EFFICACY OF TOPICAL 1% PIMECROLIMUS CREAM IN THE TREATMENT OF ATOPIC DERMATITIS

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Abstract:

Background: Topical steroids remain as the mainstay of treatment of Atopic dermatitis (AD), but associated with numerous adverse events. So, searching a non-steroidal alternative is very crucial for the management of atopic dermatitis.

Aims and objective: To evaluate the efficacy of 1% cream in atopic dermatitis.

Methods: This randomized parallel group study was conducted in the department of Dermatology and Venereology, Bangabandhu Sheikh Mujib Medical University (BSMMU), Dhaka. Patients of AD of Group A (n=20) patients were allowed to apply a thin film of Pimecrolimus 1% cream (Elidel) and Group B (n=20) were advised to apply white Vaseline to the affected skin once daily for 4 weeks. Main out come was measured fortnightly with SCORAD and statistical analysis was done with SPSS-13.

Results: SCORAD at 1st visit was 49.76 ± 17.25 in group A and 55.25 ± 13.94 in group B (p=0.275), at 2nd visit 27.39 ± 11.16 for group A and 50.05 ± 14.69 (p=0.001) and at 3rd visit 12.08 ± 6.87 for group A and 46.70 ± 14.80 for group B. After completion of treatment mean (±SD) of percent of SCORAD reduction was 76.70 ± 8.10 in group A and only 16.88 ± 8.70 in group B (p=0.001). According to physician's global assessment 9 (45.0%) patients of Pimecrolimus group and 2 (10.0%) were cleared or almost cleared. None of the patients experienced any adverse effects.

Conclusion: Twice daily application of 1% Pimecrolimus cream is effective and well tolerated in the treatment of atopic dermatitis.

Key words: Pimecrolimus, Tacrolimus, Calcinurine inhibitor, Atopic dermatitis, Eczema.

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Introduction:

Atopic dermatitis (AD) is a common skin condition affecting up to 18% of children and 2% of adults[1]. It is an itchy, inflammatory skin condition with a predilection for the skin flexures and is characterized by poorly defined erythema with edema, vesicles, and weeping in the acute stage and skin thickening (lichenification) in the chronic stage[1-2]. It has a negative impact on the quality of life (QOL) of children and their Parents and poses a therapeutic challenge to dermatologists[3]. The disease accounts for 10% to 20% of all referrals to dermatologists and about 30% of dermatologic consultations in general practice[4]. Usually the symptoms can be fairly well controlled by the judicious use of corticosteroids, also in children and topical corticosteroids have been the mainstay of treatment of AD for 40 years[5]. The local and systemic side effects of topical steroids are well recognized. Local effects include skin atrophy,

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striae, telangiectasias, hypopigmentation, rosacea, perioral dermatitis and acne. Systemic side effects include adrenal suppression, cataracts, glaucoma and growth retardation in children[6].

Pimecrolimus is a calcineurin inhibitor, it inhibits T-cell activation and maturation by inhibiting the transcription factor NFAT (nuclear factor of activated T cells) and thus the transcription and release of Th1 and Th2 cytokines[7]. To date, the safety and efficacy of tacrolimus ointment and pimecrolimus cream have been evaluated in more than 18 000 patients with atopic dermatitis and found safe and effective [8,9]. It has very few adverse effects, most the most common adverse effects of Pimecrolimus is burning and stinging sensations[10]. The current study was conducted to see the efficacy and safety of topical Pimecrolimus in the treatment of atopic dermatitis.

Methodology:

In this randomized, parallel group study forty patients with atopic dermatitis of both sexes but otherwise in good general health, were included in the study and enrolled in to two treatment groups (group-A and group-B) of equal twenty patients. Group-A patients were treated with 1% pimecrolimus cream applied twice daily for four weeks and group-B patients were advised to apply white Vaseline to the affected skin twice daily for 4 weeks. SCORAD index system was assessed at baseline and patients were assessed fortnightly. All patients were asked to report immediately if any problem develops during the study period. Finally SCORAD index was calculated at the 4th week. All information was collected in a pre designed data sheet and was recorded. Monitoring of adverse effects after 4 weeks was noted by patient's complications, query and physical examination. Data was analyzed by computer with the help of SPSS (Statistical package for social sciences) win 13 software package.

Result

Equal twenty patients with atopic dermatitis were enrolled into two groups (group-A, Pimecrolimus) and (group-B, Emollient), mean (±SD) age of the patients were 8.34±2.27 (range 2-12) years for group-A and 7.43±1.86 (range 1-12) years for group-B. Total duration of disease (mean ± SD) were 41.67±21.92 months and 34.23±19.56 months for group A and group B respectively. At entry level disease severity in terms of SCORAD was 49.76 ± 17.25 in group A and 55.25 ± 13.94 in group B (p=0.275), at 2nd visit 27.39 ± 11.16 for group A and 50.05 ± 14.69 (p=0.001) and at 3rd visit SCORAD was 12.08 ± 6.87 for group A and 46.70 ± 14.80 for group B. After completion of treatment mean (±SD) of percent of SCORAD reduction was 76.70 ± 8.10 in group A and only 16.88 ± 8.70 in group B (p=0.001). According to physician's global assessment 9 (45.0%) patients of Pimecrolimus group and 2 (10.0%) were cleared or almost cleared. None of the patients experienced any adverse effects.

Table-I

Demographic, clinical and immunological characteristics of the study population

		Group-A (Pimecrolimus)	Group-B (Emollient)
Number of patients		20	20
Sex: (M/F)		16/4	16/4
Age (years): mean ± SD (range)		8.34±2.27(2-12)	7.43±1.86(2-12)
Total duration of disease in months: mean ± SD (range)		41.67±21.92(1-96)	34.23±19.56(1-88)
Percent body involved:	up to 25%	85%	95%
	26-50%	15%	5%
Personal history of	Allergic rhinitis	11(555.0%)	7(35.0%*8
	Asthma	5(25.0%)	3(15.0%)**
Hanifin & Rajka criteria fulfill	Yes	12(60.0%)	17(85.0%)
	No	8(40.0%)	3(15.0%)***
Serum IgE level	601.30 ± 423.18	658.30 ± 211.84#	

*Chi-square test was done to measure the level of significance, p=0.695.
**Fisher's Exact test was done to measure the level of significance, p=0.204.
*** Chi-square test was done to measure the level of significance, p=0.704.
# t test was done to measure the level of significance, p=0.593.

Table-II

Distribution of clinical features

Dermatological examination	Frequency	Percent
Flexural lichenification or linearity	15	75.0
Ichthyosis palmer hyperlinearity or keratosiss pilaris	1	5.0
Tendency toward cutaneous infection	15	75.0
Tendency toward nonspecific hand or foot eczema	3	15.0
Nipple eczema	3	15.0
Cheilitis	7	35.0
Recurrent conjunctivitis	9	45.0
Dannie-morgan infra orbital fold	9	45.0
Keratoconous	5	25.0
Orbital darkening	2	10.0
Facial pallor or facial erythema	6	30.0
Pityriasis alba	10	50.0
Anterior neck fold	7	35.0
Itch when sweating	13	65.0
Food intolerance	4	20.0
Course influenced environmental & emotional factor	5	25.0
White dermatographism or delayed blanch	0	.0

**p=0.695, Fisher's Exact test was done to measure the level of significance.
*p=0.204, *Chi-square test was done to measure the level of significance.

Table-III

Distribution of SCORAD by groups

SCORAD index	Group		p
	Case (Group 1)	Control (Group 2)	value
1st visit	49.76 ± 17.25	55.25 ± 13.94	0.275
2nd visit	27.39 ± 11.16	50.05 ± 14.69	0.001
3rd visit	12.08 ± 6.87	46.70 ± 14.80	0.001
Percent of reduction from 1st visit to 3rd visit	76.70 ± 8.10	16.88 ± 8.70	0.001

*t test was done to measure the level of significance.
Data was shown as Mean ± SD.

Table-IV

Proportion of patients rated as clear or almost clear of disease based on the investigator's global assessment in 6-week vehicle-controlled studies with Pimecrolimus 1% cream

Physician's global assessment	Group-A (Pimecrolimus)	Group-B (Emollient)
Clear or almost clear	9 (45.0%)	2(10.0%)

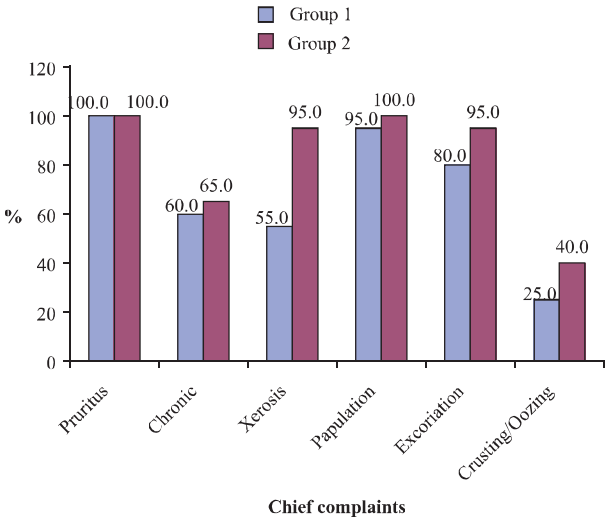

Fig.-1: *Bar diagram of complains*

Discussion:

Atopic dermatitis (AD) is a common inflammatory skin disease, causing significant physical, psychological and social distress[11]. Topical corticosteroids are the mainstay of treatment of atopic dermatitis but it has some potential adverse effects. The risk of steroidal side-effects is greater with long-term treatment and the use of potent corticosteroids[12]. For these reasons, corticosteroids are not recommended for long-term therapy, and potent preparations should not be used on the face, neck and intertriginous areas. Additionally, perceived concerns can adversely affect treatment by reducing patient compliance[12]. In a recent outpatient study, over 70% of patients were worried about using topical corticosteroids, and 24% were non-compliant because of these fears[13]. Therefore, there is currently a need for a potent, safe, non-steroidal, topical treatment for atopic dermatitis. Tacrolimus ointment, formulated for the treatment of atopic dermatitis, is the first in a class of non-steroidal topical immunomodulators and it was approved by the US-FDA in December 2000 for the treatment of atopic dermatitis in patients above 2 yrs of age. Although large multicentric studies in adults and children have confirmed the efficacy of the drug in the treatment of atopic dermatitis[13-16], few studies have conducted to see the efficacy of Pimecrolimus in atopic dermatitis. The current study was carried out to see the efficacy of topical 1% Pimecrolimus in the treatment of atopic dermatitis. It was a randomized parallel group study and conducted over forty patients of atopic dermatitis and all patients completed the treatment.

AD is a disease that primarily affects children, population particularly vulnerable to the systemic effects of several topical medications currently used to treat AD. Mean (±SD) age of the patients were 8.34±2.27 years with a range of 2 to12 years in group-A and 7.43±1.86 years with a range 1to 12 years for group-B. In similar type two 6-week randomized, double-blind, vehicle-controlled studies with Pimecrolimus comprised with children 1–17 years of age and one study with infants aged 3–23 months[17-18]. Pimecrolimus is an ascomycin derivative that is chemically unrelated to corticosteroids[19].

At base line SCORAD index in case group was 49.76 ± 17.25 and in control group was 55.25 ± 13.94 ($p>0.05$). So, at baseline both treatment groups were statistically indifferent clinically and immunologically (IgE) (Table 1). In group A, after treatment with topical 1% pimecrolimus cream disease severity was reduced to 27.39 ± 11.16 and 12.08 ± 6.87 at 2nd and 3rd visit and in group B, it was reduced to 50.05 ± 14.69 and 46.70 ± 14.80. The mean (± SD) of percent reduction of disease in group A and B was 76.70 ± 8.10 and 16.88 ± 8.70 respectively ($p=0.001$). According to physician's global assessment 9 (45.0%) patients of Pimecrolimus group and 2 (10.0%) were cleared or almost cleared, whereas in previous studies by week 6, treatment success was observed in 34.8% of children in the pimecrolimus group, compared with 18.4% of children in the vehicle group[20] and in another study in 54.5% of infants treated with pimecrolimus vs. 23.8% of vehicle-treated infants[21]. So, Pimecrolimus makes significant improvement of disease and it is marked better than only emollient. In other previous studies, 1% Pimecrolimus cream was found effective and well tolerated when used on the face and neck, which are difficult areas to treat because of the risk of local adverse events associated with the use

of higher potent topical corticosteroids [22-23]. In the present study, no instance of atrophy were reported in any patient receiving pimecrolimus cream, which is consistent with a similar type previous study, where the atrophogenic potent ial of pimecrolimus cream 1% was assessed in more detail in healthy volunteers; after 4 weeks of treatment, no evidence of skin atrophy was found in areas treated with 1% pimecrolimus cream[23]. Eichenfield et al[22] found that the efficacy and safety is sustainable on long term (26 weeks) use of 1% Pimecrolimus cream, but the current study was a short term study. So, we can conclude that 1% Pimecrolimus is safe and effective treatment modality for atopic dermatitis and we recommend to conduct further large scale prospective clinical trial to see the efficacy of 1% pimecrolimus crème in the treatment of atopic dermatitis.

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