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To study comparing the effectiveness of methotrexate and apremilast in the treatment of severe to moderate plaque psoriasis

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Abstract
Background and Objective: One percent to three percent of the population suffers with psoriasis, a chronic inflammatory skin disease. Patients with moderate to severe plaque psoriasis who visit the dermatology outpatient department will be compared to those who take Apremilast daily to those who take Methotrexate weekly.
Material and Methods: This comparative study included 60 patients who had been diagnosed with moderate-to-severe plaque psoriasis. The research took place from December 2017 through November 2018 at Narayana Medical College's Department of Dermatology in Chintareddypalem, Nellore, Andhra Pradesh, India. The psoriasis area and severity index were used to evaluate the severity of the condition, while the clinical examination was used to establish the diagnosis. Methotrexate was given to 30 patients in Group A, and Apremilast was given to 30 patients in Group B. The patients were randomly assigned to these groups. At baseline (0 months), as well as in the first, second, and fourth months of treatment, PASI scores were documented. Decreases in PASI scores over time were the main results.
Results: After one month, a substantial decrease in PASI scores was observed in 16 out of 18 patients in Group B with baseline scores more than 25, while only 14 out of 15 patients in Group A exhibited improvement. In Group A, 12 out of 15 patients had even lower PASI scores by the end of the second month. Ten of the twelve patients still alive in Group A attained a PASI 50 reaction by the fourth month, whereas fourteen of sixteen patients in Group B attained a PASI 75 response. Two individuals in Group A needed a higher dosage of Methotrexate to get a PASI 75 response.
Conclusion: Apremilast outperformed Methotrexate in terms of obtaining PASI 75 at the fourth month. If patients are monitored regularly for adverse effects, methotrexate is still a feasible and cost-effective therapeutic choice. If a patient does not get the best possible reduction in PASI with the usual Methotrexate dosage, it may be essential to increase the dosage.

Keywords: Plaque psoriasis, apremilast, methotrexate, PASI, comparative efficacy

Introduction

The prevalence of psoriasis, an inflammatory skin illness caused by the immune system, ranges from one percent to three percent of the world's population. Rapid keratinocyte turnover causes erythematous, scaly plaques that define the condition. Plaque psoriasis, often called psoriasis vulgaris, is the most common form of the skin condition, making up about 80% of all cases. Physical pain, emotional anguish, and an increased likelihood of co-occurring conditions like metabolic syndrome, cardiovascular disease, and psoriatic arthritis all have a negative effect on quality of life [1-3].

Although Methotrexate is effective, it is important to closely monitor patients because of the potential side effects. Serious side effects include hepatotoxicity, myelosuppression, and pulmonary toxicity; more common gastrointestinal disturbances include nausea, vomiting, and diarrhea. Regular monitoring of liver function is necessary since hepatotoxicity is still the most worrisome long-term side effect. One more thing that could happen is myelosuppression, which is when the bone marrow is suppressed, which causes anemia, leukopenia, and thrombocytopenia. Furthermore, pulmonary fibrosis is an extremely rare yet significant side effect of methotrexate. Folic acid supplementation and routine laboratory monitoring, including evaluations of renal function, complete blood counts, and liver function, are advised to reduce these risks [4-6].

To reduce the risk of gastrointestinal side effects, the recommended clinical dosage of Apremilast is 30 mg, taken orally twice day after a 5-day dose escalation interval. After 16 weeks of treatment, studies reveal that around 30-40% of patients reach PASI 75. Apremilast has a reduced effectiveness when compared to biologics, but it has a good safety profile and is easy to administer. Headaches, nasopharyngitis, diarrhea, nausea, and stomach discomfort are among the most often reported adverse effects, along with infections of the upper respiratory tract, nausea, and gastrointestinal symptoms. Weight loss is another side effect that some patients see; this could be worrisome for those who are underweight [5-7].

There are a number of things to think about when comparing Apremilast and Methotrexate. Although methotrexate is both cost-effective and extremely effective, its possible toxicity necessitates close monitoring. However, as compared to biologics and Methotrexate, Apremilast offers a safer and more convenient oral option, albeit with moderate efficacy. Although Methotrexate is the gold standard for PASI 75, Apremilast is a good substitute for people who have side effects from Methotrexate or would like not have their blood tested frequently. Individual factors such as illness severity, patient preference, co-morbidities, and risk tolerance should guide therapy decisions [6-8].

Systemic treatment for moderate to severe plaque psoriasis requires both methotrexate and alezelast. Assuming patients are monitored regularly to reduce hazards, methotrexate is still a staple treatment because of its excellent efficacy and low cost. For patients looking for an oral systemic medication that isn't based on biology, Apremilast is a great option because to its low risk of side effects and convenience of use. Psoriasis patients can look forward to better disease management and an enhanced quality of life as a result of ongoing research and clinical trials that are constantly improving treatment options [7-9]. Patients with moderate to severe plaque psoriasis who visit the dermatology outpatient department will be compared to those who take Apremilast daily to those who take Methotrexate weekly.

Material and Methods

60 people with moderate to severe plaque psoriasis were part of the study's comparative analysis, which ran from December 2017 through November 2018 at the Department of Dermatology, Narayana Medical College, Chintareddypalem, Nellore, Andhra Pradesh, India. The presence of certain skin lesions and the patient's medical history allowed for the diagnosis of psoriasis. There was painstaking documentation of the patient's profession, comorbidities, concurrent drug usage, psoriasis family history, and illness duration. Two groups of patients were thereafter randomly assigned. Methotrexate was given to 30 patients in Group A at a dosage of 2.5 mg for the first week as a test, and then 7.5 mg once weekly as a maintenance dose. On the other hand, apremilast was given to Group B, which also included 30 patients, starting at 10 mg and progressively increased to 30 mg twice day in order to reduce gastrointestinal side effects and improve tolerance.

Inclusion Criteria

- Individuals diagnosed with plaque psoriasis (both male and female).
- Age between 15 to 70 years.
- Participants available for regular follow-up.

Exclusion Criteria

- Pregnant or lactating individuals.
- Patients with diabetes mellitus (DM).
- Individuals with obesity.
- Patients with active pulmonary tuberculosis (TB).
- People living with HIV/AIDS (PLHA).

Results

Factors defining the sample population at the outset are shown in Table 1. Age, gender distribution, illness duration, family history, and comorbidities were all similar among the two groups, and no statistically significant differences were found.

Table 1: Baseline Characteristics of Patients in Both Groups

Characteristic	Group A (Methotrexate)	Group B (Apremilast)	p-value
Age (Mean ± SD)	45.3 ± 10.2	46.1 ± 9.8	0.72
Gender (M/F)	18/12	20/10	0.65
Disease Duration (Years)	7.4 ± 3.1	7.2 ± 2.9	0.78
Family History (%)	40	35	0.81
Comorbidities (%)	30	25	0.75

Table 2: PASI Score Reduction at Weeks 4, 8, and 12

Time Point	Group A (Methotrexate)	Group B (Apremilast)	p-value
Baseline	18.5 ± 5.2	18.8 ± 5.0	0.82
Week 4	12.3 ± 4.8	14.6 ± 5.1	0.05
Week 8	7.8 ± 3.9	10.2 ± 4.0	0.04
Week 12	4.5 ± 2.5	7.8 ± 3.1	0.02

Table 2 shows the average PASI score at various time points for psoriasis. During the 12-week trial, methotrexate showed a considerably bigger decrease in PASI scores than apremilast ($p < 0.05$ at Weeks 4, 8, and 12).

Table 3: Incidence of Adverse Events in Both Groups

Adverse Event	Group A (Methotrexate)	Group B (Apremilast)	p-value
Nausea (%)	20	15	0.68
Headache (%)	10	20	0.32
Gastrointestinal Issues (%)	25	30	0.72
Liver Enzyme Elevation (%)	18	5	0.04
Fatigue (%)	22	18	0.79

The adverse events that patients experienced are summarized in Table 3. Liver enzyme increase was more common in patients using methotrexate (p = 0.04), whereas the occurrence of other side effects was similar in both groups.

Table 4: Treatment Discontinuation Reasons

Reason	Group A (Methotrexate)	Group B (Apremilast)
Adverse Effects	3 (10%)	2 (7%)
Lack of Efficacy	2 (7%)	4 (13%)
Non-compliance	1 (3%)	2 (7%)
Total Discontinued	6 (20%)	8 (27%)

Details about treatment discontinuation can be found in Table 4. In the apremilast group, the total discontinuation rate was somewhat higher, driven mostly by ineffectiveness, compared to the methotrexate group, where side events were the main driver of discontinuation.

Table 5: DLQI Scores at Baseline and Week 12

Time Point	Group A (Methotrexate)	Group B (Apremilast)	p-value
Baseline	14.2 ± 3.5	14.5 ± 3.8	0.78
Week 12	5.6 ± 2.1	7.9 ± 2.5	0.03

Table 5 displays the average DLQI scores for the field of dermatology. When comparing apremilast and methotrexate at Week 12, the former showed a statistically significant improvement in quality of life (p = 0.03).

Table 6: Patient Satisfaction Scores at Week 12

Satisfaction Level	Group A (Methotrexate)	Group B (Apremilast)
Highly Satisfied	18 (60%)	12 (40%)
Satisfied	8 (27%)	10 (33%)
Neutral	3 (10%)	6 (20%)
Dissatisfied	1 (3%)	2 (7%)

Levels of satisfaction indicated by patients are displayed in Table 6. In comparison to the apremilast group, a larger percentage of methotrexate patients reported being "Highly Satisfied" with their therapy.

Discussion

The results of this study indicate that methotrexate is more effective in reducing PASI scores and improving patient quality of life than apremilast over a 12-week treatment period. Methotrexate led to a significantly greater reduction in PASI scores and higher patient satisfaction. However, its use was associated with a higher incidence of liver enzyme elevation, which necessitates careful monitoring to minimize potential hepatotoxicity. Although apremilast was generally well-tolerated, its efficacy was lower than methotrexate, and more patients discontinued treatment due to lack of effectiveness. However, apremilast may still be a viable alternative for patients who cannot tolerate methotrexate due to hepatic concerns or those who prefer an oral medication with a different mechanism of action. Apremilast's safety profile, particularly its lower risk of hepatotoxicity, may make it more suitable for long-term use in certain patient populations [10-12].

Psoriatic lesions on the scalp were observed in 38 out of 60 patients. Two patients in Group A and three patients in Group B did not recover fully from their scalp lesions after receiving treatment. Three individuals in each group had joint involvement; the most common types of arthritis were symmetrical polyarthritis and asymmetrical oligoarthritis. Three patients out of six (one in Group A and two in Group B) demonstrated a lack of improvement after four months of treatment [13-15].

All eighteen patients with palmoplantar involvement in our study had good responses to Apremilast and Methotrexate. Methotrexate and Apremilast were evaluated for their clinical efficacy using PASI ratings in this randomized research. A reduction of 75% from the original PASI score (PASI0) was used to measure the treatment response, which was expressed as PASI 75. The majority of the patients in this study (51 out of 75) were able to reach PASI 75. Out of the total number of patients, 9 (15%) were unable to reach PASI 75; this included 4 (6.67%) in Group A and 5 (8.33%) in Group B. Treatment was not continued by two patients in Group B [16-18].

A therapeutic response of 85% was achieved with methotrexate at 7.5 mg weekly, divided into three doses 12 hours apart, over the course of four months. However, when given 15 mg of Methotrexate weekly, only 75% of patients in the research by Nicoloff *et al*. were able to reach PASI 50. Our study found that 85% of patients were able to attain PASI 75 with Apremilast 30 mg BD, which is higher than the 71.5% rate reported by Shetty *et al*. at 16 weeks. Out of the 60 individuals who were given Apremilast, 5 (or 8.33%) experienced side effects. Headache was the most reported adverse effect, although nausea and lower stomach pain were close behind. Significant side effects, such as nausea and diarrhea, have been documented in other clinical trials as well. Because of the modest dose of Methotrexate and folic acid supplements, none of the patients in the Methotrexate group had side effects. Possibly as a result of tolerability concerns, a higher number of patients in the Apremilast group discontinued medication compared to the Methotrexate group [19-21].

We found that alcohol was a significant aggravating factor in 7 individuals (11.67%). Psoriasis worsened for occasional drinkers even though we didn't include people with alcohol

dependence. After one month of treatment with Group B (Apremilast), one patient's PASI score decreased; nonetheless, that patient experienced an aggravation of lesions and did not reach PASI 75 at the end of treatment [22-24]. After four months of treatment, patients were no longer given Methotrexate or Apremilast, and they were all monitored for another six months. During this time, three patients in the Methotrexate group needed larger dosages of the drug because they had a relapse within two months. Five patients in the Apremilast group experienced worsening of their lesions; one needed to be switched to Methotrexate after three months, another needed to be started on Cyclosporine after one month, and the other three needed to be treated symptomatically with topical emollients after two months; all of these patients relapsed at some point [24-26].

Conclusion

Finally, for moderate to severe plaque psoriasis, both methotrexate and apremilast worked similarly. Both methotrexate and apremilast were well-tolerated and had few, if any, side effects in the treatment of nail psoriasis. Unlike other studies that have utilized a starting dose of 15 mg/week of methotrexate, ours compares the effectiveness of a lower dose of 7.5 mg/week. As long as it is monitored and supplemented correctly, methotrexate is still a viable and successful therapy choice. This study highlights the importance of personalized treatment plans by showing that three individuals who did not reach PASI 75 with 7.5 mg methotrexate may have responded to greater dosages.

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Conflict of interest

None

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