

Original article

Comparative study of psoralen-UVB vs. UVB-alone therapy in the treatment of psoriasis

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Abstract *Background* Ultraviolet B (UVB) has an established role in the treatment of psoriasis. The erythemogenic and therapeutic efficacy of UVB is enhanced by oral psoralens.

Objective Our objective was to compare the efficacy and safety of psoralen-UVB (PUVB) and UVB-alone therapy in the treatment of psoriasis.

Patients and Methods This study was conducted at the Department of Dermatology, Mayo Hospital, Lahore, from June, 1996 to June, 1997. Fifty-two adult patients with stable plaque type psoriasis were enrolled, out of which 50 patients (35 males and 15 females) completed the trial, while 2 patients were lost to follow-up. All the patients were randomly divided into two equal groups and treated thrice weekly. Patients of group I were exposed to ultraviolet B two hours after taking 0.6 mg/kg body weight of 8-Methoxypsoralen, while those of group II were exposed to ultraviolet B without prior psoralen intake. The dose of UVB was given according to the skin type of these patients, all of whom belonged to type-IV skin.

Results Slightly higher rate of clearance (84%) was achieved with PUVB than that of UVB-alone therapy, where this rate was 76%. Rapid clearance of psoriasis (5.8 weeks) with lower number of treatments (17 exposures) and lower mean cumulative dose of ultraviolet B (19.4 J/cm²) were the other benefits of the combined (PUVB) therapy. Patients on UVB-alone therapy needed comparatively longer time (7.6 weeks), more number of treatments (23 exposures), and higher amount of energy (23.2 J/cm² of UVB) for clearance. Comparatively higher incidence of erythema was noted in case of PUVB therapy. Pruritus was the commonest side effect (32% in PUVB group, 28% in UVB-alone group) of either therapy. Mild recurrence was noted in two patients, one from each therapeutic group, during a ten weeks maintenance and follow-up period.

Conclusion This study has showed that concomitant use of psoralens and ultraviolet B has additive therapeutic and erythemogenic effects. Determination of the long-term hazards of this therapy needs further study and long-term follow-up.

KEY WORDS

Comparative study, ultraviolet B therapy, psoralen-UVB therapy, papulosquamous disease, psoriasis.

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Introduction

Psoriasis is a common, genetically determined, hyperproliferative and inflammatory disorder of the skin which in

its classical presentation is characterized by well-demarcated, erythematous, scaly plaques that have a predilection for the scalp and extensors of the elbows and knees. It is a disease of variable morphology and course which affects 1-3% of the world population¹ and therefore, accounts for the third most common reason for visits to dermatologists besides acne and warts.²

Psoriasis is still not completely curable, although a wide variety of treatment modalities, both topical in the form of salicylic acid, corticosteroids, tar, dithranol and ultraviolet B (UVB), and systemic agents like photochemotherapy, retinoids, methotrexate and cyclosporine are available for its control.³ The choice of therapy is determined by many factors, the most important being the age, sex, occupation, general health, the site, severity and type of psoriasis. The goal of treatment is to clear each episode of psoriasis and prevent a recurrence for as long as possible.⁴

Exposure to natural sunlight is known to improve psoriasis, but seasonal, climatic and geographic variability in solar radiation limits its therapeutic effectiveness. The development of artificial ultraviolet radiation (UVR) gave the impetus to modern day therapy. Phototherapy in the form of ultraviolet B radiation, either used alone or in combination with other topical agents e.g. coal tar and dithranol or with a variety of systemic agents like photochemotherapy and retinoids is, another useful modality for the treatment of psoriasis.⁵

Psoralens are a group of photosensitizing drugs which are ineffective when used alone, but in combination with UVR provide an effective tool for the treatment of psoriasis and a number of other photoresponsive skin disorders e.g. vitiligo and mycosis fungoides.⁶ Sakuntabhai *et al.*⁷ in a bilateral comparative study on psoriatic patients combined psoralens with

ultraviolet B and achieved higher erythemogenic and therapeutic response than that of UVB-alone. Further studies were needed in this respect; therefore, we decided to work on this subject in order to evaluate the efficacy, safety and tolerability of this new mode of therapy in the treatment of psoriasis and to compare its results with that of the commonly used phototherapy (UVB-alone) and with other studies held on this subject previously.

Patients and Methods

This study was conducted at the Department of Dermatology, Mayo Hospital, Lahore from June 1996 to June 1997. Fifty-two diagnosed patients (36 male and 16 female) with stable plaque type psoriasis were enrolled. Clinical assessment of the patients was done on the basis of severity of signs and symptoms (erythema, scaling, induration, pruritus) of disease according to a 4 grade scale (0=absent, 1=mild, 2=moderate, 3=marked). The findings obtained from a brief clinical history, general physical examination, cutaneous examination and laboratory investigations (complete blood count, antinuclear antibodies, LFTs, renal function tests) were entered on a specially designed proforma.

All the patients were randomized into two equal groups and treated on alternate days (three times a week). Patients of group I were exposed to ultraviolet B two hours after taking 0.6 mg/kg body weight of 8-MOP while that of group II were exposed to the same source of ultraviolet light without prior taking of psoralen. The first dose of UVB and subsequent incremental doses were given according to the sun reactive skin type of these patients all of whom belonged to skin type IV. The dose of UVB was increased gradually keeping in mind the response of the disease and

erythema production during the whole course of therapy. All the patients were instructed to wear UV-blocking glasses during exposure to ultraviolet radiation and in case of psoralen-UVB therapy just after taking psoralens and throughout the day after that. The face and genitals were protected by suitable clothing when not affected by psoriasis. UVB was delivered by Waldmann 1000 UVB cabin in an upright position with 26 fluorescent tubes each of 100 Watts, mounted on all the six sides of the irradiation cabin, while hands and feet UVB units were used for irradiation of the limbs.

In order to ensure proper dosimetry the radiation intensity of the radiation units was checked regularly with the help of a photometer. The dose of UVB (J/cm^2) delivered to the patients was calculated with the help of a conversion scale.

There were two phases of this study. A- Clearing phase: This phase started with the exposure of patient to the first dose of ultraviolet B (either with or without psoralen) and ended with the clearance of

scaling, erythema and induration in more than 90% area of involved skin. B- Maintenance phase: After clearing of psoriasis the last dose of ultraviolet B with which the patients cleared was kept as a maintenance dose but gradually tapered from three times weekly to two times weekly and then once a week. All the patients were followed-up for ten weeks.

Paired student t test and Fisher's exact test were used for statistical analysis of the data.

Results

Figure 1 summarizes how the study progressed. Out of the 52 enrolled patients, 50 completed the trial while 2 patients were lost to follow-up. Among the 50 evaluated patients 35 were male and 15 female. The mean age of the patients in this study trial was 37.5 years, extent of skin involvement 52.5% and the mean duration of disease 11.7 years (**Table 1**).

Twenty-one out of 25 patients cleared (84% clearance rate) on psoralen-UVB therapy, within 17 treatments, over a period of 5.8 weeks.

Figure 1 Flow diagram showing the disposition of patients

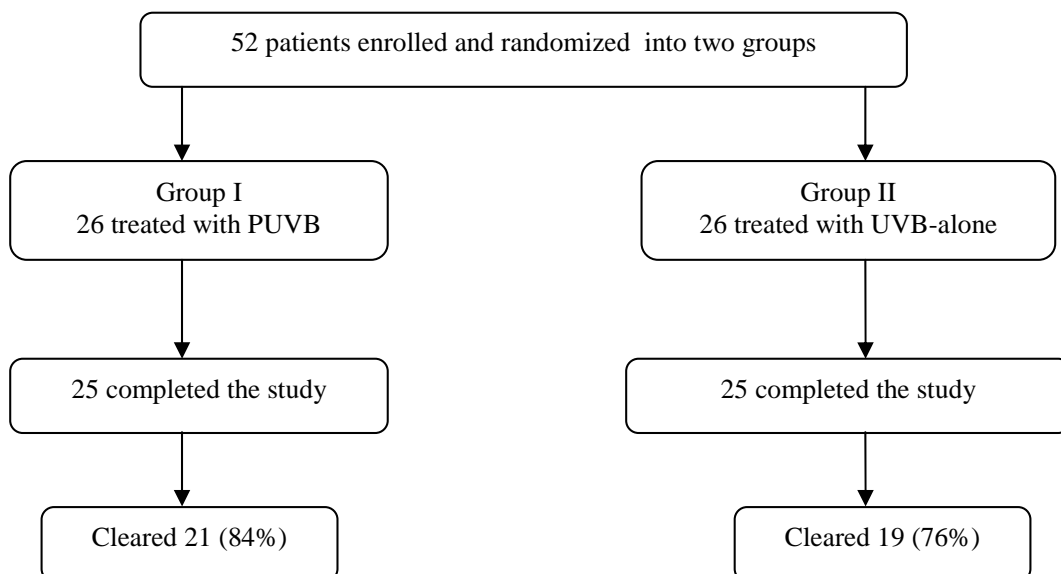


Table 1
Demographic data of patients

	Psoralen-UVB (n=25)	UVB-alone (n=25)
Age range (years)	19-57	20-54
Mean age (years)	38	37
Sex (male/female)	17/8	18/7
Extent of skin involvement	30-75%	25-80%
Mean of skin surface involved	52.2%	52.2%
Duration of disease (years)	2-23	1-21
Mean duration (years)	12.5	11

Table 2
Comparison between results of PUVB and UVB-alone therapy

	PUVB (n=25)	UVB (n=25)*
No. of patients cleared	21 (84%)	19 (76%)
No. of treatments required for clearance	17	26
Average duration of treatment (weeks)	5.8	8.7
Cumulative dose of UVB required (J/cm ²)	19.4	25.3

* $p > 0.05$

PUVB = Psoralen-ultraviolet B, UVB = Ultraviolet B, J = Joule, cm = Centimeter

The median cumulative dose required for clearance was 19.4 J/cm² (Table 2). One patient with 30% improvement, another with 20% improvement and two patients with very mild improvement were declared resistant.



Figure 2
Psoriatic plaque before and after treatment with PUVB therapy

Table 3
Comparison between side effects of PUVB and UVB-alone therapy

Side effects	PUVB (n=25) n (%)	UVB (n=25) n (%)
Pruritus	8 (32)	7 (28)
Marked erythema	3 (12)	0 (0)
Moderate erythema	4 (16)	4 (16)
Nausea	3 (12)	0 (0)
Fever and malaise	2 (8)	2 (8)
Giddiness	1 (4)	0 (0)

PUVB = Psoralen-ultraviolet B, UVB = Ultraviolet B

They were, therefore, switched over to other therapies. Nineteen out of 25 patients cleared (76% clearance rate) on UVB-alone therapy within an average number of 26 exposures, over a period of 8.7 weeks. The mean cumulative dose of ultraviolet B required for clearance was 25.3 J/cm². Two patients with 20% improvement, another with 10% improvement and four patients with quite negligible improvement were declared resistant, therefore, switched over to other therapies.

Among those who cleared on either therapies (PUVB or UVB-alone) one or two small plaques in the lumbar region were left unaffected (not healed) in one patient of each therapeutic groups. Psoriasis of the limbs was found more resistant than the trunk and, therefore, needed extra exposures for clearance.



Figure 3
Psoriatic plaque before and after treatment with UVB-alone therapy

Table 3 describes the side effects seen in two groups. Three patients (12%) on psoralen-UVB therapy developed marked erythema during the initial phase of this study which settled with omission of two treatment sessions, while four patients (16%) of each group (psoralen-UVB and UVB-alone) developed moderate erythema (also during the initial phase of study) which settled on temporary suspension of the incremental dosage. Pruritus was the complaint of 8 patients (32%) on psoralen-UVB therapy and 7 patients (28%) on ultraviolet B-alone therapy. Three patients (12%) of psoralen-UVB group complained of nausea. Fever and malaise were noted in 2 patients (8%) of each therapeutic group. Giddiness was the complaint of only 1 patient (4%) on psoralen-UVB therapy. Severe burning episodes were not noted in any patient of either therapeutic group.

Discussion

Our results show that the combined psoralen-UVB therapy is slightly better, since 84% of our patients achieved clearance on psoralen-UVB therapy as compared to 76% on UVB-alone therapy. This difference is, however, not significant statistically ($p > 0.7$). Other observations of this study were that, as compared to UVB-alone therapy, which required 8.7 weeks, 26 exposures and 25.3 J/cm^2 for clearance on average, patients could be cleared with psoralen-UVB in comparatively shorter duration (5.8 weeks), with fewer treatments (17 exposures) and on a lower median cumulative dose of ultraviolet B (19.4 J/cm^2) (**Table 1**). International studies conducted in this regard also support this aspect of our study. Sakuntabhai *et al.*⁷ in a bilateral comparison study in the treatment of psoriasis also show the superiority of the combined therapy (psoralen plus

ultraviolet B) over that of UVB-alone. They achieved more rapid clearance of psoriasis with psoralen-UVB than UVB-alone therapy. Clearance rate in their study was 88% with the use of the combined therapy (psoralen-UVB) compared to our 84% with the use of the same therapy. However, patients in their study cleared earlier within only 5 treatments compared to our 17 treatments. The mean cumulative dose of UVB required for clearance in their case was also significantly lower (4.5 J/cm^2) than our 19.4 J/cm^2 ($p < 0.005$).

The results of psoralen-UVB combination in our study are comparable with that of the same therapy used by Khurshid *et al.*⁸ We achieved a bit higher clearance rate (84%) while using 19.4 J/cm^2 of UVB compared to his 77.7% clearance rate and 25.2 J/cm^2 of UVB respectively. The average number of treatments (17 exposures) and the duration of therapy (5.8 weeks) needed for clearance in our study are comparable with his number of treatments (16 exposures) and duration of therapy (5.2 weeks) respectively.

Using PUVB therapy de Berker *et al.*⁹ achieved slightly higher clearance rate (87%) compared to our 84%. They achieved this target within 12.8 exposures, spending 16.6 J/cm^2 of ultraviolet B, compared to our 17 treatments and 19.4 J/cm^2 of UVB respectively. As there is no statistical difference among their results and ours, so the studies are in accordance with one another.

Our results of UVB-alone therapy are also comparable with the other international studies. Picot *et al.*¹⁰ while using UVB-alone therapy achieved success rate of 78.5% compared to our 76% with the use of the same therapy. The mean cumulative dose of ultraviolet B and number of

treatments needed for clearance in their study were 15.1 J/cm² and 20 treatments, respectively. Our patients on UVB-alone therapy required 25.3 J/cm² of UVB and 26 exposures for clearance when compared to them.

None of the results of the above mentioned studies matches with one another completely. This is because the response of psoriasis to therapy is not always predictable. Disease may have the same appearance, but reacts to treatment completely differently in different patients in various parts of the body, or in the same patient at different times.⁴ Apart from this, differences in the results among ours and other studies may be because of: a) difference in the source of radiation: the use of more effective narrow-band UVB in other studies^{7,9,10,11} compared to our wide-band source of ultraviolet B radiation, b) difference in the skin type of the patients: patients belonged to skin type I, II and III in international studies compared to our pigmented skin type-IV patients, c) difference in the protocol of therapy: ultraviolet B was administered according to MED by Sakuntabhai *et al.*⁷ and Picot *et al.*¹⁰ compared to our dosage system according to the skin type of the patients, and d) difference in selection of patients: guttate psoriasis responds to ultraviolet therapy better than the other types¹² and the patients of Picot *et al.*¹⁰ included this variety also, compared to our patients of only stable plaque variety. Extent of skin involvement and duration of disease may be other factors affecting the results in all these studies.

We found an increased incidence (12%) of marked erythema in our patients of PUVB group, compared to none on UVB-alone therapy and an increased incidence (16%) of moderate erythema in both of our

groups (PUVB & UVB-alone) as compared to other studies. This was also because of the more erythemogenic wide-band (290-320 nm) source of radiation and the additive effect of this band with psoralen which we used compared to the less erythemogenic narrow-band (311 nm) UVB used by Picot *et al.*¹² and the combination of the same band (311 nm) of ultraviolet radiation with psoralens by Sakuntabhai *et al.*⁷ and de Berker *et al.*⁹

Pruritus, which was the commonest complaint in our patients on either treatment, may not be solely related to ultraviolet therapy. Its frequency was not significantly higher (32%) in psoralen-UVB patients than that of UVB-alone patients (28%). Nausea is no doubt a psoralen-related side effect, and therefore confined to the patients of psoralen-UVB therapy. The incidence of this side effect was marginally low (12%) in our patients compared to 22% in Khurshid's study.⁸ Fever and malaise were the other side effects also similar in frequency in both our treatment groups (psoralen-UVB and UVB-alone). Serious episodes of burning in the form of vesicles and bullae as those reported in the literature were not observed in ours.¹³

During the 10-week maintenance/follow-up period of this study, relapse of psoriasis (defined as the degree of skin involvement of 50% or more of that recorded at the time of entry into the study) was not seen in any patient. However, mild recurrence with return of only a few guttate lesions was noted in two patients, one from each therapeutic group during the last three weeks of follow-up period.

From this study one can conclude that the combination of ultraviolet B and psoralen is as effective as ultraviolet B-alone in

terms of clearing psoriasis in shorter duration with lower cumulative dose of ultraviolet energy needed for clearance. Increased incidence of erythema in our patients is because of more erythemogenic wide-band UVB which we used compared to the less erythemogenic narrow-band UVB used in other international studies.

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