# PHOTOCHEMOTHERAPY FOR PSORIASIS WITH PSORALEN AND SUNLIGHT

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## Summary

A double blind study with systemic psoralen and sunlight exposure therapy in psoriasis is reported. Evaluation was done on the basis of clinical features, patient's subjective improvement, severity of scores and histopathology. 66.7% of patients on systemic psoralen and sunlight responded with complete clearance of lesions in 21 to 56 days and 33.3% of patients showed moderate improvement. This study shows that systemic psoralen and direct sunlight exposure is a safe and effective line of treatment for psoriasis. We feel, this method of treatment can be recommended as a routine in psoriatic patients in our country.

Fischel in 1894 introduced crude coaltar as a treatment for psoriasis and since then it has been widely used for this disease. Goeckerman in 1925[1] introduced tar and ultra violet radiation as a therapy for psoriasis with satisfactory results. Coaltar contains photosensitisers like anthracene, acridine, carbazole and phenanthrene and the beneficial effects are suggested to be due to some photochemical reaction.

In India ayurvedic physicians have been using unsaponified oil obtained from the plant Psoralea corylifolia as a topical treatment of psoriasis. Daniels in 1963[2] and Becker in 1967[3] demonstrated identical photosensitising effects in tars and psoralens. Willis and Harris in 1973[4] demonstrated the effect of topical psoralens in resistant cases of psoriasis. Parrish et al[5], Wolff et al[6] and Hajini et al[7] observed that systemic administration of psoralens with ultraviolet radiation gives significantly good results in cases of psoriasis.

Seghal et al in 1975[8] and 1978[9] reported satisfactory results in two series of 18 and 11 psoriatic patients who were treated with psoralens and direct sunlight exposure. There are however no controlled trials supporting the usefulness of psoralens in psoriasis except one repoted by Seghal et al in 1978[9].

Most of the above workers used derivatives of psoralen, whereas Hajini et al used psoralen, the parent substance which was found the most economical. They used artificial U.V. radiation from conventional U.V. radiation lamps. Majority of the above studies have been conducted in fair

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skinned population and data on effect of photochemotherapy in people of dark complexion are lacking.

In addition, while working in the Dermatology Dept. of Medical College Hospital, Alleppey, we came across a patient with vitiligo, who also had extensive lesion of psoriasis. To this patient we administered systemic psoralen combined with direct sunlight exposure, as treatment for vitiligo. To our surprise, we observed considerable improvemnt of psoriatic lesions and this improvement of psoriatic lesions started prior to the onset of repigmentation in lesions of vitiligo. All the psoriatic lesions cleared within a period of 4 to 6 weeks but it took nearly $1\frac{1}{2}$ years for clearance of vitiligo lesions. We also observed that during the above period of $1\frac{1}{2}$ years, patient did not get any relapse of psoriasis, which she used to get earlier at an interval of every 6 or 8 months. This personal observation of ours and the analysis of data published by other workers in the field gave us an impetus to try this harmless drug in a larger group of psoriatic patients and hence we undertook this controlled study.

**Material and Methods**

A total of 40 psoriatic patients belonging to varying age groups attending the Dermatology Department of Medical College Hospital, Alleppey, were selected for this study. The diagnosis of psoriasis was made on clinical grounds, and confirmed by histopathological examination. Other routine investigations like total and differential leucocyte count, R.B.C. count, routine examination of urine etc. were carried out from time to time as required for the study. Liver function tests (L.F.T.) including estimation of S.G.O.T. and S.G.P.T. were also done before and after treatment. Pregnant women, patients with abnormal L.F.T. and children below the age of 10 years were not included in the study.

The selected 40 patients were divided into 2 groups, each consisting of 20 patients. None of the patients was given any topical or systemic drug 2 weeks prior to admission to the study. In each patient, the severity of the disease was assessed and recorded on a 3 point scale based on the number of countable skin lesions.

(1) Mild.:.upto 5 skin lesions.
(2) Moderate...upto 25 skin lesions.
(3) Severe...More than 25 skin lesions.

***Group I*** (20 patients) was treated with 'Tablet X' (which was later confirmed as Manaderm brand of psoralen) followed $2\frac{1}{2}$ to 3 hours later by direct sunlight for a period of 25 to 30 minutes. Each patient received 4 tablets of 10 mg. each.

***Group II*** (20 patients) was treated in an identical manner with 4 'Tablet B' (which were later confirmed to be placebo tablets but identical to tablet X in appearance).

The regimen was continued for a period of 4 weeks in both groups. The weekly follow up and assessment of progress of treatment was carried out by a panel consisting of three dermatologists of the Department of Dermatology, Medical College Hospital, Alleppey. The persons who made the weekly assessment were totally ignorant of the nature of the tablets taken by the patients.

Response to therapy was judged as per the criterias laid down by Fitzpatric and Pathak and shown in table No. 1.

Those patients who did not show 20% to 50% improvement, when compared to original status of the disease at the end of 4 weeks' treatment were removed from the trial, irrespective of the group to which they belonged. Similarly those patients who developed

intercurrent infections, or female patients who became pregnant during the course of treatment were also dropped from the study. In all the other patients the treatment was continued for a period of 56 days (8 weeks). After 8 weeks the treatment was discontinued.

The number of days required for complete clearance of all the lesions (grade IV) were recorded. Patients in whom complete clearance did not occur within 8 weeks or those in whom the treatment was discontinued, percentage of improvement when compared to the original status of the disease was recorded as shown in table No. 1. The results were analysed in both groups for the purpose of evaluating the efficacy of psoralen.

years and in the control group it ranged from 19 to 70 years. In group I, 15 were male patients and 5 were females, whereas in group II, 14 were males and 6 were females. In the trial group (group 1) 2 patients (one female patient who became pregnant one week after starting therapy and one male patient who, 5 weeks after starting therapy, developed herpes zoster) were removed from the study. All the remaining 18 patients were given 'Tablet X' for a period of 56 days or till the clearance of all the lesions, whichever was earlier.

In group II (control group) one patient discontinued therapy after 2 weeks as he developed an intercurrent infection. In another we were forced

TABLE 1

Showing Response to Therapy (Criteria Applied by Fitzpatric and Pathak)

| Response to Therapy | | |
|---|---|---|
| Grade | Criteria | % improvement (compared to original status of the disease) |
| —1 | Psoriasis worse | 0 |
| 0 | No change | 0 |
| 1 | Minimal improvement (slightly less scaling and or erythema) | 5—20 |
| 2 | Definite improvement (partial flattening of plaques, less scaling and less erythema) | 20—50 |
| 3 | Marked improvement (complete flattening of all plaques, but borders of plaques still palpable) | 50—95 |
| 4 | Complete clearing (complete flattening of plaques including borders. Plaques may be outlined by pigmentation) | > 95 |

**Observation and Results**

A total of 40 psoriatic patients, 20 each in group I (trial group) and group II (control group) were included in the present study. The response to treatment in group I, and group II are given in Table No. II and III respectively.

In the trial group, the age of the patients ranged from 11 years to 57 to discontinue therapy after 21 days, as the disease got progressively worse as a result of which patient was not willing to continue with the same line of treatment. The age-wise and sex-wise distribution of patients in each group is shown in Table No. IV. The extent of involvement with the disease and improvement obtained after therapy in the 2 groups is shown in table No. V and VI.

TABLE 2 — Group 1

Showing Response to Treatment

| Sl. No. | No of patients | Extent of involvement | No. of days of treatment | Grade of improvement | % of improvement (compared to original state of disease) |
|---|---|---|---|---|---|
| 1 | 1 | Moderate | 56 | 4 | 100 |
| 2 | 3 | Severe | 56 | 4 | > 95 |
| 3 | 1 | Mild | 42 | 4 | 100 |
| 4 | 1 | Severe | 42 | 4 | 100 |
| 5 | 4 | Severe | 35 | 4 | 100 |
| 6 | 1 | Moderate | 28 | 4 | 100 |
| 7 | 1 | Mild | 21 | 4 | 100 |
| 8 | 2 | Moderate | 56 | III | 85 |
| 9 | 1 | Moderate | 56 | III | 65 |
| 10 | 1 | Severe | 56 | III | 60 |
| 11 | 1 | Severe | 35 | III | 60 |
| 12* | 1 | Severe | 35 | III | 40 |
| 13 | 1 | Moderate | 56 | II | 40 |
| 14* | 1 | Moderate | 7 | 0 | 0 |

* Discontinued therapy.

All the patients belonging to the trial group who continued therapy showed uniform tanning after 2 to 3 weeks, which gradually increased till all the lesions cleared. Residual hyperpigmentation was observed in 13 patients after clearance of the lesions. In general lesions on the body responded better than those on the scalp. In all patients in whom nail changes were present, they persisted even after clearance of others. In group I excellent response (Grade IV response) with complete clearance of all the lesions, was observed in 12 patients (66.7%) and moderately good response (Grade III response) in 6 patients (33.3%). The remaining 2 patients discontinued therapy. The average time required for complete clearance of all the lesions in 12 patients was 41.4 days and the time required for moderate clearance of the lesions in 6 patients was 40 days. No significant difference was observed in the time required for clearance of lesions in 14

TABLE 3

Showing Response to Treatment in Group 2

| Sl. No. | No. of patients | Extent of involvement | No. of days of treatment | Grade of improvement | % of improvement (compared to original state of disease) |
|---|---|---|---|---|---|
| 1 | 1 | Moderate | 28 | 1 | 0 |
| 2 | 1 | Severe | 28 | 1 | 0 |
| 3 | 1 | Mild | 28 | 1 | 0 |
| 4 | 1 | Moderate | 21 | 1 | 0 |
| 5 | 5 | Moderate | 28 | 0 | 0 |
| 6 | 4 | Severe | 28 | 0 | 0 |
| 7* | 2 | Moderate | 14 | 0 | 0 |
| 8 | 3 | Mild | 28 | 1 | 10 |
| 9 | 1 | Moderate | 28 | 1 | 5 |
| 10 | 1 | Severe | 28 | 1 | 5 |

* 2 patients discontinued therapy.

TABLE 4

Showing Age-wise and Sex-wise Distribution of Patients in Group 1 & 2

| Age group in years | | No. of patients | |
|---|---|---|---|
| | | Group 1 | Group 2 |
| 11 to 20 | | 1 | 2 |
| 21 to 30 | | 5 | 4 |
| 31 to 40 | | 5 | 4 |
| 41 to 50 | | 6 | 6 |
| 51 to 60 | | 3 | 3 |
| 61 to 70 | | – | 1 |
| Sex | Male | 15 | 14 |
| | Female | 5 | 6 |
| Total | | 20 | 20 |

TABLE 5

Showing Extent of Involvement in Group 1 & Group 2

| Extent of involvement | No. of patients | |
|---|---|---|
| | Group 1 | Group 2 |
| Mild | 2 | 4 |
| Moderate | 8 | 10 |
| Severe | 10 | 6 |
| Total | 20 | 20 |

TABLE 6

Showing Improvement After Treatment in Group 1 (Trial Group) and Group 2 (Control Group)

| No. of patients Group 1 | Group 2 | Grade of improvement | %of improvement compared to original state |
|---|---|---|---|
| — | 1 | –1 | 0 |
| — | 3 | 1 | 0 |
| 1 | 11 | 0 | 0 |
| — | 5 | 1 | 5 to 10 |
| 9 | — | IV | 100 |
| 3 | — | IV | >95 |
| 2 | — | III | 85 |
| 1 | — | III | 65 |
| 2 | — | III | 60 |
| 2 | — | III | 40 |

males as compared to that required in 4 females, who completed the therapy. Similary no relation was noted between the response to therapy and age of the patient or response to therapy and duration of the disease. (Fig I shows lesions before treatment and Fig. 2 shows the response after administration of 'Tablet X' for 56 days).

In control group (Group II), no significant improvement of the lesions was observed in any patient. Hence in all the patients treatment was discontinued after 4 weeks. 4 patients (including one who discontinued) showed worsening of the psoriatic lesions, whereas in 11 patients (including one who discontinued) lesions remained status quo. 5 patients showed 5 to 10% improvement at the end of 4 weeks' therapy.

In trial group, 2 patients developed gastric discomfort in the later stages of treatment and 5 patients complained of mild nausea during the course of treatment. No other side effect was observed in any patient of group I or II. The gastric irritation and nausea were controlled by symptomatic treatment with antacid gel and none of the patients was dropped out of the trial because of the above complaints. At the end of 56 days majority of the patients in group I showed pigmentation at the site of cleared lesions. This disappeared within 2 to 3 weeks of discontinuation of therapy.

There were no pre or post treatment changes in haematological or biochemical findings. Patients who showed good clinical response, revealed complete regression even on histopathological examination as shown by reformation of keratinised stratum corneum with evidence of hyperkeratosis. Complete regeneration of stratum granulosum was observed in all cases that showed grade IV clinical response, whereas partial regeneration was observed in those who showed grade III response. The cellular infiltrate in the dermis was seen to be reduced

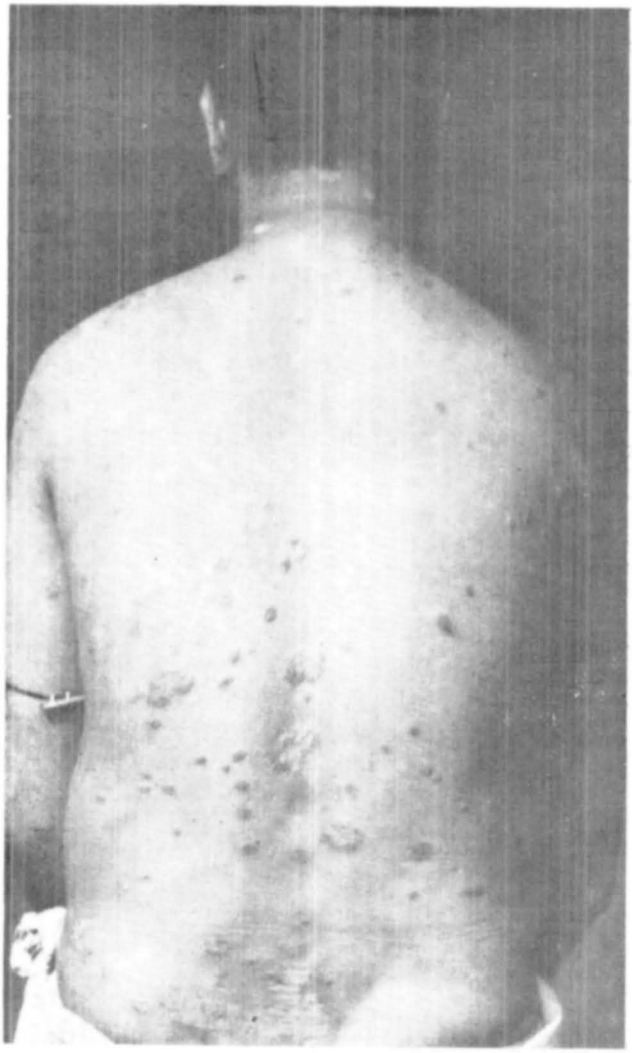

**Fig. 1** Psoriatic lesions, before treatment with tablet X.

both in those with grade III and grade IV improvement.

**Comments**

In the past psoriasis therapy had remained largely as a topical one with the disadvantages of being cumbersome and cosmetically unacceptable to patients. In later years systemic therapy with corticosteroids, methotrexate and other cytotoxic agents provided the alternative to topical therapy. These however are generally reserved for complicated cases of psoriasis which do not respond to conventional topical agents. More recently methoxsalen combined with long wave ultra violet light (puva) was used successfully by Parrish et al in 1974[7] in the treatment of psoriasis.

In India, Seghal et al in 1975[8] reported satisfactory results with trimethyl-psoralen combined with sunlight in 11 psoriatic patients. In 1978[9] they further demonstrated the usefulness of trioxasalen combined with sunlight, in a controlled study of 18 psoriatic patients. Gadgil in 1978[10] reported excellent response in 7 out of 11 psoriatic patients treated with methoxsalen combined with artificial UVA exposures. In the same year Hajini et al[7] observed complete clearance of all psoriatic lesions within 16, 40, and 45 days in 22%, 96% and 100% of a total of 70 psoriatic patients, treated with psoralen combined with artificial uv radiation.

The results of therapy are summed up in tables No. II, III and VI. It is evident that psoralen combined with sunlight is definitely effective in patients with psoriasis. In the trial group complete clearance of all the lesions was observed in 12 patients and the average time taken for complete clearance was 41.4 days. Hajini et al[7] reported an average duration of 25

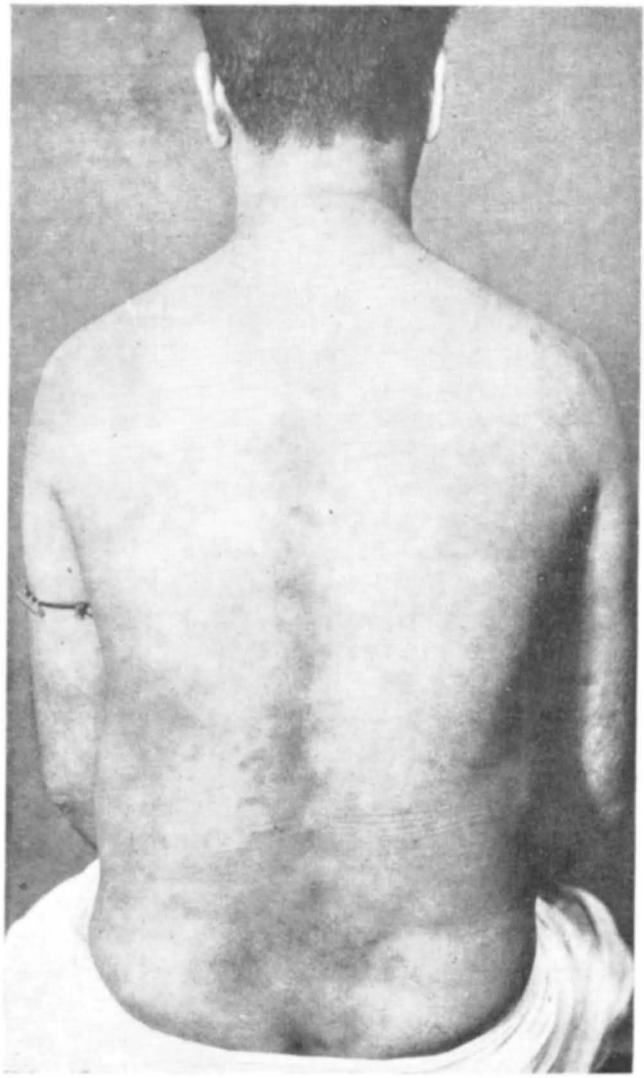

**Fig. 2** Disappearance of psoriatic lesions, after treatment with tablet X.

days ± 9.4 SD for complete clearance of lesions. They had used artificial uv light instead of sunlight. The results obtained in the present series are more or less comparable to those of Seghal et al[8,9]. According to them the time taken for complete clearance of psoriatic lesions is directly proportional to the number of irradiations. Our observations on histological regressions in proportion to the clinical improvement are comparable to those reported by Seghal et al[8,9] who also reported regeneration of stratum granulosum and reduction in the cellular inflammatory infiltrate in the dermis, in psoriatic patients treated with trimethyl psoralen combined with light exposures.

The innocuous nature of psoralen is more or less established since this drug has been used in the treatment of vitiligo for more than a decade without any serious toxic effects. Orally administered psoralens are rapidly metabolised in the liver and 90% of the drug is excreted within 8 to 12 hours. This rapid metabolisation avoids systemic toxicity.

To conclude, our study reveals that photochemotherapy with psoralen and direct sunlight is an effective, clean, quick and safe treatment for psoriatic patients in India, as an out patient regimen. It does not show the cosmetic disadvantages of the conventional coaltar treatment, or the adverse side effects of the antimetabolites.

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