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Original Article OPEN ACCESS

Safety of Topical Mometasone Furoate 0.1% Cream vs Topical Tacrolimus 0.03% Ointment in the Treatment of Atopic Dermatitis

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Abstract

Introduction: *Atopic dermatitis (AD) is an itchy, chronic, or chronically relapsing, inflammatory skin condition, affecting between 10% and 20% of children and 1% and 3% of adults. Atopic dermatitis causes significant physical, psychological and social distress. The prevalence of AD has increased steadily over the last 30 years. Topical steroids and calcineurin inhibitors are the current standard for topical anti-inflammatory therapy. Mometasone furoate cream 0.1% is a medium potency corticosteroid, effective in the treatment of atopic dermatitis in children.* ***Materials and Methods:*** *A clinical trial was conducted from September 2021 to February 2022 to compare the safety of mometasone furoate and tacrolimus in the treatment of Atopic Dermatitis. Patients of Atopic dermatitis attending outpatient department of Dermatology and Venereology, Bangabandhu Sheikh Mujib Medical University, Dhaka were the study population. Patients of atopic dermatitis diagnosed clinically and age more than 2 years were included in the study.* ***Results:*** *In this study, 73.33% of mometasone furoate treated patient and 60% of tacrolimus treated patients did not experience any side effects. Side effects recorded in group A were burning sensation (13.3%), dry skin (6.7%), Desquamation (3.3%) and irritation (3.3%) and in group B were burning(10.0%), dry skin (13.3%), desquamation (10.0%), irritation (3.3%) and erythema (3.3%) ($p>0.05$).* ***Conclusion:*** *In the light of the findings of the study we conclude that each of the treatment of mometasone furoate and tacrolimus is individually safe in the treatment of atopic dermatitis. The safety and tolerability of mometasone furoate 0.1% is almost same as that of tacrolimus in the treatment of atopic dermatitis.*

Key words: *Safetyt of mometasone furoate, safety of tacrolimus, atopic dermatitis.*

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Introduction:

Atopic dermatitis (AD) accounts for 10% to 20% of all referral to dermatologists and about 30% of dermatologic consultations in general practice. The word atopy introduced by Coca 1925 meaning out of place or strange to signify the hereditary tendency to develop allergies to food & inhalant substances[1]. Atopy is a syndrome may be defined as a genetically determined immune system maturation disorder of unknown origin, in which there is increased liability to form IgE antibodies & is frequently associated with personal or family history of atopic dermatitis, allergic rhinitis or asthma[2-4]. In atopic dermatitis(AD) there is activation of the T helper 2 (Th2) immune response, with synthesis of cytokines IL-4, IL-5, IL-10 & IL-13 and inhibition of T helper 1 (Th1) response. IL-4 & IL-5 produces elevated IgE level and eosinophilia in tissue & peripheral blood[5,6]. Pruritus is the hallmark of atopic dermatitis in all stages. 60% infantile AD present first year of life[7,8]. Pruritus is constant features and itching is paroxysmal type. Skin biopsy for histopathology show spongiosis & edema of the epidermis, hyperkeratosis and acanthosis in chronic stage along with perivascular infiltrate of in upper dermis[9,10]. Topical corticosteroids are very effective in atopic dermatitis but there frequent and long term uses, particularly in children have many side effects[11]. Mometasone furoate is a medium potency cortico-steroid, indicated for the relief of the inflammatory and pruritic manifestations of atopic dermatitis[12]. Topical calcineurin inhibitors like tacrolimus may be used as alternate of steroid. Topical tacrolimus suppresses inflammation in a similar way to steroids and is equally as effective as a mid porency steroid[10]. It dose not cause skin thinning or other steroid related

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side-effects[13]. To the best of my knowledge, no study exploring the safety of topical mometasone furoate comparing with topical tacrolimus in the treatment of atopic dermatitis has yet been conducted in Bangladesh.

Materials and Methods:

A clinical trial was conducted in department of Dermatology and Venereology, Bangabandhu Sheikh Mujib Medical University, Dhaka. The duration of the study was from September 2021 to February 2022. Patients of Atopic dermatitis attending outpatient department of Dermatology and Venereology, Bangabandhu Sheikh Mujib Medical University, Dhaka were the study population. Purposive type of non-probability sampling method was followed in this study. Inclusion criterias were patients of atopic dermatitis diagnosed clinically, patient who gave informed written consent, age more than 2 years and patients of both male and female. Exclusion criterias were known case of topical mometasone or tacrolimus hypersensitivity and patients who have been suffering from hepatic, renal, cardiovascular and hematological diseases. Patients co-existing with acute infections, neoplasia, uncontrolled hypertension and diabetes mellitus. Patients suffering from any food allergy and other skin morbidity causing acute onset of skin rash. Skin disorders likely to affect drug absorption or disorders requiring medical treatment within 5 days before the start of the study and pregnancy and lactation.

Ethical issues: The researcher was duly careful about ethical issues related to this study. In this study all patients were given an explanation of the study including the potential risks and obtainable benefits, all patients were included in the trial after taking their informed written consent, the researcher also explained them that they have the right to refuse or accept to participate in the study and they have the right to refuse during study period, if he or she desire and the patients were not gain financial benefit from this study and all data obtained during study period from the patients remained confidential.

Procedure of data collection: A total number of 60 patients were primarily selected and they were randomized using computer-generated codes into two groups (group-A and group-B), each of which included 30 patients. 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 was carefully judged. History and physical findings were recorded in a structured questionnaire. Finally those patients, who matched the inclusion and exclusion criteria according to history, physical examination and freely gave their informed consent, were selected for the study.

Intervention: Patients were divided into two groups (Group-A and group-B), group A was treated with mometasone furoate and group B with tacrolimus. Both preparations had to be administered in twice daily regimen and the duration of the total treatment period was 4 weeks. Unused medications were collected after the last assessment. Patients were clinically assessed monthly for three months. Each time the severity index of the disease were calculated and recorded and clinical photographs were taken. The final clinical assessment was done and the severity index was calculated. Six clinical signs were recorded for each case by the senior consultant in the Unit for practical purposes: erythema, edema/papulation, oozing/crusting, excoriations, lichenification and dryness. These clinical signs are the most widely used and validated in atopic dermatitis currently available scoring system: Scoring of Atopic Dermatitis (SCORAD) index, The SCORAD scored the extent, six intensity criteria, and subjective symptoms of AD. Disease extent was measured using the rule of nines. The average intensity of each clinical sign was graded on a scale from 0 to 3 (0=absent, 1=mild, 2=moderate, and 3=severe) at a representative body site, per the SCORAD protocol. Subjective symptoms, pruritus, and sleep loss were evaluated with regard to the last 3 days and nights, and all were scored by the patients. Both subjective items were graded on a 10-cm visual analogue scale. The SCORAD index formula is: A/5 + 7B/2 + C. In this formula A is defined as the extent (0–100), B is defined as the intensity (0-18) and C is defined as the subjective symptoms (0-20). The maximum SCORAD score is 103 (i.e. patients with high score are rated “worse"). Safety of the medication of the treatment was assessed by observing the side effects during follow up schedule. The SCORAD Index (SCORing Atopic Dermatitis) is a scoring index for measuring the severity of atopic dermatitis. It is intended to standardize the assessment of therapeutic studies. It was designed to be easy to use in the outpatient setting. In order to evaluate the severity of atopic dermatitis as objectively as possible, the European Task Force on atopic dermatitis has developed a method allowing consistent assessment by means of severity index called SCORAD.

The SCORAD Index is based on sub scores:

1. A (extent score based on body surface area)
2. B (intensity score based on 6 clinical findings in atopic dermatitis)
3. C (subjective symptoms)

- A=extent score=SUM (body surface area involved using rule of 9)
- B=intensity score=SUM(points for 6 criteria-erythema, edema/papulation oozing/crusting, lichenification, excoriation and dryness)
- C = subjective symptoms of pruritus and sleep disturbance = (score for pruritus from 0 to 10). SCORAD INDEX= (A/5) + (7 x B/2) + C

Data processing and analysis:

Data analysis was performed by Statistical Package for Social Science (SPSS), version-12. Statistical analyses was done and level of significance was measured by using appropriate procedures like chi square test ($\chi 2$), relative risk (RR) measurement, t-test, and proportion (d) test and others where applicable. Level of significance (p value) was set at 0.05 and confidence interval at 95%.

Results:

Total sixty patients of atopic dermatitis were enrolled and divided into group A and group B. Thirty of group A patients were treated by mometasone furoate and thirty of group B patients were treated by tacrolimus ointment. Mean age of Group A patients was 21.73 ± 4.30 and Group B was 19.70 ± 3.44. 50.0% of group A and 58.3% of Group B was from the age group 2 to10 years and 50.0% of group A and 33.3% of group B was from the age group of >10 years. Mean (± SD) age of onset was 9.37 ± 4.07 years and 7.42 ± 3.12 years in group A and group B respectively (p=0.420). Mean duration of disease was 16.60 ± 17.21 months and 28.20 ± 38.71 months in group A and group B respectively (p=0. 139).

Table I: Distribution of patients by age and mean of age at first appeared (yrs) and duration of disease (months).

Age in years	Group A (n=30)	Group B (n=30)	p value*
2 to10	15 (50.0)#	20 (58.3)	
>10	15 (50.0)	10 (33.3)	
Total	30 (100.0)	30 (100.0)	
Mean ± SD	21.73 ± 4.30	19.70 ± 3.44	0.48
	Group A	**Group B**	**p value****
Age at first appeared (yrs)	9.37 ± 4.07	7.42 ± 3.12	0.420
Duration of disease (months)	16.60 ± 17.21	28.20 ± 38.71	0.139

* unpaired t test and chi-square test** were done to measure the level of significance.

At baseline mean of total score of atopic dermatitis was 30.57 ± 13.62 and 30.90 ± 17.17 in group A and B, at 1st follow up it was 20.50 ± 13.64 and 21.17 ± 16.94 respectively in group A and B, at 2nd follow up it was 16.23 ± 12.74 and 15.83 ± 15.29 and at final follow up it was 11.87 ± 12.04 and 11.20 ± 13.85 respectively in group A and B (p>0.05). Percent reduction of severity from base line to final follow up was 69.20 ± 23.41 in group A and 74.77 ± 23.30 in group B (p=0.360).

Table II: SCORAD (Mean of total scoring of Atopic dermatitis) in different follow up

	Group A	Group B	p value*
Baseline	30.57 ± 13.62	30.90 ± 17.17	0.934
1st follow up	20.50 ± 13.64	21.17 ± 16.94	0.867
2nd follow up	16.23 ± 12.74	15.83 ± 15.29	0.913
Final follow up	11.87 ± 12.04	11.20 ± 13.85	0.846
Percent of reduction from base line to final follow up	69.20 ± 23.41	74.77 ± 23.30	0.360

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

In this study, 73.33% of mometasone furoate treated patient and 60% of tacrolimus treated patients did not experience any side effects.

Table III: Distribution of patients by side effects

Side Effects	Group A		Group B	
	N	%	N	%
With side effects	8	26.67%	12	40%
Without side effects	22	73.33%	18	60%

Side effects recorded in group A were burning sensation (13.3%), dry skin (6.7%), Desquamation (3.3%) and irritation (3.3%) and in group B were burning (10.0%), dry skin (13.3%), desquamation (10.0%), irritation (3.3%) and erythema (3.3%) (p>0.05).

Table IV: Distribution of different side effects by groups

	Group A	Group B	p value*
Burning sensation	4 (13.3)	3 (10.0)	0.688
Dry skin	2 (6.7)	4 (13.3)	0.389
Desquamation	1 (3.3)	3 (10.0)	0.301
Irritation	1 (3.3)	1 (3.3)	0.999
Erythema	0 (0.0)	1 (3.3)	0.313

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

Discussion:

Mean age of Group A patients was 21.73 ± 4.30 and Group B was 19.70 ± 3.44. Similar findings were observed by Sabry EY in his study done in Saudi Arabia to evaluate the effectiveness of combining two topical steroids, an antibiotic and an emollient as a single mixture in effectively controlling atopic dermatitis lesions in a six weeks treatment period. In total, 31 patients were assessed for eligibility to participate in this study; of these, age range of 19-26 years (mean age 22.9±2.532 years) were enrolled[14]. Gradman et al were done a study in Denmark to see the suppressive effects of topical mometasone furoate and tacrolimus on skin prick testing in children. Skin prick tests were performed in 12 children with atopic eczema before and after 2 weeks of treatment with topical mometasone furoate and tacrolimus. Both treatments significantly suppressed the allergen wheal size. Mometasone furoate reduced the histamine wheal size as well. Skin prick testing in children treated with topical glucocorticoids or tacrolimus is associated with a risk of false-negative test results[15]. Pei AY were conducted a study to observe the effectiveness of wet wrap dressings using 0.1% mometasone furoate and 0.005% fluticasone proprionate ointments in the treatment of moderate to severe atopic dermatitis in children. Various types of dressings have been used successfully in the treatment of atopic dermatitis. There was significant improvement in the disease severity from baseline during the first 2 weeks of the open application arm (p=0.043), however, additional beneficial effects were limited after week 2. Wet wraps further improved the disease severity and extent after week 2 ($p < 0.05$), and were well tolerated. They concluded that both 0.1% mometasone furoate and 0.005% fluticasone proprionate ointments are effective in the treatment of atopic dermatitis, and that wet wraps are useful in further improving refractory disease in children[16]. In our study, at baseline mean of total score of atopic dermatitis was 30.57 ± 13.62 and 30.90 ± 17.17 in group A and B and at final follow up it was 11.87 ± 12.04 and 11.20 ± 13.85 respectively in group A and B (p>0.05). Percent reduction of severity from base line to final follow up was 69.20 ± 23.41 in group A and 74.77 ± 23.30 in group B (p=0.360). The significant improvement in the SCORAD index score and its six clinical intensity signs after three and six weeks of treatment were observed by Sabry EY in his study, done in Saudi Arabia to evaluate the effectiveness of combining two topical steroids, an antibiotic and an emollient as a single mixture in effectively controlling atopic dermatitis lesions in a six weeks treatment period. Thirty one females with atopic dermatitis were enrolled in this study. Disease

severity was measured using the Severity Score of Atopic Dermatitis (SCORAD) index at baseline, 3 weeks and 6 weeks of therapy. They were treated with a mixture of mometasone furoate, fusidic acid and betamethasone valerate twice daily for six weeks. Out of the 31 enrolled cases, 20 (64.5%) satisfied the inclusion criteria. They all completed the 6-week treatment regimen and evidenced no side effects from therapy. Statistical comparison between baseline and after three and six weeks interval using ANOVA and Tukey's multiple comparison tests revealed significant improvement of SCORAD index and its six clinical intensity signs with more effective improvement after the 6-week therapy. No correlation was ever detected by the Spearman test between index score and lesions' site or with allergic co-morbidities. The combined topical therapy mixture was effective and safe in rapidly controlling treated lesions. Sabry EY also recommended that mometasone furoate; is a highly effective topical corticosteroid with a less systemic absorption and a low potential for local and systemic side effects. Once-daily use of mometasone furoate was found to result in a greater percentage improvement in total atopic dermatitis scores compared with twice-daily betamethasone valerate in that study[14]. Schnopp C et al were carried out a vehicle-controlled trial with topical steroids under wet-wrap dressings in atopic dermatitis in the department of Dermatology and Allergy, Germany. The wet-wrap dressing technique were proved to be beneficial in cases of exacerbated atopic dermatitis (AD) skin lesions. The effect of wet-wrap dressings was investigated in a controlled trial comparing a steroid (mometasone furoate 0.1%)-containing and a steroid-free (vehicle) preparation in an in-patient comparison study. 20 children aged 2-17 years with exacerbated AD were treated twice daily with wet-wrap dressings over a 5-day period. AD in treated areas significantly improved in both study arms; however, the effect was significantly better in the mometasone-treated group ($p < 0.01$). Transepidermal water loss improved in both arms without any significant differences. Staphylococcus aureus colonization decreased during the first 3 days of active treatment independently of the therapeutic modalities chosen. At day 5, colony counts further dropped on the steroid-treated lesions. Application of the wet-wrap dressing technique for exacerbated AD lesions is effective, combination with a topical steroid being superior to a steroid-free application without bearing the risk of a bacterial superinfection. The treatment of facial atopic dermatitis in children who are intolerant of, or dependent on, topical corticosteroids: a randomized, controlled clinical trial[17]. Hoeger PH were conducted a study in Department of Paediatric Dermatology, Germany. The objective of primary study was to determine the efficacy of tacrolimus in children with mild-moderate facial AD dependent on/intolerant of TCS. Treatment with topical corticosteroids (TCS) is limited due to heightened risk of treatment-associated side-effects, thus necessitating alternative AD therapies. A multicentre, double-blind (DB) study of < or = 6 weeks, followed by a 6-week, open-label (OL) phase was conducted. Two hundred patients (aged 2-11 years) were randomized 1:1 to tacrolimus (n = 99) or vehicle (n = 101) twice daily until clearance of facial AD or for a maximum of 6 weeks (DB phase). Sixteen patients receiving vehicle were allowed to switch to the OL phase at day 22. Significantly more tacrolimus-treated vs. vehicle-treated patients were cleared/almost cleared of facial AD (Investigators' Global Assessment 0/1): 74.5% vs. 51.0%, $P < 0.001$ (day 43) [57.1% vs. 36.0%, $P = 0.004$ (day 22)]. Median time to clearance was 22.0 vs. 43.0 days (tacrolimus vs. vehicle, respectively). Adverse events were mainly mild-moderate, occurring with similar frequency in both treatment groups. In children with facial dermatitis intolerant of/dependent on TCS, tacrolimus effectively controls eczema and pruritus and is well tolerated[18]. Zuberbier et al were done a study with the aim of this post hoc analysis was to evaluate whether treatment of patients with atopic dermatitis (AD) with tacrolimus can decrease the development of flares necessitating the use of a topical corticosteroid on the face and thus reduce the need for use of topical corticosteroids in this sensitive skin area. In a controlled, double-blind, multicentre study, 140 patients, aged 2 to 17 years, with facial involvement and mild to moderate disease after treatment of the initial flare with prednicarbate 0.25% cream were randomized to an intermittent treatment with tacrolimus twice daily or vehicle for 24 weeks. If a flare occurred, defined as an exacerbation (unacceptable severity of itching/scratching or onset of oozing) not controlled by study medication, patients were treated with prednicarbate 0.25% cream instead. Patients in the vehicle group needed prednicarbate treatment on the face on 20.7% of the days vs. 11.7% of the study days in the tacrolimus group ($P = 0.0024$). Fifty per cent of patients in the tacrolimus group had no flare on the face during the treatment period compared with 37.5% of patients in the vehicle group ($P = 0.012$). The median time to first flare in tacrolimus -treated patients was twice as long as in patients receiving vehicle (138 vs. 68 days, $P = 0.01$). Three adverse events (one case of skin burning) suspected to be related to use of the study medication were reported for three patients (3.9%) in the tacrolimus group. Long-term intermittent treatment of facial AD in children and adolescents with tacrolimus cream 1% does significantly reduce the need for topical corticosteroids[19]. In our study, 73.33% of mometasone furoate treated patient and 60% of tacrolimus treated patients did not experience any side effects. Side effects recorded in group A were desquamation (13.3%), dry skin (6.7%), burning sensation (3.3%) and irritation (3.3%) and in group B were desquamation (10.0%), dry skin (13.3%), burning sensation (10.0%), irritation (3.3%) and erythema (3.3%) ($p>0.05$). A study was done in Saudi Arabia to evaluate the effectiveness of combining two topical steroids, an antibiotic and an emollient as a single mixture in effectively controlling atopic dermatitis lesions in a six weeks treatment period. Disease severity was measured using the Severity Score of Atopic Dermatitis (SCORAD) index at baseline,3 weeks and 6 weeks of therapy. They were treated with a mixture of mometasone furoate, fusidic acid and betamethasone valerate twice daily for six weeks. Out of the 31 enrolled cases, 20 (64.5%) satisfied the inclusion criteria. They all completed the 6-week treatment regimen and evidenced no side effects from therapy[14].

Conclusion:

In the light of the findings of the study we conclude that each

of the treatment of mometasone furoate and tacrolimus is individually safe in the treatment of atopic dermatitis. The safety and tolerability of mometasone furoate 0.1% is almost same as that of tacrolimus in the treatment of atopic dermatitis. Study with a larger group of patients for longer period may result in superior outcome in clinical practice through improved compliance.

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