e-ISSN: 0975-1556, p-ISSN:2820-2643

Available online on www.ijpcr.com

International Journal of Pharmaceutical and Clinical Research 2023; 15(1); 976-983

Original Research Article

Efficacy and Safety of Topical Calcitriol and Topical Calcipotriol in Stable Chronic Plaque Type Psoriasis: A Comparative Study

Vinay Kumar Sinha[1], Tauseef Haider[2], Jeetendra Kumar[3]

[1]Tutor, Department of Pharmacology, Jawaharlal Nehru Medical and Hospital (JLNMCH), Bhagalpur, Bihar.

[2]Tutor, Department of Pharmacology, Jawaharlal Nehru Medical and Hospital (JLNMCH), Bhagalpur, Bihar.

[3]Associate Professor, Department of Pharmacology, Jawaharlal Nehru Medical and Hospital (JLNMCH), Bhagalpur, Bihar.

Received: 06-12-2022 / Revised: 30-12-2022 / Accepted: 20-01-2023

Corresponding author: Dr Tauseef Haider

Conflict of interest: Nil

Abstract

Background: There are not many research that contrast topical calcitriol and calcipotriol, two vitamin D derivatives that are believed to be useful in treating psoriasis. The objective of the current study was to compare and evaluate the efficacy and safety of calcitriol and calcipotriol in individuals with chronic plaque-type psoriasis that is persistent.

Methods: A total of 50 patients with chronic stable plaque-type psoriasis were randomly split into two groups of 25 each. One group received calcitriol 3 μg/g ointment for 12 weeks, whereas the other received calcipotriol 50 μg/g ointment. Clinical and subject evaluations of overall improvement were included in efficacy assessments (on a 4-point scale from 0: no change to 3: clear or almost clear). Effectiveness was also influenced by the "dermatological sum score" (DSS) from each trial visit. The safety evaluations included subject assessments of cutaneous discomfort and clinical exams of cutaneous safety (on a 5-point scale from 0: none to 4: extremely severe).

Results: Both calcitriol and calcipotriol were significantly effective ($p<0.001$) in reducing DSS, although there was no statistically significant difference between the two groups. While the mean score for the subject was 1.92 for calcitriol and 1.84 for calcipotriol, the mean score of total improvement as determined clinically was 2.20 for calcitriol and 2.16 for calcipotriol, respectively ($p > 0.05$). The discrepancies between the two groups did not differ statistically from one another. The mean worst score for cutaneous safety was higher in the calcipotriol group as compared to the calcitriol group (0.28 vs 0.04 and 0.36 vs 0.04 by clinically and by the subject, respectively). Only when the participant evaluated the safety profile was a statistically significant improvement ($p<0.05$) shown for calcitriol. Compared to calcitriol, which had only 4% documented treatment-related adverse events, calcipotriol had 24%.

Conclusions: Both topical calcitriol and calcipotriol were equally effective in treating chronic plaque psoriasis, but calcitriol had a higher safety profile due to their greater local tolerability and lower incidence of treatment-related side effects.

Keywords: Plaque Type Psoriasis, Calcipotriol, Calcitriol, Cutaneous Discomfort, Global Assessment, Cutaneous Safety.

Introduction

Skin issues such as psoriasis, which are prevalent, persistent, deforming, inflammatory, and proliferative, are greatly influenced by both genetic and environmental factors [1]. The disease affects both men and women of all ages and is prevalent throughout the world. Psoriasis prevalence varies around the world and ranges from 0.5% to about 2.5% [2]. The most prevalent type of psoriasis, known medically as Psoriasis vulgaris, is present in 90% of patients. Plaques that are symmetrically dispersed and red in colour are typical [3]. Epidermal hyperproliferation, improved antigen presentation, helper T-cell Th1 and Th17 cytokine production, T-cell expansion, and angiogenesis are the pathophysiologic features of psoriasis [4]. TNF-α is the main cytokine involved in this classic Th1-mediated illness [5].

The pathophysiology of psoriasis has also recently been linked to the cytokines IL-12 and IL-23. Naive T-cell development and differentiation into Th1 and cytotoxic T-cells are encouraged by IL-12, whilst Th17 cell survival and proliferation are supported by IL-23 [6,7]. It is clear that no single kind of therapy is best when there are numerous potential modalities of treatment for a single disease with an unknown cause. This is particularly true with psoriasis, which has a variety of alternative treatments. Therapies or therapeutic strategies frequently incorporate newer components. It is uncommon for a patient to not get multiple alternative treatments throughout his or her lifetime. Each of these various therapies has advantages and disadvantages of its own.

Despite the lack of a cure, there are numerous therapy strategies that can successfully control the illness. There are currently a variety of topical medicines available for the treatment of psoriasis, especially mild-to-moderate plaque type psoriasis. They include time-tested medications such topical vitamin D derivatives, salicylic acid, tar, topical retinoids, dithranol, and more recently, topical retinoids [8]. Several vitamin D3 derivatives, including calcipotriol, tacalcitol, maxacalcitol, and more recently, calcitriol, can be used topically to treat psoriasis [1,9]. Topical preparations of calcipotriol and other vitamin D3 analogues are probably the most widely used active topical therapy for plaque psoriasis. Although topical calcipotriol is thought to be more efficacious than topical calcitriol, this is not well established. This study was carried out to investigate the efficacy and safety of topical calcitriol and calcipotriol in stable chronic plaque type psoriasis.

Material and Methods

From March 2022 to December 2022, a total of 50 patients were chosen from the department of dermatology at the Jawaharlal Nehru Medical College and Hospital in Bhagalpur, Bihar, for this randomised, open label, parallel, comparative trial that was done there.

Sample size was calculated by the formula - Patients per group = $f(\alpha, \beta) \times 2 \times SD^2 / (d)^2$

There had to be a minimum of 25 patients in each group. With 80% power and a 0.05 likelihood of type 1 error, this was predicted to detect a difference of 4 in mean DSS across the groups, assuming a standard deviation of 5 in DSS.

All patients with stable chronic plaque psoriasis and less than 35% body surface area involvement, including male and female participants between the ages of 18 and 70, were included in this study. Patients with unstable, acute guttate, pustular, erythrodermic, or arthropathic psoriasis, a history of hypercalcaemia, renal dysfunction, calcium-based calculi, underlying medical conditions that call for the administration of systemic calcium or vitamin D supplements, body surface area involvement of greater

than 35%, use of topical antipsoriatic medication within the previous two weeks or use of systemic antipsoriatic medication within the previous eight weeks, and those with other extensive skin disease and who had severe systemic illness and pregnant women were excluded.

Based on inclusion and exclusion criteria, a total of fifty individuals with persistent plaque psoriasis were recruited for the study. With 25 patients in each group, the subjects were randomly divided into two study groups (calcitriol and calcipotriol group) in a 1:1 ratio using computer-generated random numbers. In the current study, descriptive statistical analyses were conducted. Results for categorical measurements are shown in Number (%) while those for continuous measurements were shown as Mean±SD.

When the data were not normally distributed, non-parametric tests were used, including the Mann-Whitney test for comparisons within groups and the Wilcoxon Signed Ranks test for comparisons between groups. A p-value of 0.05 or less was required for the complete test to be judged statistically significant.

Results

The two groups can be regarded as comparable ($p > 0.05$) because there was no statistically significant difference between them in terms of mean age, mean body surface area, or the proportion of males and females. (Table 1).

Table 1: Characteristics before to treatment

Variables	Calcitriol group(n=25)	Calcipotriol group(n=25)	p- value
Mean age (years)±SD	42±12.29	44.0±12.02	0.73*
Females (%)	40	40	
Males (%)	60	60	
Mean BSA(%)±SD	9.04±4.80	9.12±6.26	0.96*

* Unpaired t-test; p> 0.05 - Non-significant.

The baseline clinical variables were compared with unpaired t-test. There was no statistically significant difference between the two groups ($p >0.05$) and hence both the groups are comparable.

The group receiving either calcitriol or calcipotriol has a mean baseline DSS of 8.16±2.26 or 8.24± 2.06, respectively. There was no statistically significant difference between the groups ($p > 0.05$). (Table 2).

Table 2: DSS scores before treatment for both groups

Variables	Calcitriol group(n=25)	Calcipotriol group(n=25)	p- value
Mean age years)±SD	42±12.29	44.0±12.02	0.73*

*Mann-Whitney test; p>0.05 - Non-significant.

The baseline DSS between the two groups was compared with Mann- Whitney test. There was no statistically significant difference ($p >0.05$) between the groups.

The mean DSS was 8.16±2.26 at baseline, and it was 1.40±1.41 at 12 weeks. The difference between the mean DSS at 12 weeks post-therapy and baseline was shown to be statistically extremely significant ($P< 0.001$). (Table 3).

Table 3: Mean DSS at 12 weeks after treatment compared to baseline in the calcitriol group

Calcitriol group	Mean DSS±SD
wk-0 (baseline)	8.16±2.26
Wk-12 (end of study)	1.40±.41
p-value	<0.001*

*Wilcoxon Signed Ranks test; p<0.001- Highly significant

The comparison of DSS at baseline and at 12 wks was done by Wilcoxon Signed Ranks test. The reduction was found to be statistically highly significant (p<0.001).

The mean DSS was 8.24±2.06 at baseline, and 1.36±1.25 at 12 weeks. The difference between the mean DSS at 12 weeks post-therapy and baseline was shown to be statistically extremely significant (P <0.001). (Table 4).

Table 4: Mean DSS at 12 weeks after treatment compared to baseline in the calcitriol group

Calcipotriol group	Mean DSS±SD
wk-0 (baseline)	8.24±2.06
Wk-12 (end of study)	1.36±1.25
p-value	<0.001*

*Wilcoxon Signed Ranks test; p <0.001- Highly significant.

The comparison of DSS at baseline and at 12 wks was done by Wilcoxon Signed Ranks test. The reduction was found to be statistically highly significant (p<0.001).

When comparing the mean DSS of the two groups at 2 weeks, 4 weeks, 8 weeks, or 12 weeks of treatment, there was no statistically significant difference between the calcitriol and the calcipotriol groups (P > 0.05). (Table 5).

Table 5: At weeks 2, 4, 8, and 12, the mean DSS of the calcitriol and calcipotriol groups were compared

Week	Calcitriol group Mean DSS±SD	Calcipotriol group Mean DSS±SD	p- value
Wk- 2	6.24±2.14	6.40±1.77	0.875
Wk-4	4.32±1.77	4.48±1.44	0.704
Wk-8	2.72±1.62	2.84±1.40	0.866
Wk12	1.40±1.41	1.36±1.25	0.960

Mann-Whitney test; p >0.05 - Non-significant.

On comparing mean DSS of both groups, there was no statistically significant difference between calcitriol group and calcipotriol group at 2 weeks,4 weeks, 8 weeks and at 12 weeks of treatment.

Clinical examination at 12 weeks revealed that the mean GA score was 2.160±0.687 in the calcitriol group and 2.200±0.707 in the calcipotriol group. At 12 weeks, the subject assessed the mean GA score for the calcitriol group to be 1.920±0.909 and for the calcipotriol group to be 1.840±0.898. When comparing the mean GA scores of the two groups at 12 weeks, both clinically and by subject, there was no statistically significant difference between the two groups (P > 0.05). (Table 6).

Table 6: Clinical evaluation of improvement comparing the calcitriol group to the calcipotriol group at weeks 12

Group	Particulars	GA clinically Wk-12	GA by subject Wk-12
Calcitriol group (I)	Mean±SD	2.160±0.687	1.920±0.909
Calcipotriol group (II)	Mean±SD	2.200±0.707	1.840±0.898
I vs II	p-value	0.823	0.726

Mann-Whitney test; p >0.05 - Non-significant.

The GA scores of calcitriol group and calcipotriol group at 12 wks was compared by using Mann-Whitney test. There was no statistically significant difference between these group at 12 weeks (end of study) of treatment clinically as well as by the subject.

At week 12, the clinical and subject safety evaluations of the calcitriol and calcipitriol groups were compared.

The mean score for cutaneous safety in the calcipotriol group was higher than it was in the calcitriol group (0.28 vs 0.04). But there was no statistically significant difference between any of the groups (P > 0.05). (Table 7).

The mean score for cutaneous discomfort in the calcipotriol group was higher than it was in the calcitriol group (0.36 vs 0.04). (P<0.05) It was significant statistically (Table 7).

Table 7: Comparing the clinical and subject-level safety assessments of the calcitriol and calcipotriol groups at weeks 12

Group	Particulars	Clinically Wk-12	By subject Wk-12
Calcitriol group (I)	Mean±SD	0.040±0.200	0.040±0.200
Calcipotriol group (II)	Mean±SD	0.28±0.613	0.360±0.700
I vs II	p-value	0.079*	0.039**

Discussion

In the current study, the reduction in DSS following calcitriol 3 μg/g ointment treatment of stable chronic plaque psoriasis was statistically very significant (P <0.001).

Chronic plaque psoriasis was successfully treated with calcitriol at doses of 3 μg/g and 15 μg/g in a research by Langner A et al [11]. When used on extensive skin lesions, the larger dose (15 μg/g) did not demonstrate any therapeutic superiority over calcitriol 3 μg/g, but rather was linked to a higher risk of hypercalciuria. These results suggest that a concentration of 3 μg/g is the ideal level.

3μg/g calcitriol ointment and its excipient were compared in two placebo-controlled multicentric randomised double-blind parallel group experiments. The medication was proven in both studies to be much more efficacious than its excipient in treating mild-to-moderate plaque psoriasis [12]. With regard to demonstrating the effectiveness of calcitriol 3 μg/g ointment in the management of chronic plaque psoriasis, the current study is in agreement with the other studies.

In the current study, stable chronic plaque psoriasis was successfully treated with calcipotriol 50 μg/g ointment, and the reduction in DSS was statistically very significant (P <0.001).

According to Ashcroft DM's quantitative systematic review of randomised controlled trials with 6038 patients who had plaque psoriasis and was reported in 37 trials where patients were treated with calcipotriol ointment 50 μg/g, calcipotriol is effective in the treatment of mild to moderate chronic

plaque psoriasis [13]. Research on the use of calcipotriol ointment in the treatment of psoriasis was summarised by Scott et al. After establishing the effectiveness of the twice-daily administration of calcipotriol ointment, they discovered that it is advantageous as a first or second-line therapy option for the management of mild to moderate psoriasis [14].

With regard to demonstrating the effectiveness of calcipotriol 50 μg/g ointment in the management of chronic plaque psoriasis, the current study is in agreement with the other studies.

When therapy with calcitriol 3 μg/g ointment and calcipotriol 50 μg/g ointment were compared at 2 weeks, 4 weeks, 8 weeks, and at 12 weeks, there was no statistically significant difference ($p>0.05$) between the two groups at any post-baseline time-points in terms of reduction in DSS.

When comparing GA assessments of improvements at 12 weeks, there was no clinically significant difference between the calcitriol and calcipotriol groups ($P > 0.05$). (The main effectiveness standard) The similar result was obtained using the secondary efficacy criterion, which assesses overall improvement ($P>0.05$).

Zhu et al. conducted a multicentric, randomised, investigator-masked, parallel evaluation of the efficacy and safety of twice-daily doses of calcitriol 3 μg/g vs. calcipotriol 50 μg/g in persons with mild to moderate chronic plaque psoriasis for 12 weeks. In total, 250 subjects of both sexes were recruited. There was a statistically significant difference in favour of calcipotriol in terms of the reduction in DSS at all post-baseline time intervals, including weeks 2, 4, 8, and 12 ($p<0.01$) [10]. At week 12, both the subject's assessment and the clinical evaluation by the researcher showed that calcitriol was not inferior to calcipotriol for overall improvement.

These outcomes balance the therapeutic applicability of the calcipotriol-achieved, noticeably superior DSS lowering. He came to the conclusion that calcitriol 3μg/g ointment showed comparable efficacy to calcipotriol 50μg/g when applied twice daily for a period of 12 weeks.

The current study supported the findings of the earlier study by demonstrating the comparably effective use of calcitriol 3 μg/g and calcipotriol 50 μg/g ointments in the management of chronic plaque psoriasis. However, in our investigation, there was no significant difference in the reduction of DSS or the global assessment of improvement scores between the groups, whereas in the previous study, there was a substantial difference in favour of calcipotriol in terms of the reduction of DSS.

Ortonne et al. compared the safety and effectiveness of calcitriol 3 μg/g ointment and calcipotriol 50 μg/g ointment in a multicentric, randomised, investigator-blinded, left-right comparison of mild to moderate chronic plaque psoriasis affecting sensitive areas, such as the face, hairline, retroauricular area, and flexural areas [15]

In the 75 participants, 28% of each therapy group saw at least one target lesion disappear. The investigators considerably overestimated the global improvement from baseline for the lesions treated with calcitriol. He came to the conclusion that calcitriol ointment was superior to calcipotriol ointment for the treatment of psoriasis in sensitive areas. The efficacy of both treatments in sensitive zones was not intended to be assessed by the authors of the current investigation within the parameters of the study design. As a result, the authors were unable to verify the study findings.

Clinical evaluation of the cutaneous safety score showed that calcitriol was more locally tolerable than calcipotriol (mean scores of 0.28 vs. 0.04). 20% of the patients in the calcipotriol group had negative drug responses. These matched what local reactions would be categorised as "mild" and "moderate." The percentage of patients who had "mild" local calcitriol reactions was only 4%. Although not statistically significant ($P > 0.05$), this variation was there. The local reaction subsided within two to three days in both groups without the need to interrupt the course of treatment or take any additional medication.

The subject's assessment of cutaneous discomfort showed that the calcitriol group had better local tolerance than the calcipotriol group (mean scores 0.36 vs. 0.04). In the calcipotriol group, 24% of patients experienced "mild" or "moderate" cutaneous irritation. Only 4% of patients on calcitriol reported a "moderate" burning sensation, giving calcitriol a statistically significant advantage ($P <0.05$).

In the aforementioned study by Zhu et al., scores for cutaneous comfort and safety were significantly higher with calcitriol than with calcipotriol, demonstrating calcitriol superior safety profile (more than three times more adverse events were reported for subjects who received calcipotriol) [10].

In the aforementioned study by Ortonne et al., one participant reported one cutaneous adverse event with calcitriol, whereas seven subjects reported cutaneous adverse events with calcipotriol [15]. Calcitriol 3 μg/g was significantly better tolerated than calcipotriol 50 μg/g in terms of perilesional erythema, perilesional edoema, stinging, and burning. The subjective assessments of local tolerability and overall preference both supported calcitriol.

Conclusion

Even though calcitriol 3 μg/g ointment demonstrated a higher safety profile than calcipotriol 50 μg/g ointment in the current investigation, it was statistically insignificant clinically. However, when calcitriol 3 μg/g was compared to calcipotriol 50 μg/g, it had a noticeably improved safety profile.

The results of this study thus show that calcitriol 3 μg/g ointment and calcipotriol 50 μg/g ointment are similarly effective in treating stable chronic plaque psoriasis, with calcitriol having a higher safety profile in terms of local tolerance and inducing fewer treatment-related side events.

References

1. Griffiths CEM, Barker JNWN. Psoriasis. In: Burns T, Breathnach S, Cox N, Griffiths C, editors. Rook's textbook of Dermatology. vol 1. 8th ed. UK: Wiley-Blackwell; 2010; 20:1-20.
2. Dogra S, Yadav S. Psoriasis in India: Prevalance and pattern. Indian J Dermatol Venereol Leprol. 2010; 76(6):595-01.
3. Gudjonsson JE, Elder JT. Psoriasis. In: Goldsmith LA, Katz SI, Gilchrest BA, Paller AS, Leffell DJ, Wolff K, editors. Fitzpatrick's Dermatology in General Medicine. 8th ed. USA: McGraw Hill; 2012:197-231.
4. Richardson SK, Gelfand JM. Update on the natural history and systemic treatment of psoriasis. Advances Dermatol. 2008; 24:171.
5. Hussain I, Haroon TS. Comorbidities in psoriasis and their therapeutic implications. J Pakistan Assoc Dermatol. 2016 Dec 24;19(2):63-5.
6. Singh G, Aneja SP. Cardiovascular comorbiditiy in psoriasis. Indian J Dermatol. 2011 Sep;56(5):553-6.
7. Blauvelt A. New concepts in the pathogenesis and treatment of psoriasis: key roles for IL-23, IL-17A and TGF-β1.

Expert Rev Dermatol. 2007 Feb 1; 2(1): 69-78.
8. Aschoff R, Wozel G, Meurer M. Topical treatment of psoriasis: a systematic update. Dermatol J Dermatol Venereol Related Fields. 2003 Mar;54(3):237-41.
9. Sweetman SC, editor. Martindale: The complete drug reference. 37th edition. London: Pharmaceutical press; 2011: 1716-64.
10. Zhu X, Wang B, Zhao G, Gu J, Chen Z, Briantais P, Andres P. An investigator-masked comparison of the efficacy and safety of twice daily applications of calcitriol 3μg/g ointment vs. calcipotriol 50 μg/g ointment in subjects with mild to moderate chronic plaque-type psoriasis. J Eur Acad Dermatol Venereol. 2007 Apr;21(4):466-72.
11. Langner A, Stapor W, Ambroziak M. Efficacy and tolerance of topical calcitriol 3μg/g in psoriasis treatment: a review of our experience in Poland. Br J Dermatol. 2001;144(suppl.58):11-16.
12. Lebwohl M, Menter A, Weiss J, Clark SD, Flores J, Powers J, et al. Calcitriol 3 microg/g ointment in the management of mild to moderate plaque type psoriasis: results from 2 placebo-controlled, multicenter, randomized double-blind, clinical studies. J Drugs Dermatol. 2007 Apr;6(4):428-35.
13. Ashcroft DM, Po AL, Williams HC, Griffiths CE. Systematic review of comparative efficacy and tolerability of calcipotriol in treating chronic plaque psoriasis. BMJ. 2000 Apr 8; 320(7240):963-7.
14. Scott LJ, Dunn CJ, Goa KL. Calcipotriol ointment. A review of its use in the management of psoriasis. Am J Clin Dermatol. 2001;2(2):95-120.
15. Ortonne JP, Humbert P, Nicolas JF, Tsankov N, Tonev SD, Janin A, et al. Intra-individual comparison of the cutaneous safety and efficacy of calcitriol 3 μg g− 1 ointment and calcipotriol 50μg g−1 ointment on chronic plaque psoriasis localized in facial, hairline, retroauricular or flexural areas. Br J Dermatol. 2003 Feb;148(2):326-33.