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EFFICACY OF APREMILAST AS MONOTHERAPY IN MODERATE TO SEVERE CHRONIC PLAQUE PSORIASIS

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Abstract

OBJECTIVE

"To determine the efficacy of Apremilast as monotherapy in moderate to severe chronic plaque psoriasis in patients visiting the dermatology clinic of a tertiary care hospital".

STUDY DESIGN

The study adhered to the parameters established by a descriptive cross-sectional design framework.

PLACE AND DURATION OF THE STUDY

The research was conducted within the confines of the Department of Dermatology at Liaquat University of Medical and Health Sciences (LUMHS), Jamshoro, Hyderabad, between August 2024 and March 2025.

METHODOLOGY

This was a descriptive cross-sectional study that utilized non-probability convenience sampling of 80 patients ranging in age between 18 and 75 years with moderate to severe chronic plaque psoriasis. The administration of apremilast was done over 16 weeks with the initial dose of 10 mg, which was increased to 30 mg twice a day. PASI ≥ 75 was used to evaluate the efficacy of treatment. The analysis of the data was performed by using SPSS v26, and statistical significance was taken into account (p = 0.05).

RESULTS

The cohort under investigation comprised 80 individuals diagnosed with the condition (mean age 54.36 ± 8.24 years; 65% male, 35% female). A significant proportion of 69 patients (86.3%) exhibited a reduction of ≥75% in the Psoriasis Area Severity Index (PASI) score. The factors of shorter disease duration

(p=0.0001) and the severity of the condition (p=0.434) emerged as substantial determinants of treatment efficacy, whereas age (p=0.368) and gender (p=0.434) did not demonstrate a significant impact.

CONCLUSION

This research trial demonstrated that apremilast, used alone, can achieve high efficacy in patients with moderate to severe chronic plaque psoriasis. Most patients reported a decrease in PASI baseline score of greater than 75% after 16 weeks. Treatment response was strongly influenced by shorter disease duration and less severe baseline disease. Age and gender had no significant influence on the results. The results indicate that apremilast is a safe, convenient, and effective oral therapeutic agent for moderate to severe psoriasis, particularly for patients who present with the disease at an earlier stage.

INTRODUCTION

Psoriasis is an immune-mediated inflammatory, chronic disease of the skin that can have systemic manifestations and has a prevalence rate of about 2-3% globally [1,2]. Chronic plaque psoriasis is the most widespread of its clinical forms and is typified by erythematous scaly plaques with a relapsing-remitting progression [2]. In addition to being disfiguring, the disease also causes severe disability to quality of life, resulting in social stigma, psychological morbidity, and predisposition to comorbidities like metabolic syndrome and cardiovascular disease [3]. Even though there is no full cure to psoriasis, numerous treatment modalities such as topical agents, phototherapy, non-biological drugs, including methotrexate, cyclosporine, and acitretin, and biologic agents, exist to control the severity of the disease [4,5]. The traditional systemic treatments are usually restricted by their toxicity (hepatotoxicity, nephrotoxicity, and leukocytopenia), which limit prolonged use of these therapies [5]. Biologic agents are more effective, but they are expensive, require strict monitoring, are parenterally administered, and are prone to infections, all of which undermine adherence and sustainability in real-world practice [6,7]. Hence, there exists an urgent requirement for safe, effective, and convenient alternatives for patients with moderate to severe plaque psoriasis. In the year 2014, a new drug, apremilast, was introduced in the form of an oral small-molecule phosphodiesterase-4 (PDE4) inhibitor, which is used as a novel therapy in the treatment of moderate to severe plaque psoriasis [8]. Apremilast decreases pro-inflammatory cytokines involved in the pathogenesis of psoriasis by modulating intracellular cyclic adenosine monophosphate (cAMP) [9]. Its efficacy and tolerability have been proven in clinical trials with large decreases in PASI scores and a positive change in patient-reported outcomes [10-12]. Gastrointestinal symptoms, headache, and upper respiratory tract infections are the most reported adverse effects and occur as a rule without complications [8,9].

Nevertheless, randomized controlled studies tend to be restricted by selection bias because there is a tendency to eliminate patients with comorbidities like infections, psychiatric disorders, or metabolic diseases [13,14]. Because of this, their findings might not necessarily reflect the treatment outcomes in everyday practice. The practical evidence of apremilast in moderate to severe chronic plaque psoriasis is limited, especially in South Asian individuals, where the accessibility of treatment and comorbidities of patients vary in relation to the Western context [15,16]. The current research was to determine the efficacy of apremilast as a monotherapy in moderate to severe chronic psoriasis in plaques. It seeks to bridge the disparity between the findings of the controlled clinical trials and clinical practice to present the evidence that can be used to support clinical decision-making and drive the argument that apremilast is a safe and effective therapeutic agent in a standard dermatological practice.

METHODOLOGY

This is a cross-sectional study that was performed descriptively in the department of dermatology, LUMHS, Jamshoro, Hyderabad, with the consent of the institutional ethics committee. Patients aged 18–75 years of either gender with moderate to severe chronic plaque psoriasis (PASI >10) of more than six months' duration were included, while those with hypersensitivity to apremilast, prior use of the drug for more than four weeks, pregnancy, lactation, inadequate contraception, systemic organ impairment, or psychiatric illness were excluded. A sample size of 80 was determined using the WHO calculator with an expected efficacy of (88.7%)[10], 95% confidence level, and 7% absolute precision. Eligible participants were enrolled through non-probability convenience sampling after informed consent. Baseline demographic and clinical data were recorded, PASI scores were assessed, and apremilast was initiated at 10 mg on day 1, titrated to 30 mg twice daily by day 6, and continued for 16 weeks. At follow-up, PASI scores were reassessed and patients achieving ≥75% reduction from baseline (PASI75) were considered efficacy. Data was analyzed in SPSS version 26, where quantitative variables such as age, disease duration, and PASI were presented as mean ± SD. Categorical variables as frequencies and percentages, and the relationship between efficacy and effect modifiers was assessed using Chi-square test with $p \leq 0.05$ considered statistically significant .

RESULTS

The total sample of eighty individuals participated in the study. Their mean age was 54.36 ± 8.24 years (95% CI: 52.53–56.20). The average PASI score was 54.16 ± 23.12 (95% CI: 49.02–59.31). The mean duration of the condition was 22.29 ± 8.95 years (95% CI: 20.29–24.28). Most participants were male (65.0%), and females made up 35.0%. The majority had severe psoriasis (77.5%), while 22.5% had moderate disease (TABLE I).

Among 80 patients, treatment efficacy was observed in 69 individuals (86.3%). Eleven individuals (13.7%) showed no therapeutic response. The average age of patients with efficacy was 54.03 ± 8.49 years. Non-responders had an average age of 56.45 ± 6.29 years. There was no statistically significant difference (p=0.368). Gender also did not show a significant association with treatment efficacy (p=0.653). Among males, the response rate was 66.7% versus 33.3% among females. In the non-responder group, 54.5% were male and 45.5% were female. The duration of the disease showed a significant relationship with efficacy. Responders had a shorter mean duration (22.01 ± 8.67 years) compared to non-responders (24.0 ± 10.85 years) (p=0.0001). Disease severity also had a significant association (p=0.049). All non-responders had severe psoriasis. Among responders, 73.9% had severe disease and 26.1% had moderate disease (TABLE II).

Table I: Demographic and Clinical Characteristics of Study Participants (n=80)

Mean ± Standard Deviation		**95% Confidence Interval**
Age in years = **54.36 ± 8.24**		52.53–56.20
PASI Score = **54.16 ± 23.12**		49.02–59.31
Duration of Disease in years = **22.29 ± 8.95**		20.29–24.28
Frequency (%)		
Gender	Male	52 (65.0)
	Female	28 (35.0)
Severity of Psoriasis	Moderate	18 (22.5)
	Severe	62 (77.5)

Table II: Comparison of Patient Characteristics with Efficacy (n=80)				
Characteristics		**Efficacy**		**P-Value**
		Yes (n=69)	**No (n=11)**	
Age in years		54.03 ± 8.49	56.45 ± 6.29	0.368
Duration of Disease in years		22.01 ± 8.67	24.0 ± 10.85	0.0001
Gender	Male	46 (66.7)	6 (54.5)	0.434
	Female	23 (33.3)	5 (45.5)	
Severity of Psoriasis	Moderate	18 (26.1)	0 (0.0)	0.049
	Severe	51 (73.9)	11 (100.0)	

DISCUSSION

The current trial assessed the efficacy of apremilast as monotherapy in moderate to severe chronic plaque psoriasis. It demonstrated substantial effectiveness, with a significant clinical response: 86.3% of patients achieved a 75% reduction in PASI score from baseline at 16 weeks. This response rate is substantially higher than rates observed in pivotal phase 3 randomized controlled trials, such as ESTEEM 1 and 2, where only 28-33% of patients achieved a 75% or greater reduction in baseline PASI score at week 16 [8,9]. More recent large-scale studies, such as the DISCREET trial, reported approximately 40% [12]. Observational studies in Europe indicate long-term but relatively modest effectiveness, with 30-50% of patients achieving a 25% reduction in PASI score [10]. Discrepancies between our results and previous trials may arise from differences in patient selection, adherence, disease severity, or genetic and environmental factors specific to the South Asian population. Our cohort, primarily comprising patients with severe disease, may have been more motivated to adhere strictly to therapy, potentially increasing treatment response.

In comparison with regional data, our results are also notable. A recent study from Pakistan comparing apremilast with methotrexate found apremilast to be effective, though not significantly superior, with responses more consistent with global data [11]. The higher efficacy observed in our cohort highlights the importance of contextual factors, including healthcare access and treatment adherence, in shaping outcomes. Furthermore, our analysis showed that shorter disease duration was significantly associated with better response, suggesting that earlier initiation of apremilast may provide greater benefit. This is consistent with existing knowledge that long-standing psoriasis may become less responsive to therapy due to chronic immune dysregulation and structural changes in the skin [4,6]. In contrast, disease severity negatively influenced outcomes, as all non-responders in our study had severe disease, a finding that aligns with previous evidence that patients with advanced disease stages may be less likely to respond to systemic treatments [13]. Age and gender were not significantly associated with treatment efficacy, which is consistent with previously published reports [17].

The strengths of this study include its real-world design, which improves external validity and adds valuable evidence from a South Asian population, where studies on apremilast remain limited. The use of the ≥75% reduction in PASI score as a standardized endpoint also facilitates meaningful comparison with international research. However, some limitations must be considered. The cross-sectional design without a control group limits causal inference and

prevents direct comparison with conventional systemic therapies or biologics. The single-center recruitment and relatively small sample size may restrict generalizability. Moreover, the follow-up period was limited to 16 weeks, whereas long-term studies have demonstrated sustained efficacy and safety of apremilast for up to three years [8,10]. Importantly, our study did not systematically assess adverse events, an important limitation since gastrointestinal upset, headaches, and upper respiratory infections are among the most common side effects of apremilast [8,9].

Despite these limitations, the study demonstrates that apremilast is a highly effective and practical treatment option for patients with moderate to severe psoriasis in South Asia, particularly when initiated earlier in the disease course. Its oral administration, favorable safety profile, and suitability for patients with comorbidities, as highlighted in recent reviews [17], make it a valuable alternative to biologics, especially in regions where cost and access barriers restrict their use. Future multicenter prospective studies with larger cohorts, longer follow-up, and systematic safety reporting are recommended to validate these findings and to better define the role of apremilast in comparison with other systemic agents such as methotrexate.

CONCLUSION

This research trial demonstrated that apremilast, used alone, can achieve high efficacy in patients with moderate to severe chronic plaque psoriasis. Most patients reported a decrease in PASI baseline score of greater than 75% after 16 weeks. Treatment response was strongly influenced by shorter disease duration and less severe baseline disease. Age and gender had no significant influence on the results. The results indicate that apremilast is a safe, convenient, and effective oral therapeutic agent for moderate to severe psoriasis, particularly for patients who present with the disease at an earlier stage.

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