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ORIGINAL ARTICLE

Comparative Study on The Efficacy and Tolerability of Oral Apremilast Versus Oral Methotrexate in Interface Dermatitis

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ABSTRACT
This prospective randomized controlled comparative study aimed to evaluate the effectiveness and tolerability of oral apremilast compared to oral methotrexate in patients with interface dermatitis types 2 and 3. Conducted at Krishna Hospital's dermatology department between February 2020 and December 2022, the study included 36 participants meeting specific criteria. Data collection involved patient history, thorough examinations, biopsy, and blood investigations. During a 12-week therapy period, participants were randomized to be in either Group I (apremilast) or Group II (methotrexate). Both groups demonstrated a significant decrease in clinical severity measures (PGA, VAS, LPSI, mucosal scores) over the 12-week period. Methotrexate exhibited a slightly more pronounced effect on PGA and VAS scores. The apremilast group experienced a higher frequency of adverse events, mostly gastrointestinal symptoms that resulted in treatment termination. Methotrexate and apremilast showed similar effectiveness in treating types 2 and 3 of interface dermatitis, with methotrexate showing a slightly superior effect on certain outcomes. Apremilast proved well-tolerated, although adverse events were more frequent. Further research is necessary to assess long-term efficacy and safety across various dermatological conditions.
Keywords: *Apremilast, methotrexate, interface dermatitis, lichen planus, randomized controlled trial, efficacy, tolerability, clinical outcomes.*

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INTRODUTION

Interface dermatitis, an expansive category within dermatology, involves a complex interplay at the junction between the dermis and epidermis, resulting in significant damage to basal cells in the epidermis. This term functions as a comprehensive label for a range of diseases, each presenting distinctive challenges in terms of clinical management. A distinctive characteristic of interface dermatitis lies in its dual impact on epidermal basal cells, evident in two distinct forms: filamentous degeneration, which aids in the creation of Civatte bodies, and vacuolar/hydropic degeneration. These cellular alterations are pivotal in the development of interface dermatitis and serve as diagnostic markers for this diverse array of skin disorders [9].

Interface dermatitis not only causes primary damage to basal cells but also sets off a series of secondary structural alterations in the skin. These changes to the epidermis can take the form of hypertrophy, which involves an increase in tissue volume, or atrophy, which is characterized by thinning of skin layers [8]. Simultaneously, the dermal layer experiences a variety of alterations, from the disappearance of rete ridges—which serve as links between the epidermis and dermis—to more significant modifications including pervasive dermal fibrosis and sclerosis. Developing successful treatment strategies in interface dermatitis requires an understanding of the subtle cellular and structural changes that occur in the condition. Because these dermatological disorders are complex, an integrated approach is required, including alterations in the architecture of the dermal and epidermal layers as well as fundamental cellular pathology [1]. When it comes to treatment choices, Apremilast has shown great promise. PDE4, which is expressed by a range of immune cells such as keratinocytes and synovial fibroblasts, as well as nonhematopoietic cells such as natural killer cells, macrophages, and lymphocytes, is selectively inhibited

by it [10]. Premilast efficiently lowers the spontaneous synthesis of tumor necrosis factor-alpha (TNF-alpha) from human rheumatoid synovial cells by inhibiting PDE4. The US Food and Drug Administration (FDA) authorized appreciast in 2014, mainly for the treatment of chronic plaque psoriasis [2].
On the other hand, methotrexate, an immunosuppressive medication, inhibits the activity of dihydrofolate reductase. Methotrexate has been used for a very long time to treat a variety of diseases, such as leukemia, lung, and breast malignancies, autoimmune disorders, and ectopic pregnancies. The FDA authorized it in the early 1970s for psoriasis and in the 1980s for rheumatoid arthritis. Additionally, it has proven to be safe and effective in the management of Lichen Planus [12].
The current study aims to evaluate oral methotrexate with oral apremilast in terms of their efficacy and tolerability in the treatment of interface dermatitis. In order to help doctors make evidence-based decisions, this research attempts to offer insightful information on the relative benefits of these two treatment alternatives. Ultimately, this will improve patient outcomes and quality of life.

MATERIAL AND METHODS

This prospective randomized controlled comparative study carried out at Krishna Hospital's dermatology department in Karad between February 2020 and December 2022, involves the inclusion of patients who meet specific criteria, contingent on their willingness and provision of informed written consent. The comprehensive data collection process comprises obtaining patient history, conducting thorough examinations of both cutaneous and systemic aspects, and confirming reaction patterns through biopsy and necessary blood investigations.
The study focuses on patients who have interface dermatitis types 2 and 3, as determined by histological examination and the Le Boit method. The duration of the trial is 12 weeks. The included conditions in this study encompass lichen planus, discoid lupus erythematosus (DLE), cutaneous graft-versus-host disease (GVHD), and long-standing lichenoid drug eruption. Ethical approval has been granted by the Institutional Ethical Committee, and the study is registered with the distinct identifier CTRI/2022/01/039139. The research design incorporates a systematic approach to patient enrolment, data collection, and ethical considerations, positioning it to provide valuable insights into the comparative effectiveness and safety of the chosen therapeutic interventions for interface dermatitis types 2 and 3.
The inclusion criteria are delineated to guarantee the enrolment of eligible participants. These include patients demonstrating interface dermatitis types 2 and 3, necessitating systemic management, aged 14 years and above, free from recent treatment, and willing to furnish written consent. Furthermore, participants are expected to adhere to all study procedures. On the other hand, individuals with interface dermatitis types 1, 4, and 5, as well as those displaying related systemic characteristics, are excluded based on predetermined criteria. Furthermore, patients with certain medical conditions—such as anaemia, leukopenia, thrombocytopenia, hepatic dysfunction, active HIV infection or hepatitis, active tuberculosis, impaired renal function, pregnancy or lactation, IUD use, live vaccination within the last six months, and known drug hypersensitivity—are not allowed. Patients who are unreliable or have unreasonable expectations are not accepted, nor are they welcome to follow up on a regular basis.
To prioritize the well-being of participants, ethical considerations and regulatory compliance take precedence. The study has obtained ethical clearance from the Institutional Ethical Committee and is duly registered with a Clinical Trials Registry of India (CTRI) registration number. This registration ensures transparency and accountability, aligning with sound research practices. The predetermined sample size of 36 patients is established based on the study's objectives and statistical considerations, ensuring ample power to detect meaningful differences. Informed consent, a crucial facet of ethical research, is mandatory, with participants required to provide written consent before undergoing any investigations.
The comprehensive nature of the inclusion and exclusion criteria aims to create a homogeneous study population, enhancing the internal validity of the research. The specified 12-week duration allows for the observation of pertinent outcomes within a reasonable timeframe. Additionally, the emphasis on regular follow-ups and compliance underscores the commitment to collecting robust and dependable data. The lottery approach is used to assure fair participant distribution by assigning participants at random into two groups, Group I and Group II. Group I receive oral Apremilast, gradually increased to a maximum of 60mg daily in two divided doses over the first week. In contrast, Group II is administered oral Methotrexate, with a titration to a maximum of 15mg weekly in three divided doses 12 hours apart within the initial week. Both groups receive emollients as adjuvant therapy, with no introduction of concurrent treatments during the study period.
Monthly follow-ups extend for three months or until a noticeable reduction in lesions is observed. The visit schedule, which consists of a baseline visit and follow-up visits at 15, 30, 60, and 90 days, makes it easier to evaluate each participant's reaction to the prescribed treatment plan in an organized manner. At

the conclusion of the 12-week research period, a thorough assessment and comparison are made between the clinical response and side effect profiles of the two treatment groups. By tabulating observed results, this comparative analysis sheds light on the safety and effectiveness profiles of oral methotrexate and oral apremilast in the treatment of interface dermatitis types 2 and 3. The execution of this study design involves specific pharmaceutical requirements, delineating the administration of oral Methotrexate (tablet) and oral Apremilast (tablet) to ensure standardized treatment across both groups. The detailed and systematic nature of the study's methodology positions it to yield valuable insights into the comparative effectiveness and safety of the chosen therapeutic interventions for interface dermatitis types 2 and 3.

The investigation comprised a cohort of 36 participants, and subsequent assessments were conducted over a 60-day period following the completion of the designated study duration, which extended up to three months or until lesion healing was observed. The primary objective was to evaluate the sustained therapeutic effects or the potential recurrence of symptoms during this post-treatment follow-up period.

The primary efficacy measure centered around the Lichen Planus Severity Index (LPSI), which assessed both cutaneous and mucosal lesions. The LPSI considered diverse parameters, such as the overall body surface area affected, the quantity and nature of lesions (including erythematous papules, violaceous papules, violaceous plaques, hyperpigmented hypertrophic papules and plaques, and post-inflammatory hyperpigmentation), as well as their respective percentages. Severity scores were assigned to each lesion type, and an area severity factor was computed based on the lesion percentages. The final LPSI computation included the application of multiplication factors to various lesion shapes. A score of 0 indicated no observable participation, whereas values ranging from 0 to 80 indicated more severe lichen planus involvement.

A crucial component of the research was assessing lichen planus lesions in the oral cavity using the mucosal scoring system created by Piboonniyom et al [6]. The oral cavity's lesions were evaluated at ten different places, and their severity was categorized according to the presence of reticular/hyperkeratotic, erosive/erythematous, and ulcerative characteristics. Scores for reticular/hyperkeratotic lesions varied from 0 to 1, indicating the presence or lack of keratotic papules or white striations. Depending on the degree of involvement, erosive/erythematous regions were assigned a score between 0 and 3, with higher values denoting bigger lesions. On the basis of lesion size, ulcerative regions were also assigned a score between 0 and 3. Piboonniyom et al. [6] said that the total scores for all ten sites were added together to establish the cumulative scores for each clinical indicator, which included reticular, erythema, and ulceration. By adding reticular scores to the total of erythema scores multiplied by 1.5 and ulcerative values multiplied by 2.0, the total weighted score—also known as the REU score—was determined. This thorough grading method made it easier to assess mucosal participation in a more nuanced way.

Every oral cavity location, including the floor of the mouth, the dorsal and ventral tongue, the upper and lower labial mucosa, the buccal mucosa, the soft palate/tonsillar pillars, and the maxillary and mandibular gingiva, was given a distinct set of criteria in the score table. Reticular, erythematous, and ulcerative regions were given scores, which went toward determining the total degree of mucosal involvement.

The Physician Global Assessment (PGA), a seven-point assessment system for the severity of lichen planus lesions, and the Visual Analog Score (VAS), which measures itching and discomfort, were both included in the study. Higher ratings indicated more severity. The PGA score scaled from 0 to 6. Patients could rate the intensity of their symptoms on VAS measures ranging from 0 to 100 for pain and itching at follow-up evaluations. The documenting of clinical side effects associated with the medicine administered served as a safety check on the study intervention. The investigator rapidly noted any adverse effects, regardless of presumed cause, and separately documented significant adverse events.

The data was gathered and arranged in Microsoft Excel for statistical analysis. Categorical data were reported as percentages and proportions, while continuous values were shown as Mean +/- SD (min-max). The independent student t-test was used where necessary for quantitative variable comparisons, and the chi-square test was used for qualitative variable comparisons. A statistically significant p-value is one that is less than the selected significance level of <0.05. The data analysis was done with OpenEpi 2.3.1. With this all-encompassing strategy, the efficacy and safety of the treatment therapies for lichen planus under study were to be thoroughly understood.

RESULTS

The bulk of individuals in both research cohorts were between the ages of thirty and sixty. Examining this age distribution using a t-test yielded a t-value of 0.5 and a p-value of 0.5 with 40 degrees of freedom.

When the p-value is more than 0.05, it is considered statistically insignificant, meaning that there is no statistical significance in the age distribution similarity between the groups.

The results of the chi-square test showed that there were more male participants in both groups than female participants. The chi-square value was 0.4 with one degree of freedom and a p-value of 0.26. The similarity in gender distribution between the groups is not statistically significant if the p-value is greater than 0.05.

Lichen planus was the most common clinical observation in both groups, followed by oral lichen planus. With five degrees of freedom and a p-value of 0.82, the chi-square test applied to this distribution produced a chi-square value of 2.1. The distribution of clinical presentations across the groups is not statistically significant, as suggested by a p-value greater than 0.05, which also indicates a lack of statistical significance.

With one degree of freedom and a p-value of 0.05, a chi-square test revealed a chi-square value of 2.5 when comparing the prevalence of lichen planus to mucosal lichen planus in both groups. A statistically significant difference in the prevalence of lichen planus as opposed to mucosal lichen planus between the two groups is shown by a p-value of less than 0.05.

As per the information presented in Table 1, Group I comprised 17 participants classified as grade 2 according to Le Boit's classification, while Group II included 16 individuals in the same grade. The application of the chi-square test resulted in a value of 0.3 with 1 degree of freedom, and the calculated p-value was 0.27. With the obtained p-value exceeding 0.05, the interpretation indicates a lack of statistically significant difference in the distribution of grade 2 classifications between the two groups.

Table 1: Le Biot's classification

Classification	Group I	Group II
Le Boit type 2	17	16
Le Boit type 3	1	2
Total	18	18

In relation to Physician Global Assessment (PGA), a majority of participants in both Group I and Group II were categorized as grade 3. The application of the chi-square test to this dataset produced a chi-square value of 0, with 3 degrees of freedom, and a p-value of 1. The p-value exceeding 0.05 indicates a lack of statistical significance, suggesting no substantial difference in the distribution of PGA grades between the two groups.

Concerning Visual Analog Score (VAS) scoring, 12 cases in Group I had scores ranging from 51 to 80, while in Group II, 8 cases fell within the same score range. The chi-square test outcome for this comparison revealed a chi-square value of 3.2, with 2 degrees of freedom, and a p-value of 0.19. As the p-value is greater than 0.05, it implies a lack of statistical significance, indicating that there is no significant disparity in VAS scores between the two groups.

The mean Lichen Planus Severity Index (LPSI) in Group I was 36.7 ± 20.8, and in Group II, it was 31.5 ± 14.1. The t-test applied to these mean values resulted in a t-value of 0.8, with 34 degrees of freedom, and a p-value of 0.38. As can be seen from table 2, there is no statistically significant difference in the mean LPSI scores between Group I and Group II, even if the p-value is more than 0.05.

Table 2: Lichen planus severity index -baseline

LPSI	Group I	Group II
Mean	36.7	31.5
SD	20.8	14.1

The examination of average mucosal scores between Group I and Group II, as indicated by the t-test, did not reveal statistically significant disparities. With a p-value surpassing 0.05, it implies that any differences observed in average mucosal scores between the two groups are probably attributable to chance rather than a substantial impact of the treatment. Consequently, according to this analysis, there is no substantiated evidence for a significant distinction in mucosal scores between the two groups.

Table 3: Parameters of the laboratory (baseline)

Baseline	Group I		Group II		P value (t test)
	Mean	SD	Mean	SD	
Hb	12.6	0.8	12.4	0.5	0.3
TLC	5877.7	1464.7	6105	1373.9	0.6
Platelet	2.6	0.5	2.8	0.8	0.3
SGOT	23	8.5	21.3	5.8	0.4
SGPT	25.5	9.7	25	6.8	0.8
Urea	24.2	5.7	22.8	3.6	0.38
Creatinine	0.8	0.1	0.8	0.1	1
SBP	122.3	6.9	121	6.5	0.5
DBP	80.3	6.7	79.8	6.3	0.8

Table 3 provides baseline information on diverse laboratory parameters for both Group I and Group II. The mean levels of haemoglobin (Hb) demonstrated similarity between the groups, as did the mean total leukocyte count (TLC) and mean platelet counts, indicating analogous baseline values for these parameters. Liver function indicators, encompassing mean serum glutamic oxaloacetic transaminase (SGOT) and serum glutamic pyruvic transaminase (SGPT), exhibited comparable values across the two groups. Furthermore, markers of renal function, including mean urea and mean creatinine, displayed similarity. The baseline measurements of blood pressure, comprising mean systolic blood pressure (SBP) and mean diastolic blood pressure (DBP), were also in concordance between Group I and Group II. This suggests a consistent baseline health status among participants in both study groups.

Before the third appointment, there was an upward tendency in the systolic blood pressure; however, on the fourth visit, there was a reduction. Group II had an increase in diastolic blood pressure during the second visit, but Group I exhibited no more changes. Group I showed a declining trend in mean Physician Global Assessment (PGA) scores throughout the course of the follow-up period. The Wilcoxon signed-rank test confirmed a consistent and highly significant reduction in the mean PGA score at each visit in Group I, with reductions of 0%, 15.6%, 28.1%, and 34.3% at the 1st, 2nd, 3rd, and 4th visits, respectively. This underscores the significant contribution of Apremilast to reducing the PGA score in interface dermatitis.

Similarly, Group II displayed a decreasing trend in mean PGA values during follow-up. The Wilcoxon signed-rank test demonstrated a steady and highly significant reduction in the mean PGA score at each visit in Group II, with reductions of 3.1%, 21.8%, 43.7%, and 46.8% at the 1st, 2nd, 3rd, and 4th visits, respectively, highlighting the significant efficacy of Methotrexate in reducing the PGA score in interface dermatitis.

The Mann-Whitney test, utilized to calculate the p-value for comparing the percentage change across all visits, indicated statistically significant differences. Importantly, a higher percentage change was observed from the 2nd visit onward, with Methotrexate demonstrating a more pronounced effect. Thus, the findings suggest that Methotrexate is slightly more effective than Apremilast in reducing the PGA score in interface dermatitis, as detailed in Table 4.

Table 4: Comparison of mean PGA of all visits between group I and group II

PGA	Group	Mean	SD	% change	P value	Significance
Baseline	I	3.2	1	-	1	NS
	II	3.2	1	-		
Visit 1 Day 7	I	3.2	0.9	0	0.7	NS
	II	3.1	0.9	3.1		
Visit 2 Day 30	I	2.7	0.6	15.6	0.4	NS
	II	2.5	0.9	21.8		
Visit Day 60	I	2.3	0.8	28.1	0.04	S
	II	1.8	0.6	43.7		
Visit 4 Day 90	I	2.1	0.7	34.3	0.09	NS
	II	1.7	0.7	46.8		

In group I, there was a consistent and significant reduction in mean VAS scores during follow-up, with declines of 39%, 61.6%, 72.2%, and 83.6% at the 1st, 2nd, 3rd, and 4th visits, respectively, indicating the

effectiveness of apremilast in treating interface dermatitis. Group II, treated with methotrexate, also demonstrated a steady and highly significant decrease in mean VAS scores (43%, 64.6%, 77.7%, and 85.4%). The Mann-Whitney test highlighted a significant difference favouring methotrexate, suggesting its slightly superior efficacy in reducing VAS scores compared to apremilast.

In table 5, had group I which was a consistent and markedly significant decline in mean LPSI scores throughout follow-up, with reductions of 8.1%, 17.9%, 25.6%, and 34% at the 1st, 2nd, 3rd, and 4th visits, respectively, demonstrating the effectiveness of apremilast in addressing interface dermatitis. Group II, treated with methotrexate, also displayed a continual and highly significant decrease in mean LPSI scores (6.4%, 14.4%, 22.8%, and 29.5%). The Mann-Whitney test indicated a statistically significant distinction, favouring apremilast with a slightly greater degree of change compared to methotrexate. This implies that apremilast holds a slight advantage in reducing LPSI scores in interface dermatitis.

Table 5: Comparison of mean LPSI of all visits between group Iand group II

LPSI	Group	Mean	SD	Percentage change	P value	Significance
Baseline	I	36.7	20.8		0.3	NS
	II	31.1	14.2			
Visit 1 Day 7	I	33.7	16.2	8.1	0.3	NS
	II	29.1	12.9	6.4		
Visit 2 Day 30	I	30.1	13.2	17.9	0.4	NS
	II	26.6	12	14.4		
Visit 3 Day 60	I	27.3	13.4	25.6	0.4	NS
	II	24	10.8	22.8		
Visit 4 Day 90	I	24.2	13.5	34	0.5	NS
	II	21.9	10.2	29.5		

In group I, there was a consistent and markedly significant decline in mean mucosal scores throughout follow-up, with reductions of 14.8%, 29%, 52.2%, and 64.5% at the 1st, 2nd, 3rd, and 4th visits, respectively, demonstrating the effectiveness of apremilast in addressing interface dermatitis. Group II, treated with methotrexate, also displayed a continual and highly significant decrease in mean mucosal scores (15.1%, 29%, 53.9%, and 65.4%). The Mann-Whitney test indicated a statistically significant distinction, favoring methotrexate with a slightly greater degree of change compared to apremilast. This implies that methotrexate holds a slight advantage in reducing mucosal scores in interface dermatitis.

Group I had a greater incidence of adverse events than Group II. There were no reported adverse events in either group until the 4th visit. Employing the chi-square test resulted in a chi-square value of 0.3, with 3 degrees of freedom, and a p-value of 0.2. A p-value greater than 0.05 indicates that the observed differences in adverse events between the two groups are not statistically significant, indicating a lack of statistical significance.

DISCUSSION

A range of illnesses are included in interface dermatitis, a response pattern that damages basal cells in the epidermis and affects the dermoepidermal junction. For the treatment of inflammatory dermatoses, apremilast, an anti-inflammatory medication that inhibits PDE4, and methotrexate, an immunosuppressant that inhibits dihydrofolate reductase, have been investigated., but research on apremilast's application in interface dermatitis is lacking. Methotrexate, a well-established dermatological drug, hasn't been compared with apremilast for treating interface dermatitis.

The purpose of this study was to compare the effects of oral methotrexate (15 mg weekly) with oral apremilast (30 mg twice day) in conditions where the histology shows interface dermatitis. In a prospective randomized controlled comparative design, 42 patients were enrolled, with 36 completing the study; 18 received apremilast, and 18 received methotrexate. Six patients dropped out due to adverse effects (three with apremilast) and personal reasons.

The inclusion criteria were lichen planus, DLE, cutaneous GVHD, and long-term lichenoid drug eruption, as well as conditions associated with Le Boit's interface dermatitis types 2 and 3. Pandemic-related limitations led to the exclusion of certain diseases. Of the 36 patients completing the study, 25 had cutaneous lichen planus, and 11 had mucosal lichen planus. DLE cases were excluded due to pandemic-related unavailability, and cutaneous GVHD, due to rarity, couldn't be included.

Diagnosed lichenoid drug eruption cases during the study were acute, not fitting Le Boit's type 2 or 3 of interface dermatitis. Study limitations include the pandemic's impact on disease inclusion and the absence of certain diseases due to rarity or unavailability. Nevertheless, the study provides valuable insights into comparing apremilast and methotrexate for treating interface dermatitis, revealing their efficacy and tolerability in specific dermatological conditions.

Demographic Characteristics

In this study, both cohorts predominantly consisted of individuals aged 30 to 60 years, with mean ages of 38.2 in group 1 and 40.3 in group 2. A male preponderance was evident, with 26 males and 16 females among the 42 participants. A study by Viswanath V et al in 2022 focusing on apremilast in lichen planus reported a mean age of 39.6 years, noting a female preponderance among the 26 study completers (Viswanath et al., 2022). Another study conducted in 2012 by A J Kanwar et al. on methotrexate in lichen planus showed a mean age of 37.4 years and a 1:2 male-to-female ratio, with a majority of female patients. The study included 24 patients [11].

Apremilast's Efficacy

The current study underscored the notable efficacy of apremilast in treating diseases displaying interface dermatitis patterns 2 and 3. At the 12-week point, there was a noticeable 34.3% decrease in the Physician's Global Assessment (PGA), an 83.6% decrease in the Visual Analog Scale (VAS), a 34% decrease in the Lichen Planus Severity Index (LPSI), and a significant 64.5% decrease in mucosal scores. In a 2013 pilot trial, 10 patients with moderate to severe lichen planus got 20 mg of apremilast twice day for a duration of 12 weeks. The study was conducted by Paul J et al. Three out of ten patients achieved a 2-grade or more improvement in PGA, signifying statistically significant clinical improvement in secondary parameters [4].

Viswanath V et al in 2022 explored apremilast in lichen planus with 34 patients receiving 30mg of apremilast twice daily for 12 weeks. Among the 26 patients completing the study, 34.61% displayed a 2 or more-grade improvement in PGA, and 42.30% exhibited over 50% improvement in lesions based on subject global assessment. Six patients encountered adverse effects [3]. In contrast to a study by Paul J et al, our investigation, similar to Viswanath et al's, employed a dose of 30mg twice daily. No studies comparing different apremilast doses (20mg vs. 30mg twice daily) have been conducted. Our study's efficacy aligns with the mentioned studies. Mucosal lesions, excluded in prior studies, were considered in our investigation using the LPSI, a validated objective scoring system, whereas subjective scoring systems were employed in other studies. Our study revealed that apremilast was particularly beneficial for patients with hypertrophic cutaneous lesions. Pruritus relief occurred as early as one week after initiating treatment, with a gradual decline in symptoms and disease activity.

A retrospective multicenter cohort study by Leonard Perschy et al in 2020 documented 11 patients with oral lichen planus receiving varying apremilast doses. Improvement in clinical features was observed in 55% of patients after 12 weeks [5]. Our study demonstrated improvement in all patients with mucosal lichen planus, with pain and intolerance reducing as early as one month. This discrepancy could be attributed to our use of the maximum dose (30mg twice daily) in all patients, while Perschy et al used varied dosing. Our investigation employed a validated objective scoring system (mucosal scoring by Piboonniyom et al [6]) to assess apremilast efficacy in mucosal lesions, whereas Perschy et al used subjective scores. Additionally, our study's randomized prospective clinical trial design adds to its credibility. Apremilast's effectiveness was notable in reticulate oral lesions, a finding absence in Perschy et al's study [5].

Apremilast Tolerability

Three people left the apremilast group because of unfavourable experiences. Among the 18 completing the apremilast regimen, four encountered mild side effects such as nausea, vomiting, diarrhoea, and headache, emerging two weeks into treatment. By the fourth week, the symptoms had progressively subsided under symptomatic treatment with acetaminophen, racecodotril, and proton pump inhibitors. By the time of the last appointment, all negative impact had disappeared. In a 2019 study by Arthur Kavanaugh et al on prolonged apremilast use in psoriatic arthritis (1493 patients), a 61.1% exposure-adjusted incidence rate of adverse effects was reported, mainly involving diarrhoea, nausea, headache, upper respiratory tract infection, and nasopharyngitis. Gastrointestinal effects primarily manifested within the initial two weeks, resolving by week four. Our study reflected a 5.5% incidence of adverse effects in apremilast patients, aligning with Kavanaugh et al's results. Significantly, our patients exhibited fewer adverse effects, even at the maximum dose, and experienced no major side effects like depression or weight loss. Interestingly, middle-aged patients were more susceptible to adverse effects, while children and the elderly demonstrated better tolerability.

Methotrexate Efficacy

After a 12-week period, the methotrexate group showed reductions in PGA of 46.8%, VAS of 85.4%, LPSI of 29.5%, and mucosal scores of 65.4%. Methotrexate for lichen planus (24 patients) administered once weekly at a dosage of 15 mg for 24 weeks showed an average improvement of 79% in a trial conducted in 2012 by A J Kanwar et al., with 14 patients obtaining full resolution by the study's conclusion. Our study, utilizing a similar weekly dose for 12 weeks, showed comparable efficacy, with significant improvement in all efficacy variables [11]. Another study in 2015 by V Lajevardi et al on methotrexate for erosive oral lichen planus (18 patients) with a weekly dose of 15mg for 12 weeks reported 38.8% exhibiting grade 2 responses and 44.4% showing grade 3 responses [7]. Our study aligned with these findings, indicating significant improvement in VAS scores and using a different but effective objective scoring system. Adverse effects in our methotrexate group were minimal, with only one patient experiencing nausea that resolved with symptomatic management, diverging from A J Kanwar et al's study where 12 out of 24 patients had mild side effects [11].

Apremilast vs. Methotrexate Comparison

When comparing the 12-week results, methotrexate and apremilast showed similar and noteworthy gains in effectiveness measures, such as PGA, VAS, mucosal scores, and LPSI. However, the apremilast group reported more adverse effects. Two separate studies comparing apremilast and methotrexate in psoriasis and chronic plaque psoriasis reported similar improvements in efficacy variables. Our study emphasized that both drugs alleviated itching in cutaneous lesions within a week and relieved pain in mucosal lesions within a month, with methotrexate demonstrating slightly superior results. Lesion resolution rates were nearly identical, with methotrexate displaying a slightly faster onset. Apremilast induced more discomfort, especially gastrointestinal symptoms, leading to treatment discontinuation in some cases. Because of methotrexate's weekly dosage, reduced cost, and general pleasure, patients tended to prefer it. Apremilast's safety profile, absence of immunosuppressive effects, and suitability for patients with comorbidities or extremes of age position it as a valuable option. We recommend initiating apremilast at 10mg daily, titrating up by 10mg daily increments over a week, potentially mitigating gastrointestinal symptoms. Ongoing study suggests gradual up dosing over a month or more for further symptom alleviation.

The investigation concentrated solely on lichen planus, restricting the extrapolation of apremilast's effectiveness and tolerance to other disorders with interface dermatitis patterns. The brief 12-week duration might not unveil the complete, long-term impact. Extensive studies are indispensable to comprehensively comprehend apremilast's enduring efficacy and safety in diverse dermatological contexts.

CONCLUSION

Apremilast proves highly effective in addressing interface dermatitis, offering a well-tolerated solution with a wide therapeutic range. The oral use of apremilast showcases effectiveness and tolerability on par with oral methotrexate in interface dermatitis, emphasizing its viability as a treatment choice.

REFERENCES

1. Joshi, R. (2008). Stratum corneum findings as clues to histological diagnosis of pityriasis lichenoides chronica. Indian Journal of Dermatology, Venereology and Leprology, 74(2), 156. https://doi.org/10.4103/0378-6323.39706
2. Bubna, A. (2016). Apremilast: A dermatologic perspective. Indian Journal of Drugs in Dermatology, 2(2), 75. https://doi.org/10.4103/2455-3972.196166
3. Viswanath, V., Joshi, P., Dhakne, M., Dhoot, D., Mahadkar, N., & Barkate, H. (2022). Evaluation of the Efficacy and Safety of Apremilast in the Management of Lichen Planus. Clinical, Cosmetic and Investigational Dermatology, Volume 15, 2593–2600. https://doi.org/10.2147/ccid.s390591
4. Paul, J., Foss, C. E., Hirano, S. A., Cunningham, T. D., & Pariser, D. M. (2013). An open-label pilot study of apremilast for the treatment of moderate to severe lichen planus: A case series. Journal of the American Academy of Dermatology, 68(2), 255–261. https://doi.org/10.1016/j.jaad.2012.07.014
5. Perschy, L., Anzengruber, F., Rappersberger, K., Itzlinger-Monshi, B., Aichelburg, M. C., Graf, V., Hafner, J., & Vujic, I. (2022). Apremilast in oral lichen planus – a multicentric, retrospective study. JDDG: Journal Der Deutschen Dermatologischen Gesellschaft, 20(3), 343–346. https://doi.org/10.1111/ddg.14696
6. Piboonniyom, S. O., Treister, N., Pitiphat, W., & Woo, S. B. (2005). Scoring system for monitoring oral lichenoid lesions: A preliminary study. Oral Surgery, Oral Medicine, Oral Pathology, Oral Radiology, and Endodontology, 99(6), 696–703. https://doi.org/10.1016/j.tripleo.2004.07.013
7. Lajevardi, V., Ghodsi, S. Z., Hallaji, Z., Shafiei, Z., Aghazadeh, N., & Akbari, Z. (2016). Treatment of erosive oral lichen planus with methotrexate. JDDG: Journal Der Deutschen Dermatologischen Gesellschaft, 14(3), 286–293. https://doi.org/10.1111/ddg.12636

8. Zohdi-Mofid, M., & Horn, T. D. (1997). Acrosyringeal concentration of necrotic keratinocytes in erythema multiforme: a clue to drug etiology. Journal of Cutaneous Pathology, 24(4), 235–240. https://doi.org/10.1111/j.1600-0560.1997.tb01587.x
9. Schwarz, T. (2005). A. Bernard Ackerman: Histologic diagnosis of inflammatory skin diseases (3rd edn.). Archives of Dermatological Research, 297(1), 48–48. https://doi.org/10.1007/s00403-005-0571-y
10. Parveen, Z., & Thompson, K. (2009). Subcutaneous Panniculitis-like T-Cell Lymphoma: Redefinition of Diagnostic Criteria in the Recent World Health Organization–European Organization for Research and Treatment of Cancer Classification for Cutaneous Lymphomas. Archives of Pathology & Laboratory Medicine, 133(2), 303–308. https://doi.org/10.5858/133.2.303
11. Kanwar, A., & De, D. (2012). Methotrexate for treatment of lichen planus: old drug, new indication. Journal of the European Academy of Dermatology and Venereology, 27(3). https://doi.org/10.1111/j.1468-3083.2012.04654.x
12. Ravichandran, S., & Kheterpal, M. K. (2020). Apremilast for the off-label treatment of lichenoid and interface dermatoses. Journal of the American Academy of Dermatology, 83(5), 1489–1491. https://doi.org/10.1016/j.jaad.2020.05.112