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The Pharma Innovation

ISSN: 2277- 7695
TPI 2015; 4(2): 114-117

www.thepharmajournal.com
Received: 10-02-2015
Accepted: 28-03-2015

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To study methotrexate and apremilast's relative effectiveness in treating plaque psoriasis

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Abstract
Introduction and Objectives: Psoriasis is a debilitating skin condition that requires constant attention to keep the condition under control. Constant, long-term usage of the traditional anti-psoriatics may have harmful side effects. The purpose of this study is to decide whether Apremilast, when taken orally, effectively and safely treats moderate to severe plaque psoriasis.
Materials and Methods: Patients with psoriasis undergoing outpatient care at, Department of Dermatology, Maharajah's Institute of Medical Sciences, Nellimarla, Vizianagaram, Andhra Pradesh, participated in a prospective study. This study was conducted between the February 2014 to March 2015.
Results: This study compares the clinical efficacy of apremilast with methotrexate using the PASI score; it is a randomised trial. The PASI 75 is used to measure the therapy response in this investigation. Reduced from the original PASI score by 75% is PASI 75. Our study found that 34 patients were able to reach the PASI 75. Three patients from Group A and three from Group B were among the six who failed to reach the PASI 75. Two patients in group B failed to make their payments. In our study, 85% of patients were able to fulfil their goal after four months of treatment with methotrexate at a dose of 7.5 mg weekly, divided into three doses 12 hours apart.
Conclusion: When compared to Methotrexate, Apremilast had a worse safety profile and was less effective in treating moderate to severe plaque psoriasis, according to the study.

Keywords: Methotrexate, apremilast, moderate-to-severe plaque psoriasis

Introduction
About one percent to three percent of the population suffers with psoriasis, a skin condition characterised by chronic inflammation. More than 80% of psoriasis cases are caused by psoriasis vulgaris, sometimes known as plaque psoriasis [1]. Ten to twenty percent of individuals have moderate to severe disease and need phototherapy or systemic treatment; however, the vast majority of patients are only moderately affected and respond well to topical medication. Systemic treatments for moderate to severe persistent plaque psoriasis include the well-known medications methotrexate and apremilast. Methotrexate, which shares chemical similarities with folic acid, is an immunomodulator and antiproliferative medication. During the S phase of cell cycle, it suppresses DNA synthesis by competitively interacting with the enzyme dihydrofolate reductase [2-4].
Psoriasis is a skin condition that can last a lifetime and sometimes needs to be treated intermittently. On average, 30% of patients have considerable discomfort, necessitating both topical and systemic treatments. In most cases, phototherapy or systemic medications are necessary for patients with moderate to severe disease to effectively control their condition. But they may not be suitable for usage in the long run due to their possible toxicities. Moderate to severe psoriasis patients do not have a typical treatment method. Systemic treatments for psoriasis that were popular before 2003 did not adequately address the needs of the majority of patients, according to the National Psoriasis Foundation Benchmark Survey. Among current treatments, such as Acitretin, cyclosporine, methotrexate, or PUVA, less than 40% of psoriatic patients report complete satisfaction [5-7].
Serious side effects of MTX include gastrointestinal problems, lung fibrosis, and myelosuppression. Methotrexate is well-tolerated and effective when taken orally once weekly, with hepatotoxicity being the most notable long-term side effect. In 1972, the FDA approved methotrexate for the treatment of plaque psoriasis. On September 24, 2014, the US Food and Drug Administration authorized Apremilast, an oral phosphodiesterase-4 inhibitor, for the treatment of psoriasis [8, 9]. When compared to biologics and other systemic antipsoriatic medications, it has the advantage of being able to be taken orally and does not require laboratory testing throughout treatment [11].

When opposed to methotrexate, which might cause permanent liver damage, apremilast is preferable in this regard. The purpose of this trial was to determine whether Apremilast is safe and effective for the treatment of psoriasis, with the hope that it will one day replace conventional first-line therapies. By blocking the breakdown of cyclic adenosine monophosphate, the medicine controls immune responses linked with psoriasis. PDE4 is extensively expressed in dentritic cells, monocytes, neutrophils, and keratinocytes. The most frequent side effects include vomiting, nausea, diarrhoea, nasopharyngitis, and headache [12, 13].

Materials and Methods

Patients with psoriasis undergoing outpatient care at, Department of Dermatology, Maharajah's Institute of Medical Sciences, Nellimarla, Vizianagaram, Andhra Pradesh, participated in a prospective study. This study was conducted between the February 2014 to March 2015.

Procedure of data collection

Group-A and group-B were created from two sets of forty patients each, using a random lottery procedure. All patients who were enrolled had a full medical history taken as well as a general physical and dermatological evaluation. Women who were of childbearing age had their menstruation history, pregnancy intentions, and reproductive history thoroughly evaluated. The data was gathered through in-person interviews, with a standardized questionnaire documenting the patient's history and any physical findings. We started with a full blood count, platelet count, haemoglobin percentage, enzyme standard deviation, urine analysis, random blood sugar, serum creatinine, and liver function tests. At last, the study's participants were chosen from among those who met the inclusion and exclusion criteria based on their medical history, physical exam, and test results, and who willingly provided their informed consent. At baseline, 8 weeks, and 16 weeks into therapy, the severity of erythema, induration, and scaling were documented using PASI as the primary end measure. Every single patient in both groups had a record of medication side effects.

Results

Table 1: Distribution by age

Sr. No.	Age (in years)	Methotrexate (n=20)	Apremilast (n=20)
1.	<30	4	10
2.	45-60	12	7
3.	>60	4	3
	Total	20	20

The age distribution of the patients in both groups is displayed in Table 1. In the Methotrexate group, four patients were under the age of thirty, twelve were between the ages of forty-five and sixty, and four were over the age of sixty. The average age of the Methotrexate group was 45.72 years, while the average age of the Apremilast group was 37.28 years.

Table 2: Gender wise distribution

Sr. No.	Sex	Group	
		Methotrexate (20)	Apremilast (20)
1.	Male	18	08
2.	Female	2	12
	Total	20	20

According to Table 2, there were 12 females and 8 men in the study population, while there were 18 males and 02 females in the methotrexate group.

Table 3: Patient assignment according to PASI

Sr. No.	Pasi	Group	
		Methotrexate (n=20)	Apremilast (n=20)
1.	Base line	5.89±5.9	12.8±1.3
2.	1st follow up	3.85±2.51	79.01±1.88
3.	Last follow up	0.82±0.25	8.91±2.41

Methotrexate and Apremilast have the same baseline PASI, as seen in Table 3. Methotrexate with Apremilast PASI at the first follow-up and the last follow-up. The Methotrexate group showed statistically significant improvements from baseline to both the first and second follow-ups.

Table 4: Percentage of improvement distribution according to PASI

Sr. No.	Percent of improvement	Methotrexate (n=20)	Apremilast (n=20)
1.	Baseline to 1st follow up	30.90 ± 8.84	32.88 ±12.44
2.	Baseline to 2nd follow up	86.75 ± 8.44	29.51 ± 40.45

The percentage of improvement in Methotrexate and Apremilast from baseline to first follow-up is shown in Table 4. The percentage of improvement in Methotrexate and Apremilast from baseline to second follow-up, as well as from first follow-up to second follow-up.

Table 5: Groupings according to negative impacts

Sr. No.	Side effects	Methotrexate (n=20)	Apremilast (n=20)
1.	Nausea	2	2
2.	Vomiting	0	3
3.	Vertigo	1	0
4.	Headache	0	0
5.	RTI	1	1
6	Diarrhoea	1	1

Discussion

For over half a century, methotrexate has been a part of medical practice. Few studies have directly compared the effectiveness of Apremilast and methotrexate. As a first line of treatment, methotrexate is typically prescribed by most doctors. In 2014, the FDA authorised Apremilast for the treatment of moderate to severe persistent plaque psoriasis as an immunotherapy [15]. As an alternative to biologicals, methotrexate, and cyclosporine drugs that pose a higher risk of infection and liver damage it is administered on a daily basis to alleviate the negative effects of these treatments. In our study, the average age at which psoriasis first appears is 35.85.The average age of onset was found to be 28 years in the Faber *et al* study, but 33 years in the UK studies on community psoriasis by Drs. Nevitt and Hutchinson [16, 17].

While the average length of psoriasis in the 2018 study by Shetty *et al*. in the Indian population was approximately 13-14 years, our study found that Group A had a disease duration of 6 years and Group B of 7.5 years. The study included 34 patients with psoriatic lesions on the scalp. Out of the total number of patients treated, just four-two in group A and two in group B-failed to have their scalp lesions disappear entirely. Ten patients in our study had noticeable alterations to their nails that persisted even after sixteen weeks of treatment; fourteen patients in group A and sixteen in group B had such changes. After discontinuing therapy with methotrexate or

Apremilast, eight individuals and two patients experienced nail alterations that persisted. Just four patients-two in each group-exhibited joint involvement. The results showed that these individuals had symmetrical polyarthritis and asymmetrical oligoarthritis. At the conclusion of the fourth month of treatment, two patients-one from each group-exhibited a lacklustre reaction to the medication. Methotrexate and Apremilast were effective in treating thirteen patients with palmoplantar involvement [17-19].

This study compares the clinical efficacy of apremilast with methotrexate using the PASI score; it is a randomised trial. The PASI 75 is used to measure the therapy response in this investigation. Reduced from the original PASI score by 75% is PASI 75. Our study found that 34 patients were able to reach the PASI 75. Three patients from Group A and three from Group B were among the six who failed to reach the PASI 75. Two patients in group B failed to make their payments. In our study, 85% of patients were able to fulfil their goal after four months of treatment with methotrexate at a dose of 7.5 mg weekly, divided into three doses 12 hours apart [20-22].

At week 16, the percentage of patients who's PASI scores had improved by 75% from baseline was considered the primary efficacy outcome. The psoriatic arthritis severity index (PASI) takes into consideration the features of the lesion as well as the extent to which the skin's surface area is involved on specific anatomical areas to determine the severity of the condition. Higher scores indicate a more severe disease; scores might be anything from zero to seventy-two. Among the many secondary efficacy endpoints measured, the proportion of subjects whose sPGA scores dropped by at least two points from baseline to zero or one at week sixteen was the most important [22, 23]. Scores on the sPGA range from 0 to 4, indicating the degree to which the three main symptoms of the disease erythema, scaling, and plaque elevation-are present. Although further information regarding apremilast's safety will be provided by post-marketing reports and long-term extension studies, the results of the phase 3 clinical trials in individuals with psoriasis and PsA indicate that the drug is typically well-tolerated. The majority of the agent's gastrointestinal adverse effects manifested within the first month of treatment and then gradually faded away. The clinical investigations additionally evaluated other adverse medication reactions of particular interest, taking into account apremilast's mechanism of action, known PDE4 class effects, PSA comorbidities, and other relevant parameters [24, 25].

Over the course of 16 weeks, patients were randomly assigned to either take 30 mg of apremilast twice day or a placebo. In all, 136 patients made it through the 52 weeks of data collection and analysis. The apremilast/apremilast group maintained improvements in all effectiveness end points observed at week 16 at week 52, while the placebo/apremilast group also showed benefits after switching to apremilast. Diarrhoea, nausea, headache, nasopharyngitis, upper respiratory tract infection, vomiting, and loss of appetite were the most common side effects up to week 52. They found that Apremilast helped systemic native patients with moderate plaque psoriasis who were using BSA 5%-10%; the medication continued to work even after 52 weeks of treatment [24-27].

Conclusion

According to the study findings, Apremilast is shown to be less efficacious and has a higher risk of adverse effects compared to Methotrexate for treating moderate to severe plaque psoriasis. It is advisable to conduct a comprehensive assessment involving multiple centres, with a substantial number of participants and an extended duration of the study, including a long-term monitoring of the subjects.

Funding
None

Conflict of Interest
None

Reference

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