

PHOTOCHEMOTHERAPY FOR VITILIGO: SEVEN YEARS' EXPERIENCE AT A UNIVERSITY HOSPITAL

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Photochemotherapy has been the most successful treatment of vitiligo to date. In this study we tried to evaluate the efficacy, safety and patient acceptability of photochemotherapy (PUVA, or psoralen and ultraviolet A, therapy) for vitiligo patients treated in King Khalid University Hospital over the period of 1987-1994. The treatment success strongly depended on the number of treatments. More than 75% repigmentation was achieved in 42% of the patients who received 100 to more than 200 treatments. Unfortunately, however, only 27% of the patients received this number of treatments. Reasons for the failure of our patients to continue treatment to successful repigmentation, and recommendations for correction of this failure, are discussed. *Ann Saudi Med* 1997;17(2):175-178.

Photochemotherapy has been the most successful treatment of vitiligo to date.¹⁻⁴ Historically, photochemotherapy of "leukoderma" can be traced back as far as 3000 B.C. in Egypt and India.⁵ Modern photochemotherapy of vitiligo with psoralen and ultraviolet A (PUVA) was introduced in 1948 by El Mofty in Egypt.⁶ Since then, detailed information has become available on the efficacy and the limitations of this treatment.^{3,4,7} This therapy carries certain health risks and is time-consuming for both patients and doctors. We therefore thought it would be interesting to evaluate the efficacy of the treatment at King Khalid University Hospital. To our knowledge, this is the first report of its kind in the Middle East.

Patients and Methods

The study is retrospective and includes 142 patients with vitiligo. Patients with focal vitiligo or with the lip-tip variant were excluded from the study. Eighty-three females and 59 males were treated with PUVA in the Department of Dermatology, King Khalid University Hospital, Riyadh, over the period between 1987 and 1994. Every vitiligo patient treated with PUVA in our clinic has a PUVA chart (incorporating structured entry questionnaires and continuation sheets) in which all relevant data about his treatment, e.g., previous treatment, history of skin cancer, history of photosensitive disorders, concurrent medication, advice on contraception/fertility, psoralen dosage, UVA dosage, exposure time, degree of

improvement, side effects, laboratory work results, etc., are recorded. Data from 47 patient records were not complete and could not be used in the final analyses of the study. The charts of 95 patients (46 female and 49 male, age range 10-70 years; mean age 26) were examined for clinical data including age, sex, duration of disease, family history, previous treatment, adjuvant treatment with topical corticosteroids, localization of vitiligo (face, trunk, arms, legs, hands, feet), stability of the disease, number of treatments before start of repigmentation, total number of treatments, cumulative UVA dose, clinical side effects and laboratory abnormalities. They were also checked for the quality of data recordings. The response to treatment was

TABLE 1. Demographic and clinical data of 95 patients.

Female	46
Male	49
Age (mean)	10-70 yrs (26)
Duration of vitiligo (mean)	0.5-30 yrs (7.2)
Positive family history	48.4%
Skin phototypes*	
I	None
II	1.7%
III	16.7%
IV	50.0%
V	30.0%
VI	1.7%
Stability of the disease [†]	
Stable	57.3%
Progressive	42.7%
Localization	
Generalized	50.5%
Disseminated	48.4%
Segmental	1.1%

*Data available for 60 patients; types I-IV are determined by history, types V and VI by physical examination; [†]data available for 82 patients.

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graded as follows: poor or nil = 0%-25% repigmentation of amelanotic skin; fair = 25%-75% repigmentation of amelanotic skin; good = >75% repigmentation of amelanotic skin.

The following laboratory investigations are performed routinely at baseline, four weeks, eight weeks and at six-month intervals thereafter for all patients receiving PUVA therapy in our clinic: complete blood count, liver function tests, renal function tests and antinuclear antibodies (when needed). In addition, patients are referred to the ophthalmology clinic to check for lens abnormalities before starting PUVA and at six-month intervals during treatment. UVA irradiations are delivered by conventional PUVA cabins (Waldmann 8001 and 7001) equipped with Sylvania FR 90 T12 fluorescent tubes, which emit broad-spectrum UVA. Patients take psoralen (8-methoxypsoralen or 4,5,8-trimethylpsoralen) in recommended dosages two hours before exposure to UVA light.⁷ Patients receive two to three treatments every week. We start our irradiation schedule with 1/2 joule/cm² to 1 joule/cm², increasing at every third treatment (in absence of minimal erythematous or pigmentary response) by 20%-40% increments of the last dose up to a maximum of 7 joule/cm², which is usually the maintenance dose.

At the time of evaluation, we contacted 52 of the 95 patients. The patients were contacted by telephone and asked if PUVA therapy had been an acceptable and worthwhile treatment. They were also asked about the reasons for noncompliance and/or discontinuation of PUVA treatment, the present state of their disease, and about any long-term side effects.

Results and Discussion

Data from 25 of the 142 patient records lacked essential information, such as the extent of repigmentation and the number of treatments before the start of repigmentation. Another 22 patients were excluded from the final analyses of the study because they missed more than 50% of their scheduled PUVA treatments.

Table 1 shows the demographic and clinical data of the remaining 95 patients. It is noteworthy that the percentage of patients with a positive family history in this study (47.4%) is higher than that reported in the literature (6.25% to 38%).⁸ This is most probably due to a high prevalence of consanguineous marriages in our country.⁹ The finding that half of our vitiligo patients have skin-phototype IV is similar to that reported in the literature.^{2,8} Overall, information relating to administration and dosimetry of PUVA was well documented. However, there was often a failure to document important information such as concurrent medication (not recorded [NR] in 44%), cumulative lifetime UVA dosage (NR in 69%), history of skin cancer (NR in 73%), previous radiotherapy

TABLE 2. *Treatment results.*

Extent of repigmentation*	0-25%	25%-75%	>75%
Number of patients	64 (67%)*	19 (20%)	12 (13%)
Number of treatments to start of repigmentation (mean±SD)	23±9.1	20±7.9	17±9.0
Total number of treatments (mean±SD)	45±29	112±53	207±62
Total irradiation dose (mean±SD; joules/cm ²)	197±169	545±248	1312±597

*Only 31 of the 64 patients showed repigmentation.

TABLE 3. *Extent of repigmentation versus number of treatments.*

Number of treatments	Number of patients with repigmentation			Total
	0-25%	25%-75%	>75%	
<50	51*	1	0	52
50-99	10	6	1	17
100-199	3	11	4	18
>200	0	1	7	8
Total	64	19	12	95

*33 out of the 51 patients showed nil repigmentation.

(NR in 83%), whole-body skin examination at regular intervals during the treatment (NR in 92%), advice on contraception (NR in 95%), and reasons for early discontinuation of PUVA treatment (NR in 85%).

The results of treatment are summarized in Tables 2 and 3. We observed a trend towards an earlier start of repigmentation in the group with good response in comparison with the other groups; however, this difference was not statistically significant (Table 2). As has been described in earlier studies, certain skin areas of vitiligo, in particular acral skin, did not respond adequately despite many months of treatment.^{4,8}

In the group of 64 patients with less than 25% repigmentation, 51 patients had received fewer than 50 treatments. The reasons for the early discontinuation of PUVA therapy were not documented in 85% of the cases. We contacted 52 patients out of the 69 patients who received fewer than 100 PUVA treatments. Table 4 shows the different causes for early discontinuation of PUVA therapy as told by the contacted patients.³ Thirty-four patients did not consider PUVA an acceptable and worthwhile treatment modality of their disease. This was further supported by the fact that 23 of these patients sought treatment by folk (herbal) medicines. On further questioning of the patients, it was found that the majority (87%) were not well informed about the length of PUVA

therapy, the chances of success, or the potential side effects.

TABLE 4. Causes of early discontinuation of PUVA therapy in 52 patients.*

Poor or no response	31 (60%)
Time consuming	24 (46%)
Lack of compliance (discontinued by patient's dermatologist)	20 (38%)
Fear of side effects	15 (29%)
Clinical side effects (nausea, vomiting, headache, fatigue, excessive erythema)	6 (12%)
Other causes (claustrophobia, pregnancy, changing to PUVA-Sol, worsening of the disease)	5 (10%)

*Some patients had more than one cause.

TABLE 5. Clinical side effects of PUVA therapy in 95 patients.

Pruritus	37%
Dryness	28%
Erythema (>grade II)	22%
Nausea	20%
Headache	8%
Fatigue	6%
Other (dizziness, mottling of the skin, PUVA lentiginos, abdominal pain, vomiting, blisters, onycholysis, leukemia, leukoderma punctata, melanonychia striata and thickening and desquamation of vitiliginous skin)	Each less than 5%

An evaluation of our patients indicates that an average of 100 treatments is required to reach an overall repigmentation of 75%. Only 12 (13%) of 95 patients had a good response with repigmentation in more than 75% of the original vitiligo areas. This is much less than the results achieved in other centers. However, if one considers only the group of 26 patients who received 100 to more than 200 treatments (Table 3), the success rate (that is, more than 75% repigmentation) was at 42%. Controlled studies have yielded comparable success rates ranging from 25% to 40%.¹⁻³

As in previous studies,^{1,3,7} we found no correlation between improvement and extent of involvement at initiation of therapy, duration of vitiligo, skin phototype, age or sex of the patient. It also appears that the extent of repigmentation was not influenced by disease stability, use of adjuvant topical corticosteroids, or a positive family history of vitiligo.

Results of all laboratory tests were normal. Only eight of the 26 patients who received more than 99 treatments had eye examinations performed at regular six-month intervals. Early scattered posterior subcapsular lens

opacities were seen in two patients. Although it is difficult to interpret this finding in the absence of accurate data on the cumulative lifetime UVA dosage, a recent study has shown that patients who don't use eye protection develop acute but not chronic ocular injury.¹⁰ None of our patients had acute ocular injury (conjunctival hyperemia and/or decreased lacrimation). Other clinical side effects were seen in 48 (50.5%) of the patients (Table 5). They led to discontinuation of PUVA treatment in six patients (Table 4). These findings are not different from those reported in the literature.^{3,4,7} Long-term side effects (e.g., premature aging of the skin, premalignant and malignant skin lesions) were not observed in the relatively short period of the study.

The single most important factor in determining the response of vitiligo to PUVA therapy is the total number of treatments. Recent studies showed similar findings.^{5,11,12} For PUVA to be successful in the treatment of vitiligo, the following requirements must be fulfilled: 1) patients must be well informed about the different aspects of PUVA treatment, particularly length of therapy, side effects, and chances for success. 2) Only reliable and highly motivated patients should be treated with PUVA. 3) Close supervision by the treating physician is indispensable; this entails accurate and detailed documentation of all aspects of treatment. For this purpose, we strongly recommend the application of established guidelines for PUVA treatment of vitiligo,¹³ including the incorporation in casenotes of structured record forms and continuation sheets.

Assessment of current therapeutic practice forms an essential part of the audit process. We strongly support the practical proposition of Bilslund et al.¹⁴ for a formal multicenter audit based on published guidelines. This and similar studies could form the basis for keeping guidelines up to date.

References

1. Parrish JA, Fitzpatrick TB, Shea C, et al. Photochemotherapy of vitiligo. *Arch Dermatol* 1976;112:1531-4.
2. Lassus A, Halme K, Eskelinen A, et al. Treatment of vitiligo with oral methoxsalen and UVA. *Photodermatology* 1984;1:170-3.
3. Pathak MA, Mosher DB, Fitzpatrick TB, et al. Safety and therapeutic effectiveness of 8-methoxypsoralen, 4,5,8-trimethylpsoralen, and psoralen in vitiligo. *Natl Cancer Inst Monogr* 1984;66:165-73.
4. Honigsmann H, Fitzpatrick TB, Pathak MA, et al. Oral photochemotherapy with psoralens and UVA (PUVA): Principles and Practice. In: Fitzpatrick TB, Eisen AZ, Wolff K, et al., (eds). *Dermatology in General Medicine*. 4th edition. New York: McGraw-Hill, Inc., 1993:1728-54.
5. Ortel B, Tanew A, Honigsmann H. Treatment of vitiligo with Khellin and ultraviolet A. *J Am Acad Dermatol* 1988;18:693-701.
6. El-Mofty AM. A preliminary clinical report on the treatment of leukoderma with Ammi majus Linn. *J R Egypt Med Assoc* 1948;31:651-65.
7. Ortel B. Vitiligo treatment. In: Honigsmann H, Stingl G, editors. *Therapeutic Photomedicine, Current Problems in Dermatology*. Vol 15. Basel: Karger, 1986:265-79.

8. Ortonne JP. Disorders with circumscribed hypomelanosis: Vitiligo. In: Ortonne JP, Mosher DB, Fitzpatrick TB (eds). Vitiligo and other hypomelanosis of hair and skin. New York: Plenum Publishing Corporation, 1983:129-309.
9. Al-Mazrou Y, Farid S, Khan M. Changing marriage age and consanguineous marriage in Saudi females. *Ann Saudi Med* 1995;15:481-5.
10. Calzavara-Pinton PG, Carlino A, Manfredi E, et al. Ocular side effects of PUVA-treated patients refusing eye sun protection. *Acta Derm Venereol (Stockh)* 1994;Suppl 186:164-5.
11. Wildfang IL, Jacobsen FK, Thestrup-Pedersen K. PUVA treatment of vitiligo: a retrospective study of 59 patients. *Acta Derm Venereol (Stockh)* 1992;72:305-6.
12. Al-Aboosi MM, Ajam ZA. Oral photochemotherapy in vitiligo: follow-up, patient compliance. *Int J Dermatol* 1995;34:206-8.
13. AAD Committee on Guidelines of Care and Task Force on Phototherapy and Photochemotherapy. Guidelines of care for phototherapy and photochemotherapy. *J Am Acad Dermatol* 1994;31:643-8.
14. Bilsland DJ, Rhodes LE, Zakil L, et al. PUVA and methotrexate therapy of psoriasis: how closely do dermatology departments follow treatment guidelines? *Br J Dermatol* 1994;131:220-5.