Original article

Comparative efficacy of topical calcipotriol ointment with betamethasone valerate ointment in chronic plaque psoriasis

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Abstract

Background Topical steroids are an established therapy for localized psoriasis. Calcipotriol (vitamin D_3 analogue) is a relatively newer edition to the therapeutic armamentarium of psoriasis. We compared the efficacy and safety of calcipotriol 0.005% ointment and betamethasone valerate 0.1% ointment in the treatment of chronic plaque psoriasis.

Patients and methods One hundred diagnosed cases of chronic plaque psoriasis, 50 patients in each group, were enrolled in the study. Age range was 20-55 years for calcipotriol group with a mean of 33.6 years and 15-52 years for betamethasone valerate group with a mean age of 32.6 years. Male to female ratio was 1.17:1 in calcipotriol and 2.13:1 in betamethasone group. Patients in both groups were advised to apply the topical agents twice daily for 6 weeks. They were followed up at 2, 4 and 6 weeks. The assessment was made on the basis of PASI. Overall response was graded as clearance (>70% reduction in PASI), marked improvement (60-70% reduction in PASI), mild improvement (50-60% reduction in PASI), no change and worsening.

Results The mean PASI reduction in calcipotriol group was from 6.33 at week 0 to 1.90 at week 6, whereas betamethasone valerate ointment group showed a decrease in mean PASI from 6.22 at week 0 to 2.26 at the end of treatment. The scores for erythema, infiltration and desquamation at each follow-up i.e. 2, 4 and 6 weeks were comparable in both groups. All the three parameters were effectively reduced by both the topical modalities during six weeks treatment period, but the difference was not significant statistically when compared with each other (p>0.05). Side effects were observed with both topical agents during 6 weeks of application. Most commonly observed side effects with calcipotriol were persistent lesional erythema in 10 (20%), lesional/perilesional irritation in 7 (14%), pruritus in 4 (8%) and folliculitis in 2 (4%) of the patients. Adverse events noted with betamethasone valerate ointment were atrophy in 6 (12%), folliculitis in 5 (10%), persistent erythema in 4 (8%), pruritus in 2 (4%) and lesional irritation in 1 (2%) of the patients.

Conclusion Topical calcipotriol is as efficacious and safe as betamethasone valerate in the treatment of chronic plaque psoriasis.

Key words
Calcipotriol, betamethasone valerate, psoriasis

Introduction

Psoriasis is a common, genetically determined, proliferative and inflammatory disease of the skin, characterized by well-defined, dull-red, plaques with adherent scales, situated particularly over the extensor surfaces and the scalp. It is a disease of variable morphology and course, affecting 2-3% of the world population.[1] Prevalence of psoriasis increases with age. Early onset may be associated with more severe disease. Psoriasis vulgaris typically has a

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protracted course, with frequent recurrences and resistance to treatment.

Treatment of psoriasis depends upon age, sex, occupation, general health, intelligence and resources of the patient as well as the type, extent, duration and natural history of the disease. The objective of treatment is to clear each episode of the disease. Psoriasis is still not completely curable, although a wide variety of treatment modalities, both topical (keratolytics, corticosteroids, tar, dithranol and ultraviolet A and B) and systemic agents like methotrexate, photochemotherapy, retinoids and cyclosporine etc. are available for its control. The doctor and the patient must be goal-oriented in terms of what they want to accomplish when using a topical preparation.[1]

Topical vitamin D_3 analogue (calcipotriol) undoubtedly finds its place as the first or second-line therapy along with topical steroids for mild to moderate cases of psoriasis vulgaris, covering up to 40% of the body surface area. The major improvement occurs during the first 4-6 weeks of treatment. Mild irritant dermatitis of face and anogenital area has been reported frequently but such unwanted effects generally do not lead to withdrawal of calcipotriol[2]

Although extensively prescribed, the use of topical corticosteroids to treat psoriasis vulgaris is controversial because the therapeutic response can be variable, short lasting or associated with side effects.[3] The potent forms of topical steroids, in contrast to less potent ones, offer the best opportunity for selected patients to temporarily clear or almost clear their disease in a shorter time.[4] Following initial daily treatment, responsive patients with plaque-type psoriasis, may have their remission status extended with the use of intermittent applications of topical corticosteroids.[5]

The present study was conducted to compare the efficacy and safety of topical calcipotriol and betamethasone valerate ointment in chronic plaque psoriasis.

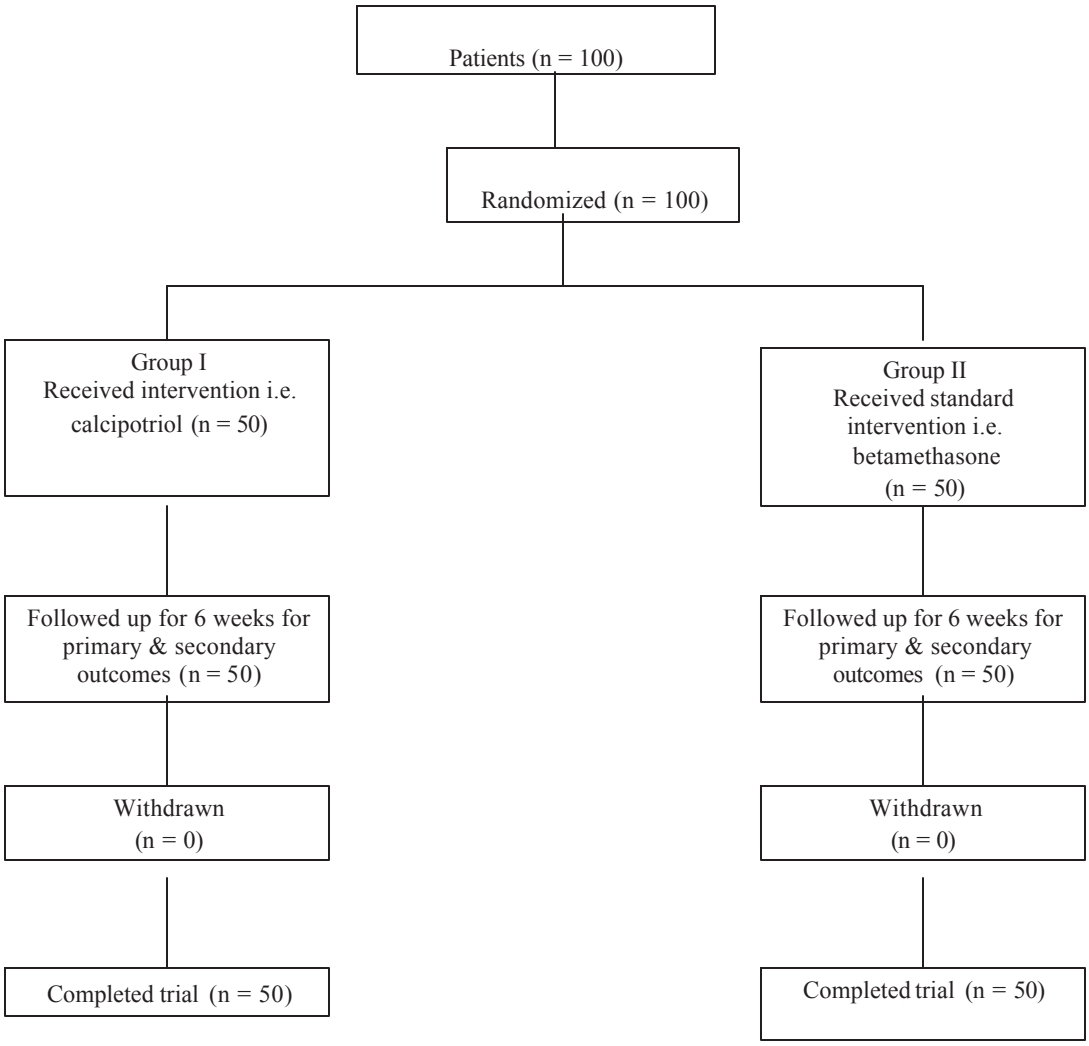
Patients and methods

One hundred diagnosed cases of chronic plaque psoriasis, aged 15 and above, of either sex, were enrolled in the trial. Fifty-six patients were enrolled at the Department of Dermatology, Jinnah Hospital, Lahore and forty-four were recruited at the Department of Dermatology, Mayo Hospital, Lahore, from February 1998 to June 2000. Patients selected in this study, were not on any systemic or topical medication for the past eight weeks and the area of involvement was less than 40% in every patient. Pregnant and breast feeding women were excluded from the study.

Eligible patients were randomized into two groups i.e., group 1 (calcipotriol group) and group 2 (betamethasone group), as shown in **Figure 1**. Both medicines, 0.005% calcipotriol ointment and 0.1% betamethasone valerate ointment, were applied twice daily for a maximum period of six weeks. The maximum allowance for calcipotriol ointment was 100 grams per week.

On the first visit, relevant history and general, cutaneous and systemic examination were conducted and recorded on a pre-designed pro forma. Laboratory investigations included hemoglobin, total and differential leukocyte counts, ESR, serum calcium and phosphate.

Figure 1 An overview of clinical study



Evaluation of severity of psoriasis

Severity of psoriasis was assessed on the basis of PASI (psoriasis area and severity index) score. The erythema (E), infiltration (I) and desquamation (D) were recorded according to a four point scale (0=absent; 1=mild; 2=moderate; 3=severe). For the assessment of Area (A), four main anatomical sites were examined i.e. the head (h), upper extremities (u), trunk (t) and lower extremities (l). Area was assigned a numerical value based on the extent of lesions in each anatomical site. The PASI score was calculated according to the following formula:

PASI = 0.1 (Eh+Ih+Dh) Ah + 0.2 (Eu+Iu+Du) Au + 0.3 (Et+It+Dt) At + 0.4 (El+Il+Dl) Al

Where E = erythema, I = induration, D = desquamation and A = area; and h = head, u = upper limb, t = trunk and l = lower limb.

Fifty patients were treated with topical calcipotriol ointment twice daily and the other fifty patients were advised to apply betamethasone valerate ointment on psoriatic plaques. Both topical modalities were applied for six weeks. Patients were assessed at 2, 4 and 6 weeks of treatment on the basis of PASI. Overall efficacy was evaluated according to the following criteria:

Efficacy

The treatment was said to be effective and further subcategorized as cleared if >70% reduction in PASI score; marked improvement if 60-70% clearance; and mild improvement if there was 50-60% improvement in disease activity. The treatment was considered ineffective if there was <50% PASI reduction or even worsening of disease.

Safety

On each visit, patients were asked and examined about any cutaneous or extracutaneous side effects.

Statistical analysis

Mean PASI reduction in both groups was compared at the end of six weeks using unpaired t test. The decrease in individual parameters i.e. erythema, infiltration and desquamation in each group, was analyzed using `paired t test'. Chi-square test was applied to the ratio of patients' overall clearance of psoriasis at the end of study. A cut-off *p* value of 5% or less was considered significant.

Results

Between February 1998 and June 2000, one hundred patients with chronic, plaque psoriasis were enrolled in this comparative study. There were 50 patients in each group. Group 1 i.e. calcipotriol group comprised of 27 males and 23 females while group 2 i.e. betamethasone group included 34 males and 16 females. Demographic characteristics are shown in **Table 1.**

Table-1 Demographic data

	Calcipotriol Group	*Betamethasone Group*
No. of patients	50	50
Age range (years)	20-55	15-52
Mean age (years)	33.60	32.66
Sex: male/ female	27/23	34/16
Extent of skin involvement	10-38%	5-40%
Mean area of skin involvement	24%	23%
Mean PASI	6.33 ± 2.23	6.27 ± 3.33

Table 2 Overall assessment of efficacy at the end of treatment

	Calcipotriol (n=50)	*Betamethasone (n=50)*
Effective therapy	50 (100%)	44 (88%)
Cleared	23 (46%)	4 (8%)
Marked improvement	27 (54%)	40 (80%)
Ineffective therapy	-	6 (12%)
No change	-	6 (12%)
Worse	-	-

Overall assessment of efficacy

All patients in these two groups showed good response to both the topically applied modalities. The treatment was 100% effective in calcipotriol and 88% in betamethasone group. Twenty three calcipotriol-treated patients showed clearance (>70% PASI reduction) [**Figure 2**], whereas betamethasone group showed clearance in 4 patients. Between 60-70% reduction in PASI (marked improvement) was seen in 27 patients of calcipotriol group and 40 patients of betamethasone group (**Table 2**).

Figure 2 Pre- and post-treatment mean PASI score in two groups.

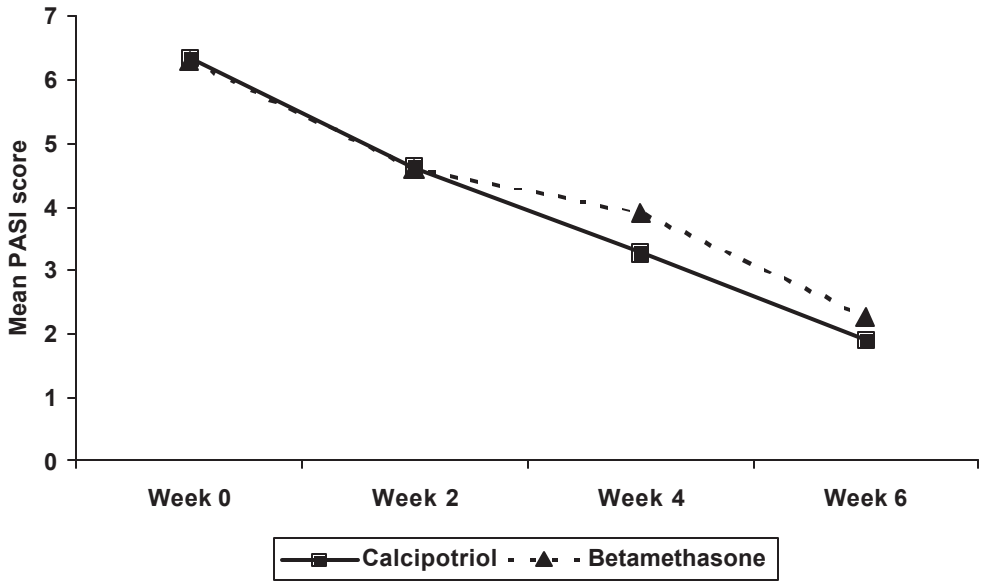


Table 3 Side effects of topical calcipotriol therapy

Side effects	*Calcipotriol group n (%)*	*Betamethasone group n (%)*
Cutaneous		
Persistent lesional erythema	10 (20%)	4 (8%)
Lesional and perilesional irritation	7 (14%)	1 (2%)
Pruritus	4 (8%)	2 (4%)
Folliculitis	2 (4%)	5 (10%)
Atrophy	-	6 (12%)
Extracutaneous		-
Nausea/ vomiting	1 (2%)	-
Headache	1 (2%)	-
Arthralgias	1 (2%)	-

Adverse events

Both drugs were well-tolerated. The common side effects seen with calcipotriol, were persistent erythema, lesional/perilesional irritation, pruritus and infections. Serum calcium and phosphate levels, before and after treatment with calcipotriol, did not show any significant change in their values. Three patients (6%) had non-dermatologic side effects (**Table 3**). Adverse events recorded in the betamethasone group included atrophy, folliculitis, persistent lesional erythema, pruritus and lesional irritation. No extracutaneous side effects were noted with betamethasone valerate ointment during six weeks study period.

Discussion

Psoriasis has always posed a therapeutic challenge and various modalities have proved beneficial in this regard. Vitamin D_3 analogues are relatively a newer therapy in psoriasis. This study clearly demonstrates that the efficacy of topical calcipotriol in the treatment of chronic plaque psoriasis is almost the same as that of betamethasone valerate. The amount of calcipotriol prescribed to each patient was

<100 gm/ week (50 µg/gm of calcipotriol) which has proved to be safe, effective and well tolerated, as shown by other studies.[6,7]

The clinical efficacy was measured using the PASI. The present study confirms the significant reduction in PASI score (69.6%) with calcipotriol over a period of 6 weeks. Similarly, treatment with betamethasone valerate showed a comparable decrease in PASI during the entire treatment period (63.8%). The results are comparable with the study by Kragballe *et al*.[6] which showed a reduction in PASI for calcipotriol and betamethasone valerate as 68.8% and 61.4%, respectively.[6] In a study by Molin *et al*.,[7] comparing calcipotriol and betamethasone valerate cream, no statistically significant reduction in PASI was noted with calcipotriol at the end of six weeks. The better response in our study is possibly due to the effective absorption of drug from its ointment form.

From second week onwards, there was a significant and constant decrease in infiltration, erythema and desquamation in both the groups. The reduction in infiltration score with topical calcipotriol was slightly greater than betamethasone valerate ointment at the end of 6 weeks, but not statistically significant (p>0.05). The reduction in infiltration score with calcipotriol is possibly due to the effective inhibition of both cell proliferation and inflammation. The erythema and desquamation scores also showed a consistent decrease at week 2, 4 and 6.

Betamethasone valerate ointment also proved to be efficacious in reducing the scores for erythema, infiltration and desquamation. However, the difference was not significant (p>0.05) at the end of treatment period.

The reduction of infiltration, erythema and desquamation imply that calcipotriol is at least as effective as betamethasone in the inhibition of both cell proliferation and inflammation. Similar results were also found in earlier studies using the same ointment formulations of calcipotriol and betamethasone in psoriasis.[6]

Betamethasone valerate ointment reduced erythema score by a relatively higher ratio at 2, 4 and 6 weeks of treatment but at the end of treatment, it was not found to be superior to calcipotriol in this regard (p>0.05). The possible reason for this effect may be that the topical steroids have known vasoconstrictor and anti-inflammatory effects which add to the better control of erythema in psoriasis.

Adverse events were seen with both the topical modalities. In our study, persistent lesional erythema was the most common side effect, seen with calcipotriol. Various studies have demonstrated the occurrence of this unwanted effect due to the local irritant effect of calcipotriol.[6] Another possibility may be allergic contact dermatitis due to topical vitamin D_3 analogues as reported by Bruynzeel *et al*.[8] Lesional/perilesional irritation was seen in a significant number of patients. It is comparable to a double-blind study conducted by Molin *et al*.[7] in which 16% of the patients had lesional irritation. Cunliffe *et al*.[4] reported this side effect in 19.5% of patients, which is higher as compared to our study. Pruritus was noticed in four patients in the present study which is possibly due to its irritant effect.

In the betamethasone group, atrophy was seen as a major side effect in 6 patients (12%). None of the patients in calcipotriol group developed this complication. In a similar comparative study by Molin *et al*.[7] where betamethasone cream was applied on 210 patients, only 3 patients showed skin atrophy.[7]

Steroids applied topically, predispose to infections. In the present study, folliculitis developed in 5 patients. Occlusive effect of ointment-base would have been an additional contributory factor in causing this problem. Only two patients in calcipotriol group suffered from folliculitis. Calcipotriol can cause such lesions by its irritant effect.[6]

Persistent erythema was seen in four patients. The late vasodilatation produced by topical potent steroids could be a possible explanation. A small number of patients developed the complaint of pruritus during treatment with betamethasone which could have been caused by contact sensitivity to this medication. In the present study, efficacy and tolerability of both topical agents were quite satisfactory.

Though calcipotriol did not show greater advantage over topical steroid in psoriasis, but it can provide an efficacious and safe alternative in patients of plaque psoriasis, showing side effects with topical steroid or showing no improvement.

From this study it is concluded that calcipotriol 0.005% ointment in plaque psoriasis is as effective as betamethasone valerate 0.1% ointment. Mild to moderate lesional irritation and pruritus is observed more commonly with calcipotriol topically as compared to betamethasone valerate ointment.

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