Journal of Pakistan Association of Dermatologists 2007; **17**: 21-27.

Original Article

Efficacy, safety and tolerability of mometasone fuorate 0.1% ointment in chronic eczema

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Abstract

Introduction Eczema covers a wide range of skin problems, which trouble people at different stages of their lives. Mometasone furoate has been reported to be an effective vasoconstrictive agent on human skin.

Objective To evaluate the therapeutic efficacy, safety and tolerability of mometasone furoate ointment 0.1% in chronic eczema following a four-week course of therapy and to record the main events in the cascade of eczema.

Patients and methods This quasi-experimental, multi-center study was conducted in four cities of Pakistan (Karachi, Lahore, Islamabad, and Peshawar) from December, 2005 to February, 2006. A total 180 patients aged ≥ 24 months of either sex with chronic eczema without secondary infection were recruited while pregnancy, known hypersensitivity to corticosteroids, presence of skin atrophy, those on systemic steroids within 28 days were excluded. Patients were instructed to apply a thin layer of ointment once daily. Tubes of mometasone furoate ointment were dispensed to the patients on days 1, 8 and 15 of the study. Patients were asked to return the used tubes at the next weekly follow-up visit. SPSS-13.0 was used for statistical analysis. Friedman test was applied to compare the significance of clinical outcome, relief in signs/symptoms and patient's comfort at $p<0.05$.

Results On first follow up 8 days after treatment, significant majority (77%) showed improvement and in 7 (4%) patients fully resolved. After 15 days, 75% showed improvement and resolved in 19% patients. After 21 days of treatment, improvement was seen in 32% and 55% had resolved. Efficacy in terms of relief in signs and symptoms on last follow up >21 days after treatment revealed significant resolution of signs and symptoms ($p<0.001$). The cumulative level of comfort on various follow up visits was found significant ($p<0.001$).

Conclusion Mometasone furoate ointment is significantly effective in relief in sign and symptoms and provides a high level of comfort after the treatment of chronic eczema.

Key words
Eczema, mometasone furoate, itching

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Introduction

Topical steroids became the mainstay in the treatment of eczema with the introduction of

hydrocortisone 30 years ago. Since then groups of topical steroids of different potency have been introduced. Unfortunately, the potency of topical steroids is often directly proportionate to the risk of side-effects. There is always a constant search for formulations which can offer greater therapeutic benefits yet possess minimum side effects.[1]

Mometasone furoate [9a, 21-dichloro-llb, 17dihydroxy-16a-methyl-pregna-14-dione-3, 20-Dione-17-(2furoate)] is a synthetic, 17-heterocyclic corticosteroid. It has been shown to be highly effective as an anti-inflammatory agent.[1]

The present study was primarily designed to evaluate the therapeutic efficacy, safety and tolerability of mometasone furoate ointment 0.1% applied once daily in chronic eczema.

Patients and methods

This was an open labeled, multicenter, non comparative study, which was conducted in different cities of Pakistan (Karachi, Lahore, Islamabad, and Peshawar) from December, 2005 to February, 2006.

Two hundred consecutive patients of either sex, age ≥ 24 months, selected from various skin OPDs with chronic eczema (> 6 weeks duration), were recruited into the study. Chronic eczema was evidenced by lichenified scaly patches and plaques on the body. Different exclusion criteria included pregnancy, known hypersensitivity to corticosteroids, presence of skin atrophy (e.g. telangiectasia and/or striae), those on systemic steroids within last 28 days, eczema with superadded infection, or application of any medication other than the study preparation to the study area. Similarly, antihistamines were discontinued one day prior to study day 1. No other medication except bland emollients or moisturizers was applied to the study area. Patients were instructed to apply a thin layer of ointment once daily. Tubes of mometasone furoate ointment were dispensed to the patients on days 1, 8 and 15 of the study depending on requirement of the patient. Patients were asked to return the used tubes at the next weekly follow-up visit (days 8, 15 and 21).

The signs/symptoms of eczema e.g. erythema, induration, crusting, scaling, excoriation and pruritus were recorded upon entry into the study (day 1 or baseline scores) and at follow-up visits on days 8, 15 and 21 using a severity scale which ranged from 0 = none to 3 = severe. The physician's overall evaluation of the response of eczema to the ointment was recorded during each visit. Each patient was assessed during every follow-up by the same dermatologist who examined the patient at the first visit. Patients' response to the treatment was also recorded during each visit.

Individual sign/symptom scores, the total sign/symptom scores, the percentage improvement in the total score and the physician's overall evaluation of change in disease was analyzed statistically. An examination for signs of skin atrophy in the target areas was made at each visit. Cosmetic acceptability on each treated site was also recorded during each visit. Institutional ethical committee approval was obtained and all efforts were made to stay true to the Declaration of Helsinki.

Dosage schedule

Mometasone furoate (0.1%) ointment applied once daily on the lesions for four weeks

Data analysis

Statistical software "SPSS-13.0" was used for statistical analysis. Frequency and percentages were computed to present the categorical variants including presenting signs and symptoms, investigator's assessment, clinical outcome, relief in symptoms and patients' comfort. Non-parametric "Friedman test" for repeated qualitative data was applied to compare the significance of clinical outcome, relief in signs/symptoms and patient's comfort at $p < 0.05$.

Results

Among 180 patients of acute and chronic eczema, 70 (38.9%) were males and 110 (61.1%) females (M:F = 1:1.6). Amongst these 83 were children ≤ 12 years.

Presenting complaints were itching, redness, dryness, induration and pinhead blisters. Median duration of presenting complaints was 180 days (Inter-quartile range = 60 to 720 days). Dryness and skin changes were the complaints of all patients but of different severity levels. Redness was found in 178 patients with different severity grades; fifty-nine (33%) had severe, 119 (66%) had moderate and 37 (21) had mild redness. Itching was reported by 174 patients out of whom majority (n=157, 90.2%) were unable to perform social and functional activities. Pinhead blisters was present in 62 (34.4%) and indurations was present in 91 (50.6%) patients **(Table 1)**.

Table 1 Presenting complaints and signs (n=180).

Presenting signs and symptoms	*n (%)*
Itching	
Minimal interference in social & functional activities	17 (09.4)
Moderate interference with social activities	61 (33.9)
Inability to perform social & functional activities	96 (53.3)
Redness	
Mild	37 (20.6)
Moderate	82 (45.6)
Severe	59 (32.8)
None	2 (01.1)
Dryness	
Mild	23 (12.8)
Moderate	119 (66.1)
Severe	37 (20.7)
None	1 (0.6)
Skin change	
Rough	40 (22.2)
Scaly	71 (39.4)
Thickened	42 (23.3)
Crusting	20 (11.1)
All	06 (3.3)
Induration	
Present	91 (50.6)
Absent	84 (49.4)

Out of 180 patients, 172 patients returned for first follow-up on 8th day after treatment. 8 were unable to continue due to various reasons. Later on, 167 patients came for second follow-up visit 15th day after treatment. Third follow-up was done after 21 days. 130 patients presented and in the last follow up that was after 21 days of the 3rd follow-up, only 60 patients reported of whom those either could not get reasonable level of comfort or missed any of the subsequent follow up visit.

Table 2 shows the severity of individual signs and symptoms at each follow up visits.

Overall effectiveness assessed by the

Table 2 Overall effectiveness in relief of symptoms

Symptoms		*Investigator's assessment*			
Itching	*N*	*No*	*Mild*	*Moderate*	*Severe*
Day-8	(172)	18 (10)	75 (42)	68 (38)	11 (6)
Day-15	(167)	39 (23)	95 (57)	30 (18)	3 (2)
Day-21	(130)	67 (52)	50 (38)	13 (10)	0 (0)
> 21 days	(60)	33 (55)	17 (28)	9 (15)	1 (2)
Redness		*No*	*Mild*	*Moderate*	*Severe*
Day-8	(172)	8 (5)	92 (53)	69 (40)	3 (2)
Day-15	(167)	34 (20)	109 (65)	22 (13)	2 (1)
Day-21	(130)	63 (48)	57 (44)	10 (8)	0 (0)
> 21 days	(60)	33 (55)	16 (27)	11 (18)	0 (0)
Dryness		*No*	*Mild*	*Moderate*	*Severe*
Day-8	(172)	20 (12)	103 (60)	46 (27)	3 (2)
Day-15	(130)	53 (32)	92 (55)	21 (12)	1 (1)
Day-21	(60)	28 (16)	23 (38)	9 (15)	0 (0)
> 21 days	(60)	28 (47)	23 (38)	9 (15)	0 (0)
Skin change		*No*	*Mild*	*Moderate*	*Severe*
Day-8	(170)	25 (15)	82 (48)	59 (35)	4 (2)
Day-15	(165)	53 (32)	67 (41)	42 (25)	3 (2)
Day-21	(130)	55 (42)	43 (33)	22 (17)	10 (8)
> 21 days	(60)	16 (27)	17 (28)	17 (28)	10 (17)
Indurations		*Absent*	*Present*		
Day-8	(170)	95 (56)	75 44)		
Day-15	(167)	121 (72)	46 (28)		
Day-21	(60)	43 (72)	17 (28)		
> 21 days	(60)	43 (72)	17 (28)		

Key: Values given in parentheses are percentages

Table 3 Clinical outcome

Follow up findings		*Investigator's Assessment*			
Clinical outcome		*Resolved*	*Improved*	*No change*	*Worse*
Day-8	(n=172)	7 (4)	133 (77)*	31 (18)	1 (1)
Day-15	(n=167)	31 (19)	126 (75)*	9 (5)	1 (1)
Day-21	(n=130)	47 (36)	75 (58)*	6 (5)	1 (1)
> 21 days	(n=60)	33 (55)*	19 (32)	6 (10)	2 (3)
Signs & symptoms					
Day-8	(n=172)	11 (6)	134 (78)*	26 (15)	1 (1)
Day-15	(n=167)	33 (20)	125 (75)*	8 (5)	1 (1)
Day-21	(n=130)	47 (36)	75 (58)*	6 (5)	1 (1)
> 21 days	(n=60)	31 (52)*	21 (35)	6 (10)	2 (3)

Key: Values given in parentheses are percentages
* Significant improvement at $p<0.001$ (By applying chi-square test).

investigator for the relief of symptoms is summarized in **Table 3**. After 8 days of treatment, complete resolution was seen in 7 (4%) patients and a significant majority of the patients (77%) showed improvement ($p<0.001$). The proportion of complete resolution and improvement was also found significant on follow visits after 15 days and 17 days ($p<0.001$). On last follow up visit after more than 21 days, mometasone

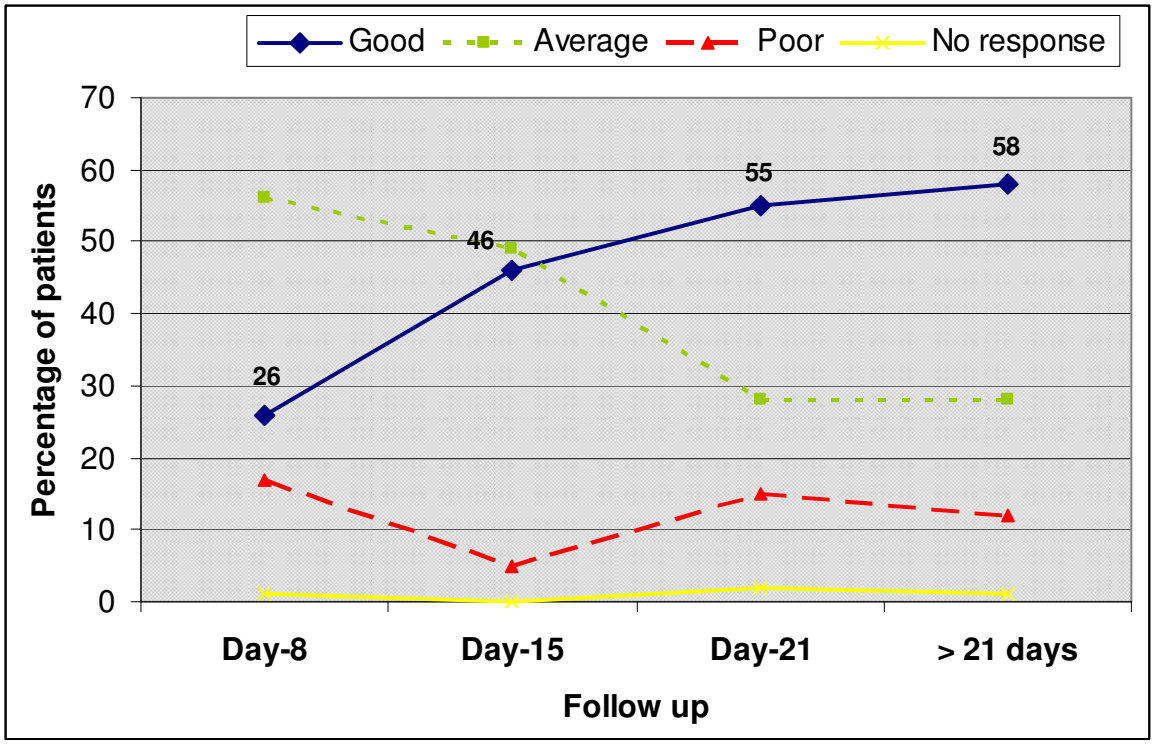

Figure 1 Overall comfort to patients on follow up visits.

resolved 55% patients and 32% showed improvement (p<0.001).

Efficacy of mometasone furoate in terms of relief in signs and symptoms was also recorded (**Table 3**). On first follow visit eight days after the treatment, signs and symptoms had been completely resolved in 6% and significant improvement in relief of the symptoms was seen in 78% (p<0.001). The same pattern of statistical significance of relief in signs and symptoms was observed on second and third follow up visits respectively after 15 and 21 days. Finally, last follow up more than 21 days after treatment revealed significant (p<0.001) resolution of signs and symptoms and relief.

None of the patients reported any local or systemic side effects. Overall level of patients' comfort was evaluated. It was found to be significant (p< 0.001, Friedman test) as shown in **Figure 1**.

Discussion

Topical corticosteroids are the treatment of choice for numerous inflammatory or hyperproliferative skin diseases. Over the years, research has focused on strategies to optimize potency and, in particular, the anti-inflammatory and immunosuppressive capacity of these drugs, while minimizing adverse effects. However, 'ideal' topical corticosteroids have not yet been synthesized. The newest topical corticosteroids used for the treatment of different dermatoses and allergic reactions of the respiratory tract (in particular asthma) are budesonide, mometasone furoate, prednicarbate, the di-esters 17,21-

hydrocortisone aceponate and hydrocortisone-17-butyrate-21-propionate, methylprednisolone aceponate, alkalometasone dipropionate, and carbothioates such as fluticasone propionate. The new molecules, compared with the well known and established corticosteroids, generally have a higher anti-inflammatory effect, good compliance among patients (only a once-daily application is needed), rarely induce cross-sensitivity reactions and have weak atrophogenicity.[2]

The present study demonstrated that mometasone furoate ointment 0.05% applied once daily for 3 to 4 weeks is an effective topical therapy in chronic eczema. It is also safe in both children and adults. Various studies have been conducted in different parts of the world to determine the safety and efficacy of mometasone furoate in different cutaneous disorders. In four multicenter clinical studies published by Medansky *et a*l.[1] the efficacy and safety of the ointment and cream formulations 0.1% of mometasone furoate, administered once daily, were compared with those of the ointment and cream formulations of fluocinolone acetonide 0.025% administered three times daily and triamcinolone acetonide 0.1% administered twice daily in chronic and moderate psoriasis. Evaluation of change in disease sign scores indicated that mometasone ointment, applied once daily, was significantly more effective (p<0.01) than fluocinolone ointment, applied three times daily, and triamcinolone ointment, applied twice daily. The ointment formulation of mometasone was significantly more effective (p<0.001) than fluocinolone ointment, applied three times daily, and equivalent to triamcinolone ointment, applied twice daily. The incidence of local adverse experiences following treatment with the ointment or ointment formulations of mometasone was minimal. Mometasone ointment and ointment provide a highly effective once-a-day treatment for moderate to severe psoriasis with minimal risk of side effects.

In another study by Faergemann *et al.*[3] 68 adult patients with atopic dermatitis were treated with Mometasone furoate. Sixty-one of 68 (90%) patients were still free of their disease after 6 months of twice weekly treatment and only one showed possible treatment related signs of skin atrophy. The number of *Staphylococcus aureus* and *Pityrosporum ovale* were significantly reduced in cleared patients. Mometasone furoate fatty cream was found successful and harmless both for treatment and as a prophylaxis in patients with atopic dermatitis.

In the study by Veien *et al*.[4] 120 patients with chronic hand eczema were treated daily with mometasone furoate fatty cream until the dermatitis cleared or for a maximum of 9 weeks. The conclusion drawn by the authors was that long-term, intermittent treatment of chronic hand eczema with mometasone furoate fatty ointment is effective and safe.

Mometasone furoate [9a, 21-dichloro-llb, 17-dihydroxy-16a-methyl-pregna-14-dione-3, 20-Dione-17-(2furoate)] is a synthetic, 17-heterocyclic corticosteroid. It has been shown to be highly effective as an anti-inflammatory agent which is approximately half as potent in suppressing hypothalamic-pituitary-adrenal (HPA) axis function as betamethasone valerate. Specifically,

mometasone furoate has a low potential for HPA axis suppression and for induction of atrophogenic effects, even after extensive application (mean baseline BSA treated, 64%).[5]

The cost-effectiveness of once-daily versus more frequent use will depend on the generalisability of the findings to the specific treatment decision and the relative product prices. Further investigations are required on the clinical and cost-effectiveness of once-daily versus more frequent use of same potency corticosteroids, specifically on mild potency products for mild to moderate atopic eczema. Outcomes should include quality of life and compliance.[6]

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