

**How to Cite:**

Yazali, M., Chandra, S., & Sura, A. (2022). Characterization and comparison of efficacy and safety of calcipotriene and clobetasol in severe chronic plaque psoriasis patients. *International Journal of Health Sciences*, 6(S5), 11338–11351. <https://doi.org/10.53730/ijhs.v6nS5.11824>

# Characterization and comparison of efficacy and safety of calcipotriene and clobetasol in severe chronic plaque psoriasis patients

**Manohar Yazali**

Ph.D. Research Scholar, Bareilly International University, Department of Pharmacology, Rohilkhand Medical College & Hospital, Bareilly, Uttar Pradesh, India

ORCID ID: 0000-0002-5394-8255,

Corresponding author Email: [yazalimanohar@gmail.com](mailto:yazalimanohar@gmail.com)

**Shalini Chandra**

Professor & Head Department of Pharmacology, Rohilkhand Medical College & Hospital Bareilly, Uttar Pradesh, India

ORCID ID: 0000-0002-1074-472X

**Amarendar Sura**

Assistant Professor Department of Pharmacology, NAMO Medical Education and Research Institute, Silvasa, DNH, India

ORCID ID: 0000-0001-6144-7445

**Abstract**--Calcipotriene and Clobetasol ointments efficiently treat psoriasis. The purpose of the study was to characterize and compare the efficacy and safety of Calcipotriene and Clobetasol in chronic plaque psoriasis patients. 70 patients with chronic plaque psoriasis were recruited and randomly divided into two groups of 35 each. One group received 0.005% Calcipotriene, and the other group received 0.05% clobetasol twice daily for 12 weeks. Efficacy evaluations comprise global improvement assessed by the clinician by using the Physician Global Assessment (PGA) score. Efficacy further included the 'Dermatological Sum Score' (DSS) and Psoriasis Area and Severity Index (PASI) score at each study visit. The safety evaluations included clinical assessment of cutaneous safety and assessment of cutaneous discomfort by the clinician as well as the subject. Calcipotriene and Clobetasol were significantly effective in reducing PASI and DSS. However, the two experimental groups have shown no statistically significant observations. The PGA score assessed clinically was 1.27 for calcitriene and 1.79 for Clobetasol ( $p>0.05$ ). The cutaneous safety score was higher in the clobetasol group compared to the Calcipotriene group. 4% of cutaneous discomfort was reported with

Clobetasol compared to 2% with Calcipotriene. Calcipotriene showed a better safety profile than Clobetasol.

**Keywords**---Plaque psoriasis, Calcipotriene, Clobetasol.

## **Introduction**

The worldwide prevalence of psoriasis varies considerably. The prevalence of psoriasis is estimated at at least 60 million people worldwide, as per the observations from the Global Burden of Disease study. In the USA, approximately 2% of the population is affected. Higher rates of psoriasis in patients have also been reported in Indian populations. (Mason et al., 2013; Mahajan et al., 2020; Alora-Palli et al., 2009)

Psoriasis may be symptomatic, with patients complaining of intense pruritus or burning. The severity of psoriasis, vital in determining appropriate therapies, may be assessed by classifying patients based on the Psoriasis Area and Severity Index (PASI) score; patients will be classified into mild, moderate, or severe psoriasis (Sofen et al., 2011)

Plaque psoriasis is the most typical type of psoriasis, characterized by plaques that are tightly defined, round-oval, or nummular (coin-sized). This form accounts for 80–90% of total psoriasis cases. Psoriasis patients show different lesion sites and variations in the amount of scaling (Mahajan et al., 2020). Erythema and scaling are the hallmark signs of exanthematic or acute inflammatory psoriasis; overall, erythema may be the predominant clinical sign of psoriasis. However, psoriasis exhibits widespread skin involvement and rapid progression, with variable courses presenting as chronic, stable plaques (Sofen et al., 2011)

Patients with psoriasis were found to have a declining quality of life like, or worse than, those with other chronic diseases, including ischemic heart disease, inflammatory bowel disease, and diabetes. Patients with psoriasis feel stigmatized by the condition, which impacts disability, leading to depression and, in some individuals, suicidal thoughts in more than 5% of patients. More broadly, worry and anxiety occur in at least a third of patients with psoriasis, and difficulties in interpersonal relations significantly impact all aspects of the patient's daily life and the implementation of their treatment (Alora-Palli, 2009; Sofen et al., 2011; Hendriks et al., 2013).

Several different severity assessment scales are employed in clinical practice, of which the most used is the Psoriasis Area and Severity Index, or PASI score. Another key scoring measure used to assess the effect of the disease on quality of life is the Dermatology Life Quality Index or DLQI. These are beneficial and validated measures for assessing the effect of treatment in patients with psoriasis (Sofen et al., 2011; Hendriks et al., 2013; Fleming et al., 2010).

In psoriasis treatment, vitamin D and its combination with other antipsoriatic agents are also commonly used. These combination treatment modalities have shown synergistic action in managing psoriatic patients by effectively controlling

the symptoms of psoriasis and decreasing adverse events like skin atrophy associated with prolonged corticosteroid therapy (Yan et al., 2016). Calcipotriene is the metabolically active form of vitamin D3, which has proven efficacy in psoriasis in various clinical trials (Feldman et al., 2012). Calcipotriene has actions on multiple fronts, like modulation of dermatological immune responses and control of hyperproliferative keratinocytes. Simultaneously, it is also known to promote the differentiation of these cells in the skin (Girolomoni et al., 2012). Clobetasol propionate cream is a super potent steroid, which is one of the modalities of treatment for this disease in India. However, long-term use results in atrophy, skin thinning, telangiectasias, and tachyphylaxis (Feldman et al., 2012; Girolomoni et al., 2012). There is little data comparing the efficacy and safety of Calcipotriene and clobetasol in psoriasis, particularly among Indian patients. Therefore, the present study was undertaken in pursuit of a comparative assessment of the efficacy and safety of Calcipotriene and Clobetasol in patients diagnosed with plaque psoriasis.

### **Material and Methods**

Our present study was a prospective randomized control study, and the comparison between efficacy and safety of Calcipotriene and Clobetasol ointment treatment was carried out from May 2021 to May 2022 at the Department of Pharmacology in collaboration with the Department of Dermatology, Venereology, and Leprosy, Rohilkhand Medical College and Hospital, Bareilly, Uttar Pradesh.

A total of 70 adult patients (age  $\geq 18$  years) were recruited who were diagnosed with mild plaque psoriasis. The following inclusion criteria were considered while recruiting the patients: male and female subjects of the age group of 18 to 60 years; subjects with stable chronic plaque psoriasis; and body surface area involvement of less than 35%. Some of the patients were not recruited based on the following exclusion criteria: those patients with unstable, acute guttate, pustular, erythrodermic, or arthropathic psoriasis, patients with a history of hypercalcemia, renal dysfunction, calcium-based calculi, underlying conditions that require the use of systemic supplements of calcium or vitamin D; body surface area involvement  $>35\%$ ; subjects who had applied topical antipsoriatic medication within the past two weeks or had used systemic antipsoriatic medication within the past eight weeks; patients who had a severe systemic illness; and pregnant women.

#### **Treatment Group**

1. Group A-Calcipotriene group: Subjects in this group were treated with Calcipotriene (0.005% w/w) (Sun Pharmaceutical Industries Ltd., Mumbai) ointment applied twice daily for 12 weeks (about 3 months).
2. Group B-Clobetasol group: Subjects in this group were treated with Clobetasol (0.05% w/w) (Sun Pharmaceutical Industries Ltd., Mumbai) ointment applied twice daily for 12 weeks (about 3 months).

**Assessment of Efficacy:**

Global assessment of improvement:

Global assessment of improvement was done clinically by the dermatologist (Physician Global Assessment (PGA) Score) at each visit. Maximum efficacy score was 5 (highly improved) (scale of 1-5).

Dermatological sum score (DSS)

1. It was the sum of erythema, plaque elevation, and scaling of the target lesion. Each sign was evaluated on a 5-point scale at each visit.

All the assessments were carried out at baseline and every two weeks for twelve weeks.

Psoriasis Area and Severity Index (PASI)

Four areas were selected (Head, trunk, upper limb and, lower limb). Each area was evaluated on a 5- point scale at each visit.

All the assessments were carried out at baseline and every two weeks for twelve weeks.

**Assessment of the safety profile:**

Adverse Drug Reactions (ADRs)

In our study, we observed Adverse Drug Reactions during the treatment period in both groups.

1. Assessment of cutaneous discomfort: The Likert scale of 5 (0–4) was used in the study to evaluate cutaneous discomfort.

2. Clinical assessment of cutaneous safety: The cutaneous assessment was also used on a Likert scale of 5 (0–4) to study local irritation.

All the assessments were carried out at baseline and every two weeks for twelve weeks. The study was approved by the institution's ethics committee, and, Informed consent was obtained from patients recruited in the study.

**Statistical analysis**

Continuous data are expressed as mean  $\pm$  standard error of mean (SEM), whereas categorical data are expressed as numbers and percentages (%). Comparative and effectiveness analysis was conducted using unpaired t-tests in both groups. A P-value  $< 0.05$  was considered statistically significant.

**Results**

Our study had 70 patients in total, with 35 patients in each group. All patients received the allocated protocol/intervention. No patient was lost in follow-up in both groups. The gender distribution is displayed in Table 1. Out of the 70 patients enrolled in the study, 40 were males and 30 were females. There was male predominance in each group. A statistically significant difference was not observed between the two groups ( $p > 0.5$ ). (Table 1).

Table 1: Baseline demographic characteristics of patients from two different treatment groups

Characteristics	Group A (n=35)	Group B (n=35)	P value
Age (years)	39.45 ± 14.72	41.52 ± 12.84*	p < 0.05
Gender			
Male	21 (60%)	19 (54.38%)	
Female	14 (40%)	16 (45.72%)	
Average Duration of Disease (years)	13.62 ± 4.82	15.26 ± 3.81**	p < 0.01
Winter exacerbation	27 (77%)	9 (26%)	
Positive family history	8 (23%)	NIL	
Average Body Surface Area	3.82 %	4.36 %	
Average Baseline Score			
Erythema	1.83 ± 0.41	1.94 ± 0.28	p > 0.05
Induration	2.76 ± 0.07	3.05 ± 0.62*	p < 0.05
Desquamation	1.97 ± 0.13	2.18 ± 0.29	p > 0.05
Scaling around the lesion	2.04 ± 0.14	2.48 ± 0.64*	p < 0.05
Irritation/Itching	3.25 ± 0.36	5.24 ± 1.14**	p < 0.01
Oedema around lesion	3.61 ± 0.48	6.19 ± 1.08	p > 0.05

Data are expressed as mean ± SEM, number of patients and, percentages (%).

\*p < 0.05, \*\*p < 0.01

Patients in the two experimental groups of this study were well matched in their demographic data (age, gender) and evenly distributed in their baseline characteristics (duration of psoriasis and current stable disease, site of lesion, affected BSA, and scores that reflect the severity of psoriasis) (table 1).

Table 2: Baseline clinical characteristics of patients from two different treatment groups

Characteristics	Group A (n=35)	Group B (n=35)	P value
Average Duration of Disease (years)	13.62 ± 4.82	15.26 ± 3.81**	p < 0.01
Stable duration (years)	1.02 ± 0.42	1.74 ± 0.95*	p < 0.05
PASI score	7.16 ± 1.38	7.93 ± 2.45*	p < 0.05
Physician Global Assessment Score (PGAS)	3.24 ± 0.53	3.94 ± 0.97*	p < 0.05
Dermatological Sum Score (DSS)	39.62 ± 8.94	41.24 ± 10.36*	p < 0.05
Site of lesion			
Trunk	12 (34.29%)	15 (42.86%)	
Extremities	23 (65.71%)	20 (57.14%)	

Data are expressed as mean ± SEM, number of patients and, percentages (%).

\*p < 0.05, \*\*p < 0.01

Table 2 shows the various baseline scores with approached and comparable mean values (not individual values) of demographic and baseline characteristics, despite randomized distribution among the different groups, which can be attributed to the good sample size for each group (n = 35).

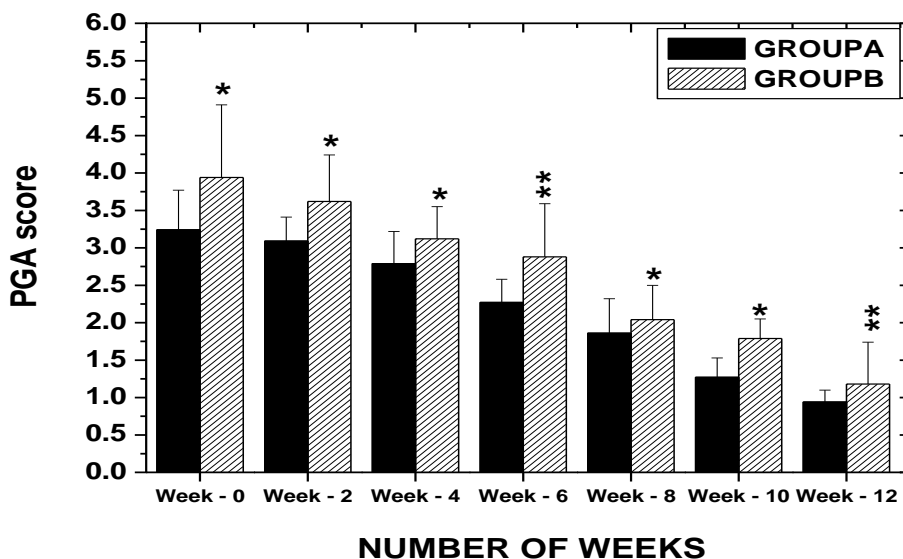


Figure 1: Comparison of efficacy outcomes-mean Physician Global Assessment (PGA) score in both groups during the treatment period.

Data are expressed as mean  $\pm$  SEM, number of patients and, percentages (%).  
\* $p < 0.05$ , \*\* $p < 0.01$

Significant improvement in symptoms was seen in all patients. Both groups saw improvement in PGA Score consistently throughout the treatment period. However, a more remarkable improvement was seen in Group A compared to Group B at the sixth week of treatment. Effectiveness outcomes in both groups were summarized in Figure 1. There was a statistical difference in outcome in the second week and the fourth week, and at the end of therapy in the twelfth week, there was a statistical difference between the two groups.

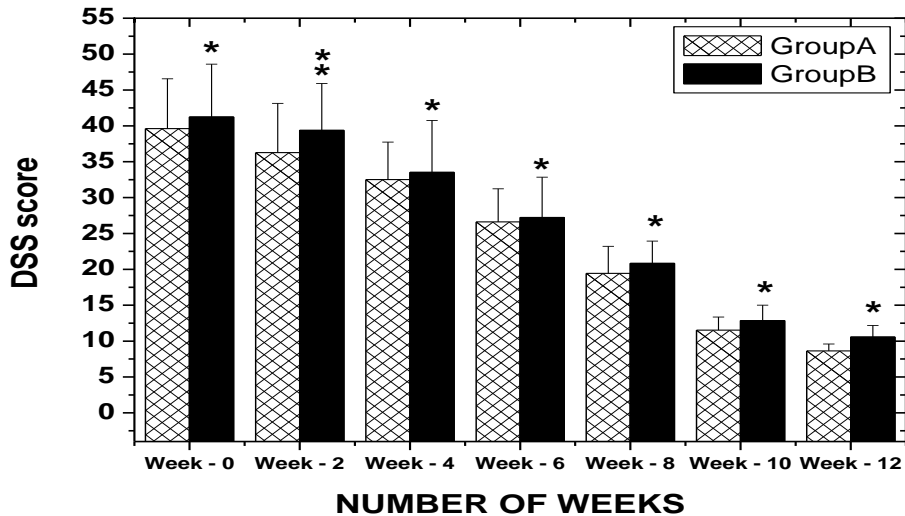


Figure 2: Comparison of efficacy outcomes-mean Dermatological Sum Score (DSS) in both groups during the treatment period

Data are expressed as mean  $\pm$  SEM, number of patients and, percentages (%).

\* $p < 0.05$ , \*\* $p < 0.01$

The baseline Dermatological Sum Score (DSS) were similar for both sides of the patient's body. The treatment with Calcipotriene and Clobetasol has resulted in a rapid and marked reduction of the DSS score during the treatment phase of the study. The most remarkable improvement was observed during the first two weeks (Figure 2). However, no significant difference between the two treatment groups was detected at the end of the treatment phase, after 12 weeks (about 3 months) of treatment, or during the follow-up period. The evaluation of the DSS data for individual parameters (psoriatic area, erythema, infiltration, scaling) revealed a slight benefit for Group A (Calcipotriene) in terms of scaling reduction during the treatment period. However, this benefit did not achieve statistical significance.

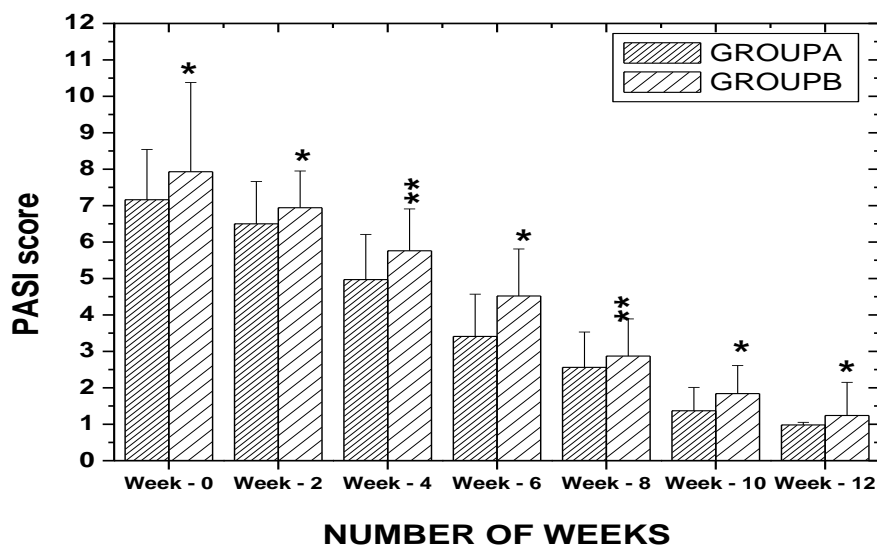


Figure 3: Comparison of efficacy outcomes-mean Psoriasis Area and Severity Index (PASI) score in both groups during the treatment period. Data are expressed as mean±SEM, number of patients and, percentages (%). \*p < 0.05, \*\*p < 0.01.

Clinical improvement in the median percent change in PASI score was observed in both groups after about two weeks of treatment. This improvement continued to increase during the study, being the fastest and greatest in the patients applying Calcipotriene ointment (Group A). A more significant decrease in total affected PASI during the treatment period was also observed in patients in Group B (Clobetasol ointment). The median percent of change in total affected PASI between baseline and the end of treatment was 41% and 38% for the Calcipotriene and Clobetasol groups, respectively ( $p > 0.5$ ) (Figure 3).

Table 3: Comparison of the safety profiles of drugs during the treatment period in both groups

Adverse Drug Reactions (ADRs)	Group A (n=35)	Group B (n=35)
Skin redness	2 (5.71%)	1(2.86%)
Skin dryness	1(2.86%)	3 (8.57%)
Burning sensation	1(2.86%)	3 (8.57%)
Itching and irritation	2 (5.71%)	2 (5.71%)
Stinging sensation	NIL	1(2.86%)
Flue like symptoms	NIL	1(2.86%)
Skin discolouration	4 (11.43%)	2 (5.71%)
Flushing	1(2.86%)	NIL

Data are expressed as number of patients and percentages (%).

In our study, we noted that the complete healing of psoriatic plaques occurred only in four patients, but not all individual lesions responded to the same extent. Both treatment regimens were well tolerated. Slight-to-moderate itching and burning at lesion sites were observed in both treatment groups, with three patients associated with Group A and five with Group B. We have not observed any statistically significant differences between these two treatment groups. However, these side effects tended to be milder. Also, we noted that no contact dermatitis occurred in any treatment group (Table 3).

### Assessment of Safety Profile of drugs

When assessed by a clinician, the mean score for cutaneous safety was greater in the Clobetasol group (0.47 vs. 0.30), although there was no statistically significant difference between the groups ( $P > 0.05$ ). When assessed by the subject, the mean score for cutaneous discomfort was greater in the Clobetasol group compared to the Calcipotriene group (0.57 vs. 0.40), but there was no statistically significant difference between the groups ( $P > 0.05$ ), as shown in [Table 4]. When comparing the Calcipotriene and Clobetasol groups, cutaneous reactions were absent more frequently in the Calcipotriene group when evaluated both by the clinician (68.57% v/s 54.28%) as well as by the patient (62.85% v/s 57.14%) as shown in [Figure 4 & 5].

Table 4: showing a global assessment of safety and cutaneous discomfort in Group A (Calcipotriene) and Group B (Clobetasol) patients

Grades	Assessed by Clinician		Assessed by Subject	
	Group A Calcipotriene	Group B Clobetasol	Group A Calcipotriene	Group B Clobetasol
NO reaction	24 (68.57%)	19(54.28%)	22 (62.85%)	20 (57.14%)
Mild reaction	8 (22.85%)	8(22.85%)	9 (25.71%)	7 (20%)
Moderate reaction	3 (8.57%)	8 (20%)	4 (11.42 %)	8 (22.85%)
Severe reaction	NIL	NIL	NIL	NIL
Very severe reaction	NIL	NL	NIL	NIL

Data are expressed as number of patients and percentages (%)

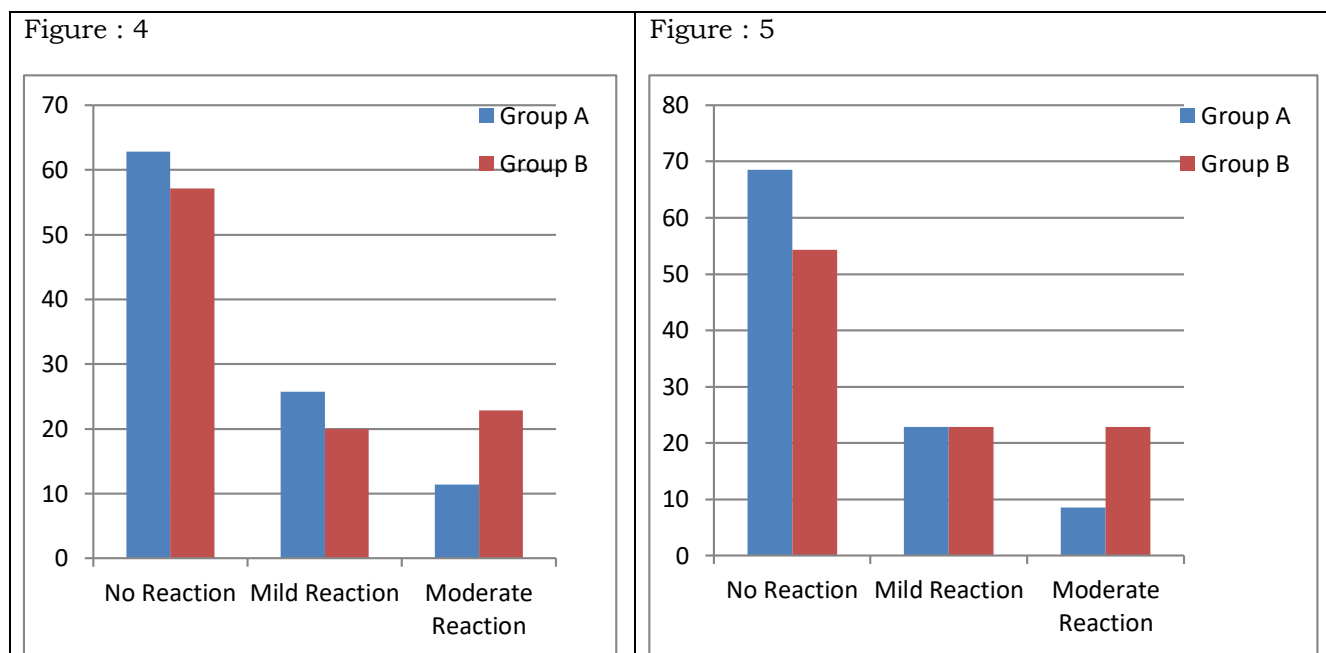


Figure 4 & 5: Showing degree of cutaneous reactions assessed by Subjects and, Clinician in Group A (Calcipotriene) and Group B (Clobetasol) patients. Data are expressed as number of patients and, percentages (%).

## Discussion

Psoriasis manifests in various forms, including chronic plaque-type, regional psoriasis (involving the scalp, napkin area, palms, and soles), exfoliative type of psoriasis, inverse flexural psoriasis, pustular psoriasis, and its variants, guttate psoriasis. The prevalent type of psoriasis is chronic plaque psoriasis (psoriasis vulgaris), which accounts for most cases. Well-circumscribed, erythematous plaques characterize psoriasis with silvery-white scales that represent a response to the inflammatory T cells, stimulating the release of cytokines. Until now, there has been no cure for psoriasis; the disease can be successfully managed by various therapeutic options, used alone or in combination.

Psoriasis manifests in various forms, including chronic plaque-type, regional psoriasis (involving the scalp, napkin area, palms, and soles), exfoliative types of psoriasis, inverse flexural psoriasis, pustular psoriasis, and its variants, guttate psoriasis. The prevalent type of psoriasis is chronic plaque psoriasis (psoriasis vulgaris), which accounts for most cases. Well-circumscribed, erythematous plaques characterize psoriasis with silvery-white scales that represent a response to the inflammatory T cells, stimulating the release of cytokines. Until now, there has been no cure for psoriasis; the disease can be successfully managed by various therapeutic options, used alone or in combination (Mason et al., 2013; Mahajan et al., 2020; Alora-Palli et al., 2009; Sofen et al., 2011; Hendriks et al., 2013).

Between Group A and Group B, baseline demographic parameters such as age and gender, as well as clinical characteristics such as redness, thickenings, and scaling, were closely matched. The study findings revealed that the PASI score and the difference in PASI score were significantly lower in Group A compared to Group B in the first and second follow-up visits, with a  $P < 0.00001$ , whereas there was no significant difference in the PASI score in either group at the final follow-up.

Calcipotriene binds to the vitamin D receptor; the vitamin D receptor is a member of the steroid receptor superfamily (Goruntla et al., 2018). Clobetasol can activate a prototypic form of the transcription factor NF (Kappa) B, a central transcriptional regulator of inflammation and immune responses. The down-regulation of epidermal growth factor (EGF) receptor on epidermal cells by clobetasol may also contribute to its antipsoriatic action. Clobetasol induces a decrease in EGF binding in a dose-dependent manner (Goruntla et al., 2018; Fleming et al., 2016). Calcipotriene and Clobetasol are effective agents with multimodal functions, exhibiting anti-inflammatory, immunomodulatory, and antiproliferative activity. Hence, Calcipotriene ointment is valuable as a first- or second-line therapy option for the management of mild to moderate psoriasis and in combination with other antipsoriatic agents for more severe psoriasis.

Safe, effective, cost-effective, and cost-effective long-term treatment and maintenance options are required to manage chronic psoriasis patients and improve their quality of life (Yan et al., 2016; Feldman et al., 2012; Girolomoni et al., 2012). Several studies reported individual antipsoriatic effects of Calcipotriene propionate (K & P, 2015; Alora palli et al., 2010; Feldman et al., 2010; Sarma, 2017). There were few research studies, published data, or articles on topical Calcipotriene versus clobetasol propionate monotherapy in limited chronic plaque psoriasis. The study also measured costs associated with treatment; these observations have detailed the best cost-effectiveness alternative in the management of chronic plaque psoriasis.

In this present study, we assessed and compared the efficacy and safety profile of topical Calcipotriene and topical Clobetasol in chronic plaque psoriasis. Based on observations in the PGA, DSS and, PASI scores, Calcipotriene ointment was more efficacious than Clobetasol ointment. Calcipotriene had a better safety profile than Clobetasol in terms of local tolerance and induced fewer treatment-related adverse events. No adverse events in either group necessitated discontinuation of therapy. Topical Calcipotriene 0.005% is effective and well-tolerated for the treatment of psoriasis. It reduces keratinocyte proliferation and enhances differentiation. These actions are mediated via vitamin D receptors located in the nucleus of keratinocytes. Clobetasol propionate 0.05% exerts anti-inflammatory, antiproliferative, and immunosuppressive actions by the induction of phospholipase inhibitory proteins (Sofen et al., 2011).

Calcipotriene has a better safety profile than Clobetasol, with a lower incidence of irritation (Sarma, 2017; Brouda et al., 2010). In our study, similar observations were noted, with patients in the Clobetasol group experiencing mild discomfort compared to the Calcipotriene group. However, this finding was not found to be statistically significant.

Topical Clobetasol ointment is known as a super potent steroid, which is one of the most preferred modalities of treatment for plaque psoriasis in India. However, its long-term usage results in skin thinning, skin atrophy, tachyphylaxis, and telangiectasias (Sarma, 2017; Brouda et al., 2010; Kaur et al., 2010). Clobetasol propionate is the most potent of the currently available topical steroids. Topical treatment of Clobetasol has established itself as a more effective mode of treatment in psoriasis patients compared to other steroid-responsive dermatoses. Clobetasol acts by delaying the rate of remission; due to such action, intermittent treatment regimens are possible with the minimum possible adverse drug reactions (Mehta et al., 2009). Whereas Calcipotriene is a vitamin D3 analogue, this causes only minimal side effects compared to Clobetasol. Calcipotriene acts by inhibiting keratinocyte proliferation, inducing anti-inflammatory action and cellular differentiation (Abramovits, 2009).

Guidelines for managing psoriasis state that when used as a control in topical steroid trials, non-medicated topical moisturizers demonstrate a response rate ranging from 15 to 47% (Kircik, 2009). The findings from our study indicated that the initial week's Calcipotriene had shown rapid improvement in symptom relief. However, at the end of the treatment, both the treatment groups were at the same level in achieving a clinical cure. Our present study highlights the more effective action of Calcipotriene ointment compared to that of Clobetasol. However, both Calcipotriene and Clobetasol are economically viable and cosmetically acceptable, but the difference in medicine cost and Pharmacoeconomics are major indicators of the economically weaker section of patients.

### **Conclusion**

Plaque psoriasis is one of the predominant types of psoriasis that does not have a complete cure. For the treatment of limited chronic plaque psoriasis, topical modalities were the mainstay. New insights into the pathogenesis of psoriasis have enabled the identification of new therapeutic targets. Target-based topical agents are being developed and tested. The advent of newer molecules and drug delivery systems will significantly expand the therapeutic armamentarium for the treatment of psoriasis.

Topical ointment therapies are a vital tool in the management of psoriasis. They are well-tolerated and safe for the patients. In our study, the efficacy of Calcipotriene was clinically more significant than Clobetasol based on improvement in global assessment score at the end of a treatment regimen. Calcipotriene had a better safety profile than Clobetasol in terms of local tolerance and induced fewer treatment-related adverse events. Clobetasol, though it was less efficacious than Calcipotriene, Clobetasol was more cost-effective and can be considered an alternative agent, especially in treating patients with low economic strata.

### **Sponsorship and Financial assistance**

Nil.

### **Conflicts of Interest**

There are none.

### Acknowledgments

We are grateful to two anonymous reviewers for their valuable comments on the earlier version of this paper.

### References

- Abramovits, W. (2009). Calcitriol 3 microg/g ointment: an effective and safe addition to the armamentarium in topical psoriasis therapy. *Journal of Drugs in Dermatology: JDD*, 8(8 Suppl), s17-22.
- Alora-Palli, M. B., Kimball, A. B., & Van Cott, A. (2009, March). A new topically applied liquor carbonis distillate (coal tar) solution helps reduce regression of plaque psoriasis after 12 weeks (about 3 months) of treatment: A 6-week comparison to Calcipotriene cream. In *Journal of the American Academy of Dermatology* (Vol. 60, No. 3, pp. AB174-AB174).
- Alora-Palli, M. B., Perkins, A. C., Van Cott, A., & Kimball, A. B. (2010). Efficacy and tolerability of a cosmetically acceptable coal tar solution in the treatment of moderate plaque psoriasis. *American journal of clinical dermatology*, 11(4), 275-283.
- Bai, K. S., & Naik, P. S. (2015). An open label prospective randomized trial to compare the efficacy of salicylic acid ointment 3% versus betamethasone dipropionate ointment in the treatment of limited chronic plaque psoriasis. *Journal of Evolution of Medical and Dental Sciences*, 4(36), 6296-6303.
- Brouda, I., Edison, B., Van Cott, A., & Green, B. A. (2010). Tolerability and cosmetic acceptability of liquor carbonis distillate (coal tar) solution 15% as topical therapy for plaque psoriasis. *Cutis*, 85(4), 214-220.
- Dewi, L. K. C., Kawiana, I. G. P., & Martini, L. K. B. (2018). Integrative model of performance improvement. *International Journal of Social Sciences and Humanities*, 2(2), 26-39. <https://doi.org/10.29332/ijssh.v2n2.116>
- Feldman, S. R., Matheson, R., Bruce, S., Grande, K., Markowitz, O., Kempers, S., & Wyres, M. (2012). Efficacy and safety of calcipotriene 0.005% foam for the treatment of plaque-type psoriasis. *American journal of clinical dermatology*, 13(4), 261-271.
- Fleming, C., Ganslandt, C., Guenther, L., Johannesson, A., Buckley, C., Simon, J. C., & Tingleff, L. V. (2010). Calcipotriene plus betamethasone dipropionate gel compared with its active components in the same vehicle and the vehicle alone in the treatment of psoriasis vulgaris: a randomised, parallel group, double-blind, exploratory study. *European Journal of Dermatology*, 20(4), 465-471.
- Girolomoni, G., Vena, G. A., Ayala, F., Cannavò, S. P., De Pità, O., Chimenti, S., & Peserico, A. (2012). Consensus on the use of the fixed combination Calcipotriene/betamethasone dipropionate in the treatment of plaque psoriasis. *Giornale Italiano di Dermatologia e Venereologia: Organo Ufficiale, Societa Italiana di Dermatologia e Sifilografia*, 147(6), 609-624.
- Goruntla, N., Arakala, G. K., Nelluri, G. P., Mounika, K. N., Pujari, S., & Byalla, M. K. (2018). Comparison of efficacy, safety, and cost-effectiveness of topical salicylic acid 6% versus clobetasol propionate 0.05% in the treatment of limited chronic plaque psoriasis. *Journal of Health Research and Reviews*, 5(2), 86.
- Hendriks, A. G. M., Keijsers, R. R. M. C., de Jong, E. M. G. J., Seyger, M. M. B., & vande Kerkhof, P. C. M. (2013). Efficacy and safety of combinations of first-line topical treatments in chronic plaque psoriasis: a systematic literature review.

- Journal of the European Academy of Dermatology and Venereology*, 27(8), 931-951.
- Kaur, I., Dogra, S., Jain, R., & Kumar, B. (2008). Comparative study of Calcipotriene (0.005%) ointment and tazarotene (0.05% and 0.1%) gel in the treatment of stable plaque psoriasis. *Indian Journal of Dermatology, Venereology, and Leprology*, 74(5), 471-4
- Kircik, L. (2009). Efficacy and safety of topical calcitriol 3 microg/g ointment, a new topical therapy for chronic plaque psoriasis. *Journal of Drugs in Dermatology: JDD*, 8(8 Suppl), s9-16.
- Mahajan, H., Deshmukh, G., Dhoot, D., Mamadi, R., & Barkate, H. (2020). Comparative Clinical Assessment of Effectiveness and Safety of Calcitriol and Calcipotriene in Mild Plaque Psoriasis. *Int. J. Clin. Dermatol*, 3, 28-31.
- Mason, A. R., Mason, J., Cork, M., Dooley, G., & Hancock, H. (2013). Topical treatments for chronic plaque psoriasis. *Cochrane Database of Systematic Reviews*, (3).
- Mehta, S., Singal, A., Singh, N., & Bhattacharya, S. (2009). A study of clinicohistopathological correlation in patients of psoriasis and psoriasiform dermatitis. *Indian Journal of Dermatology, Venereology and Leprology*, 75(1), 100.
- Sarma, N. (2017). Evidence and suggested therapeutic approach in psoriasis of difficult-to-treat areas: Palmoplantar psoriasis, nail psoriasis, scalp psoriasis, and intertriginous psoriasis. *Indian Journal of Dermatology*, 62(2), 113.
- Sembiring, T. B., Maruf, I. R., Susilo, C. B., Hidayatulloh, A. N., & Bangkara, B. M. A. S. A. (2022). Health literacy study on approaching forest and boosting immune system strategy. *International Journal of Health Sciences*, 6(1), 40-49. <https://doi.org/10.53730/ijhs.v6n1.3145>
- Sofen, H., Hudson, C. P., Cook-Bolden, F. E., Preston, N., Colón, L. E., Caveney, S. W., & Gottschalk, R. W. (2011). Clobetasol propionate 0.05% spray for the management of moderate-to-severe plaque psoriasis of the scalp: results from a randomized controlled trial. *Journal of Drugs in Dermatology: JDD*, 10(8), 885-892.
- Suryasa, I. W., Rodríguez-Gámez, M., & Koldoris, T. (2022). Post-pandemic health and its sustainability: Educational situation. *International Journal of Health Sciences*, 6(1), i-v. <https://doi.org/10.53730/ijhs.v6n1.5949>
- Yan, R., Jiang, S., Wu, Y., Gao, X. H., & Chen, H. D. (2016). Topical Calcipotriene/betamethasone dipropionate for psoriasis vulgaris: A systematic review. *Indian journal of dermatology, venereology and leprology*, 82(2).