ISSN: 2663-2187

*https://doi.org/10.48047/AFJBS.6.10.2024.6017-6025*

African Journal of Biological Sciences

Journal homepage: http://www.afjbs.com

Research Paper Open Access

# A comparative study of topical Apremilast gel versus topical Calcipotriol in mild to moderate plaque psoriasis

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Article History
Volume 6, Issue 10, 2024
Received : 17 Apr 2024
Accepted : 16 Jun 2024
doi: 10.48047/AFJBS.6.10.2024.6017-6025

**ABSTRACT**

**Introduction:** Plaque psoriasis has significant impact on patients' quality of life. Topical therapy is considered the treatment mainstay for mild-to-moderate disease according to guidelines.

**Aims**: To evaluate the clinical safety and efficacy and the patient's quality of life with topical apremilast gel versus topical calcipotriol in mild to moderate plaque psoriasis.

**Materials and methods**: This study was a single centre, prospective, parallel group, open label study. Patients were randomly allocated to any one of two groups . Patients in calcipotriol group (group C) were administered 0.005% calcipotriol for local application twice daily for 12 weeks Apremilast (group-A) were administered Apremilast Topical Gel, 2% w/w twice daily for local application on all lesions for 12 weeks.

**Results**: After baseline matching, patients treated for 12 weeks with topical apremilast had greater response compared to those treated with topical Calcipotriol ($P < 0.001$). Patients treated with topical apremilast had significantly greater improvement Psoriasis Area and Severity Index (PASI) ($P < 0.001$).

**Conclusion**: Despite recent treatment advances, unmet needs for psoriasis patients remain. Topical Apremilast offers improved efficacy in baseline matched psoriasis patients compared to topical Calcipotriol.

**Keywords**: Apremilast, Calcipotriol , Psoriasis Area and Severity Index (PASI)

## INTRODUCTION

Despite notable therapeutic advances over the past 15 years and robust use of non-biologic systemic treatments such as methotrexate, ciclosporin, acitretin and fumaric acid esters (FAE), there remains no cure for PSO and unmet needs persist for patients suffering from this chronic condition.[1] Systemic biologic treatments may be effective for severe disease but their use is often restricted due to cost and side effects. Many countries have adopted regulations that limit prescription of these expensive treatment options.
Apremilast is a versatile Small molecule. Small molecules are a novel group of agents with a low molecular weight (<1 kD) which act via the modulation of proinflammatory cytokines. They are emerging as therapeutic options in inflammatory dermatosis and other systemic inflammatory conditions owing to their ease of administration through oral or topical route with acceptable efficacy and excellent safety profile. Unlike biologic agents, small molecule drugs are relatively easy to synthesize and less expensive to be produced. Recently, there is a surge in newer small molecules being licensed for dermatological conditions and also the preexisting small molecules are being explored for newer indications . [2,3] Of these, apremilast has gained major attention from the practising dermatologists for its versatile use in psoriasis and other inflammatory skin conditions. A thorough knowledge about this drug may benefit the clinicians to tailor their treatment regimen for optimizing the efficacy and tolerability. Our aim is to evaluate the clinical safety and efficacy and the patient's quality of life with topical apremilast gel versus topical calcipotriol in mild to moderate plaque psoriasis.

## MATERIALS AND METHODS:

This study was a single centre, prospective, parallel group, open label study done in Department of dermatology , Osmania Medical College from January 2022 to January 2023. Patients were randomly allocated to any one of two groups . Patients in calcipotriol group (group C) were administered 0.005% calcipotriol ointment for local application twice daily, Apremilast (group-A) were administered Apremilast Topical Gel, 2% w/w twice daily for local application on all lesions. The procedure and purpose of the study was clearly explained individually to all study participants in their regional language. Written informed consent was obtained from all study subjects.

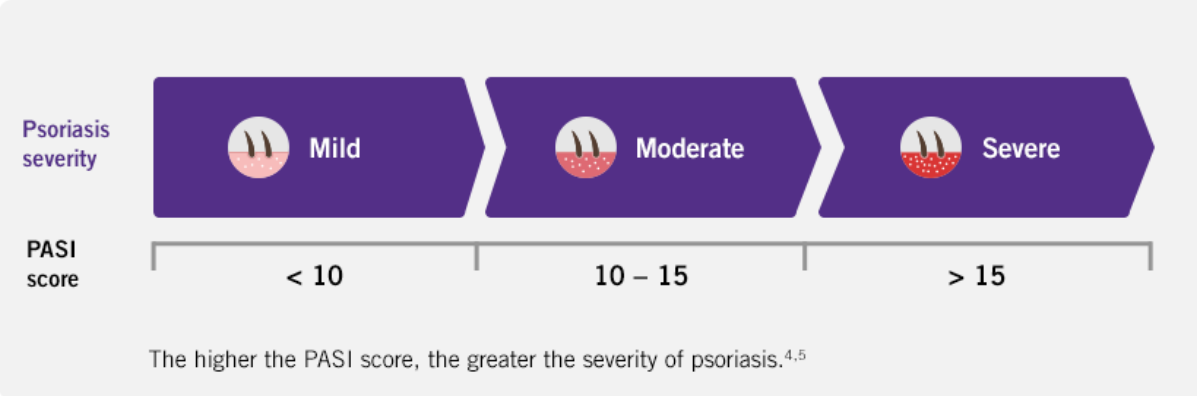
**Inclusion criteria**: Both genders of age ≥ 18 years of age, diagnosed with chronic mild to moderate plaque psoriasis i.e., 6 point sPGA score of ≤ 3 and PASI score of ≤ 10 for at least 6 months which covers less than 10% of the total Body Surface Area (BSA)

**Exclusion criteria:** Patients using topical psoriasis medications within the past 2 weeks, use of phototherapy and those taking systemic (oral, intravenous, intramuscular, or intradermal) medications for psoriasis in the past 28 days, those using steroids, immunosuppressive medications, and cyclooxygenase-2 anti- inflammatory drugs, and those using any medication conflicting with the product ingredients, Any condition, including the presence of laboratory abnormalities, other inflammatory diseases or dermatologic conditions, which confounds the ability to interpret data from the study, including other types of psoriasis (i.e., erythrodermic, guttate, inverse, or pustular psoriasis), other than plaque psoriasis. Women planning to become pregnant at the start of the study and pregnant or lactating women or women not taking medically approved birth control, Active substance abuse or a history of substance abuse within 6 months prior to signing the informed consent, who exhibited weight

loss ≥ 5% of initial body weight, Prolonged sun exposure or use of tanning booths, which may confound the ability to interpret data from the study.

**Method of Gel Application with Instructions:**

Treatment applied as a thin layer to all affected areas (Multiples of one fingertip unit (FTU) spread is recommended over the affected lesions {One FTU for approx. 100 $cm^2$ skin surface}) twice daily maximally for up to 12 weeks after the sPGA Score on 6- point scale becoming zero i.e., the lesions found to be completely cleared whichever comes first. Application to be continued for a minimum of 8 weeks regardless of clearance of lesions during this period. Patient will be advised to wear appropriate protective clothing and take measures to avoid sun exposure to the treated area.




Week 4 :Day 28 (+ 2 day window period) – Compliance Check and return of Investigational Medicinal Product ( IMP )/ Efficacy & Safety Assessment / Dispensing of medication/ Distribution of PDCs/Pregnancy monitoring (female patients).
Week 8 :Day 56 (+ 2 day window period) – Compliance Check and return of IMP / Efficacy & Safety Assessment / Dispensing of medication / Distribution of PDCs/Pregnancy monitoring (female patients).
week 12: Day 84 (+ 2 day window period) Compliance Check and return of IMP, Efficacy & Safety Assessment is done. Those patients visiting the clinic utilizing + 2 day window period on any visit will become due for the next visit as per the pre-defined visit schedule. For all patients who discontinue treatment prior to week 12, an unscheduled end of treatment visit is to be performed and last visit values will be included.

**Statistical analysis**

Inter group efficacy endpoints – the percentage of patients achieving treatment success and the percentage of patients attaining PASI were compared and analyzed using student's unpaired t test. Significance tests were two-sided using 5% significance level and 95% confidence intervals (CIs). P value of < 0.001 was taken as significant.

**RESULTS**

Patients were randomized to Apremilast group (n = 30) and calcipotriol group (n = 31) . 4 patients from apremilast group and 4 patients from calcipotriol group did not follow up with the study. (Figure 1).

**Figure-1: Flow chart showing randomization**

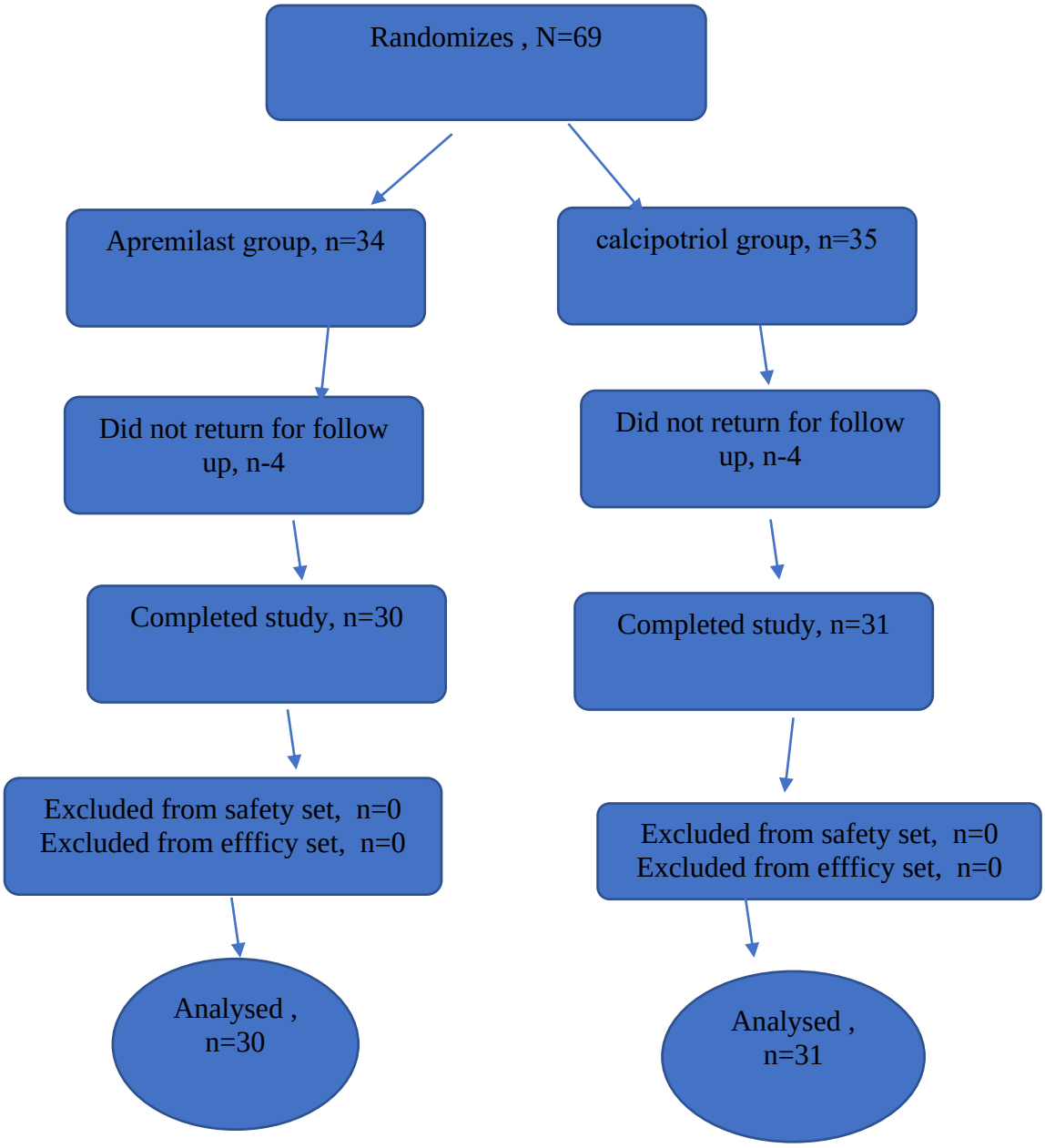


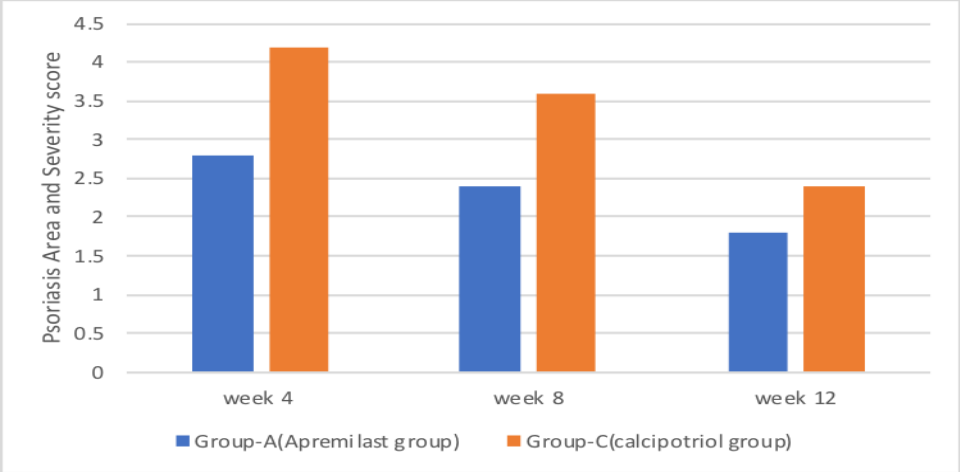

**Table-1: Patient demographics and baseline characteristics**

| | **Group-A(Apremilast group)N=30** | **Group-C(calcipotriol group)N=31** |
|---|---|---|
| Age: Mean ± SD (years) | 48.1.2 ± 4.86 | 48.8 ± 14.12 |
| Male:Female ratio | 4:11 | 14:17 |
| BSA: Mean ± SD | 3.8 ± 0.5 | 4.1 ± 1.4 |
| Duration of psoriasis: Mean ± SD (years) | 24.6 ± 10.1 | 30.1 ± 12.0 |

| | | |
|---|---|---|
| PASI: Mean | 8.1 | 7.8 |
| **Body surface area** | | |
| Week 4 | 3.46 | 3.7 |
| Week 8 | 3.6 | 3.4 |
| Week 12 | 3.1 | 3.2 |

Both groups are comparable in terms of age, gender, duration of disease, baseline PASI and body surface area.

**Figure-2: Mean Psoriasis Area and Severity Index in both groups at various weeks**




Mean PASI in Apremilast group was 2.8 and that in calcipotriol group was 4.2. was lesser in Apremilast group compared to calcipotriol group at 4 weeks. Mean PASI in apremilast group was 2.4 and that in calcipotriol group was 3.6 which was lesser in apremilast group compared to calcipotriol group at 8 weeks. Mean PASI in apremilast group was 1.8 and that in calcipotriol group was 2.4 which was lesser in apremilast group compared to calcipotriol group till 12 weeks. This statistically significant difference was maintained until 12 weeks. (1.80 vs. 2.40 :P< 0.05)

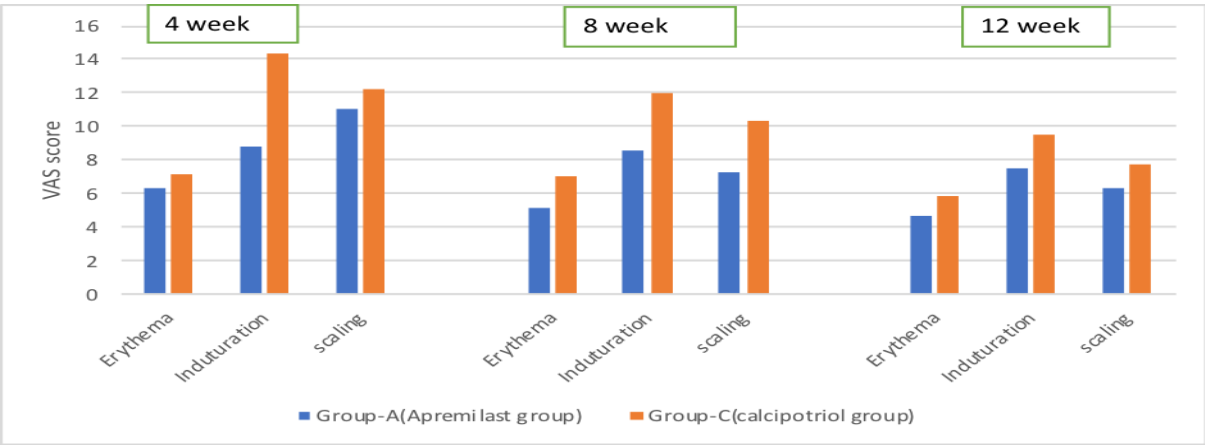


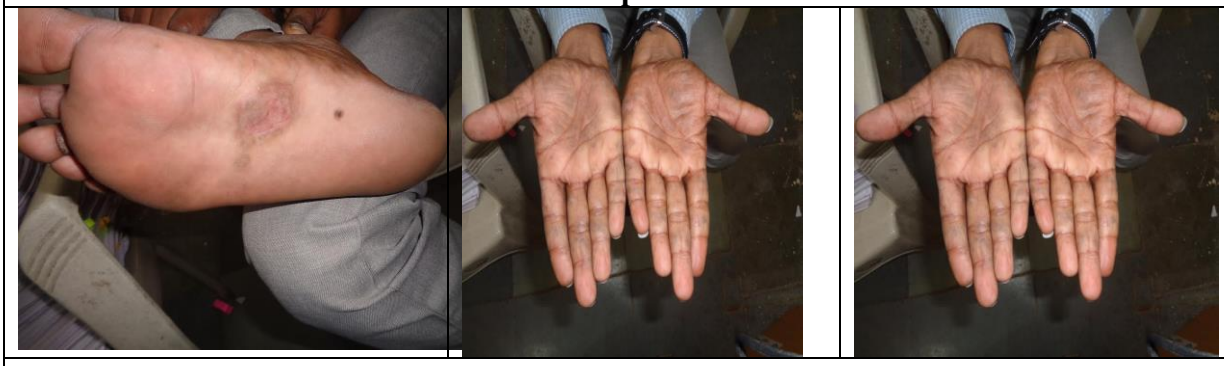

**Figure-3: Visual analog score in both groups at various weeks**

Mean VAS for erythema , induration and scaling in Apremilast group is 6.3,8.8,11 and that in calcipotriol group is 7.2,14.4, 12.2 in lesser in Apremilast group compared to calcipotriol group at 4 weeks. (P< 0.05) Mean VAS for erythema , induration and scaling in apremilast group is 5.2,8.6,7.3 and that in calcipotriol group is 7,12,10.4. was lesser in apremilast group compared to calcipotriol group at 8 weeks. (P< 0.05) Mean VAS for erythema , induration and scaling in apremilast group is 4.7,7.5,6.4 and that in calcipotriol group is 5.9,9.5,7.8. was lesser in apremilast group compared to calcipotriol group. This statistically significant difference was maintained until 12 weeks. (P< 0.05)

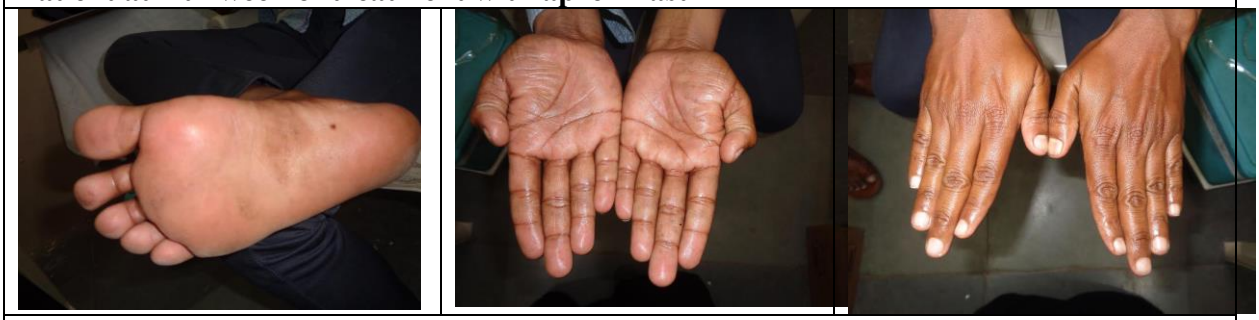
No severe adverse events or fatalities were noted nor were there any withdrawals due to adverse effect.

**Figure-4: Images at various weeks in study after treatment**

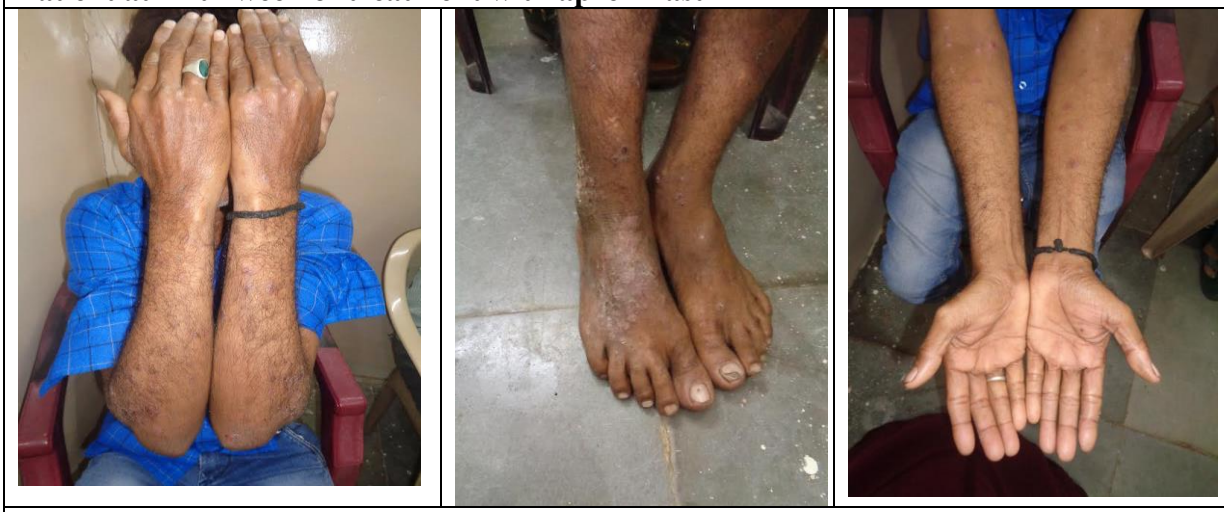
**Patient at 12 th week of treatment with calcipotriol**



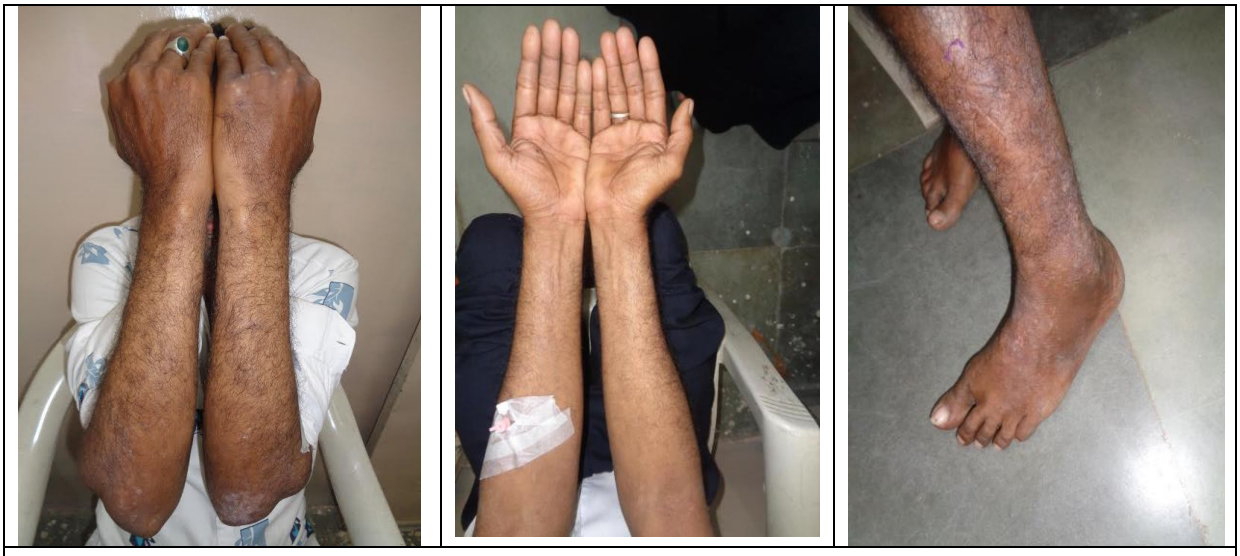
**Patient at 4 th week of treatment with apremilast**



**Patient at 12 th week of treatment with apremilast**



**Patient at 4 th week of treatment with apremilast**



**Patient at 12 th week of treatment with apremilast**

## DISCUSSION

The mechanism of calcipotriol activity has remained only partially known for a long time. However, in the last decade, a number of publications have started to discuss the immune background of psoriasis and the influence of T cells, B cells, dendritic cells, as well as cytokines in its pathogenesis [4,5,6,7]. A novel approach to the investigation of the mechanism of action of therapeutics applied in psoriasis treatment has been proposed.

Despite their established efficacy in treating psoriasis, many patients are reluctant to receive biologic agents due to safety and tolerability concerns, anxiety or fear of injection, inconvenience in administration, or loss of effectiveness over time. Patients may be hesitant to use biologics by the reported adverse effects such as tuberculosis, inflammatory bowel disease, serious infections, or depression with specific biologics. Non-biological systemic medications remain widely used with comparatively increased availability and ease of administration. Apremilast inhibits phosphodiesterase 4. Two phase 3, randomized, controlled studies showed that apremilast effectively controlled moderate to severe plaque psoriasis with acceptable tolerability and improved quality of life.[8,9,10]

In this study of Apremilast was significantly more effective than calcipotriol at end the 12 weeks of treatment in psoriasis. This higher efficacy which is apparent since the first week and was maintained till the end of 12 weeks of treatment period. Another point to be noted was that the efficacy of apremilast was effective in mild to moderate psoriasis. Apremilast was well tolerated, were noted in compared to calcipotriol. Patients were continuously getting more benefit in the Apremilast group compared to calcipotriol group in terms of treatment success as well as PASI. This suggests that extending the treatment beyond 12 weeks can help in clearing all lesions in those cases whose lesions were not clear or almost clear by 12 weeks. We conclude Topical Apremilast offers improved efficacy in baseline matched psoriasis patients compared to topical Calcipotriol. We could not find any study where the potentiating effect of apremilast to calcipotriol was studied. Although studies were available which have compared apremilast with placebo or calcipotriol + betamethasone combination.[11,12,13] The rate of development of adverse events and adverse drug reactions was low and no serious adverse results was noted also reported same by Krishnamoorthy et. al. and Mallick et. Al.[13,14] This observation was similar to previous studies of calcipotriol and apremilast.[15,16,17] Our study confirms that apremilast is well tolerated and may have a higher benefit : risk ratio for psoriasis.

Apremilast Topical Gel seems to be more effective than topical calcipotriol; however, it is more efficacious and better tolerated in the treatment of mild to moderate psoriasis. Both calcipotriol and Apremilast are cosmetically acceptable, but the difference in cost is marked in resource-poor settings. However, small sample size is the main limitation of this trial, and it is necessary to conduct a larger study in blinded manner.

## CONCLUSION

Our study proves that topical Apremilast offers improved efficacy and safety compared to topical Calcipotriol. Topical Apremilast has superior efficacy, shorter compliance, improved quality of life in mild to moderate plaque psoriasis.

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