

# COMPARISON OF PSORALEN ULTRAVIOLET A (PUVA) PHOTOCHEMOTHERAPY PLUS TOPICAL CORTICOSTEROIDS WITH PUVA PLUS BLAND EMOLLIENTS IN THE TREATMENT OF PSORIASIS

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**Background:** Psoralen Ultraviolet A (PUVA) therapy is a well-established treatment of psoriasis. The objective of the study was to compare the clinical improvement in psoriasis with PUVA photochemotherapy + topical corticosteroids and PUVA + bland emollients. **Methods:** Forty patients with chronic plaque type of psoriasis were divided into two equal groups each having 20 patients. PUVA therapy was given thrice weekly. In addition, patients of group-A were allowed to apply topical betamethasone 17-valerate 0.1% diluted 1 into 2 parts with plain vaseline twice daily. Patients of group-B were allowed to apply only plain vaseline over lesions twice daily. Clinical improvement in lesions was observed by decrease in the severity of erythema, scaling and plaque elevation. **Results:** Clearance of psoriasis was achieved in 95% of the patients treated with PUVA plus topical corticosteroids while clearance was achieved in 80% of patients treated with PUVA plus bland emollients ( $P=0.0758$ ). Median numbers of exposures for group-A were 16 & for group-B were 17.5 ( $p= 0.1029$ ). Similarly, median cumulative dose in group-A was  $64.5 \text{ J/cm}^2$  & in group-B was  $70.7 \text{ J/cm}^2$  ( $p= 0.372$ ). **Conclusion:** There is no significant difference in clinical improvement in psoriasis treated either by PUVA plus topical steroids or PUVA plus bland emollients.

**Key Words:** Psoriasis, PUVA therapy, Betamethasone 17-valerate, Emollients

## INTRODUCTION

Psoriasis is a chronic, immune mediated, inflammatory, genetically determined hyperproliferative disorder of the skin characterized by remissions and exacerbations.<sup>1</sup> The major defect in psoriasis is more than eightfold shortening of the epidermal cell cycle from 311 hours to 36 hours. Further, there is twofold increase in the proliferative cell population and 100 percent of the germinative cells of the epidermis appear to enter the growth fraction compared with 60–70 percent for normal subjects.<sup>2</sup>

Topically applied corticosteroids are of established value in the treatment of psoriasis.<sup>3</sup> They act as antimitotic, anti-inflammatory and immuno-suppressive agents. Unfortunately, these are associated with several cutaneous and systemic side effects<sup>4,5</sup> including the development of tachyphylaxis.<sup>6</sup> Even with maintenance corticosteroid therapy, relapse is 31% within 1 month and 71% within 1 year.<sup>7</sup>

Psoralen ultraviolet A (PUVA) is an effective modality for treatment of psoriasis.<sup>8</sup> Recently, it has been shown to suppress 'whn' gene that plays an active part in epidermal homeostasis and whose over-expression results in psoriasis like lesions.<sup>9</sup> It involves the use of systemic administration of a photosensitizing agent (psoralen). After that, the patient is exposed to non-ionizing radiation (ultraviolet A). This exposure results in a photochemical reaction that results in conjugation of psoralen to DNA of

keratinocytes leading to the formation of DNA adduct products and subsequent suppression of cell proliferation. It also decreases the number and function of lymphocytes, neutrophils, monocytes, macrophages and Langerhans cells.<sup>10</sup> However, long term PUVA therapy is associated with different adverse effects including skin and genital malignancies.<sup>11,12</sup>

PUVA therapy has been combined with different topical agents including bland emollients.<sup>13,14</sup> in order to get clinical improvement in the psoriatic lesions with less number of UVA exposures, reduced cumulative UVA dose and minimum number of hospital visits. The purpose of this study was to estimate whether the combination of PUVA and topical corticosteroids result in rapid clearance of lesions or not.

## MATERIAL AND METHODS

It was an interventional (quasi-experimental) study with convenient (non probability) sampling. Forty patients having chronic plaque type psoriasis, with any skin photo type, were divided into two equal groups A & B. Mean age was  $33.64 \pm 7.28$  years in group A and  $34.82 \pm 8.28$  years for group B. The diagnosis was established on clinical grounds. Study was done during a 9 months period from July 2003 to March 2004 in Dermatology Department, Nishtar Hospital Multan. Exclusion criteria were age less than 12 years; cataract or aphakia; significant renal, hepatic, respiratory or cardiac dysfunction, photo-genodermatosis, pre-existing light aggravated disease, intake of photo-toxic drugs; history of previous or existing cutaneous or internal malignancy, pregnancy or lactation, hypersensitivity to psoralens, history of ingestion of trivalent inorganic arsenic, bullous pemphigoid, pemphigus, any type of UV therapy within preceding 6 months or concomitant immunosuppressive therapy.<sup>10</sup>

Before the start of treatment, the severity of the disease of each patient was assessed by using certain parameters. The parameters were erythema, scaling and plaque elevation. Each parameter was given a score according to its individual severity i.e. severe=3, moderate=2, mild=1, and clear=0. Individual scores of each parameter were added up to reach a cumulative score reflecting the severity of disease. Decrease in the severity of erythema, scaling and plaque elevation was subjectively observed on each subsequent visit and a final cumulative score was calculated. The score calculated before the start of treatment and the score calculated on each visit were recorded.

Radiation was given by UVA light cabin having 32 UVA lamps emitting radiation between 315 – 400 nm with peak at 365 nm. Patients of both groups were given 8-methoxypsoralen orally at a dose of 0.6 mg/kg body weight 2 hours before UVA exposure. Initial UVA dose was given according to skin photo type (Table 1). Patients of group-A applied topical betamethasone 17-valerate 0.1% diluted in 1 into 2 parts with plain vaseline over lesions twice daily. Patients of group-B applied only plain vaseline to affected sites twice daily. Radiation was given thrice weekly. Subsequent increments in dose, on each visit, ranged from  $0.1 \text{ J/cm}^2$  to  $1 \text{ J/cm}^2$  (joules per square centimeter) depending upon the patients normal or psoriatic skin response. Patients having score of 2 or less were declared as 'cleared' ( $\leq 2$ =cleared). Patients having score more than 2 even after 30 exposures were declared as 'not cleared' ( $> 2$ =not cleared). Patients dropped during the treatment period were excluded from the study. Data, thus collected was analyzed by using SPSS version 8.0. P-values were calculated by using test of proportion and Mann Whitney test.

## RESULTS

The two treatment groups were well matched with regard to age and the extent/size of lesions. In patients of group-A (treated with PUVA plus topical steroids) 19 out of 20 (95%) showed clearance of psoriasis depicted by flattening of the lesions, removal of scales and disappearance of erythema with appearance of brownish black hyperpigmentation. In group-B patients (treated with PUVA plus bland emollients) 16 out of 20 (80%) patients were cleared of their lesions ( $p=0.0758$ ). P-value was calculated by using test of proportions.

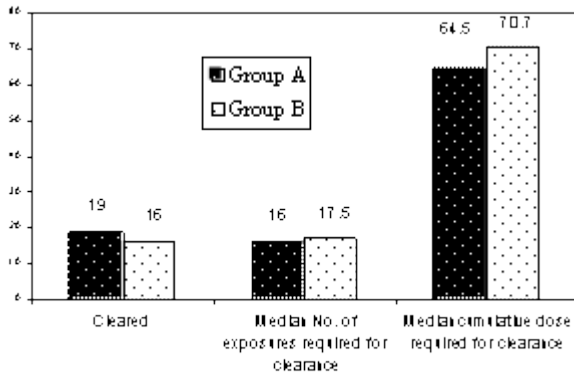
Similarly, median number of exposures for clearance of psoriatic lesions were 16 in group-A and 17.5 for group-B (p=0.1029). Cumulative UV-radiation dose required for clearance was 64.5 J/cm<sup>2</sup> for group-A and 70.7 J/cm<sup>2</sup> for group-B (p=0.372). P-values were calculated by using Mann-Whitney test. Results have been shown in figure 1.

**Table-1: Initial Dose of UVA According to Skin Type**

Skin Type	Description	Initial Dose (J/cm <sup>2</sup> )
I	Always burn, never tan	0.5
II	Always burn, Slightly tan	1.0
III	Sometimes burn, always tan	1.5
IV	Never burn, always tan	2.0
V	Moderately pigmented	2.5
VI	Deeply pigmented	3.0

Group A = PUVA+TS = PUVA plus topical steroids

Group B = PUVA plus bland emollients



**Figure-1: Comparison of results in group A (PUVA+TS) & group B (PUVA+B)**

## DISCUSSION

PUVA therapy has been used for the treatment of psoriasis for more than two decades. Currently more than 30 conditions have been successfully treated with it. Present study was done to find out whether combination of PUVA photochemotherapy with topical corticosteroids results in rapid clearance of lesions or not. No significant difference was noted between the two groups regarding clearance of lesions, median number of exposures required for clearance and median cumulative dose required for clearance. According to results obtained this combination resulted in 95% success rate as compared to 80% in other group. It means that there is only a small benefit of adding topical corticosteroids with PUVA. In the same manner, median number of exposures required in both groups (16 vs 17.5) did not show a great difference implying that both of the combination therapies have similar efficacies. In addition, total ultraviolet dose in both groups (64.5 J/cm<sup>2</sup> vs 70.7 J/cm<sup>2</sup>) showed insignificant difference again proving that patients in

both groups cleared of their lesions with similar UV radiation dose. It also showed that both groups would have equal chances of developing UV radiation related acute and chronic cutaneous side effects. The combination of PUVA and topical corticosteroids should have a pronounced anti-proliferative effect and should have been superior to the combination of PUVA and bland emollients. But this study results did not show any significant difference between two modalities. Exact cause of this phenomenon is not known. However it may due to the fact that bland emollients modulate the topical properties of the skin surface, prevent reflection/refraction of incident light by psoriatic scale and increase absorption of ultraviolet radiation in the lesions resulting in enhanced effect<sup>16</sup> approaching to that of PUVA + topical steroid combination. Another explanation is that both PUVA and corticosteroids might have same target site of action at the nuclear level. However this is an important finding showing that combining PUVA with topical steroids would result in appearance of side effects caused by both without any added therapeutic benefit.

The results of the present study are consistent with several studies done in the past. Among those, the most important work done was of Meola and his associates<sup>17</sup> who studied the effect of topical corticosteroids applied over the psoriatic lesions in combination with PUVA therapy. Their work showed no significant difference in the response of the patients whether topical corticosteroids were used or not in addition to PUVA. Similarly total ultraviolet radiation dose to which patients were exposed showed not much difference in both groups of patients. The number of hospital visits and number of exposures were also similar.

Also, the work of Dower<sup>18</sup> and Levine & his colleagues<sup>19</sup> reflected similar results. These studies clearly proved that there is no added benefit of combining topical corticosteroids with PUVA photochemotherapy. The combination of bland emollients with PUVA produce comparable results.

Different results were seen in a study done by Kostovic and his colleagues<sup>20</sup> showing rapid relief of lesions if PUVA used in combination with topical corticosteroids. This was due to the reason that the sample size used in that study was very small and insufficient to explain the difference in response to two modalities. Moreover, they used super potent topical steroid while in our study, only a potent steroid was used. Similarly only improvement, not clearance, was selected as a criterion to evaluate the efficacy of treatment.

## **CONCLUSION**

PUVA combined with topical corticosteroids has almost similar results in chronic plaque type psoriasis as compared to PUVA combined with topical bland emollients.

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