Original Article

Efficacy and Safety of Apremilast versus Methotrexate in the Treatment of Chronic Plaque Psoriasis

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Abstract

Introduction: Psoriasis is a common, chronic, inflammatory and proliferative disease of the skin, also affecting nail and joints. Although there are a range of treatment options available, none have proved to wane the symptoms fully and also they reappear in course of time.

Aim: To explore the safety and efficacy of Apremilast and Methotrexate on chronic plaque psoriasis patients.

Methods: A randomized open clinical trial was done among fifty clinically diagnosed chronic plaque psoriasis patients in the Department of Dermatology and Venereology at Combined Military Hospital (CMH), Dhaka from 1st July 2017 to 30th June 2018. Patients were divided randomly into two equal treatment groups, 25 for Methotrexate and 25 for Apremilast. Involvement of body surface by plaque psoriasis, erythema, scaling and induration were recorded in a 3 points scale before treatment and 8 weeks after starting the treatment and finally at 12th week.

Results: Reduction of psoriasis at 1st follow up in Methotrexate and Apremilast groups were 29.9±9.0 and 31.9±11.6 respectively and at 2nd follow up were 85.9±7.3 and 28.48±39.3 respectively. Significantly higher improvements were observed in Methotrexate group than Apremilast group both at 1st and 2nd follow up (p=0.001).

Conclusion: Methotrexate is a better therapeutic option than Apremilast in the treatment of chronic plaque psoriasis.

Key-words: Psoriasis, Methotrexate, Apremilast.

Introduction

Psoriasis may be regarded a substantial public heath challenge as, currently it is affecting approximately 125 million people globally[1]. Psoriasis is an inflammatory and proliferative condition of the skin which is chronic in nature and causes disfigurement of the affected part. Genetic and environmental factors- both are regarded as influencing factors to cause onset of this disease. The exact pathogenesis of psoriasis is unknown. The most typical characteristic lesions of this condition are red, scaly, sharply demarcated, indurated plaques. The disease is extensively variable in duration, periodicity of flares and extent. Morphological variants are also common[2]. Psoriasis are common in both sexes and may begin at any age, but it is uncommon under the age of 10 years. It is most likely to appear between the ages of 15 and 30 years[3].

Psoriasis is usually graded as mild (affecting less than 3% of the body), moderate (affecting 3-10% of the body) or severe. The Psoriasis Area Severity Index (PASI) is the most widely used measurement tool to assess severity of disease. PASI combines the assessment of the severity of lesions and the area affected into a single score in the range 0 (no disease) to 72 (maximal disease). Nevertheless, the PASI can be too unwieldy to use outside of trials, which has led to attempts to simplify the index for clinical use[4].

The management of psoriasis depends upon age, sex, occupation, personality, general health, intelligence and resources, as well as the type, extent, duration and natural history of the disease[5]. A broad spectrum of antipsoriatic treatments, both topical and systemic, is available for the management of psoriasis. When choosing a treatment regimen it is important to reconcile the extent and the measurable severity of the disease with the patient's own perception of his or her disease[6]. Moreover, the therapeutic options are continuously changing with the latest approval of new treatment choices for psoriasis[2]. Among the wide range of drugs available for the treatment we are principally focusing on Methotrexate and Apremilast. Methotrexate slows down the growth of skin cells and thus reduces the scale formation while Apremilast works through the immune system to moderate the inflammatory reactions[7,8].

Materials and Methods

A randomized open clinical trial was conducted among the patients who were clinically diagnosed with chronic plaque psoriasis from 1st July 2017 to 30th June 2018 at the Department of Dermatology and Venereology, CMH, Dhaka. By the method of simple random sampling 50 patients were selected who met the inclusion and exclusion criteria and divided into two groups. Twenty five patients were prescribed Methotrexate and 25 patients were prescribed Apremilast. Percentage of body surface area involved by plaque psoriasis, erythema, scaling and induration was recorded in a 3 point scale before treatment and evaluated after 8 weeks and 12 weeks giving Methotrexate and Apremilast. A representative area of psoriasis is selected for each body region. The intensity of redness, thickness and scaling of the psoriasis is assessed as none (0), mild (1), moderate (2), severe (3) or very severe (4).

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A predesigned structured questionnaire was used to record the clinical and follow up findings for each patient. Information were collected by taking clinical history and clinical examination and the data were analyzed with SPSS 16. The continuous data were expressed as mean ± SD and 't' test was used to calculate the difference in mean between two groups. The categorical data were expressed as frequency, proportion and percentage and the difference between groups was calculated by chi-square test. The level of significance was measured at <0.05 (P value).

Results

Table-I: Distribution of improvement scale after 8 weeks by group

Variable	Group			
	Improvement scale	**Group 1**	**Group 2**	**p value**
Scaling	Slight improvement	2 (8.0)	3 (12.0)	0.081
	Moderate improvement	13 (52.0)	19 (76)	
	Marked improvement	10 (40.0)	3 (12.0)	
Erythema	Slight improvement	2 (8.0)	2 (8.0)	0.999
	Moderate improvement	8(38.1)	7 (28.0)	
	Marked improvement	15 (42.9)	16 (64.0)	
Plaque	Slight improvement	3 (12.0)	5 (20.0)	0.014
	Moderate improvement	22 (88.0)	20 (80.0)	

Figure within parentheses indicates in percentage.

Group-1 = Methotrexate , Group-2= Apremilast

After 8 weeks of treatment, improvement of scaling was not significantly different between two groups (p=O.081), erythema was also improved significantly in both group 1 (p=O.999), plaque was improved significantly more in group 1 (p=0.014).

Table-II: Distribution of improvement scale after 12 weeks by group

Variable	Group			
	Improvement scale	Group 1	Group 2	p value
Scaling	Moderate improvement	5 (20.0)	8 (32.0)	0.027
	Marked improvement	7 (28.0)	10 (40.0)	
	Cleared	13 (52.0)	7 (28.0)	
Erythema	Worse	0 (0.0)	0 (0.0)	0.999
	Moderate	2 (8.0)	4(12.0)	
	Marked improvement	7 (28.0)	9(36.0)	
	Cleared	16 (64.0)	12 (48.0)	
Plaque	Moderate improvement	5 (20.0)	10 (40.0)	0.001
	Marked improvement	16 (64.0)	13 (52.0)	
	Cleared	4(12.0)	2 (8.0)	

Figure within parentheses indicates in percentage.

Group-1 = Methotrexate, Group-2 = Apremilast

After 12 weeks of treatment, improvement of scaling, erythema and plaque was significantly better is group 1 (p<0.05).

Table-III: Distribution of the patients by PASI

PASI	Group		p value
	Methotrexate (n=25)	Apremilast (n=25)	
Base line	6.9±4.8	11.9±2.8	0.001
1st follow up	4.9±3.5	8.0±1.9	0.001
Last follow up	0.8±0.4	7.9±3.4	0.001

*Fisher's Exact test was done to measure the level of significance.

Figure within parentheses indicates in percentage.

Table-III shows that the base line PASI in methotrexate and apremilast were 6.9±4.8 and 11.9±2.8 respectively. In 1st follow up PASI in Methotrexate and apremilast were 4.9±3.5 and 8.0±1.9 respectively and in last follow up PASI in methotrexate and apremilast were 0.8±0.4 and 7.9±3.4 respectively. Significant improvements were observed in methotrexate group both in baseline to 1st follow up and 2nd follow up (p<0.05).

Table-IV: Distribution of percent of improvement by group (Based on PASI)

Percent of improvement	Group		
	Methotrexate (n=25)	Apremilast (n=25)	p value*
Baseline to 1st follow up	29.9 ± 9.0	31.9 ±11.6	0.482
Baseline to 2nd follow up	85.9 ± 7.3	28.5 ± 39.3	0.001
1st follow up to 2nd follow up	78.2 ±15.0	16.2 ± 88.9	0.001

Note: Data was shown as Mean ± SD.

Table-IV shows that the percent of improvement in baseline to 1st follow up in methotrexate and apremilast were 29.9±9.0 and 31.9±11.6 respectively. In baseline to 2nd follow up percent of improvement in methotrexate and apremilast were 85.9±7.3 and 28.5±39.3 respectively and in 1st follow up to 2nd follow up the percent of improvement in methotrexate and apremilast were 78.2±15.0 and 16.2±88.9 respectively. Significant improvements were observed in methotrexate group both in baseline to 2nd follow up and 1st follow up to 2nd follow up (p<0.05).

Side effects: Side effects observed were more in patients treated with apremilast as compaired to patients treated with methotrexate. Headache, upper respiratory tract infections and mood disorder were more observed in apremilast group. Patients treated with methotrexate were more complained of nausea, vomiting and abdomianl discomfort.

Discussion

The present study showed that the base line PASI in methotrexate and apremilast were 6.9±4.8 and 11.9±2.8 respectively. In 1st follow up PASI in methotrexate and apremilast were 4.9±3.5 and 8.0±1.9 respectively and in last follow up PASI in methotrexate and apremilast were 0.8±0.4 and 7.9±3.4 respectively. Significant improvements were observed in methotrexate group both in baseline to 1st follow up and 2nd follow up (p<0.05) and the percent improvement from baseline to 1st follow up in methotrexate and apremilast groups were 29.9±9.0 and 31.9±11.6 respectively. From baseline to 2nd follow up the percent improvement in methotrexate and apremilast were 85.9±7.3 and 28.5±39.3 respectively and in 1st follow up to 2nd follow up the percent of improvement in methotrexate and apremilast were 78.2±15.0 and 16.2±88.9 respectively. Significant improvements were observed in Methotrexate group both in baseline to 1st follow up and 2nd follow up.

Armstrong et al found in their study that, there was no statistical evidence of greater efficacy for apremilast versus methotrexate[9]. Although a similar study conducted by Shetty VH et al with seventy patients above 18 years of age with chronic plaque psoriasis who

were divided into two equal groups of 35 patients and were treated with oral apremilast and oral methotrexate and were evaluated every 4 weeks for a period of 16 weeks and followed-up at 24th week. Outcome was assessed on the basis of psoriasis area-and-severity index score (PASI), psoriasis disability index (PDI) and clinical photographs. At the 16 weeks follow up the PASI score in methotrexate group was statistically significant ($p<0.05$) as compared to apremilast group[10]. Side effects were also observed and found that side effects are comparatively less common in methotrexate group patients. Thus the study concludes that, methotrexate was comparatively better tolerated and had better efficacy and safety over apremilast.

Conclusion

Psoriasis is a common, chronic and recurring skin disorder. It is a life-long disease which requires long standing treatment regimen. The long-term use of systemic drug is some how challenging and thus requires better efficacy with a single option. Among the wide range of therapeutic options available for the treatment of psoriasis, this study compares the efficacy of methotrexate and apremilast and found that, methotrexate was comparatively better tolerated and had better efficacy and safety than apremilast.

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