Research Article

Efficacy and Safety of NB-UVB Vs Methotrexate in Chronic Plaque Psoriasis- A Comparative Study

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Abstract

Introduction: Psoriasis is a chronic and proliferative inflammatory condition of the skin which is quite common in both sexes. Environmental and genetic factors both are involved in its occurrence. Various topical and systemic treatment modalities are used for psoriasis including methotrexate but phototherapy is also one of the effective treatment modality.

Objective: Objective was to compare the safety and efficacy of narrowband ultraviolet B (NB-UVB) and methotrexate (MTX) in chronic plaque psoriasis.

Methodology: In this interventional comparative study (Quasi experimental), sixty patients with more than 10% body surface area involved were enrolled according to inclusion criteria and randomly divided into two groups containing even number of patients. In group A patients were given narrowband UVB, three times a week while those in group B were given 15 mg of oral MTX weekly for twelve weeks. The response to the treatment was observed at 4^{th}, 8^{th} and 12^{th} week of therapy and two weeks after stopping therapy. The therapy was considered efficacious in patients when there was ? 50% reduction in the PASI score (Psoriasis Area Severity Index) from baseline. The group in which there was greater mean % reduction in PASI score was considered more efficacious.

Results: In group A, NB-UVB was effective in 100% of patients with excellent results in 80% of patients and good results in 20% of patients. Efficacy was seen in 100% of patients in group B with excellent response in 76.66% of patients and good response in 23.34% patients. Side effects were seen in 29.93% of patients in group 'A' and 23.34% in group 'B'. Erythema and tanning were observed in group A while nausea in group B.

Conclusion: Narrowband UVB is as good as methotrexate in both safety as well as efficacy in the treatment of chronic plaque psoriasis. Maximum improvement was seen with narrowband UVB during the first month of treatment while with methotrexate, it was seen in the 2nd and 3rd month of therapy. NB-UVB units should be introduced in all government hospitals with dermatology units so that maximum number of patients can be benefited.

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Introduction

Psoriasis is a chronic and disfiguring condition of the skin which is proliferative and common. Genetic and environmental factors play an important role in its occurrence and pathogenesis. Its typical lesions are erythematous, scaly and well demarcated plaques. Extensor surfaces and scalp are the sites of predilection.[1] Its prevalence varies in different populations from 0.1% to 11.8%. Nail changes and arthritis are common manifestations of psoriasis seen in up to 40% of patients.[2]

The pathogenesis of psoriasis is complex. There is alteration in innate as well as in the acquired immune response. There is increased activity of APCs (antigen presenting cells) along with T cells resulting in T helper 1 (Th1) cytokine production leading to increased epidermal proliferation.[1, 2]

Various topical and systemic treatment modalities used for psoriasis include tar, dithranol, salicylic acid, corticosteroids, tacrolimus, pimecrolimus, vitamin D analogues, vitamin A analogues, phototherapy, photochemotherapy, methotrexate, oral retinoids, cyclosporine, sulfasalazine and biological agents.[3]

Phototherapy is one of the most effective treatment modalities for psoriasis.[4] It can be administered in the form of narrowband ultraviolet B (NB-UVB), broadband ultraviolet B therapy (BB-UVB),UVA1, excimer laser, Psoralen ultraviolet A therapy (PUVA) and photodynamic therapy in patients of psoriasis. The NB-UVB (311nm) offers an emission spectrum which is close to spectrum required for clearing psoriasis.[5] Peripheral natural killer cell activity, immune regulatory cytokine production by both Th1 (IL-2, IFN-?) and Th2 (IL-10) cells and lymphocytes proliferation is reduced by NB-UVB in the patients of psoriasis.[6]

Methotrexate has antiproliferative, immune-suppressant and anti-inflammatory action. There is competitive inhibition of the enzyme dihydrofolate reductase which interferes with folic acid metabolic pathway thus preventing synthesis of DNA and decreases epidermal proliferation.[3,7]

Studies carried out by different groups have shown that combination of systemic methotrexate plus NB-UVB is more effective than that of NB-UVB alone.[7,8]

Methotrexate is a gold standard drug for the treatment of psoriasis for decades but side effects associated with it, mainly systemic, limit its use. NB-UVB has no systemic side effects.[6] This study compared safety as well as efficacy of NB-UVB with systemic methotrexate as to see which is more efficacious and safe, so in future therapy which is more efficacious with no or little side effects can be given to the patients of psoriasis thereby benefitting them.

Methods

Patients of plaque psoriasis presenting in dermatology department, Mayo Hospital, Lahore and fulfilling the inclusion criteria (patients with more than 10% body surface area involved, age more than 18 years and of either sex) were enrolled from May 2011 to April 2012. Pregnant or lactating females, patients with history of skin malignancy and who had been on topical therapy in the previous one month or systemic therapy for psoriasis for the last three months were excluded from the study. Patients having chronic liver disease, anaemia, diabetes, psychosis, chronic lung disease and cases in which cumulative dose of MTX exceeds 2 grams were also excluded.

By purposive non-probability sampling technique, study was performed on 60 patients of chronic plaque psoriasis, divided by balloting in to two groups (A and B), containing 30 patients in each group. In group A, patients were exposed to narrowband UVB whereas patients in group B were treated with systemic methotrexate. After taking consent, their biodata was entered in pre-designed proformas. Whole body exposure of NB-UVB was given to patients in group A three times a week. Chamber of NB-UVB consists of 24 Philips 100-W fluorescent tubes which emit radiations of wavelength from 311-313 nm. All patients were exposed to 240 mJ/cm^2 at first visit. 29 If no side effects appeared, the dose was increased by 15% from the starting dose on each visit until the lesions disappeared, which was defined by PASI score reduction to 3 or less. Genitals and eyes both were protected during the exposure by plastic shields and goggles respectively. Treatment was stopped after 36 expos-

ures and patient was followed for next two weeks. Patients in group B were given 5 mg of test dose followed by 15 mg of oral methotrexate, in three divided doses 12 hours apart, per week for 12 weeks. Topical white soft paraffin was applied on the lesions of psoriasis in both groups. The response to the treatment was observed at 4^{th}, 8^{th} and 12^{th} week of therapy and two weeks after stopping therapy. Young patients in group B were counselled about the potential side effects of MTX. Erythema, edema, blister, tanning and other side effects were noted at each visit of patients in group A while cutaneous and systemic side effects were assessed at 1^{st}, 2^{nd}, 4^{th}, 6^{th}, 8^{th}, 10^{th}, 12^{th} weeks of therapy and two weeks after stopping therapy in group B.

Data was analysed by using SPSS (Statistical package for Social Science) 20. Mean and standard deviation were used to represent the quantitative data. Percentage, frequency and proportions were used to present qualitative data. Chi-square test was applied to compare treatment groups in terms of efficacy and safety, p-value $\leq$0.05 was considered significant.

Results

In this study, 60 patients were enrolled and randomly divided by balloting into two groups containing even number of patients. Group A patients received 36 exposures of narrow band UVB with mean cumulative dose of 38.88 ± 5.56 J/cm^2, while those in group B were given 15 mg of oral MTX weekly.

The mean age in group A and B was 38.93±15.02 and 34.57±13.21 years respectively. Among 60 patients, 41 were male and 19 were female. Gender distribution of both groups is shown in Figure 1.

Mean PASI score of group A and B at baseline was 21.45±10.84 and 20.26±8.95 respectively. PASI score of both groups at follow ups is shown in Tables 1 and 2. Group A (NB-UVB) patients showed maximum reduction in mean PASI score during the first month of treatment while in group B (Methotrexate), it was seen during the second and third month of treatment. Significant reduction (p=0.000) in mean PASI score was seen in both treatment groups (Figure 2).

In group A, NB-UVB was effective in 100% of patients with excellent results in 80% of patients and good results in 20% of patients. Efficacy was seen in 100% of patients in group B with excellent response in 76.66% of the patients and good response in 23.34% (Table 3). After application of chi-square test and comparing efficacy of both groups, it was statistically insignificant (p-value = 0.754).

Side effects were seen in 29.93% of patients in group A and 23.34% in group B. Tanning was the most common side effect seen with NB-UVB. The other side effect observed in group A was erythema. Nausea was commonly seen in group B (Table 4). It was controlled with tablet domperidone and MTX was not required to be withheld. Leukopenia and deranged LFTs were other side effects seen with MTX. Deranged LFTs (twice the normal limit) were seen in 1 (3.33%) patient at 12 weeks of therapy. Therapy was stopped at 12 weeks and LFTs were coming towards the normal at the end of follow up at 14th week. The patient was followed up till LFTs came within normal range. This recovery was seen after 4 weeks of stopping MTX. There was progressive fall in TLC count from 7.5 to 3.8 at 10 wks of therapy in 1 (3.33%) patient only. TLC came to baseline 4 weeks after discontinuation of therapy. After application of chi-square test and comparing safety of both groups, it was statistically insignificant (p-value=0.559).

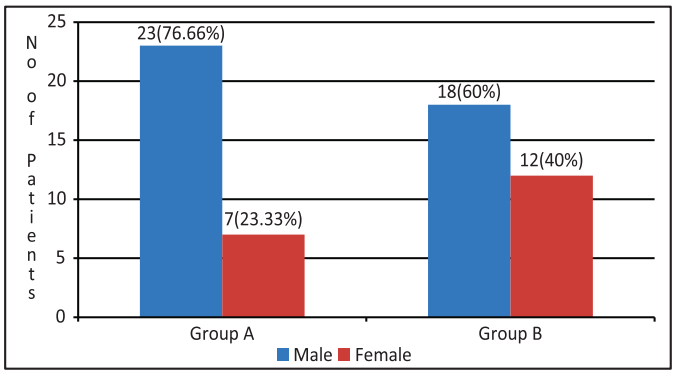

Figure-1: *Gender distribution with respect to treatment groups*
Group-A = Narrow Band UVB
Group-B = Methotrexate

Table 1: *Pasi Score Group-A (NB-UVB) n=30*

Follow Up	Minimum	Maximum	Mean	Std Deviation
Base Line	9.20	59.40	21.45	10.84
4th Week	6.80	44.00	14.96	7.95
8th Week	2.60	30.10	9.80	5.69
12thWeek	1.00	19.80	4.85	4.15
14thWeek	1.00	20.70	4.33	4.33

p-value = 0.000 (Significant: p-value<0.05)

Table 2: *Pasi Score Group B (Methotrexate) n=30*

Follow Up	Minimum	Maximum	Mean	Std Deviation
Base Line	9.20	40.70	20.26	8.95
4th Week	5.20	37.90	17.24	8.45
8th Week	3.30	25.80	11.01	5.48
12thWeek	0.20	16.80	4.77	3.25
14thWeek	0.40	16.50	4.63	3.22

p-value = 0.000 (Significant: p-value<0.05)

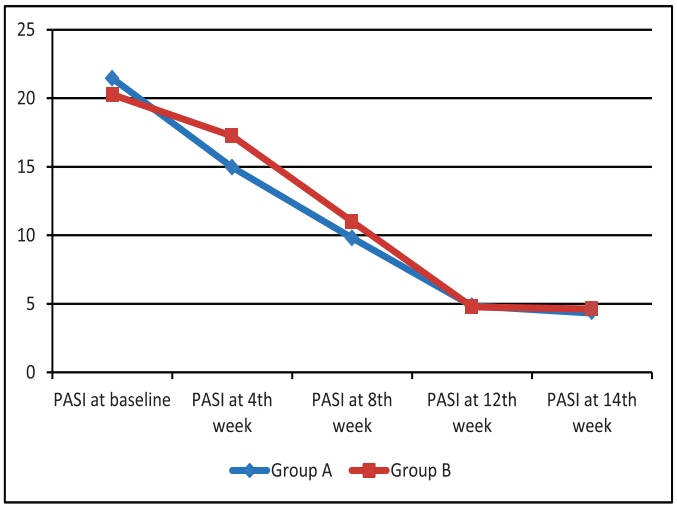

Figure-2: *Pasi Score at follow up*
Group-A = Narrow Band UVB
Group-B = Methotrexate

Table 3: *Efficacy n=60*

Efficacy(>50% PASI Reduction)	Treatment Group	
	Group-A n(%)	Group-B n(%)
Excellent (76-100%)	24(80%)	23(76.66%)
Good (50-75%)	6(20%)	7(23.34%)
Satisfactory (25-49%)	0	0
Poor (<25%)	0	0

Group-A = Narrow Band UVB
Group-B = Methotrexate
Chi-Square = 0.098
p-value = 0.754 (Insignificant: p-value >0.05)

Table 4: *Side Effects n=60*

Side Effects	Treatment Group	
	Group-A (NB UVB) n 30(%)	Group-B Methotrexate n 30(%)
Tanning	5(16.66%)	0
Erythema	4(13.33%)	0
Nausea	0	5(16.66%)
Deranged LFTs	0	1(3.33%)
Low TLC count	0	1(3.33%)
Any Other	0	0

Chi-Square test = 0.340
p-value = 0.559 (Insignificant: p-value >0.05)

Discussion:

Limited data available regarding comparison of the efficacy and safety and efficacy of NB UVB with systemic methotrexate till date. Different treatment options have been used for psoriasis. Among them methotrexate is used for decades while NB UVB is a relatively newer therapy. Studies carried out by different groups have shown that combination of systemic methotrexate plus NB UVB is more effective than that of NB UVB alone.[7,8]

Male to female ratio was 2.1:1 in our patients. Most of the literature reports the sex incidence to be almost equal. Studies from Pakistan have shown variable data.[9,10,11] This male preponderance is suppor-

ted by Indian studies.[12] The disparity between male and female was even more in group A where patients were required to visit the hospital thrice weekly. This may be due to our social constraints where most of the females cannot travel alone.

The mean age in group A and B was 38.93 (19-73) and 34.50 (17-65) years respectively which is comparable to other local and international studies.[9,10,13]

Both NB UVB and methotrexate are highly effective in the management of psoriasis. In group A (NB UVB) patients there was maximum reduction in mean PASI score during the first month of treatment while in group B (Methotrexate), it was seen during the second and third month of treatment. Since both therapies are almost equally effective at the end of study, the difference in their utility lies regarding the results required in a particular patient as certain situations demand early response. In such cases NB UVB is a better choice if facilities are available.

Mean percentage reduction in PASI was 79.07% in group 'A' at the end of treatment with NB UVB. It was effective in 100% of patients with excellent results (>75% reduction in PASI score) in 80% of patients which is comparable to study conducted by Chauhan SP et al, in which there was marked improvement (which is >75% reduction in PASI score) in 80.9% of the patients.[13] Mahajan R et al also found marked improvement in 70% of patients with NB UVB.[8]

Zulfiqar S et al compared twice weekly NB UVB with thrice weekly regime. They found >70% reduced PASI score in all the patients receiving thrice weekly NB UVB for 12 weeks. This is comparable with our study as we got >75% reduced PASI score in 80% of the patients.[14]

Dayal S et al found > 75% reduction in the PASI score in 100% of patients treated with NB UVB. This is in contrast with this current study in which there is > 75% reduced PASI score in 80% of the patients in group A. This difference may be due to the fact that mean PASI score at baseline (mean 21.45 ± 10.84 SD, range 9.20-5.40) in our study is higher than that of Dayal S et al (16.82 ± 3.90 SD, range 12.2 to 30.6).[15]

In group A, 5 patients (16.6%) developed tanning and 4 patients (13.33%) developed mild erythema. Tanning improves with passage of time in about 10 weeks.16 Erythema settled on its own by adjusting the dose and did not require any intervention. This was in accordance with the other local and international studies.[13,14,17]

The mean percentage reduction in PASI in group B was 78.50. MTX was effective in 100% of patients with >75% reduction seen in PASI score in 76.66% of patients which is comparable to results by Dogra S who found >75% reduction in the PASI score in 72% of patients given 10mg of MTX weekly. He observed >75% reduction in PASI score in 92.3% of patients given 25mg MTX weekly. Higher percentage reduction in this group is due to high weekly doses of methotrexate.18 Malik T et al found >75% reduced PASI score in 73% of patients with 10mg of methtrexate given for 8 weeks.[19]

Heydendael VMR et al and Sandhu K et al found >75% reduction in the PASI score in 100% of the patients. This difference is due to the difference in doses of MTX. 20, 21 Heydendael VMR et al started the treatment with 15mg of methotrexate weekly for 4 weeks and then increased the dose to 22.5 mg weekly while Sandhu K et al gave 0.5mg /kg of MTX weekly which is higher than the dose given in our patients.[20,21]

Karn D et al found >75% reduction in the PASI score in 57.57% of patients as compared to 76.66% of patients in our study.[22] This difference is due to the low dose of methotrexate (10mg) given to the patient by Karn D et al.

Side effects seen in group B were nausea, deranged LFTs and leukopenia. These were minor, transient and manageable. The side effects observed in our study were comparable to other local and international studies.[18,20,21]

Laboratory tests are mandatory while patient is on methotrexate. TLC and LFTs needs to be monitored

fortnightly. Vigilant monitoring of CBC is important during the initial weeks of therapy while LFTs monitoring becomes more significant in the later weeks.

NB UVB has quicker response as compared to methotrexate for the treatment of chronic plaque psoriasis. These two therapies were comparable as far as their safety profile was concerned. Side effects observed were minor, transient and were easily managed. Long term follow up is required to look for any carcinogenic and hepatotoxic effect with NB UVB and MTX respectively.

NB UVB has been used as an adjuvant therapy in the management of chronic plaque psoriasis.[4,5,7,8,23] Different studies have proved its efficacy as monotherapy.[13,14,17] It is a safe and effective mode of treatment where other topical or systemic therapies are ineffective or contraindicated (children, pregnancy, lactation, serious systemic, hepatic or cardiovascular diseases). As compared to methotrexate, use of NB UVB has limitations due to much more cost, logistics and availability of trained staff.

Conclusion:

Narrowband UVB is as good as methotrexate in the efficacy and safety in the management of chronic plaque psoriasis. Maximum improvement was seen with NB UVB during the first month of treatment while with methotrexate, it was seen in the 2nd and 3rd month of therapy. NB-UVB has less side effects as compared to methotrexate.

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Conflict of Interest: The authors declare no conflict of interest
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