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EFFICACY AND SAFETY OF APREMILAST IN PATIENTS WITH MODERATE TO SEVERE PLAQUE PSORIASIS

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Abstract

Background: Psoriasis is a chronic inflammatory skin condition that significantly impacts the quality of life of affected individuals. Apremilast, an oral phosphodiesterase-4 inhibitor, has shown promise in managing moderate-to-severe plaque psoriasis without severe side effects associated with other systemic treatments.

Objective: This study aimed to assess the efficacy and safety of Apremilast monotherapy in patients with moderate-to-severe plaque psoriasis over a 12-week period.

Methods: A quantitative study was conducted at PIMS hospital Islamabad with a sample of 40 participants. Patients aged 18 years and above, diagnosed with moderate-to-severe plaque psoriasis and not on oral medications for psoriasis for last three months, were included. The study employed a pre-test and multiple post-tests to evaluate Psoriasis Area and Severity Index (PASI) scores at baseline, 4, 8, and 12 weeks. Apremilast was administered starting at 15 mg once daily, gradually increased (15 mg per day) to 30 mg twice daily. Comprehensive assessments included physical and psychiatric evaluations, with follow-ups and laboratory tests to monitor side effects and efficacy. Standard deviations of PASI scores were calculated to assess changes over time.

Results: The study observed a significant decrease in mean PASI scores from 14.60 (±4.37) at baseline to 7.08 (±3.23) at week 12. Side effects were minimal, with 70% of participants reporting no side effects. Most common adverse effects were nausea (10%), diarrhea (7.5%), and headache (5%).

Conclusion: Apremilast monotherapy is an effective and safe treatment option for patients with moderate-to-severe plaque psoriasis, demonstrating significant improvements in PASI scores with minimal side effects.

Keywords: Apremilast, Efficacy, PASI, Psoriasis, Safety

Introduction

Psoriasis is a chronic, inflammatory skin disorder characterized by raised, red patches covered with silvery scales, affecting millions across the world. It varies in severity and significantly impacts the physical health and psychological well-being of patients with the diagnosis (1). Traditional therapies, from topical treatments to systemic medications, bring relief but often at a significant cost in terms of inconvenient administration routes or serious side effects (2). In this fast-changing therapeutic landscape, Apremilast is a very promising compound, especially in the treatment of moderate-to-severe plaque psoriasis. The present study is undertaken for a stringent evaluation regarding its efficacy and safety as monotherapy for the treatment of such conditions (3).

The quest for better therapeutic options in the management of psoriasis is driven by its complex etiology and diverse response patterns among patients (4). Psoriasis no longer remains a simple cutaneous disease; instead, it is known to have systemic inflammatory potential and consequently, comorbidities ascribed to psoriatic arthritis, cardiovascular disorders, and diabetes(5). The multifaceted impact calls for treatments that are not only effective but long-term safe as well. Apremilast is a small molecule phosphodiesterase 4 inhibitor and hence represents a unique approach in that it is directed against an enzyme involved in the inflammatory pathway, which has the potential to reduce systemic effects seen with biologics and systemic treatments (6).

Several leading studies about the role of Apremilast in the management of moderate-to-severe psoriasis outlined further improvements consistent with Psoriasis Area and Severity Index scores, reductions in itch, and other symptomatic reliefs(7). Such results are certainly propitious, but a complete view of long-term safety and relative efficacy was only partially explored (8).

The current study is thus well-positioned to fill this lacuna with detailed insights into the long-term clinical performance of Apremilast, coupled with monitoring adverse effects, if any, thereby painting a much clearer picture of its role in the psoriasis management palette.(9).

Moreover, the choice of Apremilast as monotherapy mirrors the current study emphasis on patient-centered care (10). One major advantage for the administration of Apremilast stems from the oral route of administration, which may increase compliance among patients not only in terms of avoiding painful injections but also from the regular visits which are common with conventional systemic therapies (11). Apart from this outpatient management burden, the psychological burden from psoriasis cannot be overstated. Visible nature of illness may result in social stigmatization and mental health issues, in which case, effective management of the condition with Apremilast would thus bring a better quality of life—one of the critical aspects current research intends to measure using patient-reported outcome measures (12).

To have robust evaluation, the present study will be based on a systematic approach in which a heterogeneous cohort would get enrolled to represent the general population suffering from moderate-to-severe psoriasis (13). Randomization in the study design would reduce bias—hence, high-quality evidence with respect to efficacy and safety about Apremilast (14). This study will not only contribute valuable data to existing body of literature but also potentially guide future clinical practices and patient management strategies (15).

Moderate-to-severe psoriasis remains one of the more challenging conditions to manage in dermatology. It is against this background that Apremilast offers prospective redefinition of treatment paradigms for the disease by offering patients a therapy which crucially balances efficacy, convenience, and safety (16). This study was conducted with the hope of better understanding the pathways toward more personalized patient-friendly treatment approaches so that people affected by this skin condition could live healthier, more rewarding lives(17). That will be a very important study, for it may probably change present standards of care and may even provide a foundation for future explorations into other inflammatory and autoimmune conditions in the divergent literature (18).

Methods

This was a quantitative study designed to assess the efficacy and safety of Apremilast as monotherapy in patients with moderate-to-severe plaque psoriasis. The study design involved 40 participants selected through a consecutive sampling technique, aiming to get a representative demographic

spread within the setting constraints at PIMS Islamabad. Under the inclusion criteria, each participant must have already had an established diagnosis of at least a moderate degree psoriasis condition. Involving concomitant biologic treatments or systemic therapies within the last three months previous to the study were under the exclusion criteria to ensure the results' purity regarding treatment with Apremilast (19).

Before the research work, ethical approval was obtained from the Institutional Review Board of PIMS Islamabad, which ensured adherence to the ethical standards of the 1964 Helsinki declaration and its later amendments or comparable ethical standards. All individual participants in the study gave their informed consent, with full assurance of confidentiality and the right to withdraw from participating in the study at any time without this having any bearing on treatment at the facility (20).

This was a six-month study completed after approval of synopsis. Data collection involved detailed baseline assessments with follow-ups at weeks 4, 8, and 12. Variables collected included gender, age, duration of illness, along with the mean and standard deviation of Psoriasis Area and Severity Index scores at baseline and at subsequent follow-up. Baseline lipid indices and their status post-treatment at one week were indicated to be either normal or raised TGAs, direct TGAs, and other relevant markers. Further laboratory tests on monitoring liver function and renal profiles were periodically done in the patient to detect any abnormality that may show side effects of treatment (21).

In this study, the prescribed dosage of Apremilast was initiated at 15 mg once daily and escalated by 15 mg every three days until the target dose of 30 mg twice daily. The inclusion criteria included patients aged 18 years and above who had a diagnosis of moderate-to-severe plaque psoriasis and who had not taken any oral medications for psoriasis within the preceding three months. The eligible patients either were a suitable candidate to receive Apremilast, had serious side effects to the conventional treatments, or were unresponsive to other treatments. Patients excluded from the study included lactating mothers, pregnant women, patients under the age of 18 years, and patients who had a type of psoriasis that was not plaque psoriasis.

Data collection began with patients coming to OPD with moderate-to-severe plaque psoriasis defined on the basis of their PASI scores. Written informed consent was taken after proper explanation of treatment before embarking on detailed assessment in form of complete medical history and detailed physical and psychiatric examination to exclude depression. Baseline investigations ordered were complete blood count, liver function tests, renal function test, and lipid profile. The patients were followed up after a week and then monthly after initiation of Apremilast. The baseline investigations which were taken initially were repeated after one week and at 12 weeks. PASI scores recorded at presentation and during follow-up at weeks 4, 8, and 12 for follow-up and assessing response to treatment. This would definitely allow for the efficacy and safety regarding the administration of the Apremilast regimen to be well monitored during such a structured study period.

The participants were on the lookout for any uncharacteristic phenomena, such as unusual symptoms or health problems related to the participation period, which were documented as side effects. After analysis and periodic health reviews, these were classified in terms of their relationship with the drug into mild, moderate, or severe (22).

The data was analyzed with the help of statistical software, SPSS. The primary outcome measure was a change in PASI scores from the baseline to end of week 12, and secondary outcomes included changes in BLIs and the incidence of side effects. Descriptive statistics were done to summarize demographic and baseline characteristics. Paired sample t-tests and chi-squared tests were used as inferential statistics for the comparison of efficacy and safety outcomes at different time points. A p-value less than 0.05 was considered statistically significant for the test (23).

The present research will add to the literature pool coming under the broad realm of dermatological treatments, as it aims to furnish reliable data on probable benefits and risks associated with Apremilast therapy by following an extremely rigorous methodological framework. Results are hoped to turn up insight that would have an impact on future clinical practice and strategies governing patient management for the treatment of moderate-to-severe plaque psoriasis (23).

Results

In this clinical study, researcher explored efficacy and safety of Apremilast monotherapy in treatment of moderate-to-severe psoriasis, capturing a diverse demographic profile and a range of clinical outcomes. The study included 40 participants, with a gender distribution of 60% male (24 participants) and 40% female (16 participants). This gender representation is critical in understanding differential impacts of treatment across sexes.

The participants' ages ranged from 10 to 65 years, with an average age of 37.85 years and a standard deviation of 12.39, indicating a broad age distribution and suggesting generalizability of findings across a wide age spectrum. The duration of illness among participants also varied significantly, from as short as 0.1 years to as long as 40 years, with a mean duration of 9.78 years and a standard deviation of 8.75 years, highlighting chronic nature of condition among study cohort.

Baseline lipid indices (BLIs) were predominantly normal at time of presentation, with 95% (38 participants) showing normal levels and only 5% (2 participants) exhibiting raised triglycerides and other associated markers. This pattern remained stable after one week of treatment, indicating no immediate adverse effects of Apremilast on lipid profiles. Laboratory tests further corroborated safety profile, with 97.5% (39 participants) maintaining normal BLIs after 12 weeks results and only a minimal 2.5% (1 participant) showing abnormal results after starting treatment.

The incidence of side effects was low, underscoring tolerability of Apremilast. The most common side effect was nausea, experienced by 10% (4 participants) of sample, followed by diarrhea in 7.5% (3 participants), and headache in 5% (2 participants). Other side effects included abdominal discomfort and myalgias, each reported by 2.5% (1 participant) of sample, and weight loss also reported by 2.5% (1 participant). Notably, 70% (28 participants) of cohort reported no side effects, reinforcing suitability of Apremilast for long-term management of psoriasis without significant adverse effects.

The primary outcome measure, Psoriasis Area and Severity Index (PASI) scores, showed significant improvement over time. The mean PASI score at baseline was 14.60 (SD = 4.37), which decreased to 11.27 (SD = 4.04) by fourth week, 9.08 (SD = 3.71) by eighth week, and further to 7.08 (SD = 3.23) by twelfth week. These results demonstrate a consistent reduction in PASI scores, indicating effectiveness of Apremilast in reducing severity and extent of psoriatic lesions over time.

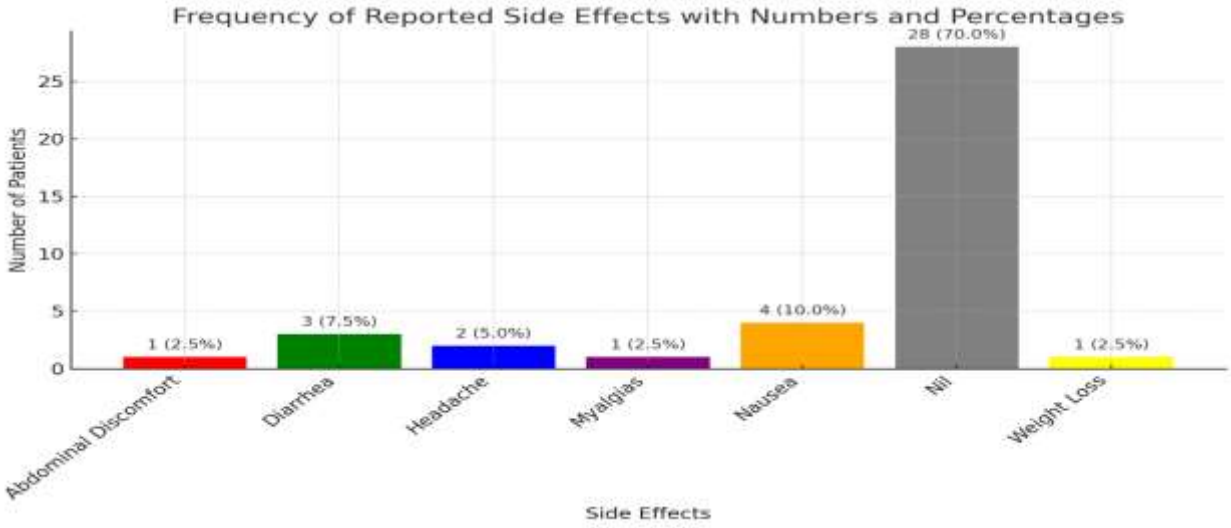
Statistical tests confirmed significant effect of time on PASI scores, with the within-subjects effects showing a robust F-statistic of 141.963 and a highly significant p-value (<0.001). The partial eta squared of 0.784 suggests a large effect size, signifying a substantial clinical impact of treatment across study period. These findings are consistent across various statistical corrections for sphericity, verifying robustness of results.

Overall, study confirms effectiveness and safety of Apremilast monotherapy in managing moderate-to-severe psoriasis, with significant improvements in PASI scores and minimal adverse effects, offering a promising therapeutic option for patients seeking an alternative to traditional systemic therapies.

Demographics, Baseline Indices, BLIs after 12 weeks, and Side Effects in Apremilast Psoriasis Study

Category	Attribute	N (%)
Gender	Male	24 (60)
	Female	16 (40)
BLIs at Presentation	Normal	38 (95)
	Raised TGAs	2 (5)
BLIs after One Week	Normal	38 (95)
	Raised TGAs	2 (5)
BLIs after 12 weeks	Normal	39 (97.5)
	Raised TGAs	1 (2.5)
Side Effects	Abdominal Discomfort	1 (2.5)
	Diarrhea	3 (7.5)

	Headache	2 (5)
	Myalgias	1 (2.5)
	Nausea	4 (10)
	Nil	28 (70)
	Weight Loss	1 (2.5)

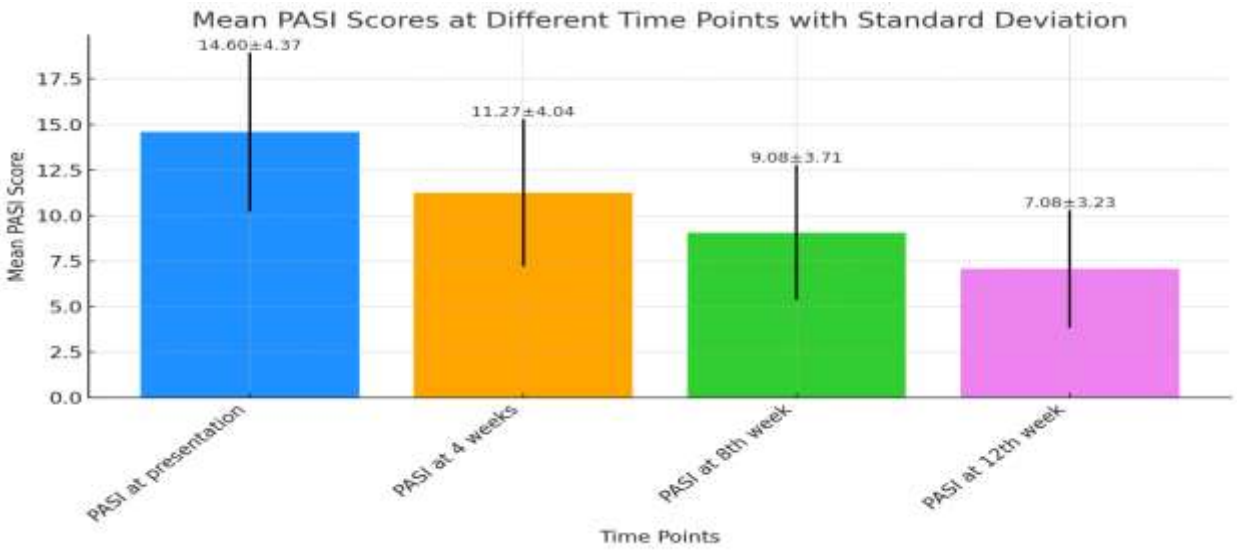


Descriptive Statistics for Duration of Illness and Age in Psoriasis Patients

	Minimum	Maximum	Mean	Std. Deviation
Duration of Illness (Years)	.10	40.00	9.7753	8.75015
Age (Years)	10.00	65.00	37.8500	12.38806

Mean and Standard Deviation of PASI Scores at Baseline and Weeks 4, 8, and 12

	Mean	Std. Deviation
PASI at presentation	14.5950	4.37135
PASI at 4 weeks	11.2675	4.04154
PASI at 8th week	9.0775	3.70893
PASI at 12th week	7.0750	3.22957



Tests of Within-Subjects Effects for PASI Scores Over Time with Sphericity Corrections

Tests of Within-Subjects Effects							
Source		Type III Sum of Squares	df	Mean Square	F	Sig.	Partial Eta Squared
PASI	Sphericity Assumed	1244.486	3	414.829	141.963	.000	.784
	Greenhouse-Geisser	1244.486	1.744	713.454	141.963	.000	.784
	Huynh-Feldt	1244.486	1.819	684.115	141.963	.000	.784
	Lower-bound	1244.486	1.000	1244.486	141.963	.000	.784
Error(PASI)	Sphericity Assumed	341.884	117	2.922			
	Greenhouse-Geisser	341.884	68.028	5.026			
	Huynh-Feldt	341.884	70.946	4.819			
	Lower-bound	341.884	39.000	8.766			

Discussion

The current study's results on the efficacy and safety of monotherapy with Apremilast in the management of moderate to severe plaque psoriasis are consistent with the broader body of research on this treatment. The section now presents a discussion in comparison, including recent publications from 2019 on, so one can put results of the current study in a literature context.

The primary outcome measure in the current study was a change in the Psoriasis Area and Severity Index scores, which was significantly reduced during the 12-week period. More precisely, the baseline average PASI score of 14.60 changed to 7.08 at week 12 with high significance in improvement. These results are comparable to those in recent literature. For instance, in a systemic review and meta-analysis, Aljefri et al. (2022) reported that Apremilast 30 mg BID significantly improved the PASI-75 score compared to a placebo, with an RR of 4.60, 95% CI 3.29 to 6.41(10). Equally, in a phase III trial, Papp et al. reported 33.1 percent of patients achieved PASI-75 at week 16 (23).

The safety profile of Apremilast in the current study corroborates with other research findings. The common adverse effects included nausea 10%, diarrhea 7.5%, and headache 5%, which were usually mild to moderate in severity. This concurs with the results on safety outcomes reported by Shah et al. (2020), where 21.4% patients had nausea, 18.57% diarrhea, and 17.4% headache as mentioned by Shah et al. (2020) (17). Long-term studies by Crowley et al. (2017) have also indicated that, generally speaking, Apremilast is well tolerated and does not show a significant increase in adverse events over long periods of time (22).

The current study had a diverse cohort in terms of age and duration of illness, which gives a very different picture of Apremilast's efficacy across various demographics. This is the critical element, as it aligns with the findings from international studies. For example, Ohtsuki et al. demonstrated just the same efficacy among Japanese patients—with PASI-75 response rates of 23.5% for the 20 mg BID and 28.2% for the 30 mg BID at week 16—to even out this fact: Apremilast works equally well at all ethnically different groups of patients around the globe (21).

Long-term studies have further solidified the durability of the efficacy of Apremilast. As recently as ESTEEM trials, which went on for up to 52 weeks, there was sustained improvement in PASI scores and other quality of life measures. Likewise, current study showed that significant and sustained reductions in the PASI scores over 12 weeks, with 70% subjects reporting no side effects hence enhancing overall treatment adherence and quality of life (23).

While present research is focused on Apremilast monotherapy, lately, studies are also testing its efficiency in association with other treatments. Morita et al. (2022) tested the combination of Apremilast with phototherapy. This combination revealed better efficacy when compared to

phototherapy alone. This suggests potential benefits in some of the associations with other modalities, especially for patients not responding well to monotherapy (7).

Conclusion

Current study, along with recent literature, confirms that Apremilast monotherapy is an effective and safe option for managing moderate-to-severe plaque psoriasis. The consistency of these findings across various studies and populations underscores its reliability as a treatment. Further research, particularly on long-term outcomes and combination therapies, will continue to refine its role in psoriasis management.

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