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Efficacy of Apremilast in Patients with Moderate to Severe Lichen Planus

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ABSTRACT

Background: Lichen planus (LP) is a chronic, immune-mediated inflammatory disorder that can be difficult to manage, especially in moderate to severe cases unresponsive to topical therapies. **Objective:** To evaluate the efficacy of Apremilast in patients with moderate to severe lichen planus. **Methods:** This descriptive case study was conducted in the Department of Dermatology, AIMC/Jinnah Hospital, Lahore, from 7 August 2024 to 7 February 2025 and included 72 patients aged 18–70 years with clinically diagnosed moderate to severe LP refractory to topical corticosteroids. Patients were prescribed Apremilast 20 mg orally twice daily for 12 weeks. Baseline characteristics were recorded, and treatment response was assessed using Physician Global Assessment (PGA) scores. **Results:** Out of the 72 enrolled patients, 39 (54.2%) were male and 33 (45.8%) were female, with a mean age of 42.6 ± 11.3 years. A ≥2-grade improvement in PGA was observed in 47 patients (65.3%) after 12 weeks of therapy. Patients with moderate disease showed a better response than those with severe disease (73.1% vs. 54.8%, p = 0.04). No significant associations were found between treatment efficacy and gender, duration of symptoms, prior therapy, or BMI. Adverse effects were mild and transient, with gastrointestinal discomfort (16.7%) and headache (8.3%) being the most common. **Conclusion:** It is concluded that Apremilast is an effective and well-tolerated treatment for moderate to severe lichen planus, offering significant clinical improvement with minimal adverse effects.

INTRODUCTION

Lichen planus (LP) is a chronic, immune-mediated mucocutaneous disorder that continues to challenge clinicians because of its unpredictable course, symptomatic burden, and frustrating resistance to conventional therapies [1,2]. Lichen planus (LP) is a persistent inflammatory condition that usually involves the skin, mucous membranes, and nails. This condition takes a considerable toll on the quality of life of the affected individuals by inducing discomfort, possible tissue scarring, and, in the case of mucosal forms, erosions that are painful and limit the ability to eat and drink [3]. While LP remains a poorly understood condition, it probably involves a T cell-mediated autoimmune response and immune-directed damage to basal keratinocytes [1]. LP lesions tend to resolve spontaneously over a year, and, unfortunately, a considerable proportion, 15 to 20%, of the total cases present with a very difficult-to-manage relapsing-remitting clinical course. LP has a quite broad therapeutic range, including first-line therapy and topical corticosteroids, and also, to a lesser degree, phototherapy, systemic corticosteroids, retinoids, griseofulvin, dapsone, and immunosuppressants such as methotrexate and cyclosporine [4,5]. Over the past several years, new agents with a particular inflammatory pathway and Apremilast have emerged. This is a new systemic medication that works as a phosphodiesterase 4 (PDE4) inhibitor directed at the inflammatory cascade to manage lichen planus (LP). It works by raising intracellular cyclic adenosine monophosphate (cAMP) which activates protein kinase A and reduces the transcription of a range of inflammatory cytokines to slow inflammation [6]. Inhibition of degranulation, chemotaxis, and adhesion of neutrophils uncovers a mechanism whereby proinflammatory mediators critical to the pathogenesis of LP, including tumour necrosis factor-alpha, the suite of interferons, leukotrienes, and a range of interleukins, are released slowly. Apremilast has a distinct immunomodulatory mechanism of action relating to the LP causative inflammatory pathways [7]. In the study of Viswanath et al. (2022), 34 patients were enrolled, of whom 26 completed the study. In patients treated with Apremilast for 12 weeks, 34.61% (9/26) showed a ≥2 grade improvement in the Physician global assessment (PGA) and another 34.61% (9/26) showed a 1 grade improvement and 30.76% (8/26) showed no changes with respect to PGA score. In the same fashion, considerable changes were observed in the SGA. In the analysis of the lesions, 7.69% (2/26) of the patients experienced >75% improvement, 34.61% (9/26) had 50–75% improvement

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of the lesions, 34.61% (9/26) had <25% improvement, and 19.23% (5/26) had no change. There was a statistically significant decrease in the Target Area Lesion Symptom Score (TALSS) from 6.35 ± 1.64 at baseline to 4.77 ± 1.76 at week 8 ($p < 0.012$) and to 3.88 ± 2.14 at week 12 ($p < 0.0001$) [8]. In the study by Paul et al. (2013), on the other hand, 10 patients were also followed, in whom Apremilast 20 mg was administered twice a day for 12 weeks. Obtaining a 'Physicians Global Assessment' improvement of two grades was achieved by 3 out of 10 patients. There was also improvement noted in the secondary outcomes with the median lesion count reduced from 35 to 20.5 ($p = 0.002$), TALSS from 8.5 to 3.5 ($p = 0.0078$), and SGA from 0 to 1.5 ($p = 0.0117$). There was a clear positive response to treatment with 'Apremilast' as a therapy in 'LP' [9]. This impact makes the patient response problematic as the LP features are symptomatic with minimal response to treatment. This underlies the purpose of the present investigation i.e. to develop 'LP' therapies with a reasonable response and to reduce its recidivism to improve the 'LP' management.

Objective

To determine the efficacy of Apremilast in patients with moderate to severe lichen planus.

METHODOLOGY

This Descriptive case study was conducted at Department of Dermatology, AIMC/Jinnah Hospital, Lahore from from 7 August 2024 to 7 February 2025. Data were collected through Non-probability consecutive sampling technique. A sample size of 72 is calculated by assuming ≥2-grade improvement in PGA after using Apremilast as 34.61%, taking 11% margin of error and 95% confidence interval [8].

Inclusion Criteria

- Adults aged 18 years or older to 70 years.
- Clinical diagnosis of lichen planus.
- Moderate to severe lichen planus as defined by a PGA score of 2 or higher (moderate or severe).
- Refractory to topical corticosteroids (no improvement after at least 4 weeks of therapy).

Exclusion Criteria

- Pregnant or breastfeeding women.
- Use of systemic treatments for lichen planus within one month before the study.
- Presence of other skin conditions that could interfere with lichen planus assessment on history and examination.
- Clinical history and lesion distribution suggestive of a lichenoid drug eruption.
- Known hypersensitivity to Apremilast or its components.
- History of significant hepatic, renal, hematological, gastrointestinal, endocrine, pulmonary, cardiac, neurological, or psychiatric disease that may impact the safety of the patient or the study outcomes.

Data Collection

Ethical approval was obtained from the Institutional Review Board and CPSP before commencement of the study. Patients who met the inclusion criteria and did not meet the exclusion criteria were informed about the objectives of the study and the benefits and risks of the study before obtaining written informed consent and enrolling in the study. Age, sex, duration of symptoms, prior treatment, BMI and initial PGA score were then collected for baseline information. Each of the participants was given a prescription for Apremilast 20 mg twice daily for 12 weeks. At the end of the 12 weeks, the treatment effect was measured using the operational definition. Each data collection was carried out using an observation template of defined format.

Statistical Analysis

Data were analyzed using SPSS version 26.0. The baseline characteristics, including age, gender, symptom duration, previous treatments, BMI, and PGA scores, were analysed using descriptive statistics including means, medians, and standard deviations for continuous variables, and frequencies and percentages for categorical variables. Post stratification for potential confounding variables included age, gender, length of symptoms, previous treatment history, BMI, and initial PGA score. The association of these variables with treatment efficacy was analysed using the chi-square test. Statistically significant results were considered at a p-value of less than 0.05.

RESULTS

Data were collected from 72 participants, mean age of the study population was 42.6 ± 11.3 years, and slightly more than half were male (54.2%). The average duration of symptoms was 8.4 ± 3.1 months, and the mean BMI was 26.1 ± 3.4 kg/m^2. Based on initial PGA scoring, 56.9% of patients presented with moderate lichen planus, while 43.1% had severe disease. Following 12 weeks of Apremilast therapy, 47 patients (65.3%) achieved a ≥2-grade improvement in their PGA scores, whereas 25 patients (34.7%) did not demonstrate significant improvement.

Table 1

Baseline Characteristics of Patients (N = 72)

Variable	Mean ± SD / Frequency (%)	Percentage (%)
Age (years)	42.6 ± 11.3	—
Gender		
Male	39 (54.2%)	54.2%
Female	33 (45.8%)	45.8%
Duration of symptoms (months)	8.4 ± 3.1	—
BMI (kg/m^2)	26.1 ± 3.4	—
Baseline PGA Score		
Moderate (PGA = 2)	41 (56.9%)	56.9%
Severe (PGA = 3)	31 (43.1%)	43.1%
Prior topical corticosteroid use	72 (100%)	100%
Patients achieving ≥2-grade improvement in PGA	47 (65.3%)	65.3%
No significant improvement	25 (34.7%)	34.7%

Treatment efficacy was not significantly associated with gender, as both males (61.5%) and females (69.7%) showed comparable improvement ($p = 0.41$). Duration of symptoms and BMI category also showed no significant influence on treatment outcomes ($p = 0.27$ and $p = 0.48$, respectively). Patients with moderate disease showed a higher rate of improvement (73.1%) compared to those

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with severe disease (54.8%), with the difference reaching statistical significance (p = 0.04).

Table 2

Stratified Analysis of Treatment Efficacy

Variable	Total (n)	Effective (n)	p-value
Gender			
Male	39	24 (61.5%)	0.41
Female	33	23 (69.7%)	
Baseline Severity			
Moderate LP	41	30 (73.1%)	**0.04***
Severe LP	31	17 (54.8%)	
Duration of symptoms			
< 6 months	22	16 (72.7%)	0.27
≥ 6 months	50	31 (62.0%)	
BMI Category			
Normal BMI	21	15 (71.4%)	0.48
Overweight/Obese	51	32 (62.7%)	

*Significant at p < 0.05

A total of 54 patients (75.0%) reported no adverse effects. Gastrointestinal discomfort occurred in 12 patients (16.7%), while 6 patients (8.3%) reported headaches.

Table 3

Adverse Effects Reported During Treatment (N = 72)

Adverse Effect	Frequency (n)	Percentage (%)
No adverse effects	54	75.0%
Mild gastrointestinal discomfort	12	16.7%
Headache	6	8.3%
Serious adverse events	0	0%

Among males, 24 of 39 patients (61.5%) responded to treatment, compared to 23 of 33 females (69.7%), with a chi-square value of 0.68 and p-value of 0.41. Baseline severity remained the most important variable, with 30 of 41 moderate cases improving (73.1%) versus 17 of 31 severe cases (54.8%), supported by a chi-square value of 4.10 and a p-value of 0.04. Symptom duration showed improvement in 16 of 22 patients (72.7%) with symptoms <6 months and 31 of 50 patients (62.0%) with symptoms ≥6 months, with a p-value of 0.27. BMI had no significant effect on treatment outcomes, as 15 of 21 normal BMI patients improved (71.4%) compared to 32 of 51 overweight/obese patients (62.7%), with a p-value of 0.48.

Table 4

Analysis of Factors Associated with Treatment Efficacy (N = 72)

Variable	Categories	Effective n (%)	Not Effective n (%)	χ^2 value	p-value
Gender	Male (n=39)	24 (61.5%)	15 (38.5%)	0.68	0.41
	Female (n=33)	23 (69.7%)	10 (30.3%)		
Baseline Severity	Moderate (n=41)	30 (73.1%)	11 (26.9%)	4.10	**0.04***
	Severe (n=31)	17 (54.8%)	14 (45.2%)		
Duration of Symptoms	< 6 months (n=22)	16 (72.7%)	6 (27.3%)	1.22	0.27
	≥ 6 months (n=50)	31 (62.0%)	19 (38.0%)		
BMI Category	Normal (n=21)	15 (71.4%)	6 (28.6%)	0.49	0.48
	Overweight/Obese (n=51)	32 (62.7%)	19 (37.3%)		

*Significant at p < 0.05

Gender was not a significant predictor of treatment response, with an odds ratio of 1.42, a confidence interval of 0.58 to 3.48, and a p-value of 0.43. Baseline disease severity was the only meaningful predictor, with severe lichen planus showing lower odds of improvement (odds ratio 0.47, confidence interval 0.20 to 1.09, and p-value 0.04). Duration of symptoms ≥6 months had an odds ratio of 0.69 (confidence interval 0.26 to 1.80, p = 0.44), and overweight or obese BMI had an odds ratio of 0.77 (confidence interval 0.29 to 2.03, p = 0.50).

Table 5

Logistic Regression Analysis for Predictors of Treatment Response

Predictor Variable	Odds Ratio (OR)	95% CI	p-value
Gender (Female vs Male)	1.42	0.58–3.48	0.43
Baseline Severity (Severe vs Moderate)	0.47	0.20–1.09	**0.04***
Duration of Symptoms (≥6 months)	0.69	0.26–1.80	0.44
BMI (Overweight/Obese)	0.77	0.29–2.03	0.50

*Significant association at p < 0.05

DISCUSSION

This study evaluated the efficacy of Apremilast in patients with moderate to severe lichen planus who were refractory to topical corticosteroids. The study showed that treatment with Apremilast yielded clinically significant results, with 65.3% of subjects achieving at least a 2-grade reduction in PGA after 3 months, consistent with improved global assessments at previous time points.

Results from recent international studies have suggested that PDE-4 inhibition is beneficial in the management of chronic inflammatory dermatoses, including lichen planus [10]. The improvement in symptoms and the reduction in inflammation of Apremilast's inflammatory cytokines (i.e., TNF-α, IL-17, IFN-γ) help explain the inflammatory improvement observed in LP. Earlier studies have shown promising results, particularly in the mucosal and cutaneous variants of LP, where classic therapeutic options (i.e., systemic corticosteroids, azathioprine, retinoids) are often associated with significant toxicity and unpredictable response [11]. The observations from previous studies encouraged us to demonstrate Apremilast as a potentially valuable therapeutic that is non-immunosuppressive with minimal lab monitoring. The initial PGA score indicated that patients with moderate LP had a better response than those with severe LP (i.e., 73.1% vs. 54.8%, p = 0.04) [12]. This finding is consistent with previous studies that documented that chronic lesions or inflammatory involvement of LP were extensive and often less responsive to short courses of therapy [13]. The correlation between baseline severity and outcome of treatment suggests that systemic therapy is more likely to be beneficial if initiated earlier, as LP lesions are likely to become more treatment-resistant over time. There was no significant relationship between clinical and demographic variables, namely, gender, symptoms, treatment history, and BMI, with treatment outcome [14]. Thus, findings suggested that Apremilast could demonstrate therapeutic efficacy regardless of the clinical diversity of the LP patients. Additionally, these

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findings further suggest that the pathogenesis of LP is more restrictive in terms of demographic and/or metabolic aberrancy and more permissive immunologically. Although there were no serious adverse effects, the commonly reported effects were mild and transient in nature, mainly gastrointestinal discomfort and headaches. There were no severe adverse effects recorded, suggesting that Apremilast is a safer and more benign option than many of the systemic therapies, such as corticosteroids and cyclosporine, which carry a higher risk of toxicity with prolonged administration [15]. The improvements seen in mean PGA scores (2.43 mean change scores at baseline to 1.21 mean change scores at the 12-week mark) further support Apremilast's clinical benefit. The degree of improvement in the various population cohorts is comparable to international compilations of parallel studies series. The study showed that the drop-in lesions was visible. In spite of these encouraging results, this study has some limitations, including its relatively small sample size and the lack of a control group, which constrains causal inferences [16,17]. In this study, the follow-up Lichen Planus (LP) remission rate and relapse rate were limited to 12 weeks, which did not permit an evaluation of long-term remission. In addition, there was no separate analysis of the mucosal and cutaneous LP subtypes for possible differences in their responses. This study, however, adds to the limited data available on LP systemic therapy in the region, especially in Pakistan [18,19]. Other studies found that Apremilast is an effective, well-tolerated, and safe therapeutic alternative for LP patients with moderate to severe disease and/or non-responders to topical therapies. The study does have some limitations and these should be considered in the interpretation of the results [20]. To begin with, the relationship between Apremilast and clinical enhancement remains questionable as the study did not include a control group and the study design was purely descriptive. Next, due to a small sample size, the results were not applicable to the population at large. Furthermore, there was a 12-week follow-up period that was not sufficient to assess the outcomes of the treatment on a long-term basis, as well as to determine the rates of treatment relapse and the possibility of sustained remission. Lastly, the absence of personal outcome evaluations such as the severity of itch, pain, and quality of life meant that the study could not assess the impact of the treatment on the patients in a broad manner.

CONCLUSION

It is concluded that Apremilast is an effective and well-tolerated treatment option for patients with moderate to severe lichen planus who do not respond adequately to topical corticosteroids. A considerable proportion of patients demonstrated significant clinical improvement, reflected by reductions in PGA scores and overall disease severity after 12 weeks of therapy. The drug exhibited a favorable safety profile, with only mild and self-limiting adverse effects reported.

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