

TREATMENT OF RESISTANT PSORIASIS WITH ORAL 8-METHOXYPsorALEN AND LONGWAVE ULTRAVIOLET LIGHT (PUVA)

A Treatment Schedule and a Follow-up Study

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Abstract. Thirty-one patients with resistant psoriasis were treated with 8-methoxypsoralen orally, followed by irradiation with long-wave ultraviolet light (PUVA). The initial irradiance was 1.4 Joule/cm², increased by 0.5 Joule/cm² at the following exposures, to a maximum of 4.2 Joule/cm². The 8-methoxypsoralen dosage was approximately 0.5 mg/kg body weight. In 17 patients psoriasis cleared completely after 10.8±3.4 exposures (mean ±S.D.). In 12 patients the healing was almost complete after 14.5±5.8 exposures. Adverse effects were negligible. After clearing, the patients were followed without further therapy. Psoriasis recurred in approximately half of those patients followed for more than 2 months, on average 5 weeks after cessation of treatment. PUVA is an effective and agreeable therapy for recalcitrant psoriasis. Further studies must be carried out to evaluate the risks of a long-term treatment.

Key words: Psoralen; Psoriasis; PUVA; UVA light

Psoralen therapy followed by exposure to long-wave ultraviolet light (UVA) has been shown to inhibit epidermal DNA synthesis (8). Recently, this photochemical procedure has been introduced into the treatment of psoriasis (5), a disorder characterized by an increased epidermal cell turnover.

The present investigation was undertaken in order to study the effect of a dose schedule with 8-methoxypsoralen (8-MOP) and UVA light in the treatment of recalcitrant psoriasis and to estimate the duration of remission after clearing.

MATERIAL AND METHODS

The material comprises 31 patients, 11 women and 20 men, with widespread psoriasis proven to be resistant to

conventional local antipsoriatic treatment. The patients were treated between January and October 1975.

Each patient received 8-MOP administered as 10 mg tablets (Meladinine®; The Memphis Chemical Co., Cairo, Egypt) 2 hours prior to UVA irradiation. The dosage was approximately 0.5 mg/kg body weight. The treatment was given three times weekly. The initial exposure time was 5 min (1.4 Joule/cm²) to both sides of the body, increased by 2 min (0.5 Joule/cm²) at subsequent exposures to a maximum of 15 min (4.2 Joule/cm²) to each side (Fig. 1).

The light source consisted of thirty-six 40 W and twelve 20 W black light tube lamps with a spectral range of 320-400 nm (Philips TL/08). The tubes were arranged in a horizontally suspended folded screen which was lowered during irradiation (Fig. 2). The light energy incident at the body surface was 4.5 mW/cm² (measured by Blak-Ray® J-221 longwave ultraviolet intensity meter). The total cost of the light equipment, which is commercially available, was approximately US \$2 000.

Controls

Before, during and after the treatment, at least every second week, the patients were photographed and blood tests were made to determine hemoglobin concentration, counts of white blood cells and thrombocytes, serum creatinine, and serum alanine aminotransferase (se-ALAT). The urine was analysed for protein and glucose.

Evaluation of clinical results

The effect of PUVA was evaluated from the photographs and the clinical observations. After complete clearing, or psoriasis remaining static for 2 weeks, the result was classified as follows: (1) complete clearing and normalisation of the skin, (2) almost complete clearing except for a few residual spots, (3) incomplete clearing with thickened lesions, and 4) unchanged.

RESULTS

Psoriasis cleared completely in 17 patients after 10.8±3.4 exposures to UVA light (mean ±S.D.). In

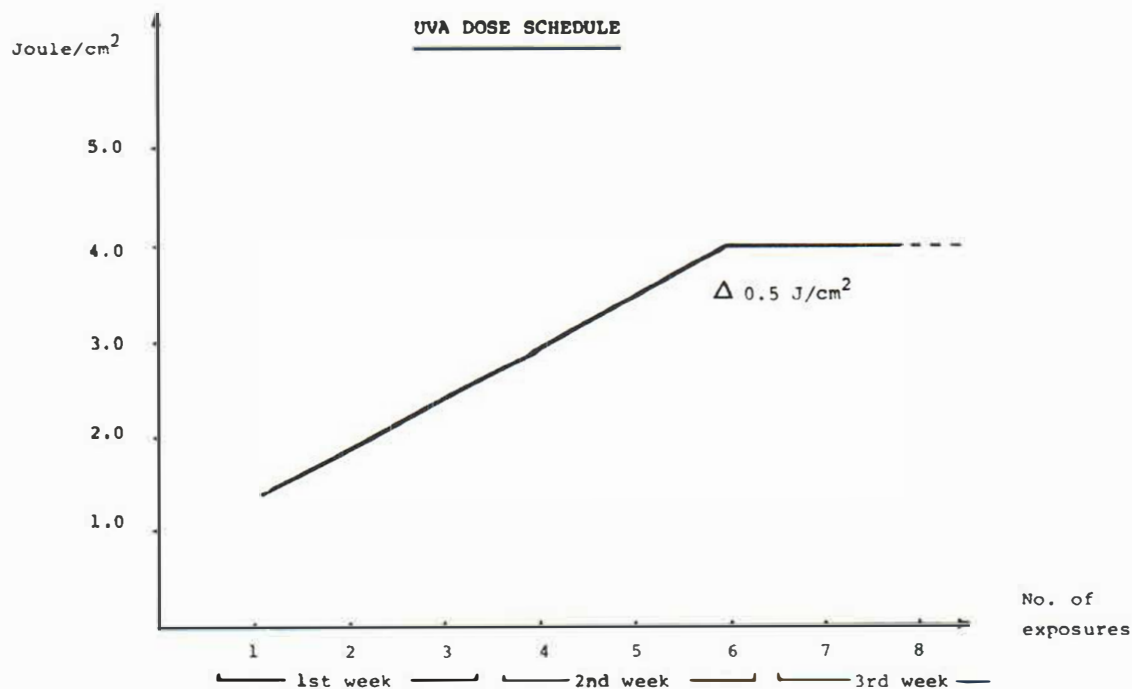


Fig. 1. The UVA dose schedule for PUVA therapy of psoriasis.



Fig. 2. UVA light source consisting of thirty-six 40 W and twelve 20 W black light tube lamps (Philips TL/08).

12 patients the clearing was almost complete after 14.5 ± 5.8 exposures (Table I). One patient improved a little and one failed to respond to the PUVA therapy. In no case was psoriasis aggravated. Five patients with psoriatic arthropathy all noticed a relief of their joint pains during therapy. This might be due to the temperature being 30–40°C below the screen.

In 2 out of 7 patients with nail psoriasis a temporary normalisation of the nail plate was noticed.

Psoriasis of the scalp was cleared only in bald or very thin-haired patients.

Recurrences

After clearing, no treatment was given during the follow-up period which ranged from one to 8 months. Psoriasis recurred, mostly of a mild degree, in half of the patients followed for more than 2 months (Table II). On average, the remission was 5 weeks (range 3 to 12 weeks).

Side-effects

After three to five exposures to UVA light, all the patients, except the one who did not respond to the

Table I. Results of photochemotherapy of psoriasis in 31 patients

Clinical response	No. of patients	No. of exposures to UVA light	Duration of treatment (days)
Complete clearing	17	10.8±3.4 ^a	23.5±7.8
Almost complete clearing	12	14.5±5.8 ^b	31.9±13.2
Incomplete clearing	1	19	44
Unchanged	1	28	64

^a Mean ±S.D.^b n.s. (0.05<*p*<0.10, Mann-Whitney's test).

therapy, developed a diffuse erythema accompanied by a slight pruritus. In 8 patients the erythema became rather pronounced, though without discomfort so severe as to require discontinuation of the therapy. In one patient a few dispersed bullae were observed.

Nausea occurred in 4 patients about 2 hours after ingestion of 8-MOP. A transient elevation of γ -ALAT was observed in 4 patients during therapy. In 3, the values were normalised promptly when alcohol was abandoned.

A diffuse hyperpigmentation, including the cleared psoriatic skin areas, developed in all patients, who regarded this as an extra gain.

DISCUSSION

In a preliminary clinical study on PUVA, Parrish et al. (5) reported clearing of psoriasis in 21 patients treated with PUVA after 12 to 20 exposures. In the extensive study of Wolff et al. (9) comprising a group of 37 patients receiving total body PUVA treatment, the number of exposures required for clearing of psoriasis was 12±6 (mean ±S.D.). The duration of treatment was 25±13 days. The light source was specially developed tube lamps emitting about 50% more UVA light energy than that used by us. The initial UVA dose ranged from 1.3 to 7.6 Joule/cm² according to the patient's MPD (minimal phototoxicity dose) which was determined prior to therapy. During the PUVA treatment the patients generally received a higher UVA dose than was the case in our study. However, their results were simi-

lar to those found in the present investigation. We used a fixed treatment schedule for all patients, raising the UVA dose slowly from 1.4 up to 4.2 Joule/cm². This procedure was simple, safe and effective, causing a minimum of adverse effects. Twelve patients did not heal entirely, despite prolongation of the therapy. In a controlled study where only one side of the patient was irradiated, Swanbeck et al. (7) found a lower percentage (about 60%) of healing on the treated side. Their less favourable results may be due to a lower UVA-dose.

About 50% of our patients stayed in remission up to 8 months after the treatment. In the study of Wolff et al. (9), after clearing, 85% of the patients who received maintenance therapy with PUVA were kept in remission for up to 400 days. This implies that several patients with latent psoriasis receive a highly active therapy which might cause late side-effects. These might include degenerative changes of the skin, cytogenetic alterations (7), or, as demonstrated in mice treated with excessive doses of psoralen plus UVA light, development of skin cancer (3), cataract and keratitis (2, 3).

More than 25 years of common use of 8-MOP in the treatment of vitiligo has proved the drug to be safe and non-toxic. A hepatotoxic effect reported in 1958 (1) could not be substantiated in subsequent investigations (4). However, as psoralens are metabolised in the liver (6) we did not give 8-MOP to patients with liver diseases, and the patients were told to abandon alcohol as long as PUVA treatment was given.

Our PUVA treatment schedule is an effective and agreeable therapy for psoriasis. However, further studies are needed to elucidate the question of long-term therapy and late side-effects of the treatment. Photochemotherapy with PUVA should probably be restricted to patients with severe, resistant psoriasis and a continuous maintenance therapy should not be given routinely.

Table II. Days of follow-up and recurrences of psoriasis in 28 patients after the last exposure to black light

Follow-up days	No. of patients	No. of recurrences
0-59	9	2
60-119	13	6
120-240	6	3
Total	28	11

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