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RESEARCH ARTICLE

Comparison of efficacy of calcipotriol and betamethasone combination with betamethasone alone in plaque psoriasis

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ABSTRACT

Background: Topical therapy constitutes the first line of management in mild to moderate psoriasis. Studies comparing the treatment outcome of topical calcipotriol and betamethasone dipropionate combination with betamethasone dipropionate alone in plaque psoriasis are few as per literature search. **Aims and Objective:** The present study evaluated the efficacy and safety of the calcipotriol and betamethasone combination in plaque psoriasis. **Materials and Methods:** Study was carried out among in and outpatients presenting to the Department of Dermatology, Sri R. L Jalappa Hospital and Research Centre attached to Sri Devaraj Urs Medical College, Kolar, for 1 year 4 months. 66 patients clinically diagnosed with plaque psoriasis were recruited. 32 patients were treated with topical calcipotriol 0.005% and betamethasone dipropionate 0.05% combination once daily and 34 with betamethasone dipropionate 0.05% twice daily topically. Clinical follow-up of patients was done using psoriasis area and severity index (PASI) at baseline, week 2, 4, 6, 8, 10, and 12. During each follow-up visit, patients were clinically examined, and the corresponding PASI scores were noted. They were also assessed for any adverse reactions. **Results:** By the end of 12 weeks, 30 patients in each group completed the study. In both the groups, the PASI scores reduced significantly from the baseline. The clinical response as well as reduction of PASI score in patients receiving calcipotriol 0.005% and betamethasone dipropionate 0.05% combination was statistically significant compared to betamethasone dipropionate 0.05% monotherapy. **Conclusion:** Calcipotriol and betamethasone combination was efficacious and well tolerated than betamethasone dipropionate monotherapy in mild to moderate plaque psoriasis.

KEY WORDS: Psoriasis; Calcipotriol; Betamethasone

INTRODUCTION

Psoriasis is a chronic autoimmune disease of skin characterized by increased epidermal proliferation, incomplete epidermal differentiation, vascular changes, and inflammation. Psoriasis vulgaris is the most common type and is characterized by well-circumscribed red raised scaly plaques. Lesions usually occur symmetrically on knees, elbows, buttocks, scalp, and areas subjected to trauma.[1] Patients with psoriasis may experience psychological difficulties, including elevated levels of anxiety and depression.[2,3] Diagnosis of psoriasis is usually done clinically and graded as mild (affecting <3% of the body), moderate (3-10%), or severe (>10%). Psoriasis area and severity index (PASI) is the most widely used measurement tool.[4,5]

Topical therapy is the mainstay of treatment for mild to moderate psoriasis. Calcipotriol, a synthetic derivative of 1,25, dihydroxy vitamin D_3 has been used topically, it acts through vitamin D receptors present on keratinocytes and lymphocytes thus

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decreasing epidermal proliferation, abnormal keratinization, and angiogenesis.[5] Vitamin D analogs suppress Th17-induced proinflammatory functions of psoriasin and koebnerisin, and thus, interfere with the inflammatory feedback loop in psoriatic skin.[6] Betamethasone, a synthetic fluorinated topical steroid, improves several markers of inflammation in psoriasis without affecting terminal differentiation. It also inhibits production of cytokines (Interleukin-1 [IL-1], IL-2, IL-8, tumor necrosis factor-α, and interferon-γ) reduce mediators of inflammation (prostaglandins, leukotrienes, and nitric oxide) decreases the abnormal CD4:CD8 ratio and the number and activity of Langerhans cells.[7,8] The present study was carried to assess the efficacy of calcipotriol and betamethasone combination versus betamethasone monotherapy.

MATERIALS AND METHODS

This study was conducted by the Departments of Pharmacology and Dermatology at Sri R. L. Jalappa Hospital and Research Centre attached to Sri Devaraj Urs Medical College, Tamaka Kolar. Duration of the study was for 16 months. The protocol was approved by the Institutional Ethics Committee, and written informed consent was obtained from the patients. It was an open label study. 66 patients who were clinically diagnosed with plaque psoriasis were randomized into two groups. Patients of either gender aged between 18 and 70 years with mild to moderate plaque psoriasis (<10% of body involvement) were included. Exclusion criteria were patients with severe psoriasis, scalp psoriasis, pustular psoriasis, and those receiving antipsoriatic drugs (vitamin D_3 analogs, corticosteroids, coal tar, anthralin, photochemotherapy, and immunosuppressants). Patients who had received calcium/vitamin D_3 analogs in the past 2 months before recruiting to the study and with history of allergy to calcium and vitamin D analogs. Pregnant and lactating women.

Demographic details were recorded at the first visit. 66 patients who were clinically diagnosed with plaque psoriasis were randomized into two groups. 32 were assigned to Group A who received combination of calcipotriol (0.005%) and betamethasone ointment (0.05%) once daily and 34 to Group B who received betamethasone ointment (0.05%) alone twice daily as topical therapy. Assessment was carried out at baseline and every 2 weeks for 12 weeks. During each visit, patients were examined for clinical response, PASI score was noted and was assessed for any adverse reactions.

PASI

The assessment of the effectiveness of new treatment for psoriasis is limited by the lack of any objective measure to determine the disease severity. Although PASI has a limitation of entirely being objective method of assessment, it remains the gold standard to measure psoriasis severity. The PASI score is calculated as follows:

$$PASI = 0.1 (E_H+S_H+I_H) A_H + 0.2 (E_U+S_U+I_U) A_U + 0.3 (E_T+S_T+I_T) A_T + 0.4 (E_L+S_L+I_L) A_L$$

Where,

		Area of extent of lesion is classified on a 7-point scale as	The severity of lesions (erythema, scaling, induration) is classified on a 5-point scale
E=Erythema or redness	H=Head	0: No involvement	0: Complete lack of involvement
S=Scaling	U=Upper limb	1: <10%	1: Mild involvement
I=Induration	T=Trunk	2: 10-29%	2: Moderate involvement
A=Area of involvement	L=Lower limb	3: 30-49%	3: Severe involvement
		4: 50-69%	4: Severest possible involvement
		5: 70-89%	
		6: 90-100%	

Statistical Analysis

Sample size was calculated taking into consideration a power of 85%, an α error of 5% to detect a difference of 0.5 in the PASI score, and drop rate of 10%, so for each group 32 patients were recruited. Data are expressed as mean ± standard deviation. Kolmogorov–Smirnov test for normality was applied and distribution was normal, so PASI was analyzed within and between groups using paired and unpaired *t*-test, respectively. Wilcoxon signed-rank and Mann–Whitney tests were also used for PASI. Categorical data were analyzed by Chi-square test. $P < 0.05$ was considered statistically significant.

RESULTS

A total of 66 patients who satisfied the inclusion criteria were recruited and were randomized to Group A (n = 32) who received combination of calcipotriol (0.005%) and betamethasone ointment (0.05%) once daily and Group B (n = 34) betamethasone ointment (0.05%) alone twice daily applied topically (Figure 1).

Percentage of male patients was more. Among them, 30.3% of patients were in the age group of 31-40 years, with 34.4% in Group A and 26.5% in Group B. The age of onset of psoriasis was between 30 and 50 years, and most of them had duration of more than 2 years in both the groups. Itchy scaly lesions were the most common presenting complaints with plaques being the most common manifestation (Table 1). The lesions were distributed over the extremities. In Group A, 33.3% of patients had lesions either in upper or lower limb alone, whereas it was 53.3% in Group B. In the rest of patients, the lesions were present at different sites including upper limb, lower limb, and trunk.

As depicted in Table 2, the mean PASI score was comparable between two groups at baseline. In Group A, there was a

Table 1: Demographic and disease parameters in Group A and Group B

Variable	Group A (*n*=32) (%)	Group B (*n*=34) (%)
Female	9 (28.1)	11 (32.4)
Male	23 (71.9)	23 (67.6)
Age years±SD		
Males	39.7±13.0	40.0±10.0
Females	39.3±3.0	35.1±8.6
Duration of psoriasis		
<6 months	4 (12.5)	2 (5.9)
6 months-1 year	2 (6.2)	4 (11.8)
1-2 years	7 (21.9)	6 (17.6)
>2 years	19 (59.4)	22 (64.7)
Educational status		
Nil	50	41.2
<10th	26.7	20.6
12th	6.7	17.6
Degree	16.7	20.6
History of smoking	9 (28.1)	13 (38.2)
History of alcohol	2 (6.2)	6 (17.6)
Presenting symptom		
Itchy scaly	28 (87.5)	31 (91.2)
Scaly	4 (12.5)	3 (8.8)
Type of lesion		
Macule+plaque	3 (9.4)	2 (5.9)
Plaque	29 (90.6)	32 (94.1)

SD: Standard deviation

Table 2: PASI score comparison within and between treatment group

Weeks	Mean±SD		*P*-value
	Group A	Group B	
Baseline (0)	4.63±1.75	3.85±1.62	0.079
2	2.46±1.20*	3.08±1.28$^{@}$	0.064
4	0.95±0.61*	2.24±1.04$^{@}$	0.0001
6	0.12±0.20*	1.37±0.75$^{@}$	0.0001
8	0*	0.70±0.46$^{@}$	0.0001
10	0*	0.24±0.24$^{@}$	0.0001
12	0*	0.08±0.12$^{@}$	0.0001

*$^{@}$*P*=0.001 compared with baseline. SD: Standard deviation, PASI: Psoriasis area and severity index

significant (P = 0.001) reduction in mean PASI scores at different follow-up visits compared to baseline, and the score was zero by week 8. In Group B also, there was a significant (P = 0.001) reduction in mean PASI scores compared to baseline, but the score was not zero even at 12-week follow-up. When PASI was also analyzed using Wilcoxon signed-rank test from baseline to each follow-up visit in both the groups and P value was statistically significant (P = 0.001). When PASI was compared between the groups, there was a significant (P = 0.0001) difference at 4, 6, 8, 10, and 12 weeks of follow-up. When Mann–Whitney test was used for between-group comparison, P value was 0.0001 from week 4 onward. The adverse effects between the treatments were compared, but it was statistically insignificant.

DISCUSSION

There were more males than females in the present study. Male:Female ratio was 2.3:1, which is similar to another study.[9] Patients were in the age group of 18-60 years, but with higher occurrence of psoriasis in the fourth decade of life.[10] Duration of psoriasis in the majority of our patients was more than 2 years in both the groups, but the duration of disease did not affect the outcome of therapy in either of these groups. There was no family history of psoriasis in the patients recruited, and seasonal variation was seen in nine patients of which six had history of exacerbation of psoriatic lesions in winter and three in summer. These findings correlated with a study where the prevalence of psoriasis was more in cooler than warmer areas.[11]

The most common presenting complaint was itchy scaly lesions in patients of both the groups. Only 10.6% had history of scaly lesions alone. The majority (92.4%) of them had plaque type of clinical manifestation which was similar to the findings of Naldi and Gambini.[12] Psoriasis preferentially affects the extremities including elbows and knees. The other less common sites are lumbosacral and intergluteal areas. In our study, 43.3% of them had lesions in the extremities which was in par with the other study.[12] In our study, all the patients were below 60 years.

Table 2 shows a significant reduction in PASI score in both the treatments compared to baseline, so the combination of calcipotriol (0.005%) and betamethasone ointment (0.05%) once daily and betamethasone ointment (0.05%) alone twice daily topical application have shown improvement in clinical response based on PASI from week 2 itself. Table 2 and Figures 2 and 3 depict comparison between treatments; the reduction is significant by week 4 with calcipotriol and betamethasone combination and by week 8 PASI score was 0, and there was complete recovery Figure 2. Patients receiving betamethasone alone showed improvement, but complete recovery was not observed until week 12 Figure 3. Hence, the combination therapy has shown to produce a better clinical response and also complete recovery.

Tolerability and safety are the important factors to be considered while treating psoriasis patients because it is a chronic disease and thus requires long-term treatment. In this 12-week follow-up study, none of the patients receiving calcipotriol and betamethasone combination presented with any adverse effects, but two of them receiving betamethasone

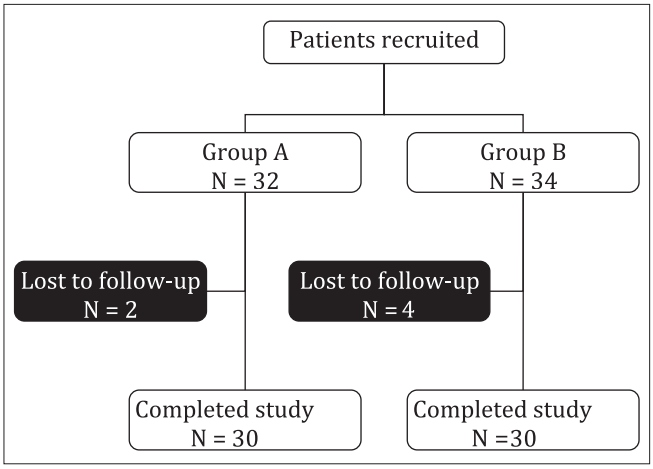

Figure 1: Flow chart showing patient recruitment

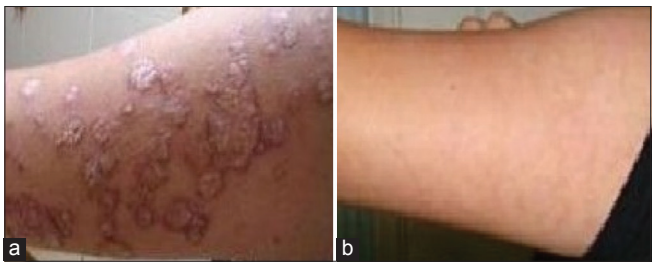

Figure 2: Combination of calcipotriol and betamethasone at 0 (a) and week 12 (b)

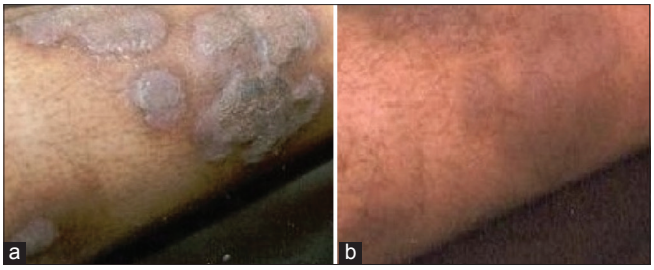

Figure 3: Treatment with betamethasone alone at 0 (a) and week 12 (b)

monotherapy had mild itching around the lesions after 2 weeks of therapy.

CONCLUSION

Patients receiving calcipotriol 0.005% and betamethasone dipropionate 0.05% combination once daily and betamethasone dipropionate 0.05% twice daily as topical therapy showed a significant decrease in PASI score from baseline to successive follow-up. However, in patients receiving combination therapy improvement was significant by week 4, and it was completely recovered by week 8. Combination therapy was found to be effective and well tolerated in the treatment of plaque psoriasis.

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