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Original Research Article

Efficacy and Safety of PUVA Therapy in Extensive Psoriasis- An Indian Experience

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ABSTRACT

Introduction- Psoriasis is a chronic, inflammatory, immune-mediated, debilitating skin disease, prevalent worldwide, affecting approximately 2%-3% of the global population. There are various treatment modalities available for extensive psoriasis which include Methotrexate, Cyclosporine, Retinoids, Oral PUVA (Psoralen and UV A) therapy, Biologic agents etc.

Aims and objectives - To assess the efficacy and safety profile of PUVA in patients with Fitzpatrick skin types IV and V who had severe plaque-type psoriasis.

Materials and methods - Ninety patients having plaque-type psoriasis with involvement of > 20% body surface area (BSA) were assigned for the study. Patients were treated with PUVA therapy. Treatment was continued for 10 weeks or until PASI 90 achieved, which-ever was earlier. Clinical improvement of skin lesions was assessed by measuring PASI scoring. Any side effects like were also noted.

Results - PASI-50 (Psoriasis Area Severity Index) (50% reduction in PASI score) was achieved by 81% (73/90) and 59 patients (65.55%) achieved PASI-90 (90% reduction in PASI score) . Mean dose required to achieve PASI-50 was 59.20±11.25 j/cm^2 and mean dose required to achieve PASI-90 was 90.11±6.06 j/cm2 in case of PUVA group. Side effects were minimal, no withdrawal of therapy required.

Conclusion - PUVA is an effective mode of treatment in extensive chronic plaque psoriasis in skin type IV and V patients with minimal side effects.

Key words- *Extensive Psoriasis, PUVA,*

INTRODUCTION

Psoriasis is a chronic, inflammatory, immune-mediated, debilitating skin disease affecting approximately 2%-3% of the global population. [1] Now a days, psoriasis may not only be considered as a disease of skin but rather a systemic disease. In India, it accounts for 2.3% of total dermatology OPD patients. [2] The choice of treatment is influenced by short-term as well as long-term considerations, and factors including the severity of the disease, the effectiveness of a given medication and its side effects, the patient's quality of life, and the ease of treatment. According to National Psoriasis Foundation, people with psoriasis on less than three percent of their body surface area are considered to have mild psoriasis. Those with three to 10 percent of the body surface area affected by psoriasis are considered a moderate case. More than 10 percent body surface area is considered severe. (The surface area of the hand equals about one percent of the skin.). [3]

Ultraviolet ray (UV ray) has been proposed as a treatment for psoriasis for a long time, PUVA acts through immuno-modulatory and anti-proliferative actions. In

addition, it acts for the generation of reactive oxygen species which damage DNA, cell membranes & cytoplasmic constituents. [4] In general, PUVA is most appropriate for persons with extensive disease that is limited to the skin; skin types III through VI, which are associated with a low risk of the development of skin cancer (Table 1), and no history of skin cancer or photodamage. [5] Psoralen ultraviolet A (PUVA) has been widely in use since the 1980s. But still expriences from India are less. We have assessed the relative efficacy and safety profile of PUVA in patients with Fitzpatrick skin types IV and V who had severe plaque-type psoriasis.

MATERIALS AND METHODS

Setting The Study was conducted at Out Patient Department (OPD) of Dermatology, Venereology & Leprosy Department of a tertiary level hospital in Eastern India.

Duration- It was done from June 2015 upto May2018.

Type of study – It was a clinical study.

Sampling methods- All patients of extensive psoriasis, attending the OPD and advised for PUVA therapy were potential cases. Eligible patients , willing to join the study, after fulfilling the inclusion Criterion and signing the Written Consent Form were included the study.

Inclusion criteria - Patients having plaque-type psoriasis with involvement of > 20% body surface area (BSA) were assigned for the study

Exclusion criteria- Unwilling patients, Patients with deranged hepatic and renal function, Patients with neurological disorder, psychiatric disorder like claustrophobia, Patients with malignancy, tuberculosis, HIV or other immunocompromised disease, other immunosuppressive therapy, infective or contagious diseases, Pregnant patient and Infants and Children were not included in the study.

Data collection procedure- A predesigned Case record form (CRF) maintained for each patient. Detail history, examination findings including PASI score, haematological and biological parameters were recorded in CRF. After fulfilling the inclusion and exclusion criteria, patients were included in the study. Clinical improvement of skin lesions was noted by measuring PASI scoring Biweekly in that proforma, any side effects like- increase in erythema, photo-onycholysis, increase of disease severity, any haematological or biochemical alteration was also noted.

Data analysis- we have calculated how many patients achieved 50% and 90% improvement. Arithmetic mean and standard deviation calculated for required time duration, total cumulative dose, and sessions required.

Phototherapy unit (departmental) -- SPIEGEL SERIES (Eco) Whole Body PHOTOTHERAPY Chamber WITH 12 TL100W/10R for PUVA was used. [Manufacturer – DERMA INDIA] [Figure]. Patients were given 8-Methoxy psoralen tablet (20 mg) followed by UVA, started at the dose of 2 j/ cm^2 thrice weekly with increment of .5j/cm^2 dose every 3rd sitting until patient has developed erythema or burning sensation over the apparently normal skin.. Treatment was continued for 10 weeks or until PASI 90 achieved, which-ever was earlier. Clinical examination, Blood investigation, PASI scoring and photograph was repeated in serial intervals during study. At the end of study, the data was compiled, tabulated, and analysed.

RESULTS

We have analysed 90 patients of chronic stable plaque psoriasis of Fitzpatrick Skin type IV and V

Table 1 Demographic profile of the cases .

Age	40.3478± 14.4575 years
Gender	M:F 2.10:1
Age of male patients	- 41.5410± 15.1411
Age of female patients	37.7931± 13.3052

At beginning the PASI score was 19.8543±5.7938, it was 19.9098±5.7302 in males, and in females it was 19.7414 ± 6.2108. After 10 weeks it became 5.7185±

8.3126, in male it was 6.5197 ± 9.4437 and in female it was 4.1552 ± 5.3773. (P = 0.2136).

PASI-50 (50% reduction in PASI score) was achieved by 81%(73/90) and 59 patients (65.55%) achieved PASI-90 (90% reduction in PASI score).

Serial changes of mean PASI is shown in table 2

Table -2. Bi-Weekly Changes in PASI

	Total patients	Male (61/90)	Female (29/90)
Age(years)		41.5410± 15.1411	37.7931± 13.3052
PASI achieved at weeks			
PASI 0 weeks	19.8543±5.7938	19.9098±5.7302	19.7414 ± 6.2108
PASI 2 weeks	16.8207± 15.0647	14.6377± 5.7397	14.5207± 5.2527
PASI 4 weeks	12.1326±6.5277	12.4082±7.3532	11.4552 ± 4.6061
PASI 6 weeks	10.0815±8.0621	10.7984±9.3805	8.5655 ± 4.3245
PASI 8 weeks	7.2978± 8.2901	8.1443 ± 9.5539	5.5552 ± 4.7795
PASI 10 weeks	5.7185± 8.3126	6.5197 ± 9.4437	4.1552 ± 5.3773

Weeks required to achieve PASI-50 was 5.0000 ± 1.4650 weeks and PASI- 90 achieved in 9.1500 ± 0.7988 weeks[Table3].

Table-3. Weeks required to achieve PASI50 and PASI90

	Number of patients	Weeks required in Total patients	Weeks required in male patients	Weeks required in female patients	Significance level
PASI 50 achieved in weeks	73/90	5.0000 ± 1.4650 [73/90]	4.6923 ± 1.4217[52/61]	5.4828 ± 1.4546[21 /29]	P = 0.0359
PASI 90 achieved in weeks	59/90	9.1500 ± 0.7988[59/90]	9.1053 ± 0.7637[38/61]	9.1905 ± 0.8729[21/29]	P = 0.6814

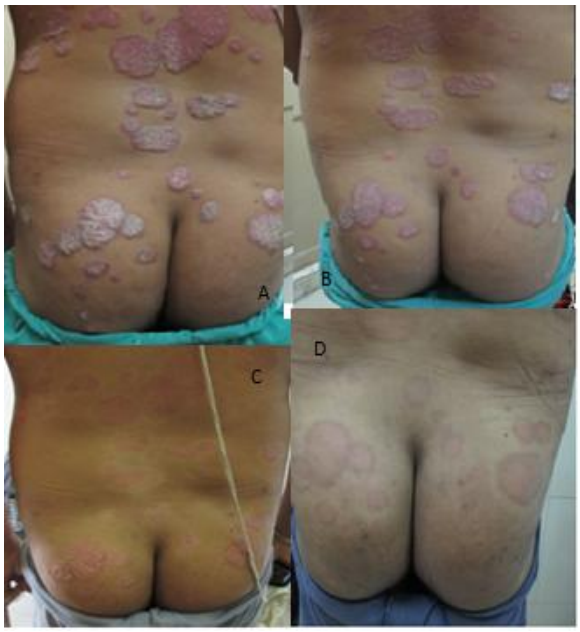
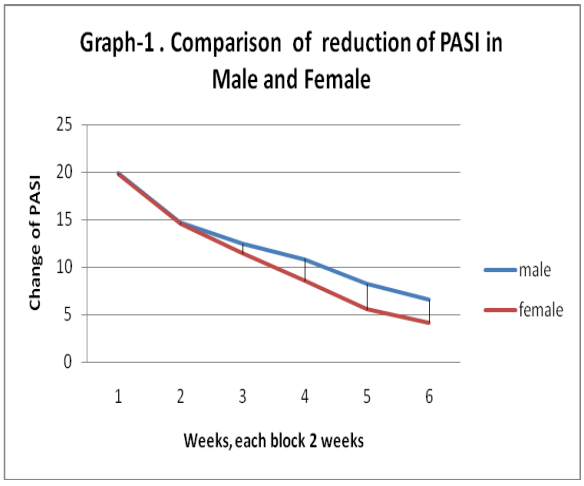


Figure-1 Serial picture of improvement. A. 0 week, B 4 weeks, C.8 weeks, D. 10 weeks

There is marginal difference of result in male and female [Graph-1].

Mean number of exposure required to achieve PASI-50 with PUVA was 14.70±4.45 (median-15) and for PASI-90 it was 27.11±2.42 (median-27). Mean dose required to achieve PASI-50 was 59.20±11.25 j/cm^2 and mean dose required to achieve PASI-90 was 90.11±6.06 j/cm2 in case of PUVA group.



No haematological and biochemical parameter changes was noticed. Side effects observed were (in decreasing frequency)-

1. Dryness and itching (43.33% each)
2. Grade 1 erythema (40%)
3. Nausea and vomiting (33.33%)
4. Pigmentation (16.67%)
5. Exacerbation of lesion (13.33%)

6. Elevated bilirubin (Total bilirubin > 2.0 mg/dl) (3.33%)

Table- 4: Laboratory changes at beginning and end

Laboratory parameters	At begining	At end	p-value
Haemoglobin	12.5100±1.5988	12.4810±1.5115	0.9427
Total leukocyte count	7803.3333±1862.9756	7840.0000±1541.2937	0.9341
Platelet	2.4113±0.5315	2.3897±0.4831	0.8693
Total bilirubin	0.7097±0.2554	0.7860±0.4189	0.3984
ALT (alanine transaminase)	30.5633± 11.3952 IU/mL	35.3033± 13.8870 IU/mL	0.1538
AST(aspartate transaminase)	29.0333± 14.0117	32.8200± 15.6123	0.3269

No side-effect was observed in 33.33% of patients.

DISCUSSION

The use of PUVA therapy revolutionized the management of psoriasis. The present study demonstrated a good efficacy of PUVA in the treatment of extensive plaque psoriasis. With PUVA, a highly effective therapy became available for severely affected persons who previously had often required hospitalization. [5] In India it accounts for about 1.4- 2.3 % of the total number of dermatology outpatients. [6,7] Approximately one-third of patients with psoriasis need phototherapy or systemic treatments for moderate to severe symptoms during the disease course. We performed a study to evaluate the efficacy of PUVA in patients with skin types IV and V (the most common Indian skin types) with chronic plaque psoriasis, because there is dearth of such evidence.

PASI-50 was achieved by 81% (73/90) and 59 patients (65.55%) achieved PASI-90 in our study. In the table of comparison of different studies on PUVA our study is comparable in efficiency of clearance, more with other Indian and Asian study with similar skin type. [4,8-10]

Treatment session in our study to achieve PASI 50 was 14.70±4.45 and 27.11±2.42 for PASI 90. The average treatment session in different Indian and Asian studies varies from 15 to 22.66 (14-48) [4,8-13] [Table -5] . Though the weekly exposures were 2 or 3 per weeks, the average session is nearly equal. All the studies had Fitzpatrick skin type IV to V, so we may consider this is the usual session period to expect significant improvement from PUVA in psoriasis in Indian or Asian skin.

Table 5- Comparison of different studies

Study	Skin type	Frequency / week	Therapeutic target	Clearance rate	Treatment session	Mean Time Weeks	mean cumulative dose j/cm^2
Tahir And Mujtaba [4]	NA	3/3		85%	17		
Kaur [8]	IV- V	3		75%	22.66		
Ahmed Asim [9]	IV V			92%	15	8	
Markham [10]	I-III	2/3		100%	19		
Gordon [11]	I - IV	2		84%	16.7		70.1
Yones [12]	I-IV V-VI	2		84% 27%	17		
Chauhan [13]	IV- V	3		82%	29.8	9.9 ± 3.5 (4–16)	93.8 ± 51.8 (40.5–224)
Dayal [16]	V-VI	2	PASI 50 PASI75	All all	12.7±4.9		7.4
Present Study	V- VI	3	PASI 50 PASI90	90% 63.33%	14.70±4.45 27.11±2.42	4.96±1.51 9.11±0.81	59.20±11.25 90.11±6.06

The mean cumulative dose (j/cm$^{2)}$ in our study was 59.20±11.25 to achieve PASI 50 and for PASI 90 it was 90.11±6.06 j/cm^2.

In a study of patients with moderate to severe Chronic Plaque Psoriasis, involving either > 20% body surface area or with a Psoriasis Area and Severity Index (PASI) of > 10 and not on any active treatment for 8 weeks were treated with PUVA, The end point of the study was complete clearance or 12 weeks (whichever occurred first), at which point treatment was stopped. They have included type IV and V skin patients. The mean cumulative dose was 99.37 ± 68.97 j/cm^2. [8] So it may be the standard cumulative

doses of PUVA for clearance of extensive PUVA. Even, other study [11] also had the median clearance dose 70.1 J/cm^2 for PUVA though majority of the patients were skin type I-IV. Almost all patients cleared their skin lesion, cleared at up to 200 J/cm^2. They also mentioned that lager plaque psoriasis had required more cumulative dose, the same finding was noted in our study but we didn't document the exact difference between the large and small plaques of extensive psoriasis patients.

Our patients with scalp lesions and nail lesions responded poor. This is the disadvantage of PUVA is that it only benefit its areas of the skin that are exposed to ultraviolet light; therefore, its use for disease of the scalp and nails is limited. [5]
We tried to analyse the difference between the male and female. The initial PASI score was marginally high in females, regression was little faster and end PASI bit less than male though the difference was not highly significant. . This may be as females are less photoexposed in regular practice, may be PUVA is more effective for them. Other reason may also there. We didn't get any reference for that.

To avoid the side effects we followed the recommended UVA exposure per skin type according to IADVL Puva guideline, [14] we also tried not to t cross the limit (2.5 j/cm^2 in type V skin. [15] The side effects are less in PUVA, that also supported by other studies [8,11] No major haematological and biological side effects were noticed in the study. In our study, most common side effects observed are dryness and itching (43.33% in both) followed by grade 1 erythema (40%). It is in contrast to study performed by Dayal et. al. [16] who observed grade 1 erythema in 100% patients receiving PUVA. In their study they also observed development of grade 2 erythema in 70% of PUVA patients, whereas in our study it was developed in none. In their study they observed pruritus in 80% patients which is much higher than incidence of pruritus observed in our study (43.33%). In our study 33.33% patients complained of nausea and vomiting. In study performed by Dayal et. al. [16] 75% patients developed nausea, which was much higher than the incidence observed in our study. Additionally Dayal et. al. [16] observed vertigo (75%), diffuse hair fall (70%) and headache (45%) in patients receiving PUVA which were not observed in our study. Though one of our patient in PUVA group developed elevated bilirubin (>2.0 mg/dl), it was a isolated finding and his pre treatment bilirubin was also high (total bilirubin – 1.5 mg/dl).

We have followed thrice weekly exposure schedule, although there are studies showed that twice weekly schedule is as efficacious as the conventional thrice weekly dosage schedule. It may improve patient compliance, though nearly all our patients maintained our thrice weekly schedule. This may also reduce the total cumulative dosage followed by long time side-effects of PUVA, but those required very long follow-up. [17-19]

CONCLUSION

In conclusion, we can say that PUVA is an effective mode of treatment in extensive chronic plaque psoriasis in skin type IV and V patients with minimal side effects. there is no significant difference of clinical improvement between patients of different gender. Thrice weekly exposure schedule is convenient to patients. Long term side-effects can only be evaluated after prolong follow up.

Conflict of interest- Nil
Financial source- none.

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