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RESEARCH ARTICLE
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COMPARISON OF EFFICACY OF METHOTREXATE VS APREMILAST IN MODERATE TO SEVERE PLAQUE PSORIASIS

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ABSTRACT

Background and Aim: Psoriasis is a chronic relapsing skin condition that can significantly affect mental and physical well-being. Due to its persistence, the use of equally safe and effective medications as a long-term treatment is necessary. The current study aimed to analyze the efficacy of methotrexate and apremilast in the treatment of moderate to severe plaque psoriasis focusing on their effectiveness, safety, and patient satisfaction, at a Tertiary Care Hospital in Karachi.

Study Design: Randomized controlled trial

Materials and Methods: This randomized controlled trial was carried out on 60 cases of plaque psoriasis in the Department of Dermatology, Jinnah Postgraduate Medical Centre (JPMC), Karachi from March 2024 to August 2024. Patients aged 18-60 years of either gender with moderate to severe plaque psoriasis were enrolled and randomly allocated to two groups. Group I (n=30); were treated with methotrexate, given 7.5 mg once a week orally. Group II (n=30); were given apremilast with an initial oral dose of 10 mg and gradually increasing to 30mg twice daily. Each patient underwent careful history taking, general examination, and complete dermatological examination using the PASI score as a baseline evaluation test.

Results: Mean age of patients was 40.64±11.5 years. Among 60 patients, there were 27 (45%) male and 33 (55%) female. The mean age of group I and group II were 40.19±11.79 and 41.09±11.21 years, respectively. The mean value of disease duration in Group I and II was 2.9±0.9 years and 3.1±1.2 years, respectively. Mean Psoriasis Area and Severity Index (PASI) score of Group I and II at baseline, six weeks, twelve weeks (3 months), and Twenty-four weeks (6 months) follow up was 24.42±7.98 and 23.86±6.21, 20.46±6.76 and 19.34±5.48, 14.89±4.86 and 12.78±3.98, and 11.68±6.52 and 8.98±5.21, respectively. Apremilast showed more effective results in treating moderate to severe plaque psoriasis than Methotrexate. The percentage reduction of score in Group I and II was 52% and 58%, respectively. There were minimum adverse effects observed in both groups.

Conclusion: Our findings show that both drugs are effective in reducing the psoriasis severity in terms of Psoriasis Area Severity Index (PASI) score. Apremilast showed overall more effective improvement in PASI scores, indicating its better outcomes in terms of effectiveness and significantly better safety with fewer adverse effects as compared Methotrexate.

Keywords: Plaque psoriasis, Methotrexate, Apremilast, Efficacy

INTRODUCTION

Psoriasis is a chronic, autoimmune, inflammatory skin disorder that involves hyperproliferation of the keratinocytes in the epidermis, with an increase in the epidermal cell turnover rate up to 10 times faster. This causes the skin to build up into bumpy patches. In Europe and the United States, the prevalence of psoriasis is between 2 and 3%, while studies in Asia shows a prevalence of 0.47% [1, 2]. The psoriasis etiology involving both environmental and genetic factors are poorly understood [3]. Emotional and psychological stress can prompt the onset and progression of psoriasis [4]. Phototherapy, salicylic acid, methotrexate, corticosteroids, retinoids, and vitamin D are different treatment modalities for psoriasis [5]. Psoriasis can be classified into different types according to location and appearance; however, the most commonly presented plaque psoriasis appears on scalp, elbows, lower back, and knees are itchy, dry, and scales covering the raised skin pitches. Psoriasis Area and Severity Index (PASI), a tool for measuring the extent and severity of psoriasis by calculating the area and intensity of body covered with disease and can be categorized into four different categories; 0 (none), 1 (mild), 2 (moderate), 3 (severe), and 4 (extremely severe).

The prevalence of psoriasis was 2.6% reported in earlier study. According to their observations, safety in treating psoriasis is particular importance to avoid comorbidities such as major depression, myocardial infarction, diabetes mellitus, and coronary artery disease found in 16.5%, 7.5%, 16.5%, and 8.4% respectively [6]. Earlier study reported that regardless of age and sex, chronic plaque psoriasis and clinical process a commonly seen (63.2%). Drugs commonly used for psoriasis, such as methotrexate, cyclosporine, and acitretin, are associated with organ toxicity and other side effects [7]. Biological drugs, although effective, have complications associated with cost, immunity, and of inconvenient administration. Thus, psoriasis could be managed by affordable treatment with less toxicity and had lower side effects [8]. Psoriasis is considered severe if it covers more than 10% of the body and if it covers 3–10 % on the slope [9, 10]. Methotrexate is generally considered the first-line treatment for chronic plaque psoriasis due to its low cost and ease of oral administration. Biological therapy and other systemic therapies, although highly effective, it is highly expensive and has the additional disadvantage of complex delivery mechanisms [11]. Considering the cost, efficacy, and good safety profile, apremilast may provide a safe, first-line solution for patients with psoriasis, which can rapidly reduce symptoms and improve disease prevention in psoriasis patients. Therefore, the present study was carried out to measure the efficacy of methotrexate and apremilast in the treatment of moderate to severe plaque psoriasis focusing on their effectiveness, safety, and patient satisfaction, at a Tertiary Care Hospital in Karachi.

METHODOLOGY

This randomized controlled trial was carried out on 60 cases of plaque psoriasis in the Department of Dermatology, Jinnah Postgraduate Medical Centre (JPMC), Karachi from March 2024 to August 2024. Patients aged 18-60 years of either gender with moderate to severe plaque psoriasis were enrolled and randomly allocated to two groups. Group I (n=30); were treated with methotrexate, given 7.5 mg once a week orally. Group II (n=30); were given apremilast with an initial oral dose of 10 mg and gradually increasing to 30mg twice daily. All patients gave informed consent before participating in the study. Individuals with pre-existing hepatotoxicity, blood disorders; those taking antiplatelet agents, anticoagulants, or iron supplements; those with any heart disease in the past six months; those who had radiotherapy for psoriasis; those who had received psoriasis medications in the past six months; who have used topical medications for psoriasis in the past two weeks; prolonged exposure to sunlight; pregnant or lactating were excluded. The scoring criteria to be included in the study was Psoriasis Area and Severity Index (PASI) score ≥ 12, affected body surface area ≥ 10%, and static Physician Global Assessment (PGA) score ≥ 2. Only patients with plaque psoriasis with moderate to severe intensity were included and lesional photography for each patient before the start of treatment was taken. The outcome of treatment was assessed using the same evaluation tool used at baseline and follow-up six weeks, twelve weeks (three months), Twenty-four weeks (six month) by comparing the PASI scores. Each patient underwent careful history taking, general examination, and complete dermatological examination using the PASI score as a baseline evaluation test.

Descriptive statistics was done using SPSS Version 23. Numerical variables such as age, disease duration, PASI score, and body mass index were expressed as mean and standard deviation whereas categorical variables such as gender, efficacy, outcomes, and side effects were described as frequency and percentages. Outcomes such as PASI score and efficacy were stratified for age, gender, and disease duration to see effect modifier. Post-stratification Chi-square test was done to compare both groups. P-value of ≤ 0.05 considered as statistically significant.

RESULTS

Mean age of patients was 40.64±11.5 years. The mean age of group I and group II were 40.19±11.79 and 41.09±11.21 years, respectively. Among 60 patients, there were 27 (45%) male and 33 (55%) female. The mean value of disease duration in Group I and II was 2.9±0.9 years and 3.1±1.2 years, respectively. Mean Psoriasis Area and Severity Index (PASI) score of Group I and II at baseline, six weeks, twelve weeks (3 months), and Twenty-four weeks (6 months) follow up was 24.42±7.98 and 23.86±6.21, 20.46±6.76 and 19.34±5.48, 14.89±4.86 and 12.78±3.98, and 11.68±6.52 and 8.98±5.21, respectively. Apremilast showed more effective results in treating moderate to severe plaque psoriasis than Methotrexate. The percentage reduction of score in Group I and II was 52% and 58 %, respectively. There were minimum adverse effects observed in both groups. Table-I represents the demographic and baseline details of patients. PASI score calculated for both groups at baseline and follow-up (six months) represented in Figure-1. The efficacy achieved in Group I and II was 11 (36.7%) and 14 (46.7%), respectively as shown in Table-II. Statistical analysis showed no significant difference between the two groups, as indicated by a p-value less than 0.005. Table-III represent the safety profile of patients.

Table-I Demographic and baseline details of patients (N=60)

Variables	**Group-I (Methotrexate) N=30**	**Group-II (Apremilast) N=30**	**Overall (Mean ± SD) N (%)**
Age (years)	40.19±11.79	41.09±11.21	40.64±11.5
Gender			
Male	14 (46.7%)	13 (43.3%)	27 (45%)
Female	16 (53.3%)	17 (56.7%)	33 (55%)
Disease duration (years)	2.9±0.9	3.1±1.2	3.0±1.1

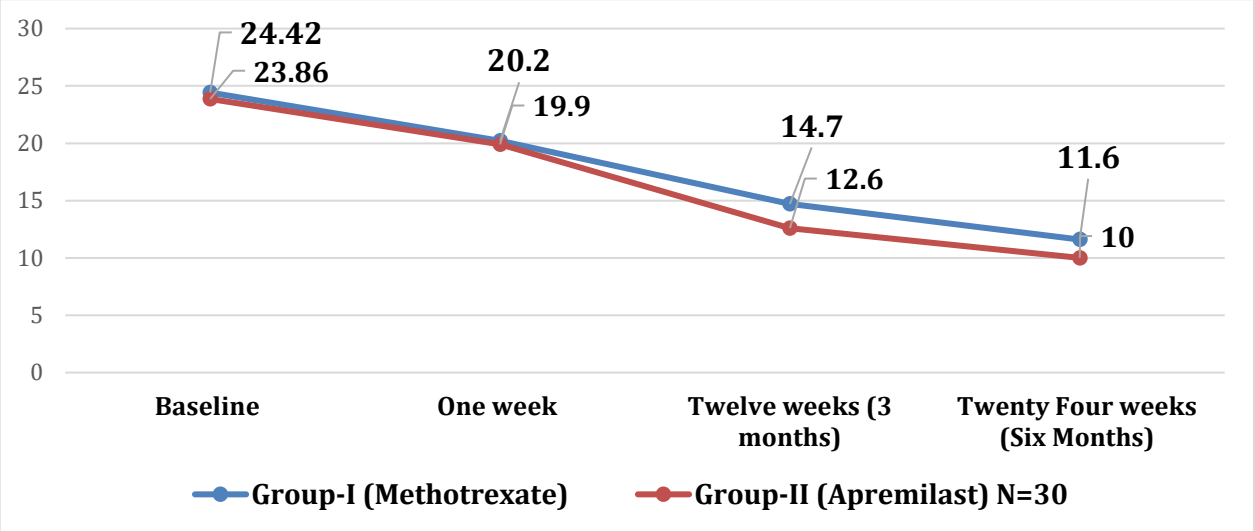

Figure-1 Comparison of PASI score calculated for both groups at baseline and follow-up (6th months)

Table-II Comparison of efficacy in both groups (N=60)

Efficacy	Group-I (Methotrexate) N=30	Group-II (Apremilast) N=30
Yes	11 (36.7%)	14 (46.7%),
No	19 (63.3%)	16 (53.3%)

Table-III Comparison of safety profile in both groups (N=60)

Side effects	Group-I (Methotrexate) N=30	Group-II (Apremilast) N=30
Diarrhea	-	2 (6.7%)
Nauseas	3 (10%)	-
Stomatitis	1 (3.3%)	-
Infection	-	1 (3.3%)
Headache	-	1 (3.3%)

DISCUSSION

The present study mainly compared the efficacy of methotrexate with apremliast in moderate to severe plaque psoriasis and reported that both drugs shown promising results in treatment of plaque psoriasis. Apremilast showed a rapid improvement in PASI scores, indicating that it is strongly active during the treatment and had significantly better safety with fewer adverse effects. Psoriasis is a chronic and relapsing skin condition that greatly affects quality of life. There are many treatment options available for psoriasis. For patients with psoriasis, any new treatment is a blessing. Treatments are available, including topical therapy in mild cases, moderate to severe systemic therapy, including methotrexate, acitretin, cyclosporine, apremilast, and biologics. In addition, combinations used based on short-term considerations, utility treatment, safety profile, severity of disease, and patient quality of life [12].

A review of large studies revealed that the average age of onset of psoriasis was 28 [13, 14]. In contrast, another study reported that age onset was 33 years, and 75% of patients developed psoriasis before age 46 [15]. Methotrexate used as treatment modalities results in 50% reduction in psoriasis severity in >75% patients. Earlier studies found that patients taking methotrexate often report mouth ulcers and gastrointestinal disorders caused by folic acid deficiency [16, 17]. Folic acid drugs administrated on methotrexate-free days to mitigate the side effects, which leads to gastrointestinal intolerance in limited patients. Others who suggested participating in follow-up studies demonstrating efficacy with long-term low-dose methotrexate without adverse effects [18].

Safety assessment of two-phase randomized trials by Ohtsuki et al. [19] reported a patient withdrawal rate of 11.2%. Only one patient (0.9%) without psychiatric history reported depressive symptoms three weeks after starting apremilast, whereas Armstrong et al. [20] reported that gastrointestinal side effects such as nausea, vomiting and headache occurred mostly during the first two to three weeks of treatment and subsequently decreased by the end of four weeks.

Yan et al. reported that there was no statistical significance in the efficacy of methotrexate and apremilast [21]. Another study revealed that seventy patients over 18 years of age with chronic plaque psoriasis were divided into equal groups of 35 patients each, who received either oral apremilast or methotrexate. They were monitored every 4 weeks for 16 weeks, at 24 weeks and follow-up. Adverse effects were also observed, with fewer reported in the methotrexate group. The study concluded that compared with apremilast, methotrexate was better tolerated and showed superior efficacy and safety [22].

The frequency of adverse events, the proportion of patients who discontinued treatment, and the time to observation of adverse events were similar among treatment groups. The most common adverse effects associated with apremilast were gastrointestinal events, such as gastroenteritis, gastrointestinal upset, nausea, vomiting, and dehydration. The frequency of these common adverse events in the apremilast group was with literature antacids, anticoagulants, or additives such as dietary advice eased, without the need to discontinue or change around therapy. In addition, two patients in our study experienced photosensitivity during the first 2 weeks of treatment with apremilast [23]. Another study

of the actual efficacy of apremilast in psoriasis also found that fever (5.6%) was the most common adverse event leading to treatment discontinuation [24].

CONCLUSION

Both Methotrexate and Apremilast shows that's they are effective in reducing the psoriasis severity in terms of Psoriasis Area Severity Index (PASI) score. Apremilast showed overall more effective improvement in PASI scores, indicating its better outcomes in terms of activeness and significantly better safety with fewer adverse effects as compared Methotrexate.

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