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Original Article

Efficacy and Safety of Topical Calcipotriol and Betamethasone in Plantar keratoderma with Fissures

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Abstract

Background: Fissured sole is a common problem in dermatology. A great number of people in our country have been suffering from plantar keratoderma which may lead to fissuring. Fissured sole is prevalent worldwide but is more common in third world countries, may be due to malnutrition, walking bare foot. No treatment available is a definitive cure. Topical calcipotriol and betamethasone valerate ointment is used in the treatment of plantar kertoderma with fissures.

Objectives: To evaluate efficacy and safety of topical calcipotriol and betamethasone valerate ointment in the treatment of plantar keratoderma with fissures as well as to determine the response on histopathological types.

Materials and methods: The clinical trial was done in the Department of Dermatology and Venereology, BSMMU, Dhaka, from January 2013 to December 2013. A total of 60 patients were included in the study which was randomly divided into two groups, each of which included 30 patients. Group A was given calcipotriol ointment at night and betamethasone velerate ointment in the morning for six weeks. Group B was given Vaseline for the same frequency and duration. Patients were clinically observed for the efficacy and side effects of the trial medicine after completion of therapy (after 6 weeks) and after 10 weeks. Baseline biopsy and histopathology, Skin scraping for fungus from the sole, random blood sugar and haemogram were done.

Result: Among 60 studied cases, age range was from 10-69 years, with most commonly affected age group was 40-49 (26.7%). Both sexes were affected with female predominance (63.3%). People of middle class socio-economic condition are more susceptible. Histopathologically it was found that more common cause of plantar keratoderma with fissured sole was psoriasis 29 (48.3%). The therapeutic response of the study group after 6 weeks showed 06 (20.0%) patient respond good, 13 (43.3%) patient respond very good and 05 (16.7%) patient respond excellent. But 04 weeks after completion of treatment (at 10 weeks) 46.7% of study group (group A) and 86.7% of group B showed no response and 53.3% of group A and 13.3% of group B showed poor response. Side effect was minimal with only 04 (13.3%) patients had burning sensation.

Conclusion: Topical calcipotriol and betamethasone velerate is effective and safe in planter keratoderma with fissures, but there is significant recurrence after discontinuation of treatment.

Key words: Plantar hyperkeratosis, Fissured sole, Calcipotriol, Betamethasone velerate.

Introduction:

It is curious that the ability to stand, walk, and run efficiently depends on the proper function of a tiny proportion of the skin. Healthy plantar skin is vital to our well being.[1] Plantar hyperkeratosis with fissured sole is not a disease rather it is one of the manifestation of different diseases, either acquired or hereditary.[2,3] Whatever may be the cause, fissured sole occurs most commonly where the sole is thickened, dried, and inelastic from inflammation. Fissures develop in the regions subjected to frequent movement and pressure. Shape, color, nature, site, number, and depth of fissures are variable in different persons in different diseases.[4] The clinical pattern of palmoplantarkeratoderma falls into three general groups with a number of additional syndromes. Major groups are diffuse, focal and punctuate

palmoplantar keratoderma. Sometimes palmoplantar keratoderma may represent wider ectodermal defects with other cutaneous, mucosal, nail, hair, teeth, and neurological abnormalities.[5] A new classification of palmoplantar keratoderma has been implicated based on histological findings and also suggested molecular mechanisms.[6] Acquired palmoplantar keratoderma can result from infection, chronic inflammation or may be a cutaneous manifestation of systemic diseases. Keratodermaclimectericum is an acquired keratoderma that appears in women at menopause. Acquired keratoderma of late onset may be a paraneoplasticdermatosis associated with intrathoracic squamous cell carcinoma.[2,7] Although a number of classifications have been published none unite satisfactorily clinical presentation, pathology, and molecular pathogenesis.[8]

Skin is both a site of vitamin D biosynthesis and a target organ of vitamin D action. Recently the increased understanding of the immunomodulatory effects of vitamin D and its analogs paralleled the growth of knowledge of the vitamin D mode of action in psoriasis and other inflammatory dermatological disorders.[9] Calcipotriol is a synthetic analog of calcitriol. Calcipotriol binds to the vitamin D receptor with the same affinity as the calcitriol although it is 100 times less active on calcium metabolism when applied topically.[10] After application of calcipotriol serum concentration is maximum within 6 hours and disappears within 48 hours. Approximately 2 to 10 percent of topically applied dose can be systemically absorbed. Vitamin D and its analogs act via its receptor to regulate cell growth, differentiation, and immune function. It has effects on inflammation.[11] Adverse effect of calcipotriole includes, irritation, photosensitivity, allergic contact dematitis, hypercalcaemia.[12]

The basic structure of all corticosteroids is the cyclopentenoperhydrophenenthrenenucleuos. Currently topical steroids are the most frequently prescribed of all dermatologic drugs. The basic molecule of steroid-cortisol, by addition or alteration of functional groups at certain positions have led to compounds of varying potencies and side effects. Substitution at the position 16 with beta methyl (beta-methasone) increases the efficacy without the concommitant increase in the sodium retaining properties. The removal, replacement or masking hydroxyl group increases the molecules lipophilicity, therefore increases the rate of percutaneous absorption as well as glucocoticoid receptor binding activity. The clinical potency of topical steroid depends not only on the inherent potency of the molecule but also on factors such as the vehicle and the nature of the skin onto which it is applied. Very occlusive vehicle such as ointment potentiates glucocorticoid effects because they provide increased hydration of the stratum corneum and increase its permeability.Topical corticosteroids exert their effects through both direct and indirect mechanism, which are mediated via glucocorticoid receptor. The effects are anti-inflammatory, antiproliferative and atrophogenic effects. Topical corticosteroids may cause HPA suppression, growth retardation, iatrogenic Cushing's syndrome if high concentration is used for long duration in a large body surface area. Locally it may cause atrophy, allergic contact dermatitis, tachyphylaxis, folliculitis, delayed wound healing.

Materials and methods:

This prospective randomized case control study was carried out on the patient of keratoderma with fissured sole in the outpatient department of dermatology & venereology BangaBandhu Sheik Mujib Medical University (BSSMU) during the period January 2013 to December 2013. After full filling the patient's selection criteria, thorough history was taken. All patients were asked regarding his/her symptoms, duration of the lesion, aggravating factors, nature of foot wear, walking habit, occupation, family history, menstrual history (in case of female). Both the soles of the feet of all patients were thoroughly examined to find out the followings- i. Number of fissures present in the soles. ii. Location of the fissures present in the soles. iii. Color of the fissures. iv. Shape and configuration of the fissures. v. Mean width of the fissures. vi. Other features presents in association with fissures in the soles. Each patient thoroughly examined to rule out any associated systemic disease that may cause fissured sole specially diabetes mellitus, hypothyroidism, hepatitis, chronic renal failure, malignancy, lupus erythomatosus, scleroderma, malnutrition.

To find out the cause, confirmation of the clinical diagnosis and exclusion of differential diagnosis, every patient was evaluated by following laboratory tests-

a. Blood for total leukocytes count, differential count, hemoglobin percentage, erythrocyte sedimentation rate, and total circulating eosinophil count.

b. Skin scraping for fungus from the sole.

c. Random blood sugar. d. Skin biopsy from sole for histopathological examination.

Then the patients were randomly allocated to one of two groups. One group was given calcipotriol ointment at night and betamethasone velerate ointment in the morning for six weeks. Other group was given Vaseline as placebo. First follow up examination was after completion of treatment (at 6 weeks). Then patients were advised to stop medication for four weeks. After that finally patients were examined at 10 weeks.

Data was collected in a predesigned data collection sheet. Data was processed and analyzed using software SPSS-12 (Statistical Package for Social Sciences). Statistical test used to analyze the data Chi-square test and student T test (Unpaired). Data processed on categorical scale were presented as frequency and percentage were analyzed by Chi-square test. While the data processed on continuous scale were presented as mean and SD and were analyzed with the help of Student t test. The level of significance was .05. The summarized data were then presented in the table and chart.

Result:

Table- I: Age distribution

Age of the patients	Group of the patient		Total
	Group A	Group B	
10-19	8 (26.7)	4 (13.3)	12 (20)
20-29	8 (26.7)	4 (13.3)	12 (20)
30-39	2 (6.7)	7 (23.3)	9 (15)
40-49	6 (20)	10 (33.3)	16 (26.7)
50-59	4 (13.3)	4 (13.3)	8 (13.3)
60-69	2 (6.7)	1 (3.3)	3 (5)
Total	30	30	60

Table- II: Sociodemographic variables

Variable	Characteristics	Case n (%)	Control n (%)	P value
Sex	Male Female Total	11(36.7) 19(63.3) 30(100)	13(43.3) 17(56.7) 30(100)	.598
Occupation	House wife Student Service Day laborer Others Total	10(33.3) 11(36.7) 3(10) 3(10) 2(6.7)	7(23.3) 7(23.3) 9(30) 1(3.3) 1(3.3)	.135
Socioeconomic condition	Lower class Middle class Upper class Total	7(23.3) 21(70) 2(6.7) 30(100)	2(6.7) 23(76.7) 5(16.7) 30(100)	.125

Table- III: Presenting signs of fissured sole of both groups

Signs of lesion	Groups		Total	P value
	Group A	Group B		
Scales	1(3.3)	4 (13.3*)	5 (8.3)	.141
Focal hyperkeratosis	24 (80)	24 (80)	48 (80)	
Diffuse hyperkeratosis	5 (16.7)	1 (3.3)	6 (10)	
Punctuate hyperkeratosis	0 (0)	1 (3.3)	1 (.7)	
Total	30 (100)	30 (100)	60 (100)	

Table- IV: Duration of suffering from fissured sole of both groups

Duration of suffering in year	Group A	Group B	Total	P value
Mean	7.8	9.2	8.5	.402
Std. deviation	6.9	5.9	6.4	
Median	5	9.5	6	

Table- V: Site of the fissures in both groups

Sites	Groups		Total	P value
	Group A	Group B		
Sides of the sole	27 (90)	28(93.3)	55(91.7)	1.00
Toes	8(26.7)	2(6.7)	10(16.7)	.038
Insteps of the sole	23(76.7)	27(90)	50(83.3)	.166
Toe cleft	2(6.7)	1(3.3)	3(5)	1.00
Heel	22(73.3)	26(86.7)	48(80)	.197
Pressure area	4(13.3)	3(10)	7(11.7)	1.00
Dorsum of the foot	3(10)	2(6.7)	5(8.3)	1.00

Table- VI: Histopathological causes of plantar hyperkeratosis with fissured sole in study population

Histopathological diagnosis	Group A	Group B	Total	P value
Chronic allergic dermatitis	10 (33.3)	9 (30)	16 (26.7)	.459
Psoriasis	12 (40)	14 (46.7)	29 (48.3)	
Keratoderma	2 (6.6)	5 (16.6)	7 (11.7)	
PRP	2 (6.6)	1 (3.3)	3 (5)	
Chronic non-specific dermatitis	4(13.3)	1 (3.3)	5 (8.3)	
Total	30 (100)	30 (100)	60 (100)	

Table- VII: Changes after completion of treatment (at 6 weeks)

Scale of improvement	Groups of patients		P value
	Group A	Group B	
No response	4 (13.3%)	22 (73.3%)	.001
poor	2 (6.7%)	2(6.7%)	
Good response	6 (20.0%)	4(13.3%)	
Very good	13 (43.3%)	1(3.3%)	
excellent	5 (16.7%)	1(3.3%)	
Total	30(100%)	30(100%)	

Table- VIII: changes 4 weeks after completion of treatment (at 10 weeks)

Scale of improvement	Groups of patients		P value
	Group A	Group B	
No response	14 (46.7%)	22 (73.3%)	.003
poor	16 (53.3%)	2(6.7%)	
Total	30 (100%)	30 (100%)	

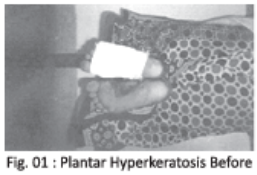

Fig. 01 : Plantar Hyperkeratosis Before Treatment (Case No.-03)

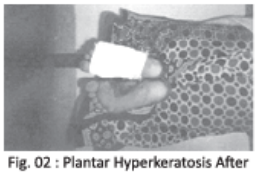

Fig. 02 : Plantar Hyperkeratosis After Treatment (Case No.-03)

Fig. 03 : Plantar Hyperkeratosis Before Treatment (Case No.-30)

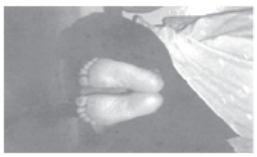

Fig. 04 : Plantar Hyperkeratosis After Treatment (Case No.-30)

Fig. 05 : Plantar Hyperkeratosis Before Treatment (Case No.-29)

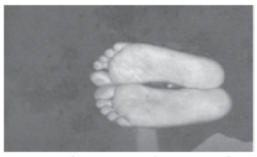

Fig. 06 : Plantar Hyperkeratosis After Treatment (Case No.-29)

Table- IX: Side effects

Side effects	Groups of patients		P value
	Group A	Group B	
Burning	3(10%)	1(3.3%)	P >.05
Asymptomatic	27 (90%)	29 (96.7%)	

Discussion:

The study was aimed to observe efficacy and safety of topical application of calcipotriol and betamethasonvelerate on plantar keratoderma with fissures, and also to determine the response of fissured sole on the basis of histopathological findings. A total of 60 patients were enrolled from OPD of the Department of Dermatology & Venereology of BSMMU for the prospective study. The mean age of group A and group B were 32.33±17.2 and 36.8±12.57 years respectively. The groups were almost identical in terms of age (P=0.256). Our study showed socioeconomic status of the majority of the patient belongs to middle class and it does not coincides with S Chidambara e.t al and they found lower class is mostly suffered from acquired keratoderma, which it may be due to more health consciousness of the middle class people than that of the lowerclass.[13] Sociodemographic study reveals that approximately 36.7% of the group A and 43.3% of the group B were male. The rest 63.3% of group A and 56.7% of group B were female. Among the total 60 subjects selected for study most common affected group was 40-49 years (26.7%) which is supported by SandepKodali[13] but differs with Chopra et al.[16] where he found it to be 27 years. Presentation of keratoderma in later years of life maybe due to the fact that the cumulative insult of constant exposure to trauma, allergens and irritants.[14] Maximum respondents of group A were students (36.7%) followed by house-wife (33.3%). On the other side maximum respondents of group B were service holder (30%) followed by house-wife (23.3%) and students (23.3%). The diseases is found to be higher in females (60%) than in males(40%), similar observation was found by M Sivakumar in his study.[15] Mean duration of suffering from fissured sole 7.8 years with a SD ± 6.9 years for group A and 9.2 years with a SD ± 5.9 years for group B. No statistical significant difference was observed in terms of duration of suffering from fissured sole. These values differ from a study carried out by A Chopra and Maninder.[16]

80% respondents of group A and similar percent respondents of group B had focal hyperkeratosis. Second highest presenting sign for group A was diffuse hyperkeratosis (16.7%) followed by scale (3.3%) S. Chidambaraet. al. in a study from North East India observed similar findings.[17] On the other side 13.3% respondents of group B had scale and 3.3% had plaque hyperkeratosis and 3.3% had punctate hyperkeratosis. No statistical significant difference was observed in terms of presenting sign of fissured sole between two groups.

Distribution of fissured sole is sometimes characteristic of the disease. In psoriasis fissure were present in the sole and insteps of the sole[18] also found in this study. Out of all patients of group A 90% had fissures on their sides of the sole and 93.3% group B had on the same location. This is supported by Belinda Longhurst, Carol Steele in a study.[19] Insteps of the sole was the next frequent site of fissures for both group A (76.7%) and group B (90%) followed by heel, 73.3% of group A and 86.7% of group B. Least common sites for fissures of both groups were toes toe cleft, pressure area and dorsum of the foot. No statistical significant difference was observed in terms sites of fissures other than toes.

In our study we found histopathologically more common cause of plantar keratoderma with fissured sole was psoriasis 29 (48.3%) followed by chronic allergic dermatitis 16 (26.7%), inherited keratoderma 7 (11.7%), Chronic non-specific dermatitis 5 (8.3%) and PRP 3 (5%) respectively and also supported by S Chidambara et.al.[17]

Considering the scale of improvement, at 6 weeks 43.3% of group A and 3.3% of group B showed excellent response. 20% of group A and 13.3% of group B showed very good response which is statistically significant (P<.05).

During therapy 3% of respondents of group A and 1% respondents of group B complaints of burning sensation 20 which was statistically not significant (P>.05).

Conclusion:

Topical calcipotriol and betamethasone velerate is effective and safe in planter hyperkeratosis with fissures, especially in cases of planter psoriasis and PRP with fissures but with significant recurrence after discontinuation of treatment.

Conflict of Interest:

None declared.

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