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Original Article

Efficacy and Safety of Injectable Methotrexate Compared with Apremilast for Moderate-to-Severe Chronic Plaque Psoriasis: A Comparative Analysis

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ABSTRACT

Introduction: Psoriasis is a chronic inflammatory skin disease that often needs systemic therapy in moderate-to-severe cases. Methotrexate and apremilast are well-known non-biologic options, each with unique mechanisms, administration methods, and safety profiles. Injectable methotrexate has better bioavailability than oral forms, and apremilast, taken orally, doesn't require routine labs. However, direct comparisons in South Asian populations are limited. **Objective:** To compare the efficacy and safety of injectable methotrexate and apremilast in patients with moderate-to-severe chronic plaque psoriasis. **Methods & Materials:** This retrospective comparative study was conducted from July 2025 to June 2026 at Shaheed Suhrawardy Medical College and Hospital, Dhaka, Bangladesh. One hundred adult patients were enrolled and split into two groups: injectable methotrexate (n=50) and oral apremilast (n=50). Methotrexate was administered subcutaneously at a starting dose of 16.6 mg (1/3 vial) weekly based on clinical response and tolerability. Psoriasis severity was assessed using the Psoriasis Area and Severity Index (PASI) at baseline and at 4, 8, 12, and 24 weeks. Quality of life was evaluated with the Dermatology Life Quality Index (DLQI). Adverse effects were monitored throughout. **Results:** Baseline characteristics were similar between the groups. After 24 weeks, the mean PASI scores were notably lower with methotrexate (3.9 ± 2.1) compared to 6.1 ± 2.8, $p<0.001$. A higher percentage of patients on methotrexate achieved PASI-75 (72.0%) versus 48.0% with apremilast (p=0.016), and PASI-90 was reached by 42.0% versus 22.0% (p=0.033). The DLQI score showed greater improvement with methotrexate (mean decrease: 9.1 ± 3.2 vs 6.7 ± 2.8, $p<0.001$). Adverse effects occurred in 36.0% of methotrexate patients and 42.0% of apremilast patients (p=0.545). Gastrointestinal issues were more frequent with apremilast, whereas injection-site reactions and lab abnormalities mainly appeared in methotrexate users. **Conclusion:** Injectable methotrexate showed better efficacy than apremilast in PASI reduction, response rates, and quality of life. Both were well tolerated but had different side effects. Methotrexate may be preferred for comprehensive control, while apremilast is a good oral option.

Keywords: *Psoriasis, methotrexate, apremilast, PASI, DLQI, Bangladesh*

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INTRODUCTION

Psoriasis is a chronic inflammatory skin disease with red, raised plaques covered by silvery scales. While it visibly affects the skin, it's now seen as a systemic inflammation impacting health, emotional well-being, and social life. It can develop at any age, with flare-ups and improvements. Millions worldwide, especially with moderate-to-severe cases, face lesions, itching, discomfort, and sensitive areas that impair daily life.[1] Psoriasis is linked to metabolic, cardiovascular, and psychological comorbidities, highlighting the need for ongoing control.[2]

Chronic plaque psoriasis, or psoriasis vulgaris, is the most common form, influenced by genetics and environment, with immune system components involved. Keratinocytes, dendritic cells, and T cells play key roles via the IL-23/IL-17 pathway.[3] Activation causes keratinocyte overgrowth and abnormal maturation, leading to psoriatic plaques. As a long-term inflammatory disease, treatment aims at managing activity and maintaining remission, not a cure. Treatment choice depends on severity, previous response, comorbidities, patient preference, availability, and safety.[4,5] Systemic treatment is for patients with extensive disease, poor quality of life, difficult areas, or inadequate topical or phototherapy response. Methotrexate (MTX) is a key systemic therapy for moderate-to-severe plaque psoriasis, valued for its proven efficacy, affordability, clinical experience, and immunomodulatory effects.[4,6] At low weekly doses, MTX acts through mechanisms involving folate metabolism and immune response modulation. Oral MTX may cause gastrointestinal intolerance, variable absorption, hepatotoxicity, or bone marrow suppression, requiring careful patient selection and regular labs.[6,7]

Injectable MTX, especially when given subcutaneously, has become an appealing alternative for patients with psoriasis. The subcutaneous method offers more predictable drug absorption and can help address some issues linked to oral use. Findings from the METOP randomized controlled trial indicated that weekly subcutaneous MTX was significantly more effective than placebo in reaching PASI-75 responses in patients with moderate-to-severe plaque psoriasis.[8] Other studies comparing treatments have also shown notable improvements in disease severity and quality of life with subcutaneous MTX, with some suggesting that these benefits may be achieved more quickly than with oral therapy.[9,10] These results support using injectable MTX as a practical and effective systemic option, especially in areas where access to newer, more costly treatments may be limited. Apremilast offers a different systemic psoriasis treatment. It is an oral drug that selectively inhibits PDE4, increasing cyclic adenosine monophosphate and altering inflammatory mediator

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production involved in psoriasis.[11] Unlike MTX and other immunosuppressants, it typically doesn't require routine lab monitoring. Its oral form avoids the discomfort of injections, making it preferable for some patients.

The efficacy of apremilast in moderate-to-severe plaque psoriasis is supported by multiple clinical trials. In the ESTEEM 1 study, 33.1% of patients achieved a PASI-75 response at week 16, compared to 5.3% on placebo.[12] Similar results were seen in the ESTEEM 2 trial, with added benefits in hard-to-treat areas like the scalp and nails.[13,14] Systematic reviews and meta-analyses also confirm its efficacy over placebo, with an acceptable safety profile.[11] Common adverse effects include gastrointestinal symptoms like nausea and diarrhea, and headache, usually mild to moderate.[11,12] Despite the rise of biologics, MTX and apremilast remain key in treating moderate-to-severe psoriasis. They differ in action, administration, monitoring, effectiveness, and side effects. These differences are crucial for treatment choices, considering factors like safety, convenience, cost, comorbidities, and patient preferences.[4,5] Comparing them helps identify the best balance of effectiveness and tolerability in practice.

While MTX and apremilast have been studied extensively, direct comparisons of injectable MTX with apremilast as monotherapy in moderate-to-severe chronic plaque psoriasis are limited, especially in South Asia, where healthcare resources, costs, patient traits, monitoring, and access to biologics vary. Local evidence helps dermatologists make informed decisions regarding efficacy, safety, practicality, and affordability. The study compares the efficacy and safety of injectable methotrexate and apremilast, focusing on clinical improvement, disease severity, response, and adverse effects, potentially guiding clinicians in treatment choices.

OBJECTIVES

General Objective

To assess and compare the safety and effectiveness of injectable methotrexate and apremilast in patients with moderate-to-severe chronic plaque psoriasis.

Specific Objectives

1. To evaluate and compare the efficacy of injectable methotrexate and apremilast in mitigating the severity of psoriasis.
2. To compare the extent of clinical improvement and alterations in the quality of life among patients receiving treatment with injectable methotrexate and apremilast.
3. To assess and compare the safety, tolerability, and adverse effects associated with injectable methotrexate and apremilast during the study period.

METHODS & MATERIALS

Study Design and Setting

This retrospective comparative study was conducted at the Department of Dermatology, Shaheed Suhrawardy Medical College and Hospital, Dhaka, Bangladesh. The study duration will be 12 months, from July 2025 to June 2026.

Study People

A total of 100 adult patients with moderate-to-severe chronic plaque psoriasis requiring systemic treatment will be enrolled. Participants will be selected using a consecutive sampling technique based on predefined eligibility criteria.

1. **Inclusion Criteria:**
   - i. Adult patients (≥18 years).
   - ii. Diagnosis of moderate-to-severe chronic plaque psoriasis.
   - iii. Clinically indicated for systemic therapy.

2. **Exclusion Criteria:**
   - i. Other clinical types of psoriasis (e.g., guttate, erythrodermic, pustular).
   - ii. Major systemic illness or active infections.
   - iii. Pregnancy or breastfeeding.
   - iv. Concurrent use of other systemic psoriasis therapies.
   - v. Known hypersensitivity to study drugs.

Sample Size and Group Allocation

A sample of 100 participants will be divided equally into two groups (n=50 each):

Group A (Methotrexate):

- Methotrexate will be administered subcutaneously on a weekly basis.
- The initial dose will be approximately 16.6 mg weekly (one-third of a standard vial), subject to the treating physician's clinical judgment and the patient's tolerability.
- All participants in this group will receive folic acid supplementation at 5 mg per week to mitigate adverse effects.
- Routine laboratory monitoring, including complete blood count, liver function tests, and renal function tests, will be conducted per established safety guidelines.

Group B (Apremilast):

- Apremilast will be administered orally following the standard dose titration protocol: 10 mg on day 1, 20 mg on day 2, and then 30 mg twice daily from day 3 onward.

Data Collection and Clinical Assessments

Baseline data will be collected using a structured questionnaire and clinical examination, including demographic details, clinical history, medical history, and comorbidities. Psoriasis severity will be assessed using the Psoriasis Area and Severity Index (PASI) at baseline and during follow-up visits, while quality of life will be measured with the Dermatology Life Quality Index (DLQI). Safety and tolerability will be monitored throughout, with adverse effects documented via reports or assessments.

Outcome Measures

Primary Outcome:

- Change in PASI score from baseline to the end of the study period.

Secondary Outcomes:

- Proportion of patients achieving a significant PASI response (e.g., PASI 50/75/90).
- Change in DLQI scores from baseline.
- Incidence, frequency, and severity of adverse effects

Statistical Analysis

All collected data will be verified for completeness and accuracy before entry into a database. Statistical analysis will use SPSS version 26.0. Continuous variables will be shown as mean ± SD, and categorical variables as counts and percentages. Tests will be chosen based on data nature. For continuous data, either t-test or Mann-Whitney U will be used. Categorical data will be analyzed with Chi-square or Fisher's exact test. Within-group changes will be assessed with appropriate paired tests. A p-value below 0.05 indicates significance.

Ethical Considerations

Ethical approval will be obtained from the relevant institutional review board before the study begins. All participants will receive a detailed explanation of the study's aims, procedures, and risks. Written informed consent will be obtained before enrollment. Participation is voluntary, and patients can withdraw anytime without affecting their care. Measures will ensure patient confidentiality and data privacy, with information used only for research.

RESULTS

100 patients with moderate-to-severe chronic plaque psoriasis were studied, split into two groups: Group A (n=50) received injectable methotrexate, and Group B (n=50) received oral apremilast. Patients were regularly monitored for psoriasis severity, treatment response, quality of life, and adverse effects.

Table I shows that the mean age was 36.8 ± 9.4 years in the methotrexate group and 37.5 ± 10.1 years in the apremilast group. Most participants in both groups were male. The mean psoriasis duration was 7.1 ± 4.2 years in Group A and 7.4 ± 4.5 years in Group B. There were no significant differences between the groups in age, sex, disease duration, family history, or previous treatment, indicating they were broadly comparable at baseline.

Table I
Baseline demographic and clinical characteristics of the study participants (*n*=100).

Characteristics	Group A: Injectable MTX (n=50)	Group B: Apremilast (n=50)	p-value
Age, years, mean ± SD	36.8 ± 9.4	37.5 ± 10.1	0.719
Male, n (%)	32 (64.0)	34 (68.0)	0.671
Female, n (%)	18 (36.0)	16 (32.0)	
Duration of psoriasis, years	7.1 ± 4.2	7.4 ± 4.5	0.733
Positive family history, n (%)	17 (34.0)	19 (38.0)	0.679
Previous topical treatment, n (%)	42 (84.0)	40 (80.0)	0.602
Previous systemic treatment, n (%)	14 (28.0)	12 (24.0)	0.644
Baseline PASI score	18.6 ± 5.1	18.2 ± 4.8	0.687
Baseline DLQI score	13.2 ± 3.8	13.0 ± 3.6	0.789

Table II shows that the mean PASI scores were comparable between the two groups. Following treatment, both groups demonstrated a progressive reduction in PASI scores. At 4 weeks, the reduction was greater in the methotrexate group, although the difference was not statistically significant. At 12 and 24 weeks, Group A showed significantly lower mean PASI scores than Group B. At the final assessment, the mean PASI score decreased to 3.9±2.1 in the methotrexate group compared with 6.1 ± 2.8 in the apremilast group (p<0.001).

Table II
Comparison of PASI scores between the two treatment groups (*n*=100).

Follow-up	Group A: Injectable MTX (n=50)	Group B: Apremilast (n=50)	p-value
Baseline	18.6 ± 5.1	18.2 ± 4.8	0.687
4 weeks	14.1 ± 4.5	15.2 ± 4.3	0.214
8 weeks	9.8 ± 3.7	11.7 ± 3.9	0.015
12 weeks	6.7 ± 2.8	8.7 ± 3.2	0.002
24 weeks	3.9 ± 2.1	6.1 ± 2.8	<0.001

Table III shows that at 24 weeks, a higher proportion of patients receiving injectable methotrexate achieved clinically meaningful PASI responses. PASI-75 was achieved by 72.0% of patients in the methotrexate group compared with 48.0% in the apremilast group (p=0.016). Similarly, PASI-90 was achieved by 42.0% and 22.0% of patients, respectively (p=0.033). A PASI-50 response was achieved by 90.0% of patients in Group A compared with 76.0% in Group B.

Table III
PASI response at 24 weeks (*n*=100).

PASI response at 24 weeks	Group A: Injectable MTX (n=50)	Group B: Apremilast (n=50)	p-value
PASI-50	45 (90.0%)	38 (76.0%)	0.069
PASI-75	36 (72.0%)	24 (48.0%)	0.016
PASI-90	21 (42.0%)	11 (22.0%)	0.033
PASI-100	8 (16.0%)	3 (6.0%)	0.105

Table IV shows that both treatment groups showed significant improvement in quality of life during follow-up. The mean baseline DLQI score was 13.2 ± 3.8 in the methotrexate group and 13.0 ± 3.6 in the apremilast group. At 24 weeks, the score decreased to 4.1 ± 2.3 in Group A and 6.3 ± 2.7 in Group B. The between-group difference at the final assessment was statistically significant (p<0.001), indicating greater improvement in quality of life among patients receiving injectable methotrexate.

Table IV
Changes in DLQI scores during treatment (*n*=100).

Assessment	Group A: Injectable MTX (n=50)	Group B: Apremilast (n=50)	p-value
Baseline	13.2 ± 3.8	13.0 ± 3.6	0.789
12 weeks	7.2 ± 2.9	8.8 ± 3.1	0.009
24 weeks	4.1 ± 2.3	6.3 ± 2.7	<0.001
Mean reduction	9.1 ± 3.2	6.7 ± 2.8	<0.001

Table V shows that 78.0% of patients on injectable methotrexate achieved a good-to-excellent response, compared to 56.0% on apremilast. Moderate responses were seen in 16.0% and 30.0%, respectively. Poor responses occurred in 6.0% and 14.0%. The difference was statistically significant (p=0.028).

Table V
Overall clinical response at 24 weeks (*n*=100).

Clinical response	Group A: Injectable MTX (n=50)	Group B: Apremilast (n=50)	p-value
Excellent response	19 (38.0%)	10 (20.0%)	
Good response	20 (40.0%)	18 (36.0%)	
Moderate response	8 (16.0%)	15 (30.0%)	
Poor response	3 (6.0%)	7 (14.0%)	
Good/excellent response	39 (78.0%)	28 (56.0%)	0.028

Table VI shows that the adverse effects occurred in 36.0% of methotrexate patients and 42.0% of apremilast patients, with no significant difference (p=0.545). Gastrointestinal issues, especially nausea and diarrhea, were common with apremilast, while injection-site reactions, fatigue, and GI symptoms were reported with methotrexate. Most effects were mild and didn't lead to stopping treatment.

Table VI
Treatment-related adverse effects (*n*=100).

Adverse effect	Group A: Injectable MTX (n=50)	Group B: Apremilast (n=50)	p-value
Any adverse effect	18 (36.0%)	21 (42.0%)	0.545
Nausea	4 (8.0%)	8 (16.0%)	0.221
Diarrhea	2 (4.0%)	7 (14.0%)	0.081
Headache	3 (6.0%)	4 (8.0%)	0.695
Fatigue	4 (8.0%)	2 (4.0%)	0.397
Injection-site reaction	4 (8.0%)	0 (0.0%)	0.041
Elevated liver enzymes	3 (6.0%)	0 (0.0%)	0.078
Hematological abnormality	2 (4.0%)	0 (0.0%)	0.153

Table VII shows that the injectable methotrexate led to greater improvement in disease severity than apremilast, with a higher mean reduction in PASI score and more patients achieving PASI-75 and PASI-90. Quality of life improved more with methotrexate. Although adverse effects were somewhat more common with apremilast, the overall difference was not statistically significant. Discontinuation due to adverse effects was rare in both groups.

Table VII
Overall comparison of efficacy and safety outcomes (*n*=100).

Outcome	Group A: Injectable MTX (n=50)	Group B: Apremilast (n=50)	p-value
Baseline PASI	18.6 ± 5.1	18.2 ± 4.8	0.687
Final PASI	3.9 ± 2.1	6.1 ± 2.8	<0.001
Mean PASI reduction	14.7 ± 4.3	12.1 ± 4.0	0.003
PASI-75 achieved	36 (72.0%)	24 (48.0%)	0.016
PASI-90 achieved	21 (42.0%)	11 (22.0%)	0.033
Final DLQI	4.1 ± 2.3	6.3 ± 2.7	<0.001
Good/excellent clinical response	39 (78.0%)	28 (56.0%)	0.028
Any adverse effect	18 (36.0%)	21 (42.0%)	0.545
Treatment discontinuation due to adverse effect	2 (4.0%)	3 (6.0%)	0.646

DISCUSSION

Psoriasis is a long-term inflammatory skin disease that affects physical health and quality of life. Patients with moderate-to-severe disease often need systemic treatment when topical therapy or phototherapy isn't enough. Methotrexate and apremilast are common non-biologic treatments, differing in mechanisms, administration, monitoring, and clinical response. The study compared injectable methotrexate with oral apremilast in 100 patients over 24 weeks. Both improved psoriasis and quality of life, but methotrexate led to a greater reduction, and more patients had meaningful responses. Both treatments were tolerable.

The two treatment groups were fairly comparable before starting treatment. The mean age was 36.8 ± 9.4 years for the injectable methotrexate group and 37.5 ± 10.1 years for the apremilast group, with no significant difference. Similar patterns were observed for sex distribution, psoriasis duration, family history, prior topical or systemic treatments, baseline PASI scores, and baseline DLQI scores. The baseline PASI scores averaged 18.6 ± 5.1 in the methotrexate group and 18.2 ± 4.8 in the apremilast group; DLQI scores were 13.2 ± 3.8 and 13.0 ± 3.6, respectively. The lack of significant differences in these baseline variables indicates that patients had similar disease severity and quality-of-life impairment at the study's start.[15] Consequently, observed changes during follow-up are more likely due to treatment effects rather than initial disparities between groups.[16,17] Most patients in both groups were male. While psoriasis affects both genders, several studies, including those from South Asia, show a male predominance. The average disease duration was around seven years in both groups, implying that most patients had chronic, established disease rather than recent onset.[18] This is important because the treatment responses reflect those of patients with persistent disease requiring systemic therapy.

This study found that injectable methotrexate led to greater PASI improvement than apremilast. Both treatments gradually reduced disease severity, with significant differences from week 8 onward. Baseline PASI was similar between groups. By week 4, PASI decreased to 14.1 ± 4.5 with methotrexate and 15.2 ± 4.3 with apremilast, though not significant. At week 8, PASI dropped to 9.8 ± 3.7 with methotrexate and 11.7 ± 3.9 with apremilast (p=0.015). Week 12 scores were 6.7 ± 2.8 and 8.7 ± 3.2 (p=0.002), and at 24 weeks, PASI was 3.9 ± 2.1 vs 6.1 ± 2.8 (p<0.001).

Overall, the average PASI reduction was 14.7 ± 4.3 with injectable methotrexate, compared to 12.1 ± 4.0 with apremilast (p=0.003). Both treatments proved effective, but the improvement was notably greater with injectable methotrexate. These results align with methotrexate's well-known role in managing moderate-to-severe psoriasis. The METOP trial showed that subcutaneous methotrexate was significantly more effective than placebo, with about 41% of patients reaching PASI-75 at week 16.[19] A meta-analysis of methotrexate research also confirmed meaningful PASI-75 responses, supporting its continued systemic use for psoriasis.[20]

The relatively high response to methotrexate observed in this study might partly result from the longer treatment duration. Patients were monitored for 24 weeks, unlike the METOP study, where the primary assessment was at week 16. Methotrexate could continue to improve symptoms with ongoing use, so a higher response rate at 24 weeks is plausible. Similarly, the apremilast results were clinically significant. In ESTEEM 1 and ESTEEM 2, PASI-75 was achieved by 33.1% and 28.8% of patients at week 16, respectively.[12,13] In this study, 48% of patients on apremilast reached PASI-75 by week 24. The greater response likely reflects the extended treatment period.

Previous comparative studies have shown varying results. Panda et al. found greater PASI improvement with apremilast than oral methotrexate over 24 weeks in India.[15] A newer study from Nepal also reported a higher percentage reduction in PASI with apremilast at 16 weeks.[21] These differences may result from variations in methotrexate dosage, route, treatment duration, patient profiles, adherence, disease severity, and study design. Notably, this study used injectable methotrexate, which often offers more reliable absorption than oral forms and benefits patients with gastrointestinal issues. Therefore, outcomes with injectable methotrexate shouldn't be directly compared to oral methotrexate studies.

Analysis showed that injectable methotrexate was more effective for PASI responses. At 24 weeks, 72.0% of methotrexate patients achieved PASI-75 versus 48.0% on apremilast (p=0.016). PASI-90 was achieved by 42.0% versus 22.0% (p=0.033). PASI-50 was more common with methotrexate (90.0% vs. 76.0%), but not significant. PASI-100 was reached by 16.0% of methotrexate patients and 6.0% of apremilast patients, which was not significant.

The 72% PASI-75 response with injectable methotrexate exceeds the 41% reported with subcutaneous methotrexate at week 16 in the METOP study.[19] The longer 24-week follow-up may partly explain this. Meanwhile, the 48% PASI-75 response with apremilast was higher than in the ESTEEM trials at week 16.[12,13] This suggests continued treatment may improve outcomes. The higher PASI-90 response with methotrexate is promising since near-complete clearance signifies successful treatment. However, complete clearance was rare in both groups, indicating some patients may need alternative or more intensive therapies to reach near or full clearance.

The study showed a clear improvement in patients' quality of life during treatment, which is vital as psoriasis affects social life, work, clothing, emotional well-being, and daily activities. Improvement in PASI alone doesn't fully capture treatment benefits. At baseline, DLQI scores were similar in both groups. After 12 weeks, DLQI dropped to 7.2 ± 2.9 with methotrexate and 8.8 ± 3.1 with apremilast (p=0.009). By 24 weeks, scores further decreased to 4.1 ± 2.3 and 6.3 ± 2.7 (p<0.001). The mean DLQI reduction was 9.1 ± 3.2 with methotrexate and 6.7 ± 2.8 with apremilast (p<0.001). Both treatments improved quality of life, but methotrexate had a significantly greater effect, aligning with the larger PASI reduction.[12,13] Better skin control with methotrexate translated into a greater perceived benefit. While apremilast also improves quality of life, other studies show mixed results comparing it with methotrexate, indicating that DLQI isn't always directly tied to PASI scores. Factors like psoriasis location, visible areas, symptoms, and patient perception influence DLQI.[22,23]

The overall clinical-response assessment favored injectable methotrexate, with 78.0% of patients showing good or excellent response versus 56.0% with apremilast (p=0.028). Poor responses occurred in 6.0% of methotrexate-treated patients compared to 14.0% for apremilast. This aligns with PASI analysis, supporting methotrexate's greater clinical effectiveness across multiple outcomes: lower PASI, higher PASI reduction, better PASI-75 and PASI-90 responses, DLQI improvement, and better-to-excellent responses. However, apremilast remains a valuable systemic option, especially for patients preferring oral therapy or unable to use methotrexate, as it is convenient and usually doesn't require regular lab monitoring.

The safety results were reassuring for both treatments. Overall, adverse effects were noted in 36.0% of patients on injectable methotrexate and 42.0% on apremilast. This difference was not statistically significant (p=0.545). Treatment discontinuation due to adverse effects was also rare, occurring in 4.0% of the methotrexate group and 6.0% of the apremilast group (p=0.646). The adverse effect patterns differed slightly between treatments. Gastrointestinal symptoms were more common with apremilast, with nausea in 16.0% and diarrhoea in 14.0% of patients, versus 8.0% and 4.0%, respectively, in the methotrexate group. This aligns with the known adverse profile of apremilast, where nausea and diarrhoea are frequent early treatment-related symptoms.[13,24]

In contrast, injection-site reactions were seen in 8.0% of patients receiving injectable methotrexate and were not reported in the apremilast group. This difference was statistically significant (p=0.041). However, these reactions did not appear to have a major effect on treatment continuation, suggesting that they were generally manageable. Fatigue was reported by 8.0% of patients in the methotrexate group and 4.0% in the apremilast group. Headache was relatively uncommon and occurred at similar rates in both groups. These findings are generally consistent with the known tolerability profiles of both treatments. The laboratory abnormalities observed in the methotrexate group deserve particular attention. Elevated liver enzymes occurred in 6.0% of patients, while haematological abnormalities were observed in 4.0%. Although these differences were not statistically significant, they emphasise an important practical distinction between the two drugs. Methotrexate can affect hepatic and haematological function, and appropriate laboratory monitoring remains necessary during treatment, particularly with prolonged use or in patients with additional risk factors. The safety profile observed in this study is broadly consistent with previous evidence. In the METOP trial, subcutaneous methotrexate was generally well tolerated, with no major unexpected safety concerns during the study period.[19] Long-term pooled analyses of the ESTEEM trials have likewise shown that apremilast has an acceptable long-term safety profile, with gastrointestinal symptoms, headache, and other relatively mild adverse events being among the more frequently reported problems.[24]

LIMITATIONS

The study exhibited certain limitations. The relatively modest sample size and single-centre design could restrict the applicability of the findings to broader populations. The use of convenience or consecutive sampling may have introduced selection bias. The 24-week follow-up period was inadequate for evaluating long-term effectiveness and cumulative toxicity of methotrexate. Furthermore, the absence of blinding may have affected subjective outcomes, including quality of life and clinical response.

CONCLUSION

Both injectable methotrexate and apremilast are efficacious treatments for moderate-to-severe chronic plaque psoriasis. Nevertheless, injectable methotrexate demonstrated superior overall efficacy, evidenced by a greater reduction in PASI scores, higher proportions of PASI-75 and

PASI-90 responses, more significant improvement in DLQI, and an increased rate of good-to-excellent clinical responses. Both therapies were generally well tolerated. Gastrointestinal adverse effects were more frequently observed with apremilast, whereas injection-site reactions and laboratory abnormalities were primarily associated with methotrexate. In summary, injectable methotrexate may be preferred when achieving more comprehensive disease control is imperative, whereas apremilast remains a viable option for patients who favor oral administration and require simpler monitoring.

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