

Efficacy of Concomitant Use of PUVA and Methotrexate in Disease Clearance Time in Plaque Type Psoriasis

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Introduction

The objective of treatment of psoriasis is to have a clearance of the disease and then to give maintenance treatment to keep the disease in remission. Quick clearance of the disease will allow the individual to continue his daily life activities thus cutting the loss of vital working hours.

PUVA and methotrexate are two time tested treatment modalities for treating psoriasis. As PUVA is less toxic and economical compared to other modalities, it is increasingly used for the treatment of widespread disease.¹ The antipsoriatic effect of PUVA has been attributed to blockage of cell proliferation as a result of the psoralen covalently binding to DNA under the influence of UVA. Alterations in the immune system caused by UVA therapy may also play a role. Though PUVA is effective, it is not without side effects. The long-term side effects may include an increased risk of melanoma² and non melanoma skin cancers, accelerated skin aging and ophthalmic abnormalities. The main drawback of PUVA is that the number of treatments required for clearance of the disease ranges from 20 to 25 which means the time interval of 1½ - 2 months in four treatments per week schedule.³

Methotrexate is given for extensive psoriasis, erythrodermic and acute pustular psoriasis, physically disabling psoriasis of the palms and soles, psoriasis in the elderly and severe psoriatic arthritis. It acts by inhibiting DNA synthesis by competitive inhibition of dihydrofolate reductase and thus exerts an anti-mitotic action on psoriatic skin. Methotrexate although having established efficacy in the treatment of psoriasis has its limitations because of long periods required for clearance of the disease and adverse effects⁴ on bone marrow, GIT, liver, kidney and lungs. Like PUVA in majority of patients the clearance time of psoriasis is two to three months.

Because methotrexate and PUVA act by different

mechanisms in psoriasis, combination may lead to rapid clearance of the disease.

Moreover their toxicity profiles are different making this combination compatible. A Medline search revealed paucity of studies on combination of PUVA and Methotrexate for treatment of Psoriasis and there was no such study from our part of the world. We evaluated the efficacy of this combination in clearance time for psoriasis in our population through a clinical trial.

An analytical study was conducted in dermatology department of PNS Shifa Karachi from March 2001 to November 2001. The aim of this study was to see if there is any reduction in clearance time of psoriasis by combining PUVA (Psoralen and Ultraviolet A radiation) and methotrexate, both modalities being started at the same time

Patients and Methods

A total of 60 male patients between 18 to 50 years of age suffering from plaque type psoriasis with PASI score of >10 were included in the study. Most of the patients were persons of Armed forces of Pakistan posted in Karachi.

Patients suffering from anaemia, thrombocytopenia, leukemia, active infection, peptic ulcer disease, ulcerative colitis, renal/hepatic disease, cardiovascular disease, cataract, preexisting light aggravated dermatoses, alcoholism and immunodeficiency were excluded from the study.

The selected patients were admitted to hospital and randomly allocated to 3 treatment groups A, B and C each group comprising 20 patients.

Group A patients were given only PUVA therapy 4 times a week according to 11011 schedule on Monday, Tuesday, Thursday and Friday. 1½ - 2 hours after oral dose of Psoralen the patients were exposed to high intensity UVA fluorescent tubes with emission spectrum between 320nm to 400nm. The PUVA Combi Light cabinet type apparatus with 48

lamps was used to give UVA radiation. The dose of oxpsoralen was 0.6 mg/kg body weight. Initial UVA dosage was based on Fitzpatrick5 skin type. Dosage was increased with every treatment depending upon skin type and erythema response. An increment of 0.5 J/cm² for skin types I to III and an increment of 1 J/cm² for skin type IV to VI was given with each treatment. As limbs are slow to respond to PUVA compared to trunk and face, half the irradiation dose was given extra to these areas. Group B was given oral methotrexate in a dose of 10 mg per week (5mg on Saturday night and 5 mg on Sunday morning).

Group C was given combination of methotrexate and PUVA therapy, both modalities being started at the same time. PUVA therapy was given as for group A patients. Methotrexate was given as for Group B patients.

PUVA was stopped in all patients in group C after clearance of the disease and maintenance treatment with methotrexate was given as outdoor. Baseline and weekly CBC, urinalysis, liver enzymes, skin examination and review of systems was carried out for all 3 groups to monitor the side effects of PUVA and methotrexate.

The Psoriasis Area and Severity Index (PASI) was used to assess clinical status. Baseline and weekly PASI scores of all patients were maintained. Endpoint in the study was taken as PASI score reduction >75%.⁶ The mean baseline PASI score before treatment was 34.25 for group A, 34.6 for group B and 33.75 for group C patients.

Results

Majority of the patients fell in skin types IV or V. The predominant symptom was itching followed by joint pains. Sunlight with summer exacerbation was provocative factor in only 4 patients, Koebner phenomenon was seen in 3. No other precipitating factor was detected. The sites of involvement, duration of disease and number of episodes were variable.

The cumulative dose of UVA radiation required for clearance of group A patients receiving PUVA alone (n=20) ranged from 150-250 J/cm² (mean-200 J/cm²). The minimum number of treatments needed for clearance was 20 and the maximum number was 25 (mean - 22.5). The clearance time for psoriasis ranged from 5 to 6 weeks (mean - 5.5 weeks).

Group B patients receiving methotrexate alone (n=20) cleared in 7 - 9 weeks time (mean - 8 weeks).

The cumulative dose of UVA radiation required for clearance of group C patients receiving both PUVA

and methotrexate (n=20) ranged from 56-108 J/cm² (mean-82 J/cm²). The patients in this group cleared in 2-3 weeks (mean-2.5 weeks) time after 8 - 12 (mean-10) PUVA sessions.

The mean PASI score reduced from 34.25 to 8.9 in group A, from 34.6 to 9 in group B and 33.75 to 8.5 in group C patients.

No significant side effects were seen except for mild erythema, pruritus, nausea and oral ulcers which were no more common in the combination group as compared to other groups. Haematological and biochemical parameters remained within normal limits throughout the study period in all the treatment groups.

S.No.	Variables	Group A	Group B	Group C
1	Patients (n)	20	20	20
2	Mean Cumulative UVA Radiation dose req. for Clearance (J/cm ²)	200 + 27.72	-	82 + 15.87
3	Mean Time of Clearance (Weeks)	5.5 + 0.32	8 + 0.89	2.5 + 0.42
4	Mean final clearance dose (J/cm ²)	21 + 1.2	-	12.5 + 1.03
5	Average no of PUVA Sessions for disease Clearance	22.5 + 1.5	-	10 + 1.6

Discussion

Treatment of psoriasis consists of a clearance phase and a maintenance phase. A rapid clearance to allow the patient to continue his daily life activities is desirable. Methotrexate and PUVA are two time tested treatment options for psoriasis. Both treatments used separately require longer time for clearance of psoriasis. As both modalities act at different stages in pathogenesis of psoriasis so their combination can have synergistic effect leading to rapid clearance of psoriasis. Moreover methotrexate causes reduction in the thickness and scaliness of psoriatic lesions thereby enhancing the effect of UVA.

Statistically significant reduction in clearance time was observed in patients who received combination therapy with PUVA and methotrexate. Most of the patients were clear of psoriasis and were able to return to normal routine after 2.5 weeks as compared to 5.5 weeks in the PUVA group and 8 weeks in the methotrexate group. Also the average cumulative dose of UVA radiation was much lower (82 J/cm²) in the combination group as compared to the group which received PUVA alone (200 J/cm²) thus minimizing the long term hazards of PUVA exposure.

The average final clearance dose of UVA was also quiet less in the combination group (12.5 J/cm²) as compared to the PUVA group (21 J/cm²). This translates into a lower maintenance dose if the patient is to be maintained on PUVA. However we

decided to maintain our patients on methotrexate in the maintenance phase due to peculiar logistic problems in the armed forces.

No significant side effects were noted and laboratory parameters remained within normal limits throughout the study period in all the treatment groups.

The combination of Methotrexate and PUVA has been rarely studied in the past. Morrison⁷ studied the effect of combination of methotrexate and PUVA on reduction of clearance time of psoriasis. Their clearance time was 6 weeks compared to ours of 2.5 weeks. However their average final clearance dose of UVA was quiet less (6.2 J/cm²) than ours (12.5 J/cm²) probably due to the priming effect of methotrexate (which was started three weeks before PUVA therapy) on psoriatic lesions. We started methotrexate and PUVA simultaneously thus saving valuable time of clearance of the disease but requiring higher last clearance dose of PUVA. This was not a concern in our study as we maintained our patients on methotrexate rather than on PUVA in the maintenance phase. There is a definite risk of carcinogenesis with methotrexate if used for a long time, but in our protocol it was given for a short duration of time.

Conclusion

It is concluded that concomitant use of methotrexate and PUVA is effective and safe mode of clearing psoriasis which helps in early return of patients to routine life. Our study is unique in a sense that we started methotrexate and PUVA at the same time as compared to previous studies in which methotrexate was started 3 weeks earlier thus saving valuable clearance time. More over this is the first study of this kind in our indigenous population. It is recommended that designation MEPUVA be assigned to this combination.

References

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Abstract

Objective: To document the efficacy of concomitant use of PUVA and methotrexate in disease clearance time in plaque type psoriasis.

Methods: Sixty male patients between 18 to 50 years of age suffering from plaque type of psoriasis with PASI score more than 10 were enrolled in the study between March 2001 to November 2001. They were divided into three groups of 20 patients each. Group A received only PUVA, Group B received only Methotrexate and group C received both PUVA and Methotrexate concomitantly. PUVA was given four times a week according to 11011 schedule. The end point for clearance of psoriasis was taken as 75% reduction in PASI score from the baseline.

Results: Group A: The minimum number of PUVA sessions needed for clearance was 20 and the maximum number was 25 (mean - 22.5). The mean clearance time was 5.5 weeks. The cumulative dose of UVA radiation ranged from 150-250 J/cm² (mean -200 J/cm²). Group B: The time required for clearance was 7 weeks at the minimum and 9 weeks at the maximum (mean - 8 weeks). Group C: The minimum number of PUVA sessions needed for clearance was 8 and maximum was 12 (mean 10). The mean time for clearance was 2.5 weeks. The cumulative dose of UVA radiation ranged from 56-108 J/cm² (mean-82 J/cm²). No significant side effects were seen in the three treatment groups.

Conclusion: The results suggest that combination of PUVA and methotrexate is an effective and safe modality for clearance of psoriasis (*JPMA* 54:453;2004).