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Original Research Article

"A COMPARATIVE STUDY OF ORAL METHOTREXATE AND COMBINATION OF ORAL METHOTREXATE AND NARROW BAND ULTRAVIOLET-B IN CHRONIC PLAQUE PSORIASIS"

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ABSTRACT:

Background: Psoriasis is a chronic common skin condition which alters the skin appearance, causes an inflammation in the outer epidermis, and proliferates the skin epidermal layers. It is influenced by both genomic and other external factors like environmental factors.

OBJECTIVES:

To know and compare the efficacy and safety of

1. Oral -Methotrexate alone.
2. Combination of both oral -Methotrexate and NBUVB for the treatment of chronic plaque psoriasis.

MATERIAL & METHODS: Study Design: Prospective hospital based observational study. **Study area:** The study was conducted in Department of Department of Dermatology, Narayana Medical College, Nellore, A.P. **Study Period:** 1 year. **Study population:** Patients of chronic plaque psoriasis not responding to any other therapeutic modality. **Sample size:** study consisted a total of 50 subjects. **Sampling method:** Simple Random sampling method. **Study tools and Data collection procedure:** Initially a detailed history regarding the age of onset, the duration of illness, past modalities of treatment, family history of the disease, seasonal variation, other triggering factors, occupation were taken. The patients were explained regarding the duration of treatment, the need for regular follow up of therapy, clinic and probable side effects that could be encountered during treatment. Complete haemogram, urine for albumin, sugar and microscopy, skin biopsy, blood sugar, liver function test, renal function test were done in all the patients before initiation of therapy and were done periodically to observe for any systemic involvement and the response to treatment was evaluated every week by PASI Score and also the patients were observed clinically for any cutaneous or systemic side effects.

Results: Among all (n=50 including group A and B, 25 of each) participants, relapse of treatment in weeks observed between the range of 6-12, mean was 9 with the standard deviation of 1.6 in group A. For group B relapse of medical regimen in weeks observed

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between the range 8-12, Mean was 10.5 with the standard deviation of 1.9 which is nearly similar in group A. This results were statistically significant as p= 0.01 where p<0.05.

CONCLUSION: From our study it, we concluded that Combination therapy of oral methotrexate and NBUVB is found to be most effective, feasible from the economic point of view as well as the side effects profile and patient compliance.

Keywords: Psoriasis; Methotrexate; NBUVB, PASI 75

INTRODUCTION:

Psoriasis is a chronic common skin condition which alters the skin appearance, causes an inflammation in the outer epidermis, and proliferates the skin epidermal layers. It is influenced by both genomic and other external factors like environmental factors.[1]The most common lesions are red, scaly, sharply demarcated plaques that appear primarily on extensor surfaces.[1] Psoriasis exhibits a chronic relapsing nature and variable clinical features. The cutaneous lesions are typically thus distinct for clinical diagnosis[1].Genetic defect and various triggering factors ex:- trauma, infections or by use of different medicines, may give rise to a psoriatic makeup in susceptible individuals[2].Psoriasis's history is as intriguing and troubling as the disease itself.

Despite extensive basic and clinical research, the exact reason why psoriasis occurs remains unknown. Almost every time, conceivable causative influence, such as microbiological, metabolic and immunologic influences has been implicated. However, proper evidence to support these facts aren't available.

Psoriasis with superficial tiny pustules on the surface is called pustular psoriasis. Overtreatment with topical tar, anthralin, steroids or systemic corticosteroids, foci of infection, pregnancy, and hypocalcaemia can all trigger it. The different types are a localised form of pustular psoriasis and a generalised form of pustular psoriasis.[3]

The treatment goal is to gain early and rapid control over disease processes, to get a longer interval of remission, to enhance better quality of life by reducing severity, and to minimize side effects. Treatment is chosen according to the patient's age, gender, occupation, personality, general health, and intelligence, extent, and time span of the disease[4]. Reassurance and emotional support are necessary measures.

Aminopterin, the first systemic folic acid antagonist, has been replaced for treating psoriasis by methotrexate, a stable analogue. Methotrexate kills cells during the S phase. It inhibits the enzyme dihydrofolatereductase, preventing tetrahydrofolate formation. This causes a significant disruption in cellular metabolism, ultimately leading to a stoppage in DNA synthesis and RNA synthesis. The medication can be administered orally, intramuscularly, or intravenously. The normal schedule consists of three consecutive doses of to 5 mg tablets taken orally 12 hours in a week. The basis for this triple dose schedule is that the psoriatic germinative cell cycle is shortened to 37.5 hours.

Anaemia, thrombocytopenia, leucopenia, active infection, peptic ulcer, ulcerative colitis, past or present alcoholism, pregnancy, lactation, and untrustworthy patient are all contraindications to therapy. Clinical response will be appreciated after a period of 3-4 weeks.

This combination was 1st demonstrated in 1982 by Paul et al.[5] An additive/synergistic therapeutic interaction between methotrexate and UVB may explain the increased

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productiveness of this combined protocol. According to Paul et al[5] study methotrexate has shown to reduce the scaliness and thickness of the lesions, thereby explaining the improved skin optics once NB-UVB is given. Both modalities might act through DNA synthesis and known to cause programmed cell death among the infiltrating lymphocytes in lesion, thus combination will result in synergistic action leading to faster recovery.

OBJECTIVES:

To know and compare the efficacy and safety of

1. Oral -Methotrexate alone.
2. Combination of both oral -Methotrexate and NBUVB for the treatment of chronic plaque psoriasis.

MATERIAL & METHODS:

Study Design: Prospective hospital based observational study.

Study area: The study was conducted in Department of Dermatology, Narayana Medical College, Nellore, A.P.

Study Period: 1 year.

Study population: Patients of chronic plaque psoriasis not responding to any other therapeutic modality.

Sample size: study consisted a total of 50 subjects.

Sampling method: Simple Random sampling method.

Inclusion criteria:

• Patients aged between 18 to 60 years.
• Both male and females.
• Patients willing for treatment, investigations and regular follow up have been included in this research after taking their informed consent.
• Patients with normal Liver function, Renal function, Hemogram and normal Chest ray.

Exclusion criteria:

• Pregnancy, Lactation, people who are < than 18.
• Currently planning to have children (both male and female patients)
• Liver dysfunction, Renal dysfunction, Chronic Alcoholism.
• Previous cutaneous malignancy.
• Patients with photosensitive disorders.
• Patients unsure about attending treatment schedule regularly.
• Patients who failed follow up after initial therapy.
• Patient with hypersensitivity to drug.
• Immuno compromised individuals and other comorbidities.

Ethical consideration: Institutional Ethical committee permission was taken prior to the commencement of the study.

Study tools and Data collection procedure:

Initially a detailed history regarding the age of onset, the duration of illness, past modalities of treatment, family history of the disease, seasonal variation, other triggering factors, occupation were taken. The patients were explained regarding the duration of treatment, the need for regular follow up of therapy, clinic and probable side effects that could be encountered during treatment.

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Complete haemogram, urine for albumin, sugar and microscopy, skin biopsy, blood sugar, liver function test, renal function test were done in all the patients before initiation of therapy and were done periodically to observe for any systemic involvement and the response to treatment was evaluated every week by PASI Score and also the patients were observed clinically for any cutaneous or systemic side effects.

Each group consisted of twenty-five patients. Group A was treated with Oral methotrexate, Group B with a combination of both oral methorexate and NBUVB. End point of treatment was PASI 75 or 12 weeks whichever was earlier.

Statistical analysis:

Data entry was done in Microsoft Excel software. Data analysis was done in Statistical Product and service solutions (SPSS). Continues variables were analysed by mean, standard deviation, median, mode, minimum and maximum. Qualitative variables were described by percentage distribution among groups. Comparison of quantitative variables was done by „t" test and qualitative variables were compared by Chi square test. P value of less than 0.05 was taken as level of significance.

OBSERVATIONS & RESULTS:

Total fifty (n=50) participants were enrolled for this research. Study participants were divided into two groups and they were 25 in numbers for each.

Table 1: Distribution of study participants with respect to their age group.

Sr. No.	Age Group (years)	Group A (Mtx)		Group B (Mtx + NBVUB)	
		Participants No.	Percentage	Participants No.	Percentage
1.	**≤ 30 years**	2	8	12	48
2.	**31 to 45 years**	18	72	10	40
3.	**46-60 years**	5	20	3	12
Total		**25**	**100**	**25**	**100**
Range		18-60 years		18-60 years	
Mean Age		35.46		33.5	
Standard Deviation		± 9.48		± 11.3	

Amongst all (n=50 including group A and B, 25 of each) participants, the participants were included from 18 years to 60 years for group A and age of eighteen years to 60 years for group B. Age of participants were made in group that is below the age of 30, 31-45 year and 46-60 years. In those groups, more number 72% (n=18) of participants were aged between 31 to 45 years for the group A. for group B also had majority of the participants from the age group 31 to 45 years and they were 40% (n=10). Only 8% (n=2) participants were aged up to thirty years in group A while in group B participants up to age 30 years were found to be

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48% (n=12). The mean age of the participant from the both group (A and B) were near about 33- 35 years.

Table 2: Distribution of study participants with respect to their gender.

Sr. No.		**Group A (Mtx)**		**Group B (Mtx + NBVUB)**	
	Gender	Participants No.	Percentage	Participants No.	Percentage
1	Male	18	72	20	80
2	Female	7	28	5	20
TOTAL		**25**	**100**	**25**	**100**

Among all (n=50 including group A and B, 25 of each) participants, the maximum number of males were observed in both the groups (A and B) they were 72% (n=18), 80% (n=20) respectively.

Table 3: Distribution of study participants according to occupational status.

Sr. No.		**Group A (Mtx)**		**Group B (Mtx+NBVUB)**	
	Occupational Status	Participants No.	Percentage	Participants No.	Percentage
1.	Coolie	3	12	5	20
2.	Farmer	13	52	8	32
3.	House wife	6	24	4	16
4.	Driver	0	0	5	20
5.	Business	2	8	3	12
6.	Student	1	4	0	0
TOTAL		**25**	**100**	**25**	**100**
Chi Square Test		**1.25**			

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Degree of freedom	**2**
p value	**0.046 (significant)**

Among all (n=50 including group A and B, 25 of each) participants, maximum number of participants were Farmers and they were 52% (n=13) and 32% (n=8) respectively for the group A and group B. Next to them House wives with the number of 24% (n=6) for group A and 20% (n=5) Drivers and same number of coolies were found in group B. only one i.e. 4 % participant was student from group A and 12% (n=3) participants were having business from study group B. no driver was included in group A as well as no one student observed in group B. This result was statistically significant as p= 0.046 where $p < 0.05$.

Table 4: Distribution of study participants according to aggravating factor that is seasonal variation.

Sr. No.	**Seasonal Variation**	**Group**	**A (Mtx)**	**Group B (Mtx+NBVUB)**	
		Participants No.	Percentage	Participants No.	Percentage
1	Yes	20	80	24	96
2	No	5	20	1	4
TOTAL		**25**	**100**	**25**	**100**
Chi Square Test			**3.65**		
Degree of freedom			**2**		
p value			**0.032**		

Among all (n=50 including group A and B, 25 of each) participants, the maximum 80% (n=20) and 96% (n=24) number of participants from group A and group B respectively had seasonal variation and these are considered as aggravating factor in study. one participant and five participants had no seasonal variation in the group A and B respectively. These results are significant statistically as p= 0.032 where $p < 0.05$.

Table 5: Distribution of study participants according to aggravating factor that is stress.

Sr. No.	**Stress**	**Group A (Mtx)**		**Group B (Mtx+NBVUB)**	
		Participants No.	Percentage	Participants No.	Percentage
1	Yes	16	64	15	60

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2	No	9	36	10	40
TOTAL		**25**	**100**	**25**	**100**
Chi Square Test			**0.56**		
Degree of freedom			**2**		
p value			**0.001**		

Among all (n=50 including group A and B, 25 of each) participants, the maximum 64% (n=16) and 60% (n=40) number of participants from group A and group B respectively had stress which is considered as aggravating factor in study. For group A, 36% (n=9) and for group B, 40% (n=10) participants has found with stress free. This results were statistically significant as p= 0.001 where $p < 0.05$.

Table 6: Distribution of study participants according to time taken for pasi 75 in weeks.

Sr. No.	**Groups**	**Time taken for pasi 75 in weeks**		
		Mean ± SD	**median**	**Range**
1.	**Group A (Mtx)**	**10.5 ± 0.9**	**10**	**9-12**
2.	**Group B (Mtx+NBVUB)**	**8.3 ± 0.7**	**8**	**7-9**
Student t test	**t ***	**45.21**		
	P	**0.001**		
Difference between group A versus B		**p < 0.01 (significant)**		

Among all (n=50 including group A and B, 25 of each) participants, time required for pasi 75 in weeks for group A had the range between 9-12, median was Ten, mean was 10.5 with the standard deviation 0.9. In group B time required for pasi 75 in weeks with the range 0f 7 to 9, having median 8, mean value is 8.3 with the standard deviation 0.7. This results were statistically significant as p= 0.01 where $p<0.05$.

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Table 7: Distribution of study participants according to their cumulative dose required for pasi 75.

Sr. No.	Groups	Cumulative Dose	
		Mean ± SD	**Range**
1.	**Group A (mg)**	**144.7 ± 16.6**	**127.5-172.5**
2.	**Group B (mg)**	**117.5 ± 9.9**	**97.5-127.5**
Student t test	**t ***	**7.70**	
	P	**0.001**	
Difference between group A versus B		**p < 0.01 (significant)**	

Among all (n=50 including group A and B, 25 of each) participants, the cumulative dose which was necessary for the participants were observed within range of 127.5-172.5 milligram, mean of those were 144.7 with standard deviation of 16.6 milligram in group A. For group B minimum cumulative dose were 97.5 mg to maximum of 127.5 mg, mean value is 117.5 with the standard deviation of 9.9, This results were statistically significant as p= 0.01 where p<0.05.

Table 8. Distribution of study participants according to their observed side effects on medication during study.

Sr. No.	Side Effects	Group A (Mtx)		Group B (Mtx+NBVUB)	
		Participants No.	Percentage	Participants No.	Percentage
1.	Erythema	0	0	4	16
2.	Headache	3	12	1	4
3.	Malaise	9	36	1	4
4.	Nausea	8	32	1	4
5.	Pruritus	0	0	1	4
6.	Nil	5	20	17	68
TOTAL		**25**	**100**	**25**	**100**

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Chi Square Test	**0.267**
Degree of freedom	**2**
p value	**0.006**

Among all (n=50 including group A and B, 25 of each) participants, In group A,maximum 36% (n=9) number of participants had Malaise. Next to them 32% (n=8) participants were felt Nausea. 12% (n= 3) participants had Headache. A few 20% (n=5) participants did not developed any side effects. None of participants showed Pruritus and Erythema.

For group B 68% (n= 17) participants does not developed any side effects while 16% (n=4) participants had Erythema. Headache, Malaise, Nausea and Pruritus those side effects were observed by only one participant with 4% for each. This results were statistically significant p=0.006 as p<0.05.

Table 9. Distribution of study participants according to their treatment relapse in weeks.

Sr. No.	**Groups**	**Relapse of treatment in weeks**	
		Mean ± SD	**Range**
1.	**Group A (Mtx)**	**9 ± 1.6**	**6-12**
2.	**Group B (Mtx+NBVUB)**	**10.5 ± 1.9**	**8-12**
Student t test	**t ***	**3.278**	
	P	**0.001**	
Difference between group A versus B		**p < 0.01 (significant)**	

Among all (n=50 including group A and B, 25 of each) participants, relapse of treatment in weeks observed between the range of 6-12, mean was 9 with the standard deviation of 1.6 in group A. For group B relapse of medical regimen in weeks observed between the range 8-12, Mean was 10.5 with the standard deviation of 1.9 which is nearly similar in group A. This results were statistically significant as p= 0.01 where p<0.05.

DISCUSSION:

In our study Patients of age between 18-60 years were included. In group A, 8% belonged to age < 30 years, 72% belonged to 31-45 years, 20% belonged to 46-60 years, while in group B, 48% belonged to < 30 years ,40% belonged to 31-45 years ,12% belonged to 46-60 years. The mean age of the participants from the both group (A and B) were nearly about 33-35 years. This type of age distribution is seen in similar study done by Faber et al[6].

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Among all participants, the maximum number of patients were males in both the groups (A and B) - 72% ,80% followed by females (A and B) -28%, 20% respectively[7], similar findings were seen in study conducted by Sharma Tet al al[7].

In our study, maximum number of participants were farmers by occupation (52% -group A and 32%- group B) followed by house wives (24% - group A and 16% -group B), Cooli (12% - group A and 20% group B), Business (8% -group A and 12% group B), Students (4 % - group A and 0% group B), Drivers (group A- 0 % and group B 20%). Similar findings were seen in study done by Bedi TR et al.[8,9]

In our study, 48% from group A had past medication history of taking allopathic drugs,while in group B it is 44%. 4% in group A while in group B 0% took ayurvedic medication. 20% in group A and 40% in group B took both medication (Allopathic and Ayurvedic), and 28% in group A and 44% in group B did not use any medication. Similar findings were seen in study done byKaur I, Kumar B. et al.[10]

In our study, 80% and 96% from group A and group B respectively had seasonal variation, while 20% in group A and 4% in group B had no seasonal variation, seen similarly in study done by HenselerT,Christophers E et al.[11]

In our study, group A (64%) and group B (60%) respectively had stress which is considered as aggravating factor in study, while 36% in group A and 40% in group B were stress free, such a finding was found in a similar study conducted by Hell E et al[12].

In our study, both the groups were observed for Pasi measurements at an interval of baseline,4 weeks and 8 weeks. In group A, mean value was 35.7 with standard deviation 6.8 at baseline. After 4 weeks the mean value was 36.8 with standard deviation 5.8 and mean value was 16.8 with standard deviation 4.4 after 8 weeks in group A. The pasi measurements for group B were mean value 36.6 with standard deviation 5.9 at baseline, mean 27.4 with standard deviation 4.6 after 4 weeks and mean 11 with standard deviation 3 after 8 weeks, similarly shown in Bischoff R, DeJong EM. [13]

In our study, the time required for pasi 75 in weeks was observed in both groups in which group B had a mean value of 8.4 ± 0.7 and group A had a mean value of 10.5 ± 0.9. These values correlated well with the study conducted by Paul BS et al .[5]

In our study, the cumulative dose required for the participants were observed between range of 127.5-172.5 milligram in group A, while for group B cumulative dose were 97.5 mg to 127.5 mg, similar findings were seen in study done by Paul et al[5].

In this research, relapse of treatment in weeks were observed between the range of 6-12 in group A, for group B relapse of treatment in weeks were observed between the range of 8-12, similar findings were seen in a study done by Dayal S, Mayanka,et al[14] Epstein E,et al[15].Asawanoda Pet al[16].

From our study we came to opinion that combined therapy (MTX+NBUVB) was better than monotherapy (MTX).

CONCLUSION:

From our study it, we concluded that Combination therapy of oral methotrexate and NBUVB is found to be most effective, feasible from the economic point of view as well as the side effects profile and patient compliance. Though there are wide range of modalities offered for the treatment of disease of the skin it is a challenge to treat chronic plaque psoriasis and depends on depth, nature and chronicity.

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