Original Article

Comparative Efficacy of Topical Calcipotriol (0.005%) Versus Topical Corticosteroid (Betamethasone 0.1%) in Treating Plaque Type Psoriasis

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Abstract

A clinical trial was carried out to compare the efficacy of topical calcipotriol (0.005%) and topical corticosteroid (betamethasone 0.1%) in the treatment of plaque type psoriasis. The study was conducted from January 2012 to August 2012 and patients of plaque type psoriasis attending outpatient department of Dermatology and Venereology, Bangabandhu Sheikh Mujib Medical University, Dhaka were the study population. Patients were divided into two groups, group A was treated with topical calcipotriol (0.005%) ointment and group B with topical corticosteroid (betamethasone 0.1%) ointment. The mean baseline PASI score was 6.7 ±4.5 and after 8 weeks, the mean PASI score was 2.0 ±1.4 for group A and mean baseline PASI score was 5.5 ±4.2 and after 8 weeks, the mean PASI score was 2.5 ±1.4 for group B. There was statistically significant reduction in PASI score from base line after 8 weeks of treatment in both treatment groups ($p < 0.001$). After 8th week of treatment moderate response was 11(73.3%) in group A and 9(60%) in group B. Very good response was 4 (26.7%) in group B and 2 (13.3%) in group A and minimal response of treatment occurs equally 2 (13.3%) in group A and group B. In the light of the findings of the study we conclude that each of the treatment of calcipotriol(0.005%) and betamethasone (0.1%) is individually effective. Further multicenter, randomized, double-blind study should be conducted with large sample size.

Key words: *Efficacy of calcipotriol, efficacy of corticosteroid (betamethasone), plaque type psoriasis.*

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Introduction

Psoriasis is a common, chronic and recurrent inflammatory disease, characterized by scaling plaques of varying sizes and covered by grayish white or silvery white scales, affecting approximately 2% of the population and leads to considerable impairment of the quality of life of the affected patients.[1,2] Both genetic and environmental factors have been implicated in the pathophysiology of psoriasis.[3] About 35% of patients with psoriasis have a family history of the disease. Treatment of psoriasis involves, traditional therapeutic agents targeted abnormal keratinocyte proliferation and differentiation or induced general immunosuppression, thereby producing temporary improvement, partial response, or serious adverse effects. However, the vast majority of patients approximately 80-90% present with relatively mild disease and have only limited involvement of the skin, which can be well-controlled with topical therapy.[4,5] Calcipotriol ointment is a synthetic topical vitamin D analog considered being as effective as other vitamin D analogs.[6,7] At appropriate concentration, calcipotriol causes a decrease in the proliferation and an increase in the morphologic and biochemical differentiation of keratinocytes, hence regulate their proliferation and differentiation.[8] Calcipotriol ointment has been extensively evaluated for the treatment of chronic plaque-type psoriasis and has been shown to be effective, in a number of short-term and long-term clinical trials.[9] Betamethasone is a class III potency, synthetic, fluorinated topical steroid. They inhibit production of cytokines (IL-1, IL-6, IL-8, tumor necrosis factor-α, interferon-γ), reduce mediators of inflammation (prostaglandins, leukotrienes, nitric oxide), decrease the abnormal CD4:CD8 ratio and the number and activity of Langerhans' cells.[10]

For decades, topical corticosteroids, particularly high-potency steroids, have been the mainstay in the topical treatment of psoriasis. Psoriatic patients with thick, plaques often require treatment with the highest potency corticosteroids and associated with multiple side effects with long term use.[11] Calcipotriol is generally considered to be as effective as corticosteroid (betamethasone), in some studies in plaque psoriasis. Topical calcipotriol (0.005%) is found more effective than the conventional topical corticosteroid (betamethasone 0.1%) in some studies.[12-14] An effective therapeutic options for plaque psoriasis is limited & the results are somewhat not satisfactory to some extent. Therefore the purpose of the present study was to compare the efficacy level of topical calciprotriol (0.005%) and topical corticosteroid (betamethasone 0.1%) in plaque type psoriasis in Bangladesh.

Materials and Methods

A clinical trial was carried out in the department of Dermatology and Venereology, Bangabandhu Sheikh Mujib Medical University (BSMMU), Dhaka, Bangladesh. Thirty patients clinically and histopathologicaly diagnosed as chronic plaque type psoriasis were enrolled. Fifteen patients were treated with topical calcipotriol (0.005%) ointment (Group-A) and fifteen patients with topical corticosteroid (betamethasone 0.1%) ointment (Group-B). Purposive type of non-probability sampling method was followed in this study. Inclusion criteria's were all patients reported with chronic plaque type psoriasis, in the department of Dermatology and venereology of BSMMU, Dhaka during the study period, Psoriasis Area And Severity Index (PASI) < 7 (mild type), patients having serum calcium level within normal limit, age 18 years or above with both sexes and participants who will give the consent and willing to comply with the study procedure. Exclusion Criterias were acute guttate, pustular, severe or erythrodermic psoriasis, psoriasis which is predominantly located in the skin folds, face or scalp, treatment for plaque type psoriasis with corticosteroid agents, vitamin D analogues, or tacrolimus within the last 3 months, systemic anti-psoriatic treatment or PUVA within 16 weeks period prior to visit, pregnant or lactating women, patients under treatment with retinoids or antibiotics, patient with known or suspected renal / hepatic disease/ hematological disease and history of acute or chronic active infections.

Procedure of data collection:

Complete history, general physical and dermatological examinations were done for all enrolled patients. For women of reproductive age reproductive history, menstrual history, lactation and pregnancy plan were carefully judged. History and physical findings were recorded in a data sheet. Baseline investigations included complete blood count (total count, differential count of white blood cell), platelet count, Hb%, ESR, serum creatinine, serum alanine transaminase, random blood sugar, serum calcium level, serum albumin, serum total protein and pregnancy test as required were done. Finally those patients, who matched the inclusion and exclusion criteria according to history, physical examination and laboratory reports and freely gave their informed consent, were selected for the study. Photographs of all lesions at baseline and at the end of 8th week were taken for subsequent assessment and further compare. Erythema, induration and scaling were recorded in term of PASI (Psoriasis Area and Severity Index) at baseline, after 4th weeks and 8th weeks of therapy as the tool of main outcome measure. Adverse effects of the drugs among all patients of two groups were noted.

Scoring of psoriasis

Severity of psoriasis were scored by using psoriasis area and severity index PASI formula, in which the body was divided into four areas Head (H), Upper limb (U), Trunk (T) and Lower limb (L). Erythema (E), Induration (I) and Desquamation (D) were measured for each area with a scale ranging zero (none), 1 (mild), 2 (moderate), 3 (severe) and 4 (very severe). Erythema and induration were measured as visual impression and palpation of the lesion in place of ideal chromometer and ultrasound respectively. Body surface was measured with Patients' palm, taken as 1% total body surface area.

Head area: one palmer surface of hand = 10% of head area, Upper limb: two palmer surface of hand = 10% upper limb area, Trunk area: three palmer surface of hand = 10% trunk area, Lower limb: four palmer surface of hand = 10% lower limb area.

PASI was calculated using the following formula:

0.1 (EH + IH + DH) A H + 0.2 (EU + IU + DU) AU + 0.3 (ET + IT + DT) AT + 0.4 (EL + IL + DL) AL.[15]

Severity of plaque type psoriasis can be classified according to PASI score. Psoriasis can be defined as severe when PASI score >12, moderate when PASI score 7-12 and mild when PASI score <7. Percentage of PASI score reduction is used for assessment the efficacy of drug and prognosis of plaque type psoriasis. The percentage of PASI score reduction can be describe as 4 grades. When PASI reduction <50% it can be defined as minimal response, 50% - <70% as moderate response, 70% - <90 % as very good response and >90% as excellent response.

Intervention:

Group A were treated with Calcipotriol (0.005%) twice daily and group B were treated with topical corticosteroid (Betamethasone 0.1%) twice daily. They were treated for the period of 8 weeks. The results of the cases of both group A and group B were evaluated at the end of 8 weeks. Patients were examined at baseline, and after 4 weeks of treatment followed by re-examination at weeks 8. The severity of psoriasis were evaluated by a single

investigator at the center, using the psoriasis area and severity index (PASI). Laboratory parameters, were measured before enrollment in the study and at the end of the follow-up period. Follow-up laboratory investigations were complete blood count (Total and differential count of White blood cell, hemoglobin and ESR, Platelet count ($\times 10^9$/L), Serum alanine transaminase (S. ALT), serum creatinine, serum calcium level, random blood sugar and serum total protein and serum albumin level. Data analysis was performed by Statistical Package for Social Science (SPSS), version-16. Statistical analyses were done and level of significance were measured by using appropriate procedures like chi square test (χ^2), paired and unpaired t-test. Level of significance (p value) was set at 0.05 and confidence interval at 95%.

Results

Table I shows the mean ±SD age was 34.7±12.7 years and 34.5±15.8 years in group A and group B respectively. Male was found 7 (46.7%) in group A and 8 (53.3%) in group B. Family history of same disease was found 4(26.7%) in group A and 1(6.7%) found in group B. Regarding the duration of illness, most of the patients suffered 1- 5 years in both groups, which were 8 (53.3%) and 10(66.7%) in group A and group B respectively. The mean duration of illness was 5.5±3.7 years in group A and 4.4±3.5 years in group B. There is no statistically significant difference between two groups in terms of age, sex, family history of same disease and duration of illness (p value >0.05).

Table I: Distribution of patients by baseline characteristics

	Group A (n=15)		Group B (n=15)		t/chisquare value	P value
Age (in year)	**n**	**%**	**n**	**%**		
≤20	1	6.7	3	20.0	0.05	0.960^{ns}
21-30	7	46.7	6	40.0		
31-40	3	20.0	1	6.7		
41-50	2	13.3	1	6.7		
>50	2	13.3	4	26.7		
Mean±SD	34.7	±12.7	34.5	±15.8		
Sex						
Male	7	46.7	8	53.3	0.13	0.715^{ns}
Female	8	53.3	7	46.7		
Family history of disease						
Yes	4	26.7	1	6.7	2.16	0.141^{ns}
No	11	73.3	14	93.3		
Duration of Illness (years)						
1-5	8	53.3	10	66.7	0.78	0.443^{ns}
6-10	6	40.0	4	26.7		
>10	1	6.7	1	6.7		
Mean±SD	5.5	±3.7	4.4	±3.5		

Group A: Calcipotriol Group B: Betamethasone

Ns=Not significant, P value reached from unpaired t-test and chi square test.

Mean Psoriasis Area and Severity Index (PASI) score of Group A and Group B at baseline was 6.7±4.5 and 5.5±4.2 respectively. The mean percentage of PASI reduction after 4th week of treatment was 39.4 and 35.4 in group A and group B (p value >0.05). The mean percentage of PASI reduction after 8th week of therapy was 59.6 in-group A and 60.7 in-group B respectively. The mean different was not statistically significant (p value >0.05) between both groups

Table II: Comparison of Reduction of Psoriasis Area and Severity Index (PASI) in two groups.

	Group A (n=15)		Group B (n=15)		t value	P value
PASI	Mean	±SD	Mean	±SD		
Base line	6.7	±4.5	5.5	±4.2	1.39	0.174[ns]
Reduction after 4th weeks (%)	39.4		35.4		1.46	0.155[ns]
Reduction after 8th weeks (%)	59.6		60.7		-.20	0.802[ns]

ns==Not significant, P value reached from unpaired t-test.

Table III shows that after 8th week of treatment, moderate response is 11(73.3%) and 9(60%), very good response is 4 (26.7%) and 2 (13.3%) in group A and group B respectively.

Table III: Comparison of grading of PASI percentage reduction in two groups.

Grading of (%) PASI reduction	Group A(n=15)		Group B(n=15)		Chi value	P value
	n	%	n	%		
Minimal response <50	2	13.3	2	13.3		
Moderate response 50 to <70	11	73.3	9	60.0	0.867	0.648 [ns]
Very good response 70 to <90	2	13.3	4	26.7		
Excellent response >90	0	0	0	0		

ns=Not significant, p value-0.648 reached from chi square test.

Table IV shows that mean baseline PASI score was 6.7 ±4.5 and after 8 weeks, the mean PASI score was 2.0 ±1.4 for group A and mean baseline PASI score was 5.5 ±4.2 and after 8 weeks, the mean PASI score was 2.5 ±1.4 for group B. There was statistically significant reduction in PASI score from base line after 8 weeks of treatment in both treatment groups ($p < 0.001$).

Table IV: Comparison of PASI score before to after treatment in two groups.

Groups	Mean baseline PASI score with SD	Mean PASI score after 8th week with SD	*t*-value	P value
Group A	6.7 ±4.5	2.0 ±1.4	12.94	<0.001*
Group B	5.5 ±4.2	2.5 ±1.4	7.37	<0.001*

*Paired t test was done to measure the level of significance.

Hb%, ESR, total WBC, platelet count and serum ALT change are not statistically significant (p value >0.05) between two groups during baseline and 8th weeks follow-up.

Table V: Comparison of Laboratory reports at baseline and at follow-up in two groups.

Investigation	Group A (n=15)		Group B (n=15)		t value	P value
	Mean	±SD	Mean	±SD		
Hb (gm/dl.)						
Baseline	12.3	±1.9	13.2	±1.0	-1.64	0.111^{ns}
8^{th} weeks	12.4	±1.8	13.0	±1.2	-1.12	0.273^{ns}
ESR (in 1^{st} hr.)						
Baseline	22.7	±18	17.0	±11.9	1.03	0.313^{ns}
8^{th} weeks	19.1	±15.1	15.3	±8.3	0.85	0.401^{ns}
WBC ($\times 10^9$/L)						
Baseline	9.2	±2.3	9.0	±1.9	0.23	0.819^{ns}
8^{th} weeks	8.5	±2.3	8.9	±2.3	-0.37	0.715^{ns}
Platelet count (($\times 10^9$/L))						
Baseline	276	±62.6	270.7	±54	0.25	0.805^{ns}
8^{th} weeks	255.6	±36.5	259.1	±45.1	-0.24	0.815^{ns}
Serum ALT (U/L)						
Baseline	29.5	±11.8	24.1	±10.5	1.33	0.195^{ns}
8^{th} weeks	27.8	±15.2	26.0	±7.3	0.41	0.683^{ns}

Group A: Calcipotriol Group B: Betamethasone, ns=Not significant,
P value reached from unpaired t-test.

Discussion

In our study showed statistically significant reduction in PASI score from base line after 8 weeks of treatment in both treatment groups ($p<0.001$). These findings were consistent with other studies.[15-17] Molin et al conducted a study and showed that the mean reduction in the PASI in patients treated with calcipotriol was 3.3 and in patients treated with betamethasone 2.8. The reduction in PASI was statistically significant in both treatment groups. The mean percentage reduction in the PASI from baseline to end of treatment was 47.8% in patients treated with calcipotriol and in patients treated with betamethasone 45.4%. In patients treated with calcipotriol, the mean reduction in thickness score from baseline to end of treatment was 2.59 and with betamethasone 2.25. Similarly the change in scores for redness and scaliness showed a highly significant reduction from baseline to end of treatment but there was no difference between calcipotriol and betamethasone groups. The overall assessment of treatment response showed 58% of patients treated with calcipotriol cream cleared or achieved marked improvement as compared with 56% in the betamethasone group.[15] Cunliffe et al conducted a study of 6 weeks in 409 patients. Efficacy as measured by the Psoriasis Area and Severity Index (PASI) were assessed at 2,4 and 6 weeks. The reduction in PASI was statistically significant in all time points for both treatment groups. At the completion of 6 weeks of treatment, the mean reduction in the PASI in patients treated with calcipotriol was 5.50 and in patients treated with betamethasone 5.30. The overall assessment of treatment response at 6 weeks showed 61.2% of patients treated with calcipotriol cream clearance or achieved marked improvement as compared with 50.5% in the betamethasone group. Calcipotriol ointment was as effective as betamethasone 17-valerate ointment as measured by the PASI and superior as measured by self-assessment in patients with stable plaque psoriasis.[16] Kragballe et al carried out a study to observe the therapeutic efficacy of topical calcipotriol and betamethasone in psoriasis in a multicentre randomized, double blind right/left trial. Three hundred forty five patients with psoriasis vulgaris of symmetrical distribution were treated twice daily for 6 weeks with calcipotriol ointment and betamethasone ointment randomly assigned to opposite side of the body. The main outcome measures were Psoriasis Area and Severity Index (PASI), the investigators assessments of erythema, thickness and scaling at weeks 2, 4 and 6. The reduction in PASI was statistically significant in all time points for both treatment groups.

At the completion of 6 weeks of treatment, the mean reduction in the PASI in patients treated with calcipotriol was 68.8% and in patients treated with betamethasone 61.4%. The overall assessment of treatment response at 6 weeks showed the score for erythema, thickness and scaling were significantly lower with calcipotriol cream than betamethasone cream. The patients considered that 82.1% of calcipotriol treated sides and 69.3% of betamethasone treated sides had improved greatly or cleared up by the end of treatment. Thus calcipotriol ointment was superior to betamethasone ointment in psoriasis vulgaris.[17]

A study was conducted by Dahri et al and 60 patients were enrolled for the study and divided into two equal Groups namely Group A and Group B. In that study a total number were divided into two groups, each having 30 patients, designated as group - A Calcipotriol ointment alone. While in the group-B we applied calcipotriol plus Betamethasone combined therapy. The improvement in the parameter of PASI seen during the period of Day 0 - 90 and percentage change observed in group-A is 67.89% i.e. the mean change from 14.08±0.33 to 4.52±0.22. While improvement in the parameter of PASI seen during the period of day 0-day 90 and percentage change, observed in Group B (Calcipotriol plus Betamethasone) combination is more pronounced i.e. the change in mean from Day 0-90 is 12.81±0.35 to 2.37±0.36, with the percentage change of 81.495 ($p<0.001$) . The results are highly significant i.e. ($p<0.001$) and showing great improvement in patient's symptoms. They conclude that Betamethasone plus Calcipotriol therapy is more efficacious as it produces less adverse effects than Calcipotriol alone, therefore it may be recommended that monotherapy can be replaced with once daily Calcipotriol Betamethasone combination.[18] Calcitriol ointment has been extensively evaluated for the treatment of chronic plaque-type psoriasis and has been shown to be effective, safe, and well-tolerated in a number of short-term and long-term clinical trials.[19]

In the light of the findings of the study we conclude that each of the treatment of calcipotriol(0.005%) and betamethasone (0.1%) is individually effective. Study with a larger group of patients for longer period may result in superior outcome in clinical practice through improved compliance.

References

1. Neimann AL, Porter SB, Elfand JM. The epidemiology of psoriasis. Expert revision of dermatology 2006; 1(1): 63-75.
2. Fenton C, Plosker G. Calcipotriol/Betamethasone dipropionate: A review. Am J Clin Dermatol.2004;5:463-78.
3. Ashcroft DM, Li Wan Po A, Griffiths CE. Therapeutic strategies for psoriasis. J Clin Pharm Ther.2000;25:2-10.
4. Douglas WS, Poulin Y, Decroix J. A new calcipotriol/betamethasone formulation with rapid onset of action was superior to monotherapy with betamethasone dipropionate or calcipotriol in psoriasis vulgaris. Acta Derm Venereol. 2002;82:31-5.
5. Gelfand JM, Weinstein R, Porter SB. Prevalence and treatment of psoriasis in the United Kingdom. Arch Dermatol. 2005;141:1537-41.
6. Charakida A, Dadzie O, Teixeira F. Calcipotriol/Betamethasone dipropionate for the treatment of psoriasis. Expert Opin Pharmacother. 2006;7:597-606.
7. Kragballe K, van de Kerkhof PC. Consistency of data in six phase III clinical studies of a two-compound product containing calcipotriol and betamethasone dipropionate ointment for the treatment of psoriasis. J Eur Acad Dermatol Venereol. 2006;20:39-44.
8. Langely RG, krueger GG & Griffiths, CE. Psoriasis: epidemiology, clinical features, and quality of life. Annals of the rheumatica 2005;64(2): 18-23
9. Koo JY. Current consensus and update on psoriasis therapy: a perspective from the U.S. J Dermatol. 1999;26:723-33.
10. Guenther L, Cambazard F, Van de Kerkhof PCM. Efficacy and safety of a new combination of calcipotriol and betamethasone dipropionate (once or twice daily) compared to calcipotriol (twice daily) in the treatment of psoriasis vulgaris: a randomized, double-blind, vehicle-controlled clinical trial. Br J Dermatol 2002; 147:316-23.
11. Kaufmann R, Bibby AJ, Bissonnette R. A new calcipotriol/betamethasone dipropionate formujlation is an effective once daily treatment for psoriasis vulgaris. Dermatology.2002;205:389-93.
12. Kragballe K, Gjertsen B, de Hoop D, et al. Double-blind, right/left comparison of calcipotriol and betamethasone valerate in treatment of psoriasis vulgaris. Lancet. 1991;337:193-6.

13. Guenther LC. Calcipotriol / Betamethasonedipropionate: Daivobet / Dovobet. Therapy. 2005; 2: 343-48.

14. Cassano N, Miracapillo A, Coviello C, Loconsole F, Bellino M,& Vena GA. Treatment of psoriasis vulgaris with the two-compound product Calcipotriol obetamethasone dipropionate followed by different formulations of calcipotriol. Clin Drug Investig. 2006; 26(4): 227-33.

15. Molin L., Topical calcipotriol combined with phototherapy for psoriasis. The results of two randomized trials and a review of the literature. Calcipotriol-UVB Study Group. Dermatology. 1999;198(4): 375-381.

16. Cunliffe WJ, Berth-Jones J, Claudy A, et al. Comparative study of calcipotriol (MC 903) ointment and betamethasone 17-valerate ointment in patients with psoriasis vulgaris. J Am Acad Dermatol. 1992;26:736-43.

17. Kragballe K, Austad A. A 52-week randomized safety study of a calcipotriol/betamethasone dipropionate two-compound product in the treatment of psoriasis. British Journal of Dermatology 2006; 6: 1155-1160.

18. Dahri GM,. Samdani AJ, Qazi N, Laghari MJ, Mashori GR, Wagan MA. To compare the role of calcipotriol alone versus combination with betamethasone in mild to moderate psoriasis. Sindh Univ. Res. Jour. (Sci. Ser.) 2010; 42 (1):69-72.

19. Johann EG and James TE. Psoriasis. Fitzpatrick's dermatology in general medicine. 7th edi. Sanfransisco,USA; McGraw-Hill Publisher; 2008.pp.169-193.