **Obvious clinical improvement, with no comparable differences between various low UVA doses, was noted in patients with M and SS, accompanied by histopathological changes towards normalization of collagen.**
Conclusions: **After 20 sessions, it appears that lower doses of UVA (5, 10 J/cm^2) are as beneficial as the relatively higher dose (20 J/cm^2) in the treatment of M and SS.**

Key words: **low-dose UVA-histopathology; Morphea; morphometry; systemic sclerosis.**

Scleroderma is a connective tissue disorder characterized by thickening and sclerosis of the skin. Two types of scleroderma exist, circumscribed morphea (M) and systemic scleroderma (SS) (1).

Patients with M have one or multiple circumscribed, ivory-white, indurated, sometimes confluent plaques (2). Although the disease has a self-limited course, the lesions may lead to disfigurement, or if they extend over joints, result in contractures (3).

The pathogenesis of scleroderma has not been completely delineated. It may result from an increased synthesis of type I and III collagen (4) with decreased collagenase 1 production. Such changes are believed to occur through the inappropriate activation of dermal fibroblasts by cytokines produced by skin-infiltrating helper T-cells (5).

SS has been designated as a collagen vascular disease. The pathophysiology of SS can be understood on the basis of the following concepts: injury of the vessel wall; disturbed immune response; and defective control of connective tissue metabolism (6).

The hallmark of SS is the sclerotic changes in the skin and tissues such as the heart, lungs, submucosa and muscularis of gastrointestinal tract (GIT). Widespread vascular lesions may be a prominent feature of certain cases. The digital arteries may be severely involved and changes of endarteritis may be seen in the lungs, heart, GIT, muscle and kidney. Raynaud's phenomenon is usually, but not invariably the earliest feature of the disease (7).

Numerous modalities including D-penicillamine, penicillin, antimalarial drugs, cyclosporin A, interferon gamma and topical or systemic glucocorticoids have been used in the treatment of M and SS and found to be not very rewarding (8).

Different types of phototherapy have been suggested for sclerosing skin disease such as photopheresis (9, 10), bath psoralen UVA (PUVA) photochemo-

therapy (11), oral PUVA therapy (12) and topical cream PUVA therapy (13). High-dose ultraviolet A (UVA)-1 therapy (130 J/cm^2) was found to be effective and superior to low-dose UVA-1 (20 J/cm^2) in five patients with M (14). However, in another study low-dose UVA-1 therapy was shown to be equally effective in the treatment of M without risks of acute or long-term side effects (15). SS was treated successfully with medium dose (60 J/cm^2) (16) and low-dose (30 J/cm^2) (5) UVA-1 phototherapy.

In 2000, El-Mofty et al., proved that low-dose broad-band UVA phototherapy was a very effective and safe treatment modality for M (17).

The mechanisms by which UVA exerts its effects on scleroderma are unknown. Photoimmunologic studies indicate that the keratinocytes (18), epidermal Langerhans cells (19), mast cells (20) and helper T-cells (21) may be target cells in UVA radiation-induced immunomodulation. It was found that the production of collagenase by UVA is dose dependent and is directly proportional to the amount of UVA up to 60 J/cm^2 (22). However, it was found that a satisfactory response could be achieved with low dose of UVA (20 J/cm^2) early in the treatment (17). The aim of the present study was to define the lowest effective broad-band UVA dose in the treatment of M and SS.

Patients and methods

Patients

In this study, we treated patients complaining of cutaneous sclerosis (67 M and 17 SS) with different low doses of broad-band UVA therapy (320–400 nm), three times a week for 20 sessions. Patients were *randomly* divided into three groups receiving 5, 10 and 20 J/cm^2, respectively, aiming at finding out the least dose of UVA that would bring about a satisfactory degree of improvement for these patients.

Morphea: Of 67 M patients who started UVA therapy, 63 completed the study. Dropouts were not related to therapy. They were 43 females and 20 males with ages ranging between 3 and 66 years. Disease duration varied between 1 month and 10 years.

Nine patients were skin type III, 37 patients were skin type IV and 17 patients were skin type V according to Fitzpatrick's classification (23). Of the 63 patients, 27 presented with circumscribed plaques, 12 presented with linear M and 24 presented with disseminated M.

Clinically, all lesions were indurated as assessed by palpation. This induration was associated with hypo- or hyperpigmentation, sclerotic changes, and in one patient, with flexion deformity of the fingers.

The patients were divided randomly into three groups (Table 1).

1. *Group I:* (16 patients) received 5 J/cm^2/session for 20 sessions.
2. *Group II:* (21 patients) received 10 J/cm^2/session for 20 sessions.
3. *Groups III:* (26 patients) received 20 J/cm^2/session for 20 sessions.

Systemic sclerosis (SS): Seventeen patients complaining of SS were included in this study, two patients dropped out. Of the 15 patients who continued the therapy, 12 were females and three were males. Their ages ranged between 18 and 63 years. Disease duration varied between 1 and 30 years. Four patients were skin type III, seven patients were skin type IV and four patients were skin type V according to Fitzpatrick's classification (23).

The patients were divided into three groups (Table 2).

1. *Group I:* (two patients) received 5 J/cm^2/session for 20 sessions.
2. *Group II:* (eight patients) received 10 J/cm^2/session for 20 sessions.

Table 1. Clinical data of patients in the morphea group

	Group I (5 J/cm^2)	Group II (10 J/cm^2)	Group III (20 J/cm^2)
No. of patients	16	21	26
Sex			
Male	10 (62.5%)	5 (23.8%)	5 (19.2%)
Female	6 (37.5%)	16 (76.2%)	21 (80.8%)
Age (years)	3–47	6–51	6–66
Mean	17.88–13.00	22.14 ± 12.90	20.85 ± 14.75
Disease duration (mon)	2–8	1–120	1–120
Mean	20.68 ± 22.69	25.48 ± 33.12	23.54 ± 24.46
Clinical presentation			
Circumscribed plaques	7	12	8
Linear	3	1	8
Disseminated	6	8	10

Table 2. Clinical data of patients in the systemic sclerosis group

	Group I (5 J/cm^2)	Group II (10 J/cm^2)	Group III (20 J/cm^2)
No. of patients	2	8	5
Sex			
Male	–	2 (257%)	1 (20%)
Female	2 (100%)	6 (75%)	4 (80%)
Age (years)	33–50	29–60	18–63
Mean	41.50 ± 12.02	42.87 ± 11.54	37.60 ± 17.50
Disease duration (mon)	18–120	12–360	18–48
Mean	69.00 ± 72.12	87.00 ± 127.92	30.00 ± 12.00
Clinical presentation			
Generalized	–	3	2
Acrofacial	2	5	3

3. *Group III:* (five patients) received 20 J/cm^2/ session for 20 sessions.

Methods

A complete history was obtained for every patient before starting UVA therapy. Inspection of the skin lesions as regards site, colour (hypo- or hyperpigmented), pattern of lesions (circumscribed, linear or disseminated) and palpation of the lesions for skin thickening, induration, atrophy and sclerosis were performed. Clinical assessment was done before starting UVA therapy, every week and at the end of the study period (20 sessions). The clinical response was assessed subjectively by palpation of the skin lesions for skin softening. It was graded as very good response (marked skin softening, almost normal skin texture), good response (moderate softening), fair response (mild softening) and poor response (no change in skin texture).

Other associated manifestations such as Raynaud's phenomenon, trophic changes, grip strength, flexion deformity, joint mobility, etc. were assessed subjectively by investigstors and patients. Routine laboratory studies as complete blood picture, liver and kidney function tests and ophthalmologic examination were performed at the onset of UVA therapy.

Histopathology

Pre- and post-treatment skin specimens were obtained from some M patients (four from group I, 5 J/cm^2; five from group II, 10 J/cm^2; and seven from group III, 20 J/cm^2) from the same plaque, and stained with H&E for routine histopathologic examination. Specimens were subjected to a morphometric study. A Jena Zeiss morphometric eyepiece (× 15) was used to measure:

1. thickness of the longitudinal collagen bundles;
2. width of spaces between collagen bundles.

Morphometric results of random cases were double-checked using 'CAS-200' image analyser. Results were found to be parallel.

Phototherapy

Total body irradiation with UVA (320–400 nm) was given three times a week for 20 sessions. During therapy patients wore protective goggles and covered the genitals. Patients were divided into three groups.

1. *Group I:* (16 M and two SS) received 5 J/cm^2/ session.
2. *Group II:* (21 M and eight SS) received 10 J/cm^2/ session.
3. *Group III:* (26 M and five SS) received 20 J/cm^2/ session.

Equipment

The source of UVA was a Waldmann Medizin technik UVA cabin 7001 equipped with 40 UVA lamps and PUVA 1000 cabin containing 26 lamps of Waldmann type F 85/100 W- PUVA with a spectrum of 315–400 nm and a maximum at 365 nm.

Data management and statistical analysis

The data were coded and entered on an IBM compatible personal computer using the statistical package SPSS ver. 9.0. The mean and standard deviation were used to summarize the quantitative data. Clinical data of the 63 patients were assessed using a one-way analysis of variance (ANOVA) and Pearson's chi-square test (χ^2) as indicated. In a subgroup of M patients ($n = 16$), morphometric analysis of histopathological differences between groups was assessed using non-parametric tests, namely, the Kruskal–Wallis test and the Wilcoxon signed ranks test. For all tests probability level was considered significant at $P < 0.05$.

Results

Morphea

Clinical study: Results are shown in Tables 3 and 4 for the three different groups (5, 10 and 20 J/cm^2).

(a) Softening started before the sixth session in 12 of 16 patients in group I, in nine of 21 patients in group II and in nine of 26 patients in group III.
(b) Factors including age, sex, disease duration and type of the clinical lesion had no statistically significant correlation with the degree of response in the M group, the *P*-values for these being 0.737, 0.936, 0.662 and 0.636, respectively.
(c) *Clinical observations:* Early indurated lesions, whether hypo- or hyperpigmented, responded very well to UVA phototherapy, while old, fibrotic, atrophic, scarred, sclerotic and/or shiny white lesions remained rather unchanged. The sizes of the indurated plaques were reduced gradually from the periphery to the centre towards the end of the treatment sessions. Erythematous lesions cleared leaving hyperpigmentation that faded gradually. The hypo- and hyperpigmented lesions gradually reverted to match almost the colour of the surrounding normal skin by the end of treatment period. In patients with indurated lesions affecting the limb contour, reduction of skin sclerosis resulted in an increase in the limb circumference. Improvement of joint mobility in the patient with flexion deformity was observed when softening of the skin induration occurred.

Lesions on the trunk responded in the same degree and at the same time as lesions on the extremities, except in two patients where abdominal lesions regressed earlier than limb lesions. Areas with little or no UVA exposure because of anatomic reasons showed minimal change (e.g., axilla, submammary areas, etc. especially in obese patients). Hair did not regrow in patients with *en coup de sabre*, although the skin lesion itself showed fair improvement. In only one patient showing band-like M around the wrist who received 20 J/cm^2/session, the lesions were aggravated, erythema increased and pain exacerbated.

The only side effect observed, apart from generalized tanning, was temporary pruritus, which occurred in three patients (one from each dose group) and disappeared after application of topical emollients.

Comparison of the clinical results between the three M groups: There was no significant difference among the three groups regarding the session at which the clinical response started, or the degree of improvement at the end of treatment period (Tables 3 and 4). Comparison of the number of sessions needed to show the start of response among groups I, II, III, revealed no statistically significant difference (Table 3). The same results were obtained as regards the degree of improvement, which showed no statistically significant difference among the three groups (Table 4).

Results of the histopathological study: Before starting UVA phototherapy, histopathological examination of the skin biopsies revealed apparently normal epidermis and papillary dermis. Collagen bundles in the reticular dermis appeared thickened, hypocellular and closely packed with fine, slit-like spaces between them. Most of the subcutaneous fat was replaced by newly formed collagen, which appeared thick, pale, hypocellular and hyalinized. Eccrine glands, normally

Table 3. Comparison of the effect of UVA dosage on number of sessions needed to start the response in morphea patients

			ANOVA	
Group	No. of patients	Mean no. of sessions to start response ± SD	*F*	*P*-value
Group I (5 J/cm^2)	16	6.37 ± 3.87	0.798	0.455
Group II (10 J/cm^2)	21	8.38 ± 6.25		
Group III (20 J/cm^2)	26	7.61 ± 3.84		

Table 4. Comparison of the effect of various UVA doses on the degree of response in morphea patients

Group	Very good response	Good response	Fair response	Poor response	Chi-square (χ^2)	*P*-value
Group I					2.389	0.881
($n = 16$)	3	3	8	2		
%	18.8	18.8	50.0	12.5		
Group II						
($n = 21$)	4	6	8	3		
%	19.0	28.6	38.1	14.3		
Group III						
($n = 26$)	8	7	9	2		
%	30.8	26.9	34.6	7.7		

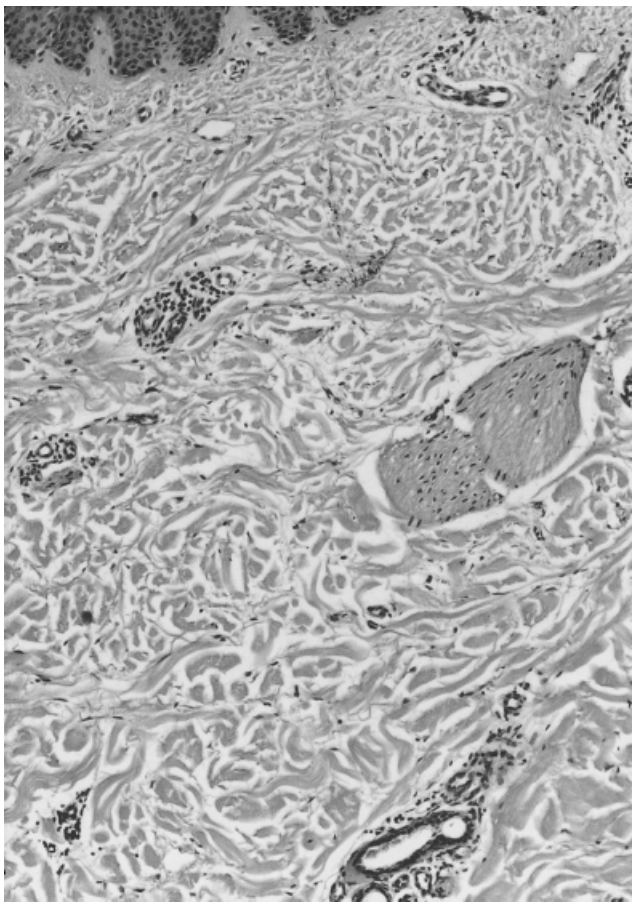

Fig. 1. Pretreatment biopsy of a morphea patient receiving 10 J/cm^2/session, showing thickened collagen bundles with slit-like spaces inbetween (H&E, ×200).

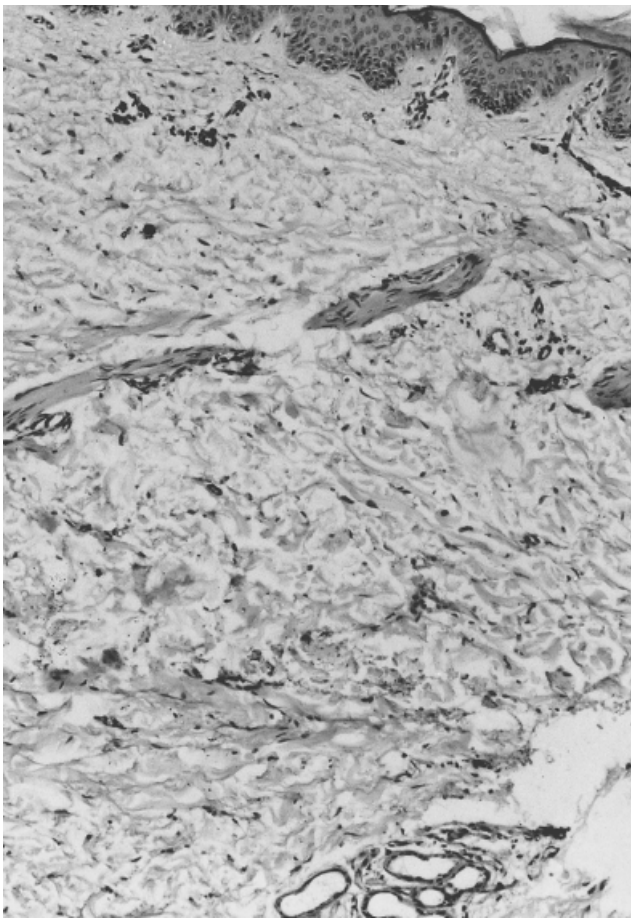

Fig. 2. Post-treatment biopsy of the same morphea patient showing a dramatic response with short, loose collagen bundles and widening of the spaces inbetween (H&E, ×200).

marking the dermal–subcutaneous junction, appeared atrophic and surrounded by collagen instead of subcutaneous fat. A mild–to-moderate lymphocytic infiltrate was noted within the papillary dermis, mainly surrounding vascular spaces. Few scattered lymphocytes were occasionally noted between the thickened collagen bundles of the reticular dermis (Fig. 1). Following phototherapy, the collagen bundles appeared thinner, individually arranged and loose with widening of the spaces between them. Some eccrine glands appeared surrounded by subcutaneous fat (Fig. 2).

These differences were more obvious in the subgroups of M treated with 20 and 10 J/cm^2/session, than in the subgroup receiving 5 J/cm^2/session. In the latter group, the thickness of collagen bundles showed no difference after treatment; however, they appeared shorter and loose with increased spacing than before treatment.

The mean results of the morphometric study of pre- and post-treatment biopsy specimens of some of the M patients are presented in Table 5.

Using the Kruksal–Wallis test there were no significant differences between the three groups at the start of the study as regards the thickness of collagen bundles ($P = 0.594$) and width of spaces in-between them ($P = 0.678$). Post-treatment assessment did not show any significant difference among the three groups as regards the thickness of collagen bundles ($P = 0.279$) and width of spaces in-between them ($P = 0.369$).

Systemic sclerosis (SS)

1. *First group (5 J/cm^2, two patients):* The first sign of improvement appearing as softening of the sclerotic lesions was seen before the ninth session in both patients. The degree of softening was fair in both patients.
2. *Second group (10 J/cm^2, eight patients):* The start of softening ranged between the ninth and 28th sessions. The degree of softening was good

Table 5. Measurements in microns (μm) of the morphometric study of pre- and-post-treatment biopsy specimens of some morphea patients from the three dose groups

Group I (5 J/cm^2) pre-ttt, $n = 4$		Group I (5 J/cm^2) post-ttt, $n = 4$		Group II (10 J/cm^2) pre-ttt, $n = 5$		Group II (10 J/cm^2) post-ttt, $n = 5$		Group III (20 J/cm^2) pre-ttt, $n = 7$		Group III (20 J/cm^2) post-ttt, $n = 7$	
Collagen thick (μm)	W. of spaces (μm)	Collagen thick (μm)	W. of spaces (μm)	Collagen thick (μm)	W. of spaces (μm)	Collagen thick (μm)	W. of spaces (μm)	Collagen thick (μm)	W. of spaces (μm)	Collagen thick (μm)	W. of spaces (μm)
24	9.12	17.5	35	28	18	15.6	10	24.8	14.25	20.85	19.33
25	13.16	23.6	15.28	23.6	18.5	18.75	28.8	23.6	20.6	32	24.16
32	22.5	27.5	19	22	15.8	23	47.5	21.75	17.6	28.16	44.6
38.5	25	27.27	21.9	37.12	16	27.2	22.4	32.5	20	27.33	16.66
				23.5	22	18.7	33.75	21	17.2	22.33	14.83
								35.6	20.3	22.75	20.2
								35.2	22.75	30.8	27.2
Mean 29.87	17.44	23.96	22.79	26.84	18.06	20.65	28.49	27.77	18.95	26.31	23.85
SD 6.76	7.53	4.66	8.57	6.16	2.50	4.50	13.85	6.41	2.80	4.38	10.07

Pre-ttt vs. post-ttt (5 J/cm^2), $n = 4$		Pre-ttt vs. post-ttt (10 J/cm^2), $n = 5$		Pre-ttt vs. post-ttt (20 J/cm^2), $n = 7$	
Collagen thick.	W. of spaces	Collagen thick.	W. of spaces	Collagen thick.	W. of spaces
P-value 0.068	1.00	0.080	0.500	0.735	0.176

Ttt = treatment, collagen thick. = collagen thickness, w. of spaces = width of spaces in-between collagen bundles, SD = standard deviation.

in three patients, fair in four patients and poor in one patient.

3. *Third group (20 J/cm^2, five patients):* The start of softening ranged between the sixth and 23rd sessions. The degree of softening was good in two patients, and fair in three of them.

Clinical observations

(a) Factors including age, sex, disease duration and type of the clinical lesion had no statistically significant relationship to the degree of response in the SS group, the P-values for these being 0.231, 0,071, 0.758 and 0.082, respectively.

(b) Raynaud's phenomenon, which was reported in five patients, improved in three. This improvement appeared in the form of diminution in frequency of attacks, cold sensation, cyanosis and pain felt in the digits and healing of associated ulcers. However, recurrences during winter were not prevented.

(c) Joint mobility and function improved and in few patients returned to almost normal levels. Increased circumference of some affected limbs was observed after softening of the indurated lesions, whereas non-lesional skin remained unaffected.

(d) It was noted that in some cases of SS, which continued UVA sessions until 30 sessions or more (after the study period and before writing this paper), a better degree of response was achieved.

Comparison of the clinical results between the three SS groups: Studying the difference in number of sessions needed to start response (Table 6) and the degree of response (Table 7) among the three subgroups of SS revealed no statistically significant difference, $P = 0.501$ and 0.678, respectively.

Comparison between the M and the SS groups: Start of response was significantly delayed in patients with generalized SS in relation to M patients ($P = 0.001$), where the mean number of sessions to start the response was 16.4 sessions in SS patients and 7.6 sessions for M. However, there was no significant difference in the degree of response between M and SS groups ($P = 0.804$).

Discussion

Different types of phototherapy have been suggested for sclerosing skin disease, such as photopheresis (9, 10), bath PUVA photochemotherapy (11) and oral PUVA therapy (12). The most recent advance in phototherapy for scleroderma is UVA-1 radiation.

Table 6. Comparison of the effect of UVA dosage on number of sessions needed to start the response in systemic sclerosis patients

Group	No. of patients	Mean no. of sessions to start response ± SD	ANOVA	
			F	*P*-value
Group I (5 J/cm^2)	2	9.50 ± 0.70	0.734	0.501
Group II (10 J/cm^2)	8	14.62 ± 6.50		
Group III (20 J/cm^2)	5	12.80 ± 4.02		

Table 7. Comparison of the effect of various UVA doses on the degree of response in systemic sclerosis patients

Group	Good response	Fair response	Poor response	Chi square (χ^2)	*P*-value
Group I				2.317	0.678
($n = 2$)	0	2	0		
%	–	100	–		
Group II					
($n = 8$)	1	4	3		
%	12.5	50.0	37.5		
Group III					
($n = 2$)	0	3	2		
%	–	60	40		

UVA-1 irradiation alone without prior photosensitization of the skin by psoralen can induce clearance of sclerotic lesions and bears the advantages of being more comfortable than PUVA; avoiding the possible gastric upsets, less possibility of carcinogenic effect, in addition to its safety for children (15). Low-dose broad-band UVA also was found to be a very effective and safe line of treatment for localized M (17).

UVA could induce synthesis of collagenase via production of singlet oxygen (24) or through the release of signalling peptides as interleukin-1, interleukin-6 (25) or through production of hydrogen peroxide (26), TNF- and alpha-melanocyte-stimulating hormone-MSH) (which could explain the normalization of the hypopigmented lesions of M associated with skin softening) (27). UVA-1 also depletes skin-infiltrating T-cells through the induction of apoptosis (28).

Stege et al. (1997) (14) found that the high-dose UVA-1 therapy (130 J/cm^2/session) was superior to the low-dose UVA-1 therapy (20 J/cm^2/session) in the treatment of patients with localized scleroderma. Several other studies proved that using UVA-1 in a dose of 20 J/cm^2 four times a week for 6 weeks, then once a week for another 6 weeks was able to produce an excellent response in the treatment of localized scleroderma (5, 15, 29, 30). However, in previous studies limited numbers of patients have been examined. Recently, daily treatment with medium-dose UVA-1 (60 J/cm^2) resulted in marked softening of the skin after nine to 29 exposures in four patients with SS. Besides clinical improvement there was an increase in joint mobility and skin temperature (16). In another study, low-dose UVA-1 (30 J/cm^2) was given four times a week for 8 weeks, then three times a week for another 6 weeks to eight SS patients with resultant softening of acrosclerotic skin, reduction of stiffness, enhanced mobility and even clearance of peripheral piecemeal necrosis (5). It seems that increasing the session numbers to 30 sessions gives better treatment results, as observed in some of our patients and in other studies that used even 40 sessions in their treatment protocol (31).

Using broad-band UVA in a dose of 20 J/cm^2 for 20 sessions in the treatment of M, EL-Mofty et al. (2000) reported excellent clinical response with changes observable by routine histopathology and by computerized image analysis (17).

As most other dermatology centres have no access to UVA-1 therapy due to its high cost (13), we performed the present study on a large number of patients using different low doses of broad-band UVA radiation (5, 10 and 20 J/cm^2/session) for 20 sessions.

The main aim of this study was to know if smaller doses of UVA (5 and 10 J/cm^2) would be as beneficial as the relatively higher dose of 20 J/cm^2 in the management of localized and systemic scleroderma. Three dose groups of patients were therefore randomly formed receiving 5, 10 and 20 J/cm^2. The clinical and histopathological results showed that there was no statistical difference in the start of response and the degree of improvement between the three dose regimens in both M and SS.

On comparing the session number at which the first sign of improvement was seen, no statistically significant difference was found between the three dose regimens utilized. The same applies for the degree of softening of lesions. These two observations

hint that the least dose (5 J/cm^2) will bring about the same degrees of improvement as higher doses (10 and 20 J/cm^2).

Comparable results were observed by histopathologic examination of post-treatment biopsy specimens. After treatment, the structure of dermal collagen appeared individually arranged and thinned, and collagen bundles were separated by wider spaces. However, such changes were less observable in the group receiving 5 J/cm^2/session.

It was observed in the present study that a satisfactory response was obtained with early indurated lesions whether hyper- or hypopigmented, whereas late, fibrotic, sclerotic, shiny white plaques showed fair to poor response. This means that UVA did not reverse scarring or atrophy, and treatment should be started as early as possible to minimize residual deformity. Although softening of the indurated plaques may occur spontaneously within months, yet, UVA could induce it in a few weeks; thus preventing further progress of the disease and minimizing its complications as joint contracture and muscle atrophy.

In the present study, a total of 20 sessions was needed to reach a satisfactory therapeutic response with a maximum dose of 20 J/cm^2/session. Therefore, cumulative doses of 100, 200 or 400 J/cm^2 were utilized in the three patient groups without significant difference in the degree of response clinically. This is in comparison with previous studies where larger cumulative doses of 600 (15) or 3900 J/cm^2 (5) were utilized. Studying the difference in number of sessions needed for the start of response and degree of response among the three dose groups of SS revealed no significant statistical difference. However, on comparing the three M groups with the three groups of SS, a highly significant statistical difference was found in favour of M groups, where a smaller number of sessions was needed to start showing a response to UVA therapy.

Results of the present study show that a satisfactory clinical response could be achieved almost equally with various low doses of UVA (5, 10 and 20 J/cm^2/session) in patients with M and SS. To our knowledge, this is the first study aiming at the evaluation and comparison of such low doses of UVA in the treatment of a large number of patients with M and SS. Patients with M showed earlier and better therapeutic response than SS patients; indurated lesions with shorter disease duration responded better than the old fibrotic lesions. It is therefore suggested as an effective line of therapy in early lesions of M, and as an adjuvant therapy in SS.

It is concluded that UVA therapy in low doses is an effective and safe line of treatment in M and SS. The systemic effects of different doses of UVA therapy in scleroderma and their mechanism of action on the molecular level are presented in further studies.

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