Original Article

Placebo Controlled Study on the Efficacy and Safety of Calcipotriol in the Treatment of Mild to Moderate Psoriasis

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ABSTRACT

Background: Calcipotriol is a vitamin D analogue that has been used now a day as monotherapy in mild to moderate psoriasis. We have conducted a placebo-controlled clinical comparative study to assess the efficacy and safety of calcipotriol in the treatment of psoriasis.

Objective: To assess the efficacy and safety of calcipotriol in comparison with placebo in patients with mild to moderate psoriasis.

Study Design: Experimental Study

Place and Duration of Study: This study was conducted in the Department of Pharmacology and Therapeutics, Basic Medical Sciences Institute, Jinnah Postgraduate Medical Centre (JPMC), Karachi from January 2008 to March 2008.

Materials and Methods: Sixty patients with mild to moderate psoriasis were enrolled after obtaining their informed written consent and were divided into two groups, A and B. Group-A was administered calcipotriol and Group-B was considered as placebo group for three months. The study parameter (Psoriasis Area and Severity Index, PASI) score was noted after every fifteen days (02 weeks) and were evaluated statistically at the end of the study period.

Results: The significant changes in mean ± SEM values were noted for the efficacy of calcipotriol during the period from day 0 to day 90 in group-A (calcipotriol) v/s group-B (placebo). According to the statistical evaluation, a reduction in the symptoms of the disease was found up to 67.8% in group A, and 0.5% in group-B. The difference between the results of both groups was noted to be highly significant ($P<0.001$).

Conclusion: Calcipotriol as monotherapy is observed to be significantly superior to placebo in terms of efficacy and safety in the treatment of psoriasis.

Key Words: Calcipotriol, placebo, psoriasis, psoriasis area & severity index.

INTRODUCTION

Psoriasis is a common, non-contagious skin disorder that causes rapid skin cell reproduction resulting in red, dry patches of thickened skin. The dry flakes and skin scales are thought to result from the rapid buildup of skin cells. Psoriasis commonly affects the skin of the elbows, knees, and scalp.[1] Psoriasis affects the life cycle of skin cells and causes cells to build up rapidly on the surface of the skin, forming thick silvery scales and itchy, dry, red patches that are some times painful.[2] Approximately 2-3% of the population worldwide is affected by psoriasis.[3] However, commonly accepted and validated diagnostic criteria are lacking. Psoriasis patients when compared to those with other dermatological disorders are among those who suffer from highest impact on their quality of life. Several lifestyle factors including alcohol and smoking have been associated with psoriasis. There is also evidence of association with other diseases including cancer. Psoriasis also accounts for considerable treatment costs, which should always be taken into consideration together with the relevant clinical outcome parameters.[4] Although the effect of psoriasis on a person's quality of life can be substantial, it is not well correlated with the extent of cutaneous involvement of the estimated 4.5 million adults in the United States who have psoriasis, about 450,000 indicate that at least 3% of their body surface area is currently involved, and only about 100,000 patients indicate at least 10% skin involvement. About 500,000 adults in the United States describe their psoriasis as being a substantial problem.[5]

Psoriasis is a skin condition that can take many forms. Most people live with just one of the types below, although there are rare cases in which a patient may experience more than one type. Plaque psoriasis is the most common type of psoriasis; nearly 90% of the people who live with psoriasis can have this skin lesion. Guttate psoriasis is the second most common type of the disease that accounts for up to 10% of people which usually affects people under age 30 years. Inverse psoriasis also called seborrheic psoriasis; this psoriasis develops in skin folds such as the armpits, groins, under the breasts, around the genitals and buttocks. Pustular

psoriasis, in which white blisters are commonly surrounded by red skin, is the hallmarks of pustular psoriasis. Erythrodermic psoriasis is the least common form of psoriasis that results in inflammation, itching, and a painful red rash that may peel and often covers the entire body. Psoriatic arthritis that affects up to 30% of people with psoriasis, which usually develops 5 to 10 years after the original diagnosis of psoriasis, although it can show up before a skin diagnosis.[6]

The primary cause of psoriasis remains unknown. Abnormal epidermal cell kinetics and abnormal activation of immune mechanisms are thought to be the major contributors and treatment may affect one or both of these mechanisms.[7] Calcipotriol is a vitamin D_3 analog, acts not only to inhibit cell proliferation and enhance cell differentiation in the skin of patients with psoriasis, but also appears to have effects on immunologic markers that are thought to play a role in the etiology of the disease. Calcipotriol ointment 50 micrograms/gm twice daily provided similar or superior efficacy to several other anti-psoriatic agents in adult patients with mild to moderate psoriasis.[8]

This study evaluated the role of calcipotriol alone v/s placebo in treatment of psoriasis and to verify efficacy and safety of calcipotriol.

MATERIAL AND METHODS

This study was conducted in the Department of Pharmacology and Therapeutics, Basic Medical Sciences Institute, Jinnah Postgraduate Medical Centre (JPMC), Karachi. The patients were selected from Department of Dermatology JPMC, Karachi during the period from January to March 2008. A total of 60 patients were enrolled in this study after taking their written consent to complete the full course of therapy and were divided into two equal groups named group-A and group-B.

Inclusion Criteria:

- Patients with mild to moderate psoriasis.
- Patients of either sex (male or female)
- Age 18 years or above.
- Patients suffering from psoriasis with percentage of Body Surface Area (BSA) affected by psoriasis ≤ 10%.

Exclusion Criteria:

- Patients suffering from hepatic or renal diseases.
- Pregnant or lactating women.
- Patients under treatment with retinoids or antibiotics.
- Patients with other skin diseases.
- Any other chronic ailment requiring prolonged treatment.
- Allergy to study medication.

We have used calcipotriol ointment 50 micrograms/gm twice daily in group-A patients and severity of the disease was assessed by Psoriasis Area and Severity Index (PASI). The severity of psoriasis has traditionally been evaluated by objective measurement of the extent of the body surface affected and consideration of the subtype of psoriasis, degree of disability and feasibility of topical therapy. The Psoriasis Area and Severity Index (PASI) score can be used as such a measurement of psoriasis severity. It includes the amount of body surface area affected by psoriasis in addition to three major symptoms i.e., redness, inflammation and scaliness of the skin lesion.[9]

Study Design: A total number of 60 patients of either sex were enrolled and divided into two groups, each group having 30 patients, designated as group-A (calcipotriol ointment alone), while in group-B we had used ointment base only. All the values were taken as mean ± SEM. The primary efficacy measurement was the mean change in (PASI) score from baseline to the endpoint i.e., at day 90. In our study, there were many quantitative variables therefore; we had applied chi-square. Student t-test was used to analyze the data at P value 0.05 for statistical significance.

RESULTS

Our final analysis included 60 patients, who had completed the whole study period. The age, sex, marital status and family history was recorded and as shown in Table-1. In group-A, a total of 30(50%) patients were studied, in which 18(60%) were male & 12(40%) were female, mean age was 33.5 years, range 18.5 years, in which 18(66.6%) had positive family history of psoriasis and 9(33.3%) patients had no family history of such disease. In group-B, a total of 30(50%) patients were studied having 17(56.6%) were male and 13(43.3%) were female, the mean age was 32.5 years, range 18.5 years, among those 16(64%) patients had positive family history of psoriasis and 9(36.3%) had no family history of such disease.

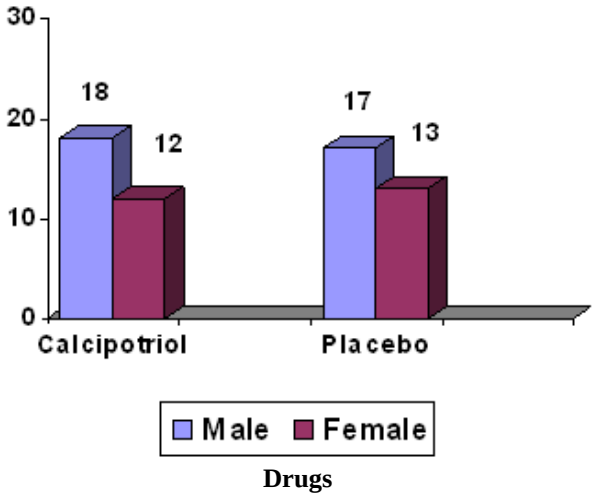

Figure No.1: Gender Distribution of Study Subjects

Table No.1: Demographic, Social & Professional Variables of Patients

Total study subjects (n=60)	Calcipotriol group (n=30) (%)	Placebo group (n=30) (%)		*P*-value*
Male	60.0%	Male	56.6%	<0.05
Female	40.0%	Female	43.3 %	<0.05
Age 20-39 (yrs)	31.6 ± 0.4	Age 20-39	31.60 ± 0.4	-
Age 40-60 (yrs)	51.8 ±0.5	Age 40-60	51.80 ±0.5	-
Educated	33.3 %	Educated	33.3 %	<0.05
Uneducated	66.6 %	Uneducated	66.6 %	<0.05
Laborers	66.6 %	Laborers	66.6 %	<0.05
Farmers	16.6 %	Farmers	16.6 %	<0.05
Drivers	13.3 %	Drivers	13.3 %	<0.05
Extra works	3.3 %	Extra works	3.3 %	<0.05
Married	66.6 %	Married	66.6 %	<0.05
Un-married	33.3 %	Unmarried	33.3 %	<0.05

The basic demographic variables shown in percentages and chi-square of association were applied for significance.

Table No.2: The Efficacy of Calcipotriol in Mild to Moderate Psoriasis

Improvement after calcipotriol treatment in weeks	*t* test	Mean Difference	*P*-value	95% Confidence Interval	
				Lower	Upper
WEEK-1	4.8	4.0	0.003	2.0	6.0
WEEK-3	5.7	5.5	0.000	3.3	7.6
WEEK-6	6.4	7.0	0.000	4.6	9.3
WEEK-9	6.0	6.0	0.000	3.7	8.2
WEEK-12	5.4	5.0	0.001	2.8	7.1

DISCUSSION

This present study demonstrates statistically significant changes in both groups in the parameter of PASI. In group-A, we applied calcipotriol local application once daily and observed a reduction of 67.89% in PASI at the end of study ($p<0.001$).

Our study match with the study of Austad et al (1997)[10], who conducted two parallel trials of 6 and 8 weeks and observed a reduction of 58.7% and 50.9% which are nearer to our results. The improvement in the parameter of PASI seen during the period of Day 0-90 and in group-A (calcipotriol) 15.5±8.8 pre-treatment after three months 14.00±7.937 were improved, p-value <0.05 and results were highly significant in our study. In case of safety of calcipotriol 3.00 ±1.5, p value >0.317 results were insignificant. The results of our study are also matching with results of Schwartzel et al (1996)[11] who conducted two trials comparing twice daily and once daily regimens of calcipotriol in 480 patients, the efficacy wise percentage change in PASI scores and observed a more than 60% reduction in once daily regimen i.e., in accordance to our study.

Lebwohl and colleagues (1998)[12] evaluated the use of calcipotriol and corticosteroids for the treatment of mild to moderate psoriasis and after two weeks of daily combination therapy 40 subjects (out of 44 demonstrated, 50% are greater improvement in Psoriasis Area and Severity Index (PASI) at the end of 6 months treatment, 76% of subjects shown remission. The researcher in this study also found the calcipotriol in combination was tolerable to the patients and that this combination improved remission, rates in the 2nd phase of sequential therapy. In our study about 67.3% reduction seen in PASI, scores and no patients in this group complained about itching or irritation. These results and observations are seen in accordance with the study of Lebwohl and colleagues. But in our study calcipotriol had improved 67.89% as compared placebo in the treatment of psoriasis. The improvement in the parameter of PASI seen during the period of Day 0-90 and in group-A (calcipotriol) 15.5±8.8 pre-treatment after three months 14.00±7.937 were improved, p-value <0.05 and results were highly significant in our study. In case of safety of calcipotriol 3.00 ±1.5, p-value >0.317 results were insignificant.

A review of medical literature from 1996 to 2002 was conducted using guidelines set by QUORUM statement criteria. In monotherapy studies, corticosteroids caused fewer adverse drug reactions compared to vitamin D analogues and tazarotene. Irritant contact dermatitis was the main side effect seen with vitamin D analogues.[8]

Calcipotriol is a synthetic analog of vitamin D_3 that inhibits keratinocyte proliferation and induces terminal differentiation. Calcipotriol is effective for psoriasis and a few studies have reported efficacy in nail psoriasis. This study shows the efficacy of calcipotriol in 24 patients with nail psoriasis. In this study, 14 patients showed significant clinical improvement after 3 months of therapy, and two of them became completely lesion-free after another 2 months. Topical calcipotriol is an effective treatment for nail psoriasis; its high tolerability allows its prolonged usage without severe side effects. Therefore, it can be considered to be a safe topical treatment in chronic cases.[13] According to the study of thaci et al[14] calcipotriol solution is an effective, safe, well-tolerated and cosmetically acceptable treatment modality. He found that this treatment was found to be a valuable supplement to previously available and established treatments for scalp psoriasis

CONCLUSION

Calcipotriol as monotherapy is observed to be significantly superior to placebo in terms of efficacy and safety in the treatment of psoriasis.

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