PUVA Treatment in Sclerodermatoid Spectrum of Dermatologic Diseases: Our Initial Experience

Sharon Baum MD, Felix Pavlotsky MD, Dorit Shpiro MD and Henry Trau MD

Phototherapy Unit, Department of Dermatology, Sheba Medical Center, Tel Hashomer, Israel
Affiliated to Sackler Faculty of Medicine, Tel Aviv University, Ramat Aviv, Israel

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Sclerodermatoid disorders represent a spectrum of diseases that include different types of scleroderma: systemic sclerosis, localized and generalized morphea, as well as sclerodermic graft versus host disease. These chronic disorders affect the microvasculature and loose connective tissues in many organs including the skin. Scleroderma may occur in skin (designated morphea) as both localized and generalized form and as systemic disease. The latter is often progressive and fatal.

Numerous therapeutic options have been reported for this disease spectrum, but until now no therapy has proven effective. Recent studies suggest that various forms of ultraviolet A therapy [1,2] may be highly effective in the management of sclerodermatoid disorders with the most current advance being UVA1 (360–400 nm) irradiation [3–5]. We present our initial experience with psoralen plus ultraviolet A (320–400 with a peak of approximately 360 nm) therapy in sclerodermatoid disorders.

UVA = ultraviolet A

Patient Descriptions

Five patients were included in the present report; their profiles are summarized in Table 1. The age range of the four males and one female was 13–66 years. One patient had generalized morphea, two were diagnosed with systemic sclerosis and two with sclerodermic GVHD. The duration of the disease ranged from 6 months to 8 years. Previous therapy with conventional treatment modalities did not result in

GVHD = graft vs. host disease

Table 1. Patients' data in the study

Patient no.	Gender	Age (yrs)	Disease duration	Treatment duration	Total dose (J/cm^2)	Response (%)
1	Female	56	SS 8 years	19 mos	483	100%
2	Male	66	SS 2 yrs	1.5 mos	20	>70%
3	Male	27	Gen. morphea 6 mos	10 mos	288	>70% and hair regrowth
4	Male	13	GVHD 1 yr	2 mos	12	>70%
5	Male	34	GVHD 6 mos	3 mos	44	>70%

SS = systemic sclerosis

significant improvement in any of the patients.

Our treatment regimen included 0.5 mg/kg of 8-methoxypsoralen 1.5 hour prior to exposure to irradiation from a UVA cabinet (Waldmann UV 1,000 K). The treatment was given three times weekly. The initial UVA irradiation dose was 0.5 J/cm^2 and was increased by 0.5 J/cm^2 at every second treatment in all cases. Dose adjustments were performed as previously described [2]. After complete improvement was achieved it was continued once a week as maintenance therapy. In our practice we do not usually perform pretreatment (minimal erythemal dose) measurements and reserve them for photosensitive individuals only.

Therapeutic effectiveness was assessed by patients' self-evaluation. The skin lesions were examined before, during and after phototherapy by palpation for tethering and thickening of the skin and joint mobility. Complete blood count, liver function tests, antinuclear factor levels and ophthalmologic evaluation were performed before treatment, and every 3 months during and following the treatment.

Comment

The treatment resulted in a remarkable softening of the sclerotic lesions in all patients as early as 6 weeks of treatment, which is consistent with previous reports. The treatment was well tolerated and showed remarkable healing of skin lesions. No adverse side effects were observed.

Recent reports demonstrated that UVA1 has beneficial effects for both localized and systemic scleroderma [3,4]. However, the long-term side effects of UVA1 have not yet been fully studied. Moreover, by using psoralen with UVA (PUVA), the cumulative ultraviolet dose can be reduced. Thus, von Kobyletzki et al. [3] reported a total UVA1 dose of 1,500 J/cm^2 compared to 480 J/cm^2 maximally used in our study.

Cost-effectiveness is another consideration. UVA1 equipment is much more expensive and the treatment time per session much longer than with the old UVA machine. Since the response rate was greater than 70% as early as 6 weeks from the start of treatment, this treatment is clearly more cost-effective.

The mechanism of action of PUVA (or UVA1) in sclerodermatoid disorders remains unclear at present. However, three different disease processes can act as potential targets [5]: a) vascular alterations with endothelial cell damage, b) autoimmune activity – perhaps related to the decrease of CD34+ cells in the dermis during disease activity, and c) disturbances in the control of connective tissue synthesis.

The interaction between T cells and dermal fibroblasts might play a pivotal role in the pathogenesis of scleroderma. UVA is known to cause apoptosis of skin-infiltrating T cells and has been effective in T cell-mediated skin diseases such as psoriasis, atopic dermatitis and cutaneous T cell lymphoma [5]. UVA1 not only depletes skin-infiltrating T cells through the induction of apoptosis, but also up-regulates the expression of collagenase-1 in dermal fibroblasts. PUVA treatment may decrease the amount of collagen by directly inhibiting its synthesis and/or stimulating collagenase activity. The ultraviolet-induced production and release of cytokines, such as tumor necrosis factor or interleukin 6, may also be responsible for decreased collagen synthesis.

In conclusion, phototherapy seems to be a valuable contribution to the poor therapeutic armamentarium for sclerodermatoid disorders. Whatever the mechanism, our observation suggests PUVA therapy may be an effective treatment for patients with sclerodermatoid disorders who are undergoing skin changes. Further studies with a larger number of patients seem justified and desirable.

References

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Correspondence: Dr. S. Baum, Dept. of Dermatology, Sheba Medical Center, Tel Hashomer 52621, Israel.
Phone: (972-3) 530-2419
Fax: (972-3) 530-2443
email: baumdr@zahav.net.il