

ORAL TRIMETHYLPsorALEN IN THE TREATMENT OF VITILIGO

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Abstract. One hundred adult patients and 18 children with various clinical types of vitiligo, were treated with oral trimethylpsoralen (Trisoralen®, P. B. Elder Co.) followed by exposure to sunlight or an artificial ultraviolet radiation source. In 61 of the adult patients, more than 80% of the vitiliginous areas became repigmented, 18 patients repigmented 50-80%, 13 repigmented less than 50% and 8 patients failed to repigment at all. In all of the children, more than 80% of the treated vitiliginous patches became repigmented. No side effects were observed. A follow-up study of the retention of the new pigment revealed that 72 adults (out of 76 followed-up) and 10 children (out of 11) without any treatment had retained 95% or more of the new pigment, 18 months after the completion of treatment. Oral trimethylpsoralen is therefore suggested for the treatment of vitiligo.

Key words: Vitiligo; Psoralens; Pigmentation; Melanocytes

It has been known for thousands of years that certain plant extracts, locally applied or orally administered, can cause a repigmentation of vitiliginous skin if followed by ultraviolet radiation exposure.

Pure psoralens have been isolated from these preparations. Scientific investigation of the compounds was first reported by Fahmy & Abu-Shady in 1947 (4). The most potent psoralens with photosensitizing properties were found to be, psoralen, 4-methylpsoralen, 5,8-dimethylpsoralen, 5-methoxypsoralen and 8-methoxypsoralen.

Oral or topical 8-methoxypsoralen has proved to be effective in the management of vitiligo (5, 6, 7). It has been the most commonly used psoralen derivative until the recent development of a new, potent, synthetic psoralen, 4',5',8'-trimethylpsoralen.

Clinical studies carried out in other countries by numerous investigators have given promising therapeutic results of the drug in the treatment of vitiligo (1, 2, 3, 8, 9, 10).

The purpose of the present investigation was to determine the efficacy of trimethylpsoralen and the permanency of regained pigment on a large series of patients.

MATERIALS AND METHODS

Trimethylpsoralen was studied in 118 patients with different types of vitiligo, selected for the trial from the Dermatological Clinic of "A. Syngros" Hospital. There were 100 adults ranging in age from 17 to 65 and 18 children

Table 1. *Clinical material and the percentages of the body surface covered by vitiliginous lesions*

Patients	Percentage of body surface covered by lesions			
	<10%	10-25%	25-50%	>50%
Adults				
♂	16	16	15	3
♀	13	17	11	9
Children				
♂	8	-	-	-
♀	10	-	-	-

Table II. *Evaluation of therapeutic results obtained with the use of oral trimethylpsoralen in the treatment of vitiligo*

Patients	UV-light source	Degree of healing			
		Nil	<50%	50-80%	>80%
Adults	Natural sunlight	6	7	5	52
	UV-lamp	2	6	13	9
Children	Natural sunlight	-	-	-	18
	UV-lamp	-	-	-	-

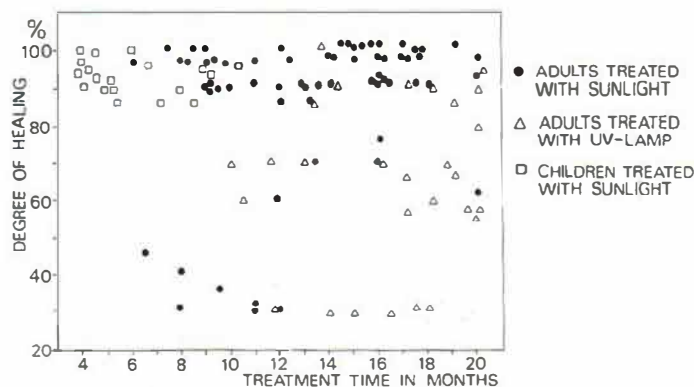


Fig. 1. The degree of healing at the end of the treatment period. Note the good results for the children group after relatively short treatment periods.

ranging in age from 4 to 12. Fifty of the adults and 10 of the children were females.

The diagnosis was based on the clinical examination alone. The patients were classified in four groups according to the percentage of their body surface covered by vitiliginous lesions (Table I).

Every patient was subjected to a battery of investigations: blood count, urine analysis, blood sugar, liver function tests and estimation of blood cholesterol, prior to the commencement of the trial and every fortnight thereafter.

Two 5 mg tablets of trimethylpsoralen were taken daily by each patient, followed by exposure to sunlight or artificial ultraviolet radiation source (●Original Hannau Hohen-sonne, HI-FI 550) 2–3 hours later, for 5 minutes. This period was gradually increased in the subsequent days to a maximum of 45 minutes for the sunlight exposure and 60 minutes for the exposure to UV light irradiation at 120 cm exposure distance. Seventy adults and all the children were using sunlight as the ultraviolet radiation source.

Clinically, the response to the treatment was evaluated by the appearance of pigmentation in the areas of vitiligo. Four grades were used for judging the repigmentation: <50%, 50–80%, and >80% of the vitiliginous lesions, and no response, as nil.

RESULTS

The results are summarized in Table II and Fig. 1.

With natural sunlight as the light source, 52 adult patients repigmented more than 80% of their vitiliginous areas treated, 5 patients repigmented 50–80%, 7 patients repigmented less than 50%, and 6 patients failed to repigment at all. With the UV-lamp as the light source, 9 adult patients repigmented >80% of their vitiliginous areas treated, 13 patients repigmented 50–80%, 6 patients repigmented <50% and 2 patients failed to repigment whatsoever. All children became almost completely cured (more than 80%). The mean duration of the treatment was 14 months for the adults and 6 months for the children.

The first signs of repigmentation were observed 6–8 weeks after the onset of the trial. Repigmentation started around the hair follicles or at the borders of the vitiliginous lesions (Fig. 2).

No side effects due to the administration of the

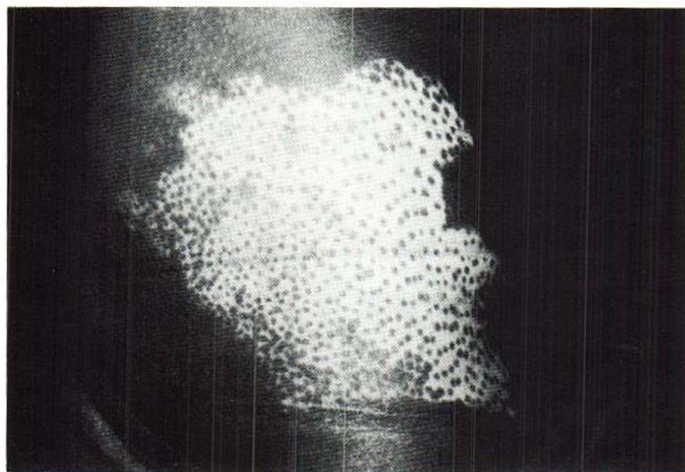


Fig. 2. Perifollicular pigmentation 6 weeks after the beginning of treatment.

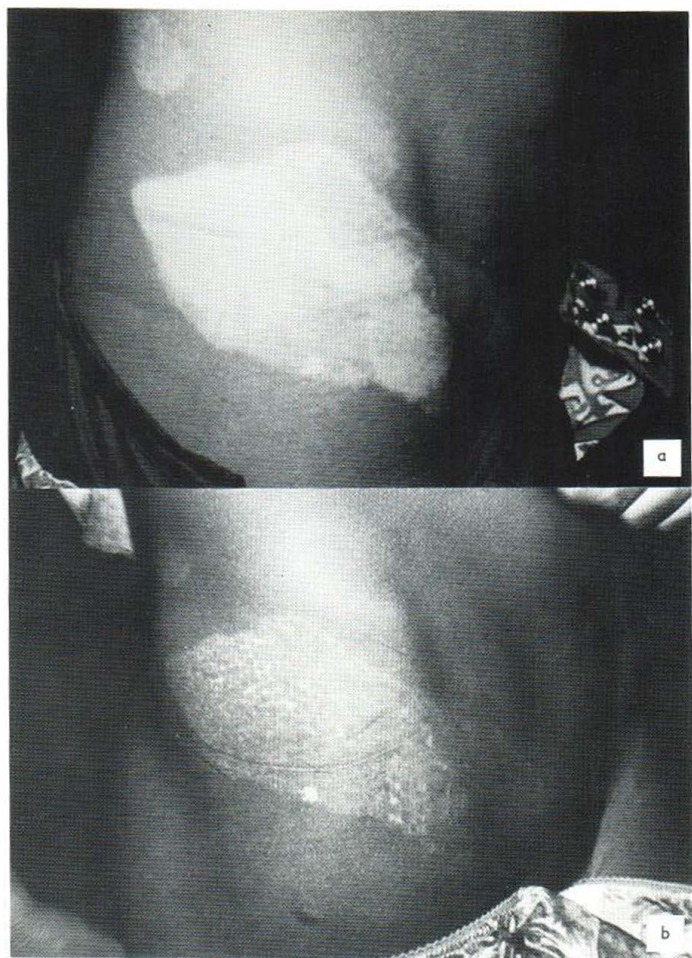


Fig. 3. (a) Before treatment; (b) 3 months after the beginning of treatment.

drug were observed. The laboratory investigations to which the patients were subjected revealed no abnormality.

A follow-up study of the retention of the new pigment revealed that 72 adults (out of 76 followed up) and 10 children (out of 11) without any treatment, had retained 95% or more of the new pigment 18 months after the completion of treatment (Figs. 3, 4).

DISCUSSION

It is still unknown how trimethylpsoralen works in vitiligo. Some papers have suggested the direct activation of melanocytes, which increase in size, number and enzymatic activity (5, 10). According to some investigators, repigmentation occurs by the division and migration of melanocytes from the hair follicles and the borders of vitiliginous lesions (5).

The results of our study, which was carried out on the largest number of patients ever reported to be used for a clinical trial of trimethylpsoralen, revealed that the drug is of especial therapeutic value in children and adults who have suffered from the disease for short periods only, a view that has been expressed in earlier papers (11, 12).

Natural sunlight seems to provide better therapeutic results than does the UV-lamp, and it is therefore recommended for the treatment of vitiligo with oral trimethylpsoralen.

The lack of toxicity of the drug, as demonstrated in our study, provides further proof of the safety of its use, especially in children.

The results of the follow-up study of the retention of the new pigment in 87 patients, confirm that repigmentation due to trimethylpsoralen may be regarded as permanent.



Fig. 4. (a) Before treatment; (b) 8 months after the beginning of treatment, and 18 months after the completion of treatment.

In conclusion, the results of this investigation demonstrate the safety and efficacy of oral trimethylpsoralen in the treatment of vitiligo.

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