PHOTOCHEMOTHERAPY OF PSORIASIS WITH ORAL 8-METHOXYPSORALEN (8-MOP) AND SOLAR IRRADIATION (PUVASOL THERAPY)*

LESLIE MARQUIS † AND G. M. RANGWALA ‡

Summary

48 patients having psoriasis were studied with puvasol therapy. Pretreatment haemogram, platelet count, liver and renal functions were done. To begin with 40 mgm of 8 MOP were given at 10–30 a.m. and at 12-30 p.m. sunlight exposure for period varying from 5-30 minutes. After 8 to 12 weeks tri bi and weekly maintenance therapy was given. The sunlight exposure calculated by the photometer was 8-12 Joules/cm$_2$ per day. The grading of response was undertaken on the basis of three different aspects. (1) Subsidence of lesions, Grades were given as excellent with 100 % subsidence, good with 90—100%, fair with 50—90% and poor with less than 50% subsidence. (2) Statistical point score as per Wallace's classification and depending on type and morphology of lesions and (3) Response related to duration of therapy.

Of 38 patients with psoriasis vulgaris, 21 (82%) showed excellent to good response. All six cases of psoriasis erythroderma (100%) showed excellent to good response. Of the three cases of pustular psoriasis, 1 showed 90-100% and 2, 50—90% subsidence. 1 case of flexural psoriasis showed 50—90% subsidence.

Puvasol therapy proved to be effective, non-toxic and inexpensive in psoriasis. In the erythrodermic and pustular phase for the first time the results were encouraging.

The ideal treatment for psoriasis still remains elusive. An ideal treatment for psoriasis should be (1) oral not topical (2) ambulatory—not involving loss of working hours (3) inexpensive (4) non-toxic if given for a long time. (5) It should not interfere with patient's sense of well being or social activities. and (6) the therapeutic response should compare with other well established regimes. (7) It should cure 100% cases with no relapses. Photochemotherapy to some extent satisfies the above criteria.

Mochella[1] reviewing the systemic chemotherapy of psoriasis (table 1) found that drugs like methotrexate, cyclophosphamide, hydroxyurea, azaribine, mycophenolic acid and steroids though valuable in psoriasis, did not prevent frequent relapses. Further their severe toxicity out-weighed their utility. Compared to these drugs, 8 methoxypsoralen is a relatively safe drug, though the potential toxicity namely cutaneous

* Paper presented at VIIth Annual Conference of I.A.D.V. & L. at Srinagar in May 1979.

† Prof. Dermatology & Venereology,
T. National Medical College
Hon. & Head : Department of Dermatology & Venereology
B. Y. L. Nair Charitable Hospital, Bombay

‡ Post Graduate.

Received for publication on 21—8—1979.

SYSTEMIC CHEMOTHERAPY OF PSORIASIS (MOCHELLA)

DRUG	DOSE	RESULT	RELAPSE	RESISTANCE	TOXICITY
1. METHOTREXATE (M.T.X.)	2·5 -5 mg. DAILY 0·02–0·5 mg/Kg. WEEKLY, BIWEEKLY	80%	FREQUENT	10 %	HEPATIC, HAEMATOLOGIC. CITRACT, POTENTIAL CARCINOGENICITY.
2. CYCLOPHOSPHAMIDE	50-200 mg/DAILY	50%	—	20%	IMMUNOSUPPRESIVE, BRONCHOPULMONARY INFECTION
3. HYDROXYUREA	500 mg B.D.	65%	70%	FREQUENT	"FLU" SYNDROME, VASCULITIS
4. AZARIBINE	125 –200 mg/DAILY Kg	80%	20 %	—	MUSCULOSKELETAL, CNS THROMBOEMBOLIC PHENOMENON.
5. MYCOPHENOLIC ACID (M.P.A.)	1600 - 4800 mg.	97%	3-8 WEEKS. ON STOPPING DRUG	10%	NAUSEA, DIARRHOEA, ANOREXIA, URINARY TRACT BURNING, URGENCY & FREQUENCY.
6. STEROIDS SYSTEMICALLY & TOPICALLY	20 – 60 mg.	100%	RELAPSE & REBOUND	—	WELL KNOWN COMPLI-CATIONS PROHIBITS USE IN ROUTINE PSORIASIS
7. PSORALEN (8 MOP)	40 mg 2 HOURS BEFORE IRRADIATION	GOOD TO EXCELLENT	—	—	RELATIVELY SAFE DRUG POTENTIAL TOXICITY (MELANOMA RISK)

carcinoma and melanoma risk should be kept in mind.

Historical Review

In 1890 Finsen introduced the artificial U. V. Lamp. Goeckermann[2,3] in 1925 demonstrated the utility of coaltar + U. V. R. in psoriasis. In 1928 Oppenheim[4] tried tryptoflavin and U. V. R. and Tulifan[5] in 1941 used oral sulpha + U. V. R. in psoriasis. In 1953 Ingram[6] popularised conventional coaltar and diathranol + U. V. R. In 1962 Allyn[7] tried topical psoralen + U. V. R. and Oodoze[8] in 1967 used oral psoralen + U. V. R. In 1974 Walters et al[9] studied topical 8MOP + black light and in 1974 Fitzpatrick et al[10] convincingly demonstrated the value of 8MOP + Puvasol in psoriasis. EL Mofty [11] in 1976-77 also used 8MOP + Puvasol in psoriasis. On the Indian side, workers like Sehgal[12,13,14], Hajini[15] Bhutani[16], Bedi[17] and Dutta[18] have contributed further in assessing the utiliy of 8MOP + U. V. R. in psoriasis.

Material and Methods

At the department of Dermatology, Nair Hospital, Bombay, cases of psoriasis were randomly selected for 8MOP + Puvasol therapy. 48 cases of psoriasis was studied. Their mean age was 30–40 years. 38 cases had psoriasis vulgaris, 6 cases psoriatic erythroderma, 3 cases palmo-plantar pustular psoriasis and one case flexural psoriasis. 11 cases were new cases diagnosed for the first time and others were suffering from the disease for 6 months to 30 years. Investigations like Haemogram, platelet count, SGOT, SGPT, blood urea, serum creatinine and routine urine examinations were undertaken. Patients already on oral steroids and topical applications of coaltar, salicylic acid or local steroids were treated after stopping therapy and after an interval of 15 days.

Methodology

40 mgm of 8MOP was given daily to all patients at 10·30 a. m. and after 2 hours at 12-30 p. m. they were exposed to sunlight (5–30 minutes). 8–12 weeks later as patients started to show response frequency of exposure was gradually decreased to thrice a week, twice a week and later once a week. The sunlight exposure calculated by the photometer amounted to 8–12 Joules/cm^2 daily.

Grading of Response

Response was assessed in three ways. (1) clearance of lesions ; excellent when 100% lesions cleared, good when 90–100%; cleared, fair when 50–90% cleared and poor when less than 50% of lesions cleared. (2) A statistical point score was maintained as per Wallace's classification and depending on the type and morphology of the lesions and (3). morphological responses with respect to duration of therapy.

Results of Photochemotherapy in Psoriasis

Of the 38 cases of psoriasis vulgaris, 53% showed an excellent response, 28% good and 18% fair response in 1–7

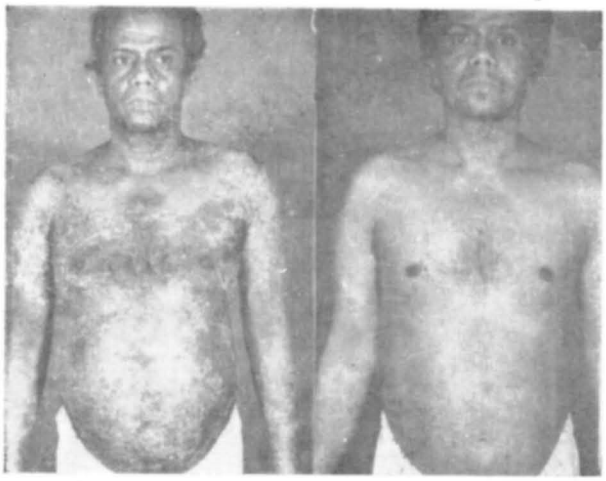


Fig. 1 Before and after treatment

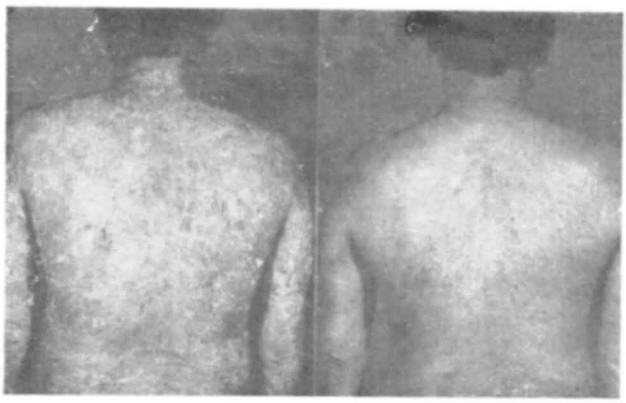


Fig 2 Before and after treatment

weeks. In the erythrodermic phase; of 6 cases 5 (83%) showed an excellent response (Photograph 1 & 2) and 1 a good response in 5-7 weeks. Of 3 cases of pustular psoriasis, 1 showed a good response and 2 cases fair response. One case of flexural psoriasis showed fair response in 4-6 weeks. (Table 2.)

The response of psoriasis vulgaris at the various sites is shown in Table 3. The lesions on the trunk responded earliest within 1-3 weeks; the limbs in 3-6 weeks. Scalp lesions and lesions on the palms and soles took a longer time for clearance. The hairy nature of the scalp and the thick keratin over the palms and soles may interfere with solar irradiation.

The morphological subsidence with respect to duration of treatment is shown in Table 4. The papules disappeared first in (1-4 weeks) followed by scales and plaques regressing in 4-6 weeks. Erythema and pustules subsided by 6-7 weeks. Pruritis a subjective symptom showed subsidence at variable times.

The subsidence of lesions in relation to prior treatment showed that cases diagnosed and treated for the first time cleared in a short time of 1-3 weeks. Patients who had received topical therapy responded in 1-4 weeks. Patients on topical steroids or systemic steroids therapy showed little or no improvement in the first 3 weeks and then showed gradual response and

TABLE 2

RESULTS OF PHOTOCHEMOTHERAPY IN PSORIASIS

CLINICAL TYPES	NO. OF PTS.	EXCELLENT 100%	%	GOOD 90-100	%	FAIR 50-90%	%	DURATION OF TREATMENT (WKS)
1. PSORIASIS VULGARIS	38	20	53%	11	29%	7	18%	1-7 WKS.
2. ERYTHRODERMA	6	5	83%	1	17%	–	–	5-7 WKS.
3. PUSTULAR	3	–	–	1	33%	2	77%	4-6 WKS.
4. FLEXURAL	1	–	–	–	–	1	100%	7 WKS.

TABLE 3

PSORIASIS VULGARIS -RESPONSE OF SITES

	SITE OF LESION	DURATION OF RESPONSE (WKS)
1.	TRUNK - CHEST, ABDOMEN, BACK	1 - 3 WEEKS
2	LIMBS - UPPER, LOWER	3 - 6 WEEKS
3.	SCALP	4 - 6 WEEKS
4.	PALMS AND SOLES	5 - 7 WEEKS

clearance by the end of 7 weeks of puvasol therapy.

(Graph 1) shows the statistical score subsidence (mean) in weeks (Psoriasis + Puvasol). At the beginning of puvasol therapy the score was 17.5 points, by the 4th week it was 3.7 points and by the 6th week 0.1 point.

(Graph 2) shows the bio-statistics of puvasol therapy in various types of psoriasis. In psoriasis vulgaris by the 2nd week most patients had a 50% response (17.2 — 10.9 points) and by the end of the 4th week 99% response (17.2—0.16 points). In patients with psoriasiform eyrthroderma there was no response for 3 weeks (25-20.5 points) but by the end of 4-5 weeks (25-9 points) 75% response was seen, and by the 7th week 100% response. In pustular psoriasis the first 3 weeks there was no response and only by the end of the 6th week was 80% response seen. Statistically the t value = 2.76, S value = 2.38 and p value < 0.01 and $p > 0.005$. The improvement observed after treatment is statistically significant as P value is less than 0 01.

Side Effects

Nausea as a side effect was minimal, and disappeared on continuation of treatment and when advised not to take the drug on an empty stomach. There was no evidence of hepatic, renal or haematological abnormalities.

One case lost 9 kg body weight which may be attributed to loss of thick scales. Laboratory investigation on this patient showed low total protein, albumin and globulin, but no changes in liver function tests or renal function. He was kept on very high protein diet, and within a month gained weight, but the total protein, albumin and globulin were same as base line level.

One case showed painful phototoxic erythema after 3 weeks of treatment. No flare up of lesions or Koebner's phenomena was observed.

Discussion

The rationale of the use of 8MOP in photochemotherapy of psoriasis is the inhibition of increased DNA synthesis within the psoriatic plaque by the interaction of psoralen molecules and light energy in the U. V. A. ranges 320–400 um Photoexcited methoxsalen (triplet state) can transfer the absorbed ultraviolet energy to DNA by forming monofunctional single strand photo adducts with thymine bases on further irradiation

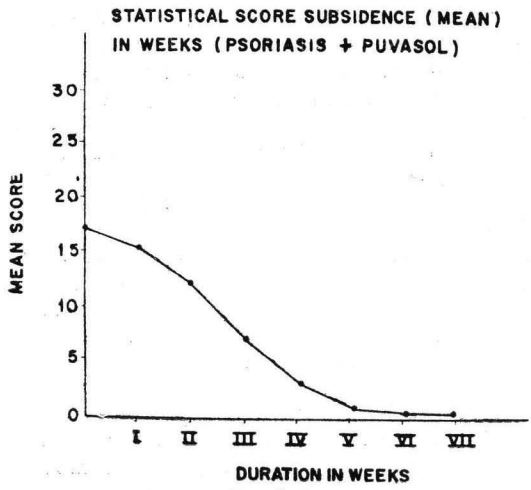
TABLE 4

MORPHOLOGICAL SUBSIDENCE IN WEEKS

TYPE	PAPULE	SCALE	PLAQUE	ERYTHEMA	PUSTULE	PRURITUS	PIGMENTATION
P.VULGARIS	1 - 4	1 - 4	2 - 5	2 - 6	-	1 - 6	—
ERYTHRODERMA	—	3 - 6	4 - 6	4 - 7	-	3 - 7	—
FLEXURAL	—	—	5	PERSISTED	-	PERSISTED	—
PUSTULAR	—	—	—	—	4 - 6	-	—

SUBSIDENCE IN RELATION TO PRIOR TREATMENT

	NO. OF PTS.	SUBSIDENCE IN WEEKS
1) NO TREATMENT	11	1 - 3 WEEKS
2) TOPICAL	9	1 - 4 WEEKS
3) TOPICAL STEROIDS	11	3 - 5 WEEKS
4) SYSTEMIC STEROIDS	17	3 - 7 WEEKS
TOTAL	48	



Graph 1

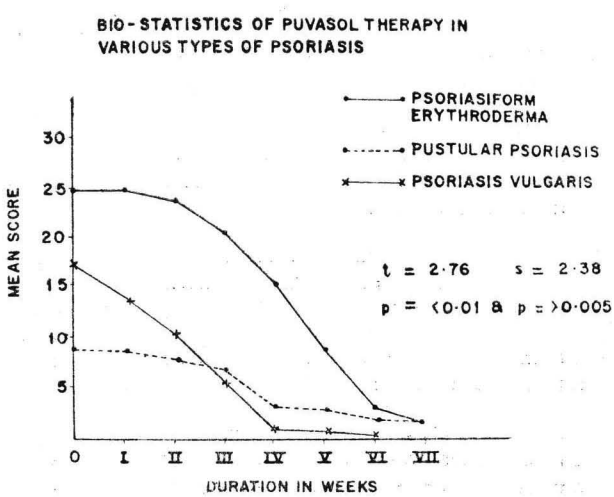
interstrands cross links (bifunctional adducts) between opposite pyrimidine bases. This leads to inhibition of DNA synthesis[19,20,21] and may be the mechanism by which 8MOP exerts its beneficial effect in hyperproliferative skin disease such as psoriasis.

Nonetheless, any agent known to bind DNA after U. V. irradiation poses a theoretical risk of carcinogenicity and this notion should be evaluated against the background of information available at present[23]. The relationship between fair complexion, extreme sun exposure and skin cancer have been well proved[24,25] as also the melanoma risk with excessive sun exposure. UV-B light itself has a clear oncogenic potency[25,26]. It has also been believed that potential oncogenic effect occurs with psoralen and U. V. light[23,27,28]. With psoralen and sunlight or UV-A in vitiligo and psoriasis, no malignancies have been so far reported in man[10,19,29,30,31,32,33,34].

However, Stern et al[23] in a study of 1373 patients reported 30 cases with a total of 48 basal cell and squamous cell carcinoma. The incidence was 2.63 (95% confidence limits = 1.91 to 3.90) times for age, sex and geographically matched population. Relative risk to patients with ionizing radiation was 3.68 (99% confidence limits 2.42 to 8.69). Patients with previous cutaneous carcinoma had a relative risk of 10.22 (99% confidence limits, 4.78 to 37.08). A higher than expected proportion of squamous cell carcinomas and an excess of squamous cell carcinomas in areas not exposed to sun were seen. They conclude that new patients with known histories of ionizing — radiation exposure or skin tumors should be given 8MOP photochemotherapy only if they understand the risks and have disabling psoriasis untreatable by other means.

Puvasol therapy differs from artificial PUVA in that UV-B, visible light and infrared radiation accompany the UV-A.

These fractions of the electromagnetic spectrum may make a significant contribution to the erythemogenic or therapeutic effect of puvasol therapy. In a city like Bombay the sun provides UV-A. source that does not require extra floor space, no travel to treatment centres and no cost. But puvasol



Graph 2

therapy cannot be continued in the rainy season when it is cloudy and dark (3 months – June-August). This therapy is feasible only during the summer or winter seasons.

Excessive heat or cold, insects and lack of privacy may seem to be trivial consideration, but these may result in loss of treatment days. Besides exposure to the sun at specific hours may make treatment difficult for office workers.

In this study puvasol therapy was found to be effective, non-toxic and inexpensive in psoriasis. In the erythrodermic and pustular phases, for the first time the results were encouraging.

Acknowledgements

Our thanks are due to Dr. M. S. Kenkre, Dean, Topiwala National Medical College and B.Y.L. Nair Hospital for his kind permission to utilise the hospital records for publication and to Mr. S. Venkitesan for his secretarial help.

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FALSE

Vasoconstrictor (VC) assay system for corticosteroids is much used and valuable, but these tests do not always parallel therapeutic effect on various dermatosus. For example, it has been shown that in psoriasis the assessment of therapeutic effect is based on techniques such as the DNA synthesis test in hairless mice for antimitotic activity. Again many workers prefer to use the more clinical approach of measuring suppression of experimentally induced contact allergic dermatitis by a particular steroid preparation. More techniques are being currently evaluated in this field of therapeutics.

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