

# Comparative Clinical Assessment of Effectiveness and Safety of Calcitriol and Calcipotriol in Mild Plaque Psoriasis

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**Abstract:** Introduction: Psoriasis is defined as chronic disease of the skin which is treated by topical drugs, systemic drugs or phototherapy depending on its severity. Vitamin D analogues are also commonly used in psoriasis, and its combination with topical corticosteroids (TCS) has shown to have synergistic action leading to more effective control of symptoms of psoriasis as well as decrement in adverse events like skin atrophy associated with prolonged TCS therapy. The present study was undertaken in pursuit of comparative assessment of effectiveness and safety of calcitriol and calcipotriol in patients diagnosed with mild psoriasis. Material and methods: This was a multicentre, retrospective data analysis and comparison between calcitriol and calcipotriol ointment done at 129 dermatology clinics across India after obtaining ethics committee approval. The data charts were identified by generating a list of all patients who were prescribed clobetasol and calcitriol as fixed dose combination for 2 weeks followed by either calcitriol (group 1) or calcipotriol (group 2) for 4 weeks at all clinics, using medical record database. Results: Out of 1076 records, a total of 630 patients met inclusion criteria. Improvement in symptoms was seen in all patients. Improvement in Physician Global assessment Score (PGAS) and Psoriasis Area and Severity Score (PASI) was seen consistently throughout the treatment period in both the groups, but greater improvement was seen in calcitriol group as compared to calcipotriol group at day 42 ( $p < 0.05$ ). Overall, the adverse effects in calcitriol group were less as compared to calcipotriol group. Conclusion: The findings of the present study suggests that calcitriol offers better effectiveness and safety over calcipotriol in maintenance phase of treatment of mild to moderate psoriasis and also it can serve as better option to maximise the therapeutic effect of topical corticosteroid as a fixed dose combination in acute phase of treatment.

**Keywords:** Psoriasis, Calcitriol, Calcipotriol, Topical Corticosteroid, PASI, PGAS

## 1. Introduction

Psoriasis is defined as chronic disease of the skin which is typified by two key pathological features i.e. abnormally increased proliferation of keratinocytes and inflammation of the involved skin [1]. Psoriasis is treated by topical drugs, systemic drugs or phototherapy depending on its severity. Due to its chronicity, relapses are not uncommon in patients with psoriasis, particularly when there is stoppage of topical therapy [2].

Topical corticosteroids (TCS) are the mainstay of topical therapy of psoriasis. Owing to the adverse effects caused by

TCS, their long term use is not feasible in clinical practice [3]. Vitamin D analogues are also commonly used in psoriasis, and its combination with TCS has shown to have synergistic action leading to more effective control of symptoms of psoriasis as well as decrement in adverse events like skin atrophy associated with prolonged TCS therapy [4].

Calcitriol is metabolically active form of vitamin D3 which has proven efficacy in psoriasis in various clinical trials [5, 6]. Calcitriol has multimodal actions like modulation of dermatological immune responses, control of hyper proliferation of keratinocytes and at the same time it is known to promote differentiation of these cells in the skin [7]. Thus, calcitriol might serve as an effective option in place of another

commonly used vitamin D derivative i.e. calcipotriol in the management of psoriasis [8]. There is very limited data on direct comparison of effectiveness and safety of calcitriol and calcipotriol in psoriasis, especially in Indian patients.

Hence the present study was undertaken in pursuit of comparative assessment of effectiveness and safety of calcitriol and calcipotriol in patients diagnosed with mild psoriasis.

## 2. Material and Methods

This was a multicentre, retrospective data analysis and comparison between calcitriol and calcipotriol ointment done at 129 dermatology clinics across India after obtaining ethics committee approval. The data charts were identified by generating a list of all patients who were prescribed clobetasol and calcitriol as FDC for 2 weeks followed by either calcitriol and calcipotriol for 4 weeks at all clinics, using medical record database. Adult patients (age ≥18 years) diagnosed with mild plaque psoriasis were included. Additionally, only those patients were included whose Psoriasis Area and Severity Score (PASI) was below 7 and records of Physician Global Assessment Scores (PGAS) were available. All safety data were also included in analysis. If an AE was not re-recorded in the chart at a follow-up visit, it was assumed that the AE had been resolved. Patients who discontinued the treatment due to AEs in different regimes were recorded in the study outcomes. Effectiveness analysis was compared by unpaired t test in both the groups. A p value <0.05 was considered significant.

## 3. Results

Out of 1076 records, a total of 630 patients met inclusion criteria and their baseline demographics are summarized in Table 1. All the records were divided into two group. Both the groups received clobetasol and calcitriol as FDC initially for 2 weeks, thereafter Group I received calcitriol and group II received calcipotriol for 4 weeks. Of the 630 patients, 352 were in Group I and 278 were in Group II respectively.

Table 1. Baseline parameters in both the treatment groups.

	Gr 1 (calcitriol)	Gr 2 (calcipotriol)	P value
N	352	278	
Male	227	167	
Female	125	111	
BSA	2.75±1.02	2.58±0.94	0.23
Mean Age	41.17±11.31	40.8±11.08	0.15
Mean duration months	3.15±1.11	3.09±1.25	0.46
Baseline scores			
PASI	6.07±1.31	5.95±1.23	0.38
PGAS	3.81±0.50	3.79±0.60	0.4

Improvement in symptoms was seen in all patients. Improvement in PGAS and PASI was seen consistently throughout the treatment period in both the groups, but greater improvement was seen in group 1 as compared to group 2 at day 42 (figures 1 & 2). Effectiveness outcomes in

both the groups are summarized in Table 2. There was no statistical difference in outcome at day 14 and day 28 but at the end of therapy at day 42, there was statistical difference between two groups.

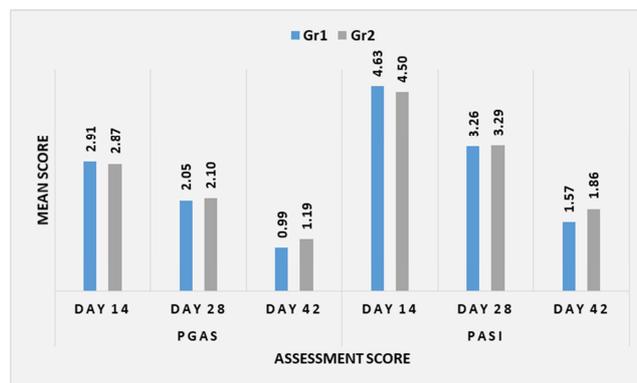


Figure 1. Mean PASI and PGAS over the treatment period in both the groups.

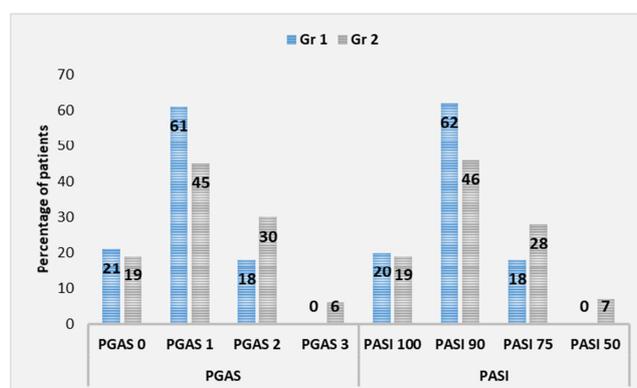


Figure 2. Percentage of patients achieving various PASI and PGAS over the treatment period in both the groups.

Table 2. Effectiveness outcomes-mean PGAS and PASI scores during the treatment period in both the groups.

PGAS	Gr1 (calcitriol)	Gr2 (calcipotriol)	p-value
Day 14	2.91±0.65	2.87±0.68	0.35
Day 28	2.05±0.69	2.10±0.78	0.3
Day 42	0.99±0.61	1.19±0.84	<0.05
PASI			
Day 14	4.63±0.62	4.50±0.65	0.4
Day 28	3.26±0.69	3.29±0.75	0.34
Day 42	1.57±0.58	1.86±0.78	<0.05

The adverse effects encountered in both the treatment groups are shown in table 3. Overall, the adverse effects in calcitriol groups were less as compared to calcipotriol i.e. calcitriol was better tolerated.

Table 3. Safety profile in both the treatment groups.

Adverse effects	Group-1 N (%)	Group-2 N (%)
Erythema	14 (3.9)	22 (7.9)
Scaling around the lesion	8 (2.2)	14 (5)
Irritation/Itching	10 (2.8)	33 (11.8)
Edema around lesion	6 (1.7)	7 (2.5)

## 4. Discussion

Psoriasis is known to adversely affect the quality of life, jeopardising the routine activities, and some patients may even suffer from depression. Owing to its chronic nature, patients with mild to moderate psoriasis requires prolonged topical therapy. Few critical factors which play a major role in optimal treatment outcome are patient compliance and adverse effect profile of the drug [9, 10]. Fouere et al in their study revealed that patients affected with psoriasis gave weightage to such topical formulations which are non-oily, has less adverse effects and easy to apply [11].

TCS monotherapy in the treatment of psoriasis is associated with array of adverse effects like atrophy or thinning of skin, striae formation, etc. [12]. The addition of the Vitamin D3 analogue not only augments the efficacy of TCS but its safety profile is also improved [8]. This has been proven in various clinical trials with varying regimens like evening and morning or alternate day administration of clobetasol propionate and vitamin D derivative [8, 13]. There are very few studies related to efficacy and safety of fixed dose combination of TCS and vitamin D analogue and that too in Western countries. So this study will be first of its kind in India to provide such evidence along with comparative assessment of effectiveness and safety of calcitriol and calcipotriol.

The present study confirmed the effectiveness of fixed dose combination of clobetasol and calcitriol as well as of calcitriol as maintenance therapy. There are few clinical trials which also have documented similar improvement with combination therapy either as morning/evening or alternate day regimen of TCS and vitamin D derivative [14-16].

In the present study there was almost similar reduction in PGAS in both calcitriol and calcipotriol groups, except at day 42 where results were in favour of calcitriol and the difference between calcitriol and calcipotriol groups was statistically significant [ $p < 0.05$ ]. PGAS gives a better perspective of disease control [17]. However, it is recommended by all majority of the regulatory bodies like European Medicine Agency (EMA), United States Food and drug Administration (USFDA) that PGAS should be used along with PASI evaluation in studies related to psoriasis [18].

The mean PASI score reduction was consistently seen in both calcitriol and calcipotriol groups and the reduction was comparable till day 28. But greater reduction was seen in calcitriol group as compared to calcipotriol group at day 42 and the difference was statistically significant ( $p < 0.05$ ). Improvement on PGAS and PASI score in both the groups indicate that both calcitriol and calcipotriol have good effectiveness, but greater improvement was seen in both these parameters with prolonged therapy of calcitriol as compared to calcipotriol. Similar results were found in a randomised clinical trial which evaluated the efficacy and safety of calcitriol ointment and calcipotriol ointment in patients of mild to moderate plaque psoriasis. In this clinical trial, patients with bilaterally symmetrical psoriasis lesions with equal severity on both sides were involved to negate the

effect of inter subject variability bias. Calcitriol was applied on one side and calcipotriol on the other side. It was found that global improvement score had shown statistically significant greater improvement in calcitriol group as compared to calcipotriol group [19].

One of the key challenge in topical therapy of psoriasis is the adverse effect profile of these drugs and hence the resulting poor patient compliance [17]. In the present study the adverse effects encountered with calcitriol were significantly less as compared to calcipotriol. Similar safety profile was reported in other such clinical trials [19, 20]. In a study by Ortonne et al. the patient acceptability was found to be excellent in 80% of the patients treated with calcitriol as compared to only 57% in calcipotriol group in patients with flexural lesions, while the overall tolerability was better in calcitriol group i.e. 49% as compared to calcipotriol group i.e. 10.7% and the difference was highly statistically significant ( $p < 0.0001$ ). This study concluded that calcitriol is more effective and safe as compared to calcipotriol particularly in sensitive areas [19].

Zhu et al in their study had reported that adverse effects like erythema, burning, irritation, etc. were all significantly less in patients treated with calcitriol as compared to calcipotriol. In the same study number of patients with severe category of skin discomfort score at the end of treatment was significantly less in patients treated with calcitriol as compared to calcipotriol ( $p = 0.02$ ) [20]. Similar safety profile was seen in study by Liao et al wherein calcitriol ointment was applied in sensitive areas like face [21]. Even on long term use up to 78 weeks, the safety profile of calcitriol was found to be excellent [22].

## 5. Conclusion

Vitamin D3 analogues i.e. calcitriol and calcipotriol are important class of topical drugs for management of psoriasis. The findings of the present study suggests that calcitriol offers better effectiveness and safety over calcipotriol in maintenance phase of treatment of mild psoriasis and also it can serve as better option to maximise the therapeutic effect of topical corticosteroid as a fixed dose combination in acute phase of treatment.

## Source of Support

This study was carried out with the help of Glenmark Pharmaceuticals Ltd, Mumbai in terms of collecting all medical records and its analysis.

## Ethics Committee Approval

Obtained prior to the start of the study.

## Conflicts of Interest

All the authors do not have any possible conflicts of interest.

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