ADIS DRUG EVALUATION

Drugs 1998 Jan; 55 (1): 145-163
0012-6667/98/0001-0145/$19.00/0

Topical Mometasone

A Review of its Pharmacological Properties and Therapeutic Use in the Treatment of Dermatological Disorders

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Synopsis

Mometasone, a synthetic 16α-methyl analogue of beclomethasone, is classified as a 'potent' glucocorticoid for dermatological use. It is available as 0.1% cream, ointment and lotion formulations for the treatment of patients with inflammatory glucocorticoid-responsive dermatoses.

In patients with atopic dermatitis, the effects of mometasone 0.1% applied once daily over 2 to 3 weeks were similar to those of other glucocorticoids of similar potency, such as betamethasone dipropionate 0.05% twice daily and methylprednisolone aceponate 0.1% once daily. Mometasone 0.1% was significantly superior to twice-daily application of less potent glucocorticoids such as

clobetasone 0.05%, hydrocortisone 1.0%, hydrocortisone butyrate and hydrocortisone valerate 0.2%. In patients with seborrhoeic dermatitis, mometasone 0.1% was more effective than ketoconazole 2.0% and hydrocortisone 1.0% in trials lasting 4 or 6 weeks. In the management of scalp psoriasis and psoriasis vulgaris, mometasone 0.1% applied once daily for 2 to 8 weeks was generally more effective than other glucocorticoids of similar or weaker potency such as betamethasone valerate 0.1%, fluocinolone acetonide 0.025%, fluticasone propionate 0.005%, triamcinolone acetonide 0.1% and hydrocortisone 1.0% and as effective as diflucortolone valerate 0.1%. Alternate day application of mometasone 0.1% for 2 weeks was as effective as once-daily application in maintaining symptom control in a small number of patients with psoriasis vulgaris.

Although mometasone demonstrates greater anti-inflammatory activity and a longer duration of action than betamethasone, it has low potential to cause adverse systemic effects such as suppression of the hypothalamic-pituitary-adrenal (HPA) axis. Moreover, its atrophogenic potential is low and no greater than that of other glucocorticoids in its class, such as betamethasone valerate. Transient, mild to moderate, local adverse effects such as burning, stinging, folliculitis, dryness, acneiform eruptions and signs of skin atrophy have been reported with mometasone. Mometasone has shown a low risk of primary sensitisation and cross-reactions in preliminary patch test studies.

Mometasone is a well tolerated topical glucocorticoid effective in the management of patients with atopic dermatitis, seborrhoeic dermatitis, scalp psoriasis and psoriasis vulgaris. In addition to its low potential for causing primary sensitisation and cross-reactions with other topical glucocorticoids, mometasone offers the convenience of once-daily administration.

Pharmacological Properties

Mometasone has high lipophilicity and displays greater *in vitro* affinity for glucocorticoid receptors in rat epidermis than betamethasone dipropionate. In suppressing erythema induced by ultraviolet (UV)-B light, mometasone showed greater activity and a longer duration of action than betamethasone dipropionate and betamethasone valerate. However, it showed little potential to suppress the hypothalamic-pituitary-adrenal axis in patients and healthy volunteers.

An *in vitro* study on human fibroblasts and keratinocytes reported the antiproliferative effects of mometasone to be negligible or small compared with those of betamethasone valerate. No clinical or histological signs of skin atrophy were observed in 6 volunteers after 12 months of once-daily application of mometasone 0.1% cream. Some clinical trials have found the atrophogenic potential of mometasone to be low and similar to that of hydrocortisone, prednicarbate, betamethasone valerate and methylprednisolone aceponate. However, in one trial, mometasone 0.1% ointment was associated with a significantly greater incidence and severity of skin atrophy and telangiectasia than methylprednisolone aceponate 0.1% ointment.

Little topically applied mometasone reaches the systemic circulation. In human volunteers, only 0.7% of mometasone 0.1% ointment was systemically absorbed after a contact time of 8 hours without occlusive dressing. After application of 10g 0.1% ointment under occlusion, the plasma concentration of mometasone peaked at about 130 ng/L in 12 hours and then declined rapidly.

Therapeutic Use

Atopic dermatitis. In short term studies (≤6 weeks) once-daily mometasone 0.1% cream or ointment was significantly more effective in reducing total sign and symptom severity scores than twice-daily clobetasone 0.05% ointment,

clobetasone 0.05% cream, hydrocortisone butyrate cream, hydrocortisone valerate 0.2% cream and hydrocortisone 1.0% cream and as effective as once-daily methylprednisolone aceponate 0.1% cream or twice-daily betamethasone dipropionate 0.05% ointment in the treatment of moderate to severe atopic dermatitis.

Seborrhoeic dermatitis. Once-daily application of mometasone 0.1% solution was more effective and showed a faster onset of action than ketoconazole 2.0% shampoo applied twice weekly over 4 weeks in the treatment of patients with moderate to severe seborrhoeic dermatitis. Significantly greater improvement was observed after 6 weeks with mometasone 0.1% cream applied once daily than with hydrocortisone 1.0% cream applied twice daily.

Psoriasis. Mometasone 0.1% lotion or ointment applied once daily was significantly more effective than twice-daily betamethasone valerate 0.1% lotion or ointment over 2 to 8 weeks in 3 trials in patients with scalp psoriasis or psoriasis vulgaris. The once-daily application of mometasone 0.1% cream, lotion or ointment formulations produced significantly greater reductions in total psoriatic symptom scores than once-daily hydrocortisone 1% ointment, twice-daily fluticasone propionate 0.005% ointment, triamcinolone acetonide 0.1% lotion or ointment or 3-times-daily fluocinolone acetonide 0.025% cream or ointment. In patients with psoriasis vulgaris, mometasone applied once daily was as effective as twice-daily diflucortolone valerate 0.1% ointment and triamcinolone acetonide 0.1% cream. Results of a preliminary short term study suggest that application of mometasone 0.1% ointment on alternate days may be as effective as once-daily application in maintenance therapy in patients with psoriasis vulgaris.

Tolerability

Topical mometasone 0.1% cream was associated with local cutaneous adverse effects in 1.6 and 7.0% of 319 adult and 74 paediatric patients, respectively. The most commonly encountered adverse effects included stinging, burning, pruritus, folliculitis, dryness, acneiform/erythematous eruptions, tenderness and signs of skin atrophy. These adverse effects were transient and of mild or mild to moderate intensity.

Preliminary patch test studies have reported that the risk of primary sensitisation or cross-reaction with mometasone is low, even in patients known to be hypersensitive to glucocorticoids.

Dosage and Administration

Mometasone 0.1% cream, ointment or lotion is indicated for the symptomatic relief of inflammation and pruritus in patients with glucocorticoid-responsive dermatoses. It should be applied without occlusion to the affected areas once daily. Like other topical glucocorticoids, mometasone should not be used in patients with primary cutaneous viral, bacterial or fungal infections, rosacea, acne, perioral dermatitis, or perianal or genital pruritus. It may be used with caution in children aged ≥2 years.

Mometasone (fig. 1) is a synthetic 16α-methyl analogue of beclomethasone for topical use in glucocorticoid-responsive, inflammatory dermatological conditions.

Structure-activity relationship studies indicate that glucocorticoid 17-monoesters would be more potent anti-inflammatory agents than the respective 21-esters and insertion of a halogen atom in position 21 would make them resistant to degradation by esterases in the epidermis.[1] Structure-binding relationships in cultured human skin cells have shown that halogenation at the 9α-position, esterification of 17-OH and presence of chloride at the 21-position result in increased affinity for

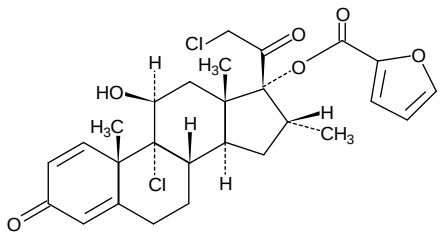

Fig. 1. Structural formula of mometasone.

glucocorticoid receptors.[2] Studies using the 9α,11β-hydroxy series of glucocorticoids in animal models of skin inflammation found that topical anti-inflammatory activity of the 21-chloro 17(2′-furoate) compound (mometasone) was 4- to 6-fold greater than that of topical betamethasone valerate.[3,4]

Topical mometasone is available as a 0.1% cream, ointment or lotion and has been classified as a 'potent' glucocorticoid[1] (table I). However, a recent study evaluating the effects of various topical glucocorticoids on skin thickness and inhibition of experimentally induced contact dermatitis in 22 nickel-sensitised women found the effects of mometasone 0.1% cream to be similar to those of the 'less potent' glucocorticoid clobetasone 0.05% cream, and significantly less than those of clobetasol propionate 0.05% cream.[5]

1. Pharmacological Properties

1.1 Mechanism of Action

The precise mechanism by which glucocorticoids exert their anti-inflammatory effect is unknown. In general, glucocorticoids bind to specific glucocorticoid receptors (GCR) present in the cytoplasm; their binding to the GCR is accompanied by dissociation of the heat shock proteins. The unoccupied GCR is associated with 2 heat shock proteins (hsp90) which promote glucocorticoid binding and prevent binding of GCR to DNA.[6] The glucocorticoid-GCR complex then moves into the nucleus and binds to DNA at specific regions, known as the glucocorticoid response elements, of certain genes. This binding results in increases in the production of lipocortin-1, a protein of the annexin superfamily, which directly inhibits the activity of phospholipase A_2 (thereby decreasing production of pro-inflammatory prostaglandins, leukotrienes and thromboxanes) and leucocyte migration.[7-9] There is also an increase in production of an inhibitory factor (IκBα), which diffuses into the cytosol and binds to nuclear factor-κB (NF-κB). This binding prevents translocation of NF-κB to the nucleus and suppression of various gene products regulated by NF-κB (e.g. cytokines and adhesion molecules).[10,11]

Other glucocorticoid binding sites and receptor subtypes have also been identified.[12,13] In contrast to the classical glucocorticoid receptor (glucocorticoid receptor α), another receptor (glucocorticoid receptor β) is not activated by glucocorticoid binding. The β-type receptor has been suggested to inhibit the effects of the hormone-activated receptor, probably by competing for the glucocorticoid response elements.[14]

A specific glucocorticoid receptor protein has been identified in the epidermis and dermis of both

Table I. Potency classification of cream and ointment formulations of topical glucocorticoids (adapted from Mori et al.[1])

Compound	Concentration (%)
Less potent	
Clobetasone	0.05
Hydrocortisone butyrate	0.25-2.5
Moderately potent	
Prednicarbate	0.25
Triamcinolone acetonide	0.1
Potent	
Betamethasone dipropionate	0.05
Betamethasone valerate	0.1
Diflucortolone valerate	0.1
Fluocinolone acetonide	0.025
Fluticasone	0.05
Methylprednisolone aceponate	0.1
Mometasone	0.1
Very potent	
Betamethasone dipropionate	0.1
Clobetasol	0.05
Ulobetasol	0.05

human and rat skin.[15,16] The number of receptors in the dermis exceeds that in the epidermis although the receptors appear to be physicochemically similar at both locations.[17] Mometasone and most of its putative metabolites exhibit greater *in vitro* receptor affinity (measured by inhibition of ^{3}H-triamcinolone acetonide binding) than alclomethasone propionate and betamethasone dipropionate, but equal to that of betamethasone valerate in the rat epidermis and dermis.[18]

In common with other glucocorticoids, mometasone inhibits the arachidonic acid pathway by directly and indirectly inhibiting the enzyme phospholipase A_2.[19,20] Recent *in vitro* studies have suggested additional mechanisms by which mometasone may provide benefit in inflammatory conditions, e.g. potent and significant reduction of leukotriene production by peripheral blood mixed leucocytes,[21] and inhibition of the production of cytokines, interleukin (IL)-4, IL-5,[22] IL-1, IL-6 and tumour necrosis factor α (TNF-α).[23] Two small studies in patients with psoriasis (n = 6 to 7 per study), published in abstract form, found that treatment with topical mometasone (concentration and formulation not stated) decreased methionine enkephalin levels in lesional psoriatic skin in parallel with clinical improvement[24] and reduced cellular infiltrate and expression of activation antigens on keratinocytes and vessels in the affected skin.[25]

Using inhibition of ultraviolet (UV)-B-induced erythema as an indicator of anti-inflammatory effect, topical mometasone 0.1% cream displayed an anti-inflammatory effect 2- to 4-fold greater and of significantly longer duration than that of other glucocorticoids of similar potency such as betamethasone dipropionate or betamethasone valerate in 10 healthy volunteers.[26] The anti-inflammatory effect of mometasone was similar to that observed with methylprednisolone aceponate 0.1% in 20 volunteers[27] (table II). Subjects were exposed to a 2.6 to 3.0 minimal erythema dose (MED) of UV-B light and the inhibition of skin blood flow was monitored either visually[27] or by laser Doppler blood flowmetry.[26] The relative anti-inflammatory effects were as follows: mometasone = methylprednisolone aceponate > betamethasone dipropionate > betamethasone valerate.

1.2 Systemic Effects

The major risk with the topical use of potent glucocorticoid preparations is their potential to cause hypothalamic-pituitary-adrenal (HPA) axis suppression. In randomised,[27-31] double-blind,[27,30] parallel-group[28-30] or nonblind[31,32] studies in healthy male volunteers[27,28,31,32] and patients with allergic rhinitis[29] or psoriasis,[30] administra-

Table II. Anti-inflammatory activity of mometasone. Vasoconstrictor assays in human volunteers measuring the relative inhibition of ultraviolet (UV)-B light-induced erythema

Reference	Dose of UV-B	No. of volunteers	Agents	Reduction in skin blood flow (AU) measured by laser Doppler flowmetry			Visually assessed suppression of erythema intensity after 8h (% of subjects)		
				5h	12h	24h	total	residual	none
Bjerring[26]	109.2 mJ/cm^2 (2.6 MED)	10	VEH	0	0	0			
			MOM 0.01% cr	3.60**	3.92**	4.02**			
			BMD 0.05% cr	1.62*	1.16**	NS			
			BMV 0.1% cr	1.24*	1.04	NS			
Kecskés et al.[27]	3 MED	20	VEH						100
			MOM 0.1% ung				67.5	27.5	5.0
			MPA 0.1% ung				87.5	12.5	

Abbreviations and symbols: AU = arbitrary units; BMD = betamethasone dipropionate; BMV = betamethasone valerate; cr = cream; MED = minimal erythema dose; MOM = mometasone; MPA = methylprednisolone aceponate; NS = value not stated; ung = ointment; VEH = vehicle; 0 = no activity; * $p < 0.05$; ** $p < 0.01$ *vs* vehicle.

Table III. Effects of multiple doses of mometasone on the hypothalamic-pituitary-adrenal axis in healthy male volunteers and patients with allergic rhinitis[29] or psoriasis[30]

Reference	Study design	Treatment	Duration (days)	No. of subjects	Effect on serum cortisol levels
Brannan et al.[28]a	r,pg	MOM 1,2,4mg intranasal	Single dose	8	DEX > PL ≡ MOM
		MOM 2,4,8mg oral		8	
		DEX 0.2,0.4,0.4mg oral		8	
		PL			
Brannan et al.[29]a	r,pg	MOM 200μg intranasal od	36	16	PRE > PL ≡ MOM
		MOM 400μg intranasal od		16	
		PRE 10mg oral od		16	
		PL		16	
Bressinck et al.[30]	r,db,pg	MOM 0.1% ung od 15 g/day	21	24	MOM ≡ HYD
		HYD 1.0% ung od 15 g/day		24	
Higashi & Katagiri[32]	nb	MOM 0.1% ung 10 g/day (20 h/day)b	5	5	No effect on serum cortisol levels
Kecskés et al.[27]	r,db	MOM 0.1% ung 30 g/day (22 h/day)b	5	11	MOM ≡ MPA
		MPA 0.1% ung 30 g/day (22 h/day)b		10	
Visscher et al.[31]	r,nb	MOM 0.1% cr 16 g/day (11 h/day)b	5	12	MOM > HYD
		HYD 0.1% cr 16 g/day (11 h/day)b		12	

a Abstract.

b Application under airtight occlusion.

Abbreviations and symbols: cr = cream; db = double-blind; DEX = dexamethasone; HYD = hydrocortisone butyrate; MOM = mometasone; MPA = methylprednisolone aceponate; nb = nonblind; od = once daily; pg = parallel group; PL = placebo; PRE = prednisolone; r = randomised; ung = ointment; ≡ indicates similar effect; > indicates significantly greater effect.

tion of mometasone either by nasal, oral or topical routes did not produce any clinically significant decrease in serum cortisol levels, and no symptoms of HPA axis suppression were observed in any of the patients (table III).

Oral dexamethasone, but not intranasal or oral mometasone, caused marked dose-related decreases in area under the plasma cortisol level versus time curve, urinary free cortisol levels and morning plasma cortisol levels compared with placebo.[28] In another study, the plasma cortisol response to a 6-hour infusion of tetracosactide (250μg) was significantly lower in prednisolone-treated patients than in placebo recipients ($p < 0.01$), while the response in the 2 groups treated with mometasone was similar to that of the placebo group.[29]

While the once-daily application of either mometasone or hydrocortisone (without occlusion) for 21 days was not associated with a decrease in plasma cortisol levels from pretreatment values,[30] another study, using the medications under airtight occlusive dressing, found significantly lower plasma cortisol levels in the mometasone-treated group than in the hydrocortisone-treated group ($p = 0.0220$) after 5 days.[31] Plasma cortisol reached pretreatment levels within 7 days after discontinuing treatment in both groups. Furthermore, adrenocorticotrophic hormone levels did not change and the tetracosactide test evoked normal rises in plasma cortisol levels, indicating that adrenocortical insufficiency had not developed.[31] Daily application of mometasone and methylprednisolone aceponate under airtight occlusion decreased serum cortisol in 5 of 11 and 3 of 10 volunteers, respectively.[27]

In patients with glucocorticoid-responsive dermatoses, mometasone 0.1% cream or ointment applied once daily for up to 12 weeks was not associated with a significant change in mean plasma cortisol levels from baseline, and the effect of mometasone was found to be similar to that of hydrocortisone 1.0%, clobetasone 0.05%, hydrocortisone butyrate, betamethasone dipropionate

0.05% or betamethasone valerate 0.1% creams applied twice daily.[33-38]

In common with hydrocortisone and dexamethasone, topical mometasone has also been shown to cause dose-dependent immunosuppression, as evidenced by inhibition of oxazolone-induced local lymph node activation in mice. Mometasone 0.1 to 1.0% decreased the activation of T cells ($CD4^+$/$CD25^+$), antigen presenting cells (Ia^+/$CD69^+$) and B cells (Ia^+/$B220^+$) and decreased draining lymph node cellularity.[39]

1.3 Local Effects

The therapeutic efficacy of topical glucocorticoids depends primarily on their anti-inflammatory potency,[40] but in dermatoses such as psoriasis vulgaris, where there is increased cellular turnover, an antimitotic effect is useful.[41] The antimitotic activity of glucocorticoids is, however, closely correlated with skin atrophy, which is considered to be the major local adverse effect of these agents.[42]

The results of an *in vitro* study[43] and some clinical trials[37,44-46] suggest a low risk of skin atrophy with the use of mometasone. However, the local effects of mometasone on the skin should be addressed in long term studies in greater numbers of patients.

In an *in vitro* study of human fibroblasts and keratinocytes, monolayer cell lines were exposed to different concentrations of glucocorticoids for 5 days. Although all drugs tested inhibited fibroblast and keratinocyte proliferation as a function of their concentration, the effects were more marked with conventional fluorinated compounds like betamethasone valerate.[43] The inhibitory effects of mometasone on fibroblast and keratinocyte chemotaxis and contraction of collagen gels were negligible or small compared with those of betamethasone valerate.

Using a newly developed technique to measure collagen synthesis *in vivo*,[47] mometasone 0.1% cream once daily was reported to be similar to betamethasone valerate 0.1% cream twice daily in decreasing the levels of procollagen propeptides (carboxy-terminal propeptide of type I procollagen, amino-terminal propeptide of type I procollagen and amino-terminal propeptide of type III procollagen) in abdominal skin suction blister fluid from 15 healthy male volunteers (table IV). Ultrasonic measurement did not reveal any decrease in skin thickness over the 1-week study period.

In a randomised double-blind study,[44] application of mometasone 0.1% ointment once daily for 6 weeks did not markedly reduce the thickness of normal human skin (as assessed by pulsed A- and B-mode ultrasound). The effect of mometasone was similar to that observed with twice-daily hydrocortisone 1.0% ointment or prednicarbate 0.25% ointment; skin thickness returned to its baseline value within 3 weeks of discontinuing these agents. One long term study in 6 healthy volunteers did not observe any clinical or histological signs of skin atrophy after 12 months of mometasone 0.1% cream application.[46] The use of ≤10g mometasone 0.1% ointment or cream once daily for 6 to 12 weeks, in 57 patients with a variety of glucocorticoid-responsive dermatoses, was associated with skin atrophy (1 patient) and telangiectasia (4 patients).[36] Application of mometasone 0.1% ointment under occlusive dressing for 6 weeks induced a significantly greater incidence and severity of visually assessed skin atrophy ($p < 0.001$) and telangiectasia ($p < 0.001$) on the forearms of 20 healthy volunteers than similar application of methylprednisolone aceponate 0.1% ointment.[27] However, in another study once-daily application of 200mg mometasone or methylprednisolone aceponate or 0.1% hydrocortisone under occlusion did not significantly alter ultrasound-assessed skin thickness in 10 volunteers after 3 weeks.[48]

A 6-week clinical trial in 50 patients with psoriasis found that although the efficacy of mometasone 0.1% ointment was significantly greater than that of hydrocortisone 1% ointment, the incidence of visually assessed cutaneous atrophy was minimal with both agents.[45] Clinical improvement was also found in all 33 patients with glucocorti-

Table IV. Atrophogenic potential of mometasone. Summary of studies carried out in healthy adult volunteers and patients[45]

Reference	Trial design	Treatment × duration	No. of volunteers	Effect on skin	Relative effect of mometasone
Brasch[46]	o	MOM 0.1% cr od × 12mo	6	No clinical or histological signs of skin atrophy seen	
Hoffman et al.[48]	r,db	MOM 0.1% 200mg[a] od × 3wk MPA 0.1% 200mg[a] od × 3wk HYD 0.1% 200mg[a] od × 3wk V	10 10 10 10	Reduction in skin thickness, assessed by ultrasound, was not significantly different between various groups at day 22 ($p = 0.05$)	MOM ≡ MPA ≡ HYD ≡ V
Katz et al.[45]	bpc	MOM 0.1% ung od × 6wk HYD 1.0% ung od × 6wk	51[b] 51[b]	Signs of skin atrophy seen in 2 patients at end of study period. Mild skin thinning in 1 patient with both MOM and HYD and moderate telangiectasia in 1 patient with MOM	MOM ≡ HYD
Kecskés et al.[27]	r,db	MOM 0.1% ung[a] 3×/wk × 6wk MPA 0.1% ung[a] 3×/wk × 6wk	20 20	MOM was associated with a higher visually assessed incidence of atrophy and telangiectasia than MPA	MOM > MPA
Kerscher et al.[44]	r,db	MOM 0.1% ung od × 6wk HYD 1.0% ung bid × 6wk PRD 0.25% ung bid × 6wk V	12 12 12 12	All applications, including V, decreased skin thickness. MOM did not markedly reduce thickness of normal human skin	PRD ≡ MOM ≥ HYD ≡ V
Koivukangas et al.[47]	o	MOM 0.1% cr od × 7 days BMV 0.1% cr bid × 7 days	15 15	Reversible decrease in dermal collagen synthesis, but no reduction of skin thickness was observed with either MOM or BMV	MOM ≡ BMV

a Application under occlusive dressing.

b Patients with moderate to severe psoriasis vulgaris.

Abbreviations and symbols: bid = twice daily; BMV = betamethasone valerate; bpc = bilateral paired comparison; cr = cream; db = double-blind; HYD = hydrocortisone; MOM = mometasone; MPA = methylprednisolone aceponate; o = open; od = once daily; PRD = prednicarbate; r = randomised; ung = ointment; V = vehicle; ≡ indicates equivalent effect; ≥ indicates a trend towards greater effect; > indicates significantly greater effect, $p < 0.001$ *vs* MPA.

coid-responsive dermatoses, and only 4 patients showed slight signs of skin atrophy on visual assessment after 4 to 12 weeks of treatment with mometasone 0.1% cream.[37] These findings indicate that mometasone may offer some dissociation of potent anti-inflammatory effect from the risk of inducing dermal atrophy.

1.4 Pharmacokinetic Properties

The extent of percutaneous absorption of topical glucocorticoids depends on the vehicle, the condition of the epidermal barrier and the use of occlusive dressings.

In a Japanese trial,[32] 10 g/day of mometasone 0.1% ointment was applied under occlusion for 20 hours/day for 5 days in 5 healthy male volunteers. Plasma concentrations of mometasone peaked at 130 ng/L after 12 hours and declined rapidly (15 ng/L after 72 hours). Only 0.00076% of the total administered dose was excreted in urine as mometasone and its metabolite, 6β-hydroxy mometasone. There are no published studies concerning the pharmacokinetic profile of mometasone cream or ointment in patients with an inflammatory dermatological condition. Animal studies have reported percutaneous absorption of 2 to 6% of topically applied [^{3}H]mometasone ointment and cream.

Only 0.7% of [^{3}H]mometasone 0.1% ointment was systemically absorbed in humans after an 8-hour contact period without occlusive dressing.[49] After oral administration of 1mg mometasone as a solution, the plasma drug concentration in 6 male volunteers peaked at about 0.15 ng/L at 30 minutes and then declined rapidly.[50]

2. Therapeutic Use

2.1 Atopic Dermatitis

Mometasone has been reported to be effective in the management of moderate to severe atopic dermatitis in children and adult patients (table V).

2.1.1 In Children

Three randomised, single-blind comparative trials in children, aged between 6 months and 12 years, compared once-daily mometasone 0.1% cream with twice-daily application of less potent glucocorticoids such as clobetasone 0.05% cream,[38] hydrocortisone 1.0% cream[35] and hydrocortisone valerate 0.2% cream.[51] One double-blind trial,[52] in paediatric and adult patients evaluated the efficacy of mometasone 0.1% cream versus a glucocorticoid with similar potency, methylprednisolone aceponate 0.1% cream.

Patients had not received systemic glucocorticoids within 28 days or used topical glucocorticoids within 7 days. For inclusion, patients presented with at least 3 signs and symptoms of atopic

Table V. Comparative efficacy of mometasone versus other topical glucocorticoids in the management of moderate to severe atopic dermatitis. Summary of results from randomised, single-blind, parallel group studies

Reference	Treatment × duration (wk)	No. of patients treated (evaluated)	Treatment outcome	
			decrease in total sign and symptom severity score (%)	overall assessment (% of patients successfully treated)[a]
In children (aged between 6mo and 12y)				
Lebwohl et al.[51][b]	MOM 0.1% cr od × ≤ 3	111[c]	87.2**	
	HYDV 0.2% cr bid × ≤ 3	112[c]	78.6	
Rafanelli et al.[38]	MOM 0.1% cr od × 3	30 (30)	86.1**	50.0*
	CLO 0.05% cr bid × 3	30 (30)	66.1	6.7
Vernon et al.[35]	MOM 0.1% cr od × ≤ 6	24 (23)	95**	
	HYD 1.0% cr bid × ≤ 6	24 (19)	75	
In adults (including elderly patients aged ≤70y)				
Bianchi[52][d]	MOM 0.1% cr od × 15 days	58[e] (56)		95
	MPA 0.1% cr od × 15 days	64[e] (63)		86
Giannetti et al.[53][b]	MOM 0.1% cr od × ≤ 15 days	61	97.4***	
	CLO 0.05% ung bid × ≤ 15 days	61	83.6	
Hoybye et al.[34]	MOM cr[f] od × 3 and first 3 days/wk × 3	49 (48)		85**
	HYDB cr[f] bid × 3 and first 3 days/wk × 3	45 (38)		71
Marchesi et al.[54]	MOM 0.1% ung od × ≤ 3	30 (30)		100
	BMD 0.05% ung bid × ≤ 3	30 (30)		100

a Successful treatment was defined as clearance or excellent or good (≥75%) improvement in the target area compared with baseline.

b Abstract.

c Patients with topical hydrocortisone-unresponsive, severe atopic dermatitis.

d Double-blind study.

e Age of patients ranged from 6mo to 65y.

f Formulated in a fatty cream base; concentration of active drug not stated.

Abbreviations and symbols: bid = twice daily; BMD = betamethasone dipropionate; CLO = clobetasone; cr = cream; HYD = hydrocortisone; HYDB = hydrocortisone butyrate; HYDV = hydrocortisone valerate; MOM = mometasone; MPA = methylprednisolone aceponate; od = once daily; ung = ointment; * $p \leq 0.02$; ** $p \leq 0.01$ *vs* comparator; *** $p = 0.0005$ *vs* CLO.

dermatitis, namely erythema, induration and pruritus, at the designated target area.[38] One study included patients showing 5 signs and symptoms of atopic dermatitis [erythema, lichenification, skin surface disruption (crusting and scaling), excoriation and pruritus].[35] The total sign and symptom severity score was required to be ≥6[38] or ≥8 with an erythema score of ≥2[35] according to a 4-point scale (0 = none; 1 = mild; 2 = moderate; 3 = severe). Body surface area (BSA) affected by disease ranged from ≤50%[38] to between >15 and ≤65%[35] and the duration of symptoms varied from 1 to 72 months.

Mometasone was significantly superior to clobetasone from the fourth day in reducing the severity of pruritus (by 35.4% and 17.2%, respectively; $p < 0.05$), and from the seventh day in reducing the severity of induration (by 53.5% and 35.9%, respectively; $p < 0.05$). At the end of the 3-week study period, mometasone was significantly superior to clobetasone in reducing the total sign and symptom severity score (by 86.1% and 66.1%, respectively; $p < 0.01$). In the physician's global evaluation, performed at the end of the treatment period, 50% of the mometasone-treated patients were clear of symptoms compared with 6.7% of the clobetasone-treated group ($p < 0.02$).[38]

In another trial, 15 of 24 patients in the mometasone group and 15 of 24 patients in the hydrocortisone group were withdrawn from treatment before the 6-week end-point (median duration 3 weeks) because of clearing of symptoms. Mean improvement in total sign and symptom severity score was 95% for mometasone 0.1% cream versus 75% for hydrocortisone 1.0% cream ($p = 0.01$). Patients with >25% of BSA affected also showed greater improvement in favour of mometasone (92 *vs* 62%; $p = 0.01$).[35]

A large study published in abstract form compared mometasone with hydrocortisone valerate for ≤3 weeks in paediatric patients with severe atopic dermatitis unresponsive to topical hydrocortisone.[51] Improvement in total sign/symptom severity scores was significantly superior with mometasone (87.2 *vs* 78.6%; $p < 0.01$). Mometasone-treated patients also experienced significantly greater improvement in lichenification and pruritus at days 15 and 22 than hydrocortisone valerate-treated patients. Cost data from the study revealed that a full 21-day course of mometasone 0.1% cream was significantly less expensive than a similar course of hydrocortisone valerate 0.2% cream ($p < 0.001$), although actual costs were not stated.

2.1.2 In Adults

Three randomised, single-blind trials compared mometasone with hydrocortisone butyrate (both formulated as a test fatty cream),[34] mometasone 0.1% cream with clobetasone 0.05% ointment[53] and mometasone 0.1% ointment with betamethasone dipropionate 0.05% ointment[54] in adult patients with stable or slowly progressive typical atopic dermatitis affecting ≤50% of BSA (table V). Erythema, induration and pruritus were present in all enrolled patients and the duration of disease in one study[34] was >1 year in the majority of patients. Scores of 0 to 3 (none to severe) were assigned to the signs and symptoms and the total score at study entry was ≥4.5[34] or ≥6.[54] Global evaluation scores of 1 to 6 (cleared to exacerbation) were assigned after treatment.[34,54]

Mometasone improved pruritus significantly better than hydrocortisone butyrate ($p = 0.0069$), although there was no difference between the 2 groups with regard to improvement in erythema or induration. After 6 weeks, 85% of patients in the mometasone-treated group had cleared symptoms or showed marked improvement compared with 71% of patients in the hydrocortisone butyrate group ($p = 0.0025$).[34] In the second trial, mometasone and betamethasone dipropionate caused complete clearance of symptoms in 16 of 30 and 15 of 30 patients, respectively. In addition, good improvement was achieved in the remaining patients of both groups after 3 weeks.[54] A study, published in abstract form, found the effects of mometasone to be significantly superior to those of clobetasone after 15 days ($p = 0.0005$).[53]

Two randomised, double-blind studies found the effects of once-daily application of mometa-

sone 0.1% cream to be similar to those of glucocorticoids of similar potency applied once daily, such as betamethasone valerate 0.1% cream over 4 weeks[55] and methylprednisolone aceponate 0.1% cream over 15 days.[52] However, a significantly larger number of patients in 1 trial preferred betamethasone valerate to mometasone ($p < 0.005$) on the basis of odour, consistency, ease of smearing and feeling of penetration into the skin.[55]

2.2 Moderate to Severe Seborrhoeic Dermatitis

Two randomised, comparative studies have been conducted in patients with moderate to severe seborrhoeic dermatitis.[56,57] All antiseborrhoeic agents were prohibited for at least 2 weeks before the initiation of treatment and systemic glucocorticoids were prohibited for at least 4 weeks. Erythema and scaling were required for enrolment and were rated for severity using an ordinal scale of 0 to 3 (none to severe). Pruritus, if present, was rated for severity but was not a prerequisite for enrolment. The investigators rated efficacy of treatment on a scale of 1 (cleared) to 6 (exacerbated).

A double-blind study in 54 adult patients (aged 22 to 85 years) compared the effects of mometasone (0.1% solution once daily) with those of ketoconazole (2% shampoo twice a week) for up to 4 weeks. After 2 weeks, 17 of 27 patients in the mometasone group (63%) had clearance or marked improvement of symptoms compared with 6 of 22 patients in the ketoconazole group (27%). After 4 weeks, 85% of patients in the mometasone-treated group and 63% of patients in the ketoconazole-treated group were judged to have clearance or marked improvement of symptoms. Mometasone exerted a faster onset of action than ketoconazole, achieving significantly greater improvements in symptom scores for pruritus, erythema and scaling after 2 weeks (fig. 2).[56]

A single-blind multicentre trial in 117 patients (aged 13 to 70 years) compared the effects of mometasone (0.1% cream once daily) with those of hydrocortisone (1.0% cream twice daily) applied for 6 weeks. After 3 weeks, total symptom score improvement was significantly greater in the mometasone group than in the hydrocortisone group (92.5 *vs* 84.7%; $p < 0.01$). At treatment endpoint, total symptom score improvement was 96.7 and 91.4%, respectively, ($p = 0.02$), and 83% of patients in the mometasone group were clear of symptoms compared with 66% in the hydrocortisone group ($p = 0.01$). These results indicate that mometasone was more effective than hydrocortisone in the treatment of seborrhoeic dermatitis and that maximum beneficial effects were evident within 3 weeks. However, signs and symptoms recurred in the majority of patients in both treatment groups within 2 weeks of discontinuation of treatment.[57]

2.3 Moderate to Severe Psoriasis

Patients (aged between 12 and 90 years) with moderate to severe scalp psoriasis[58,59] or psoriasis

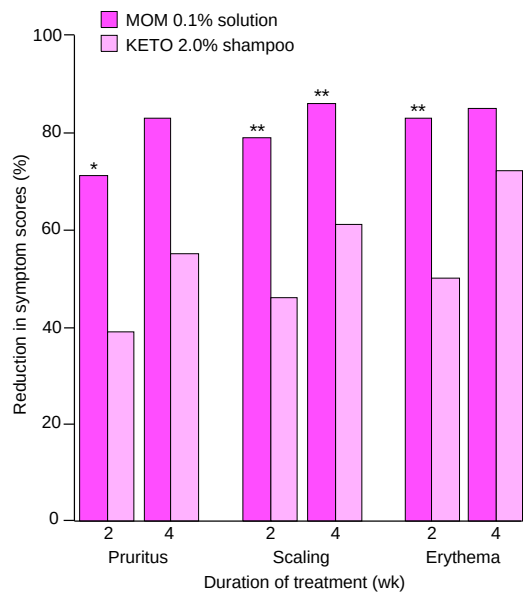

Fig. 2. Comparative efficacy of mometasone in seborrhoeic dermatitis. Reduction in total severity scores of pruritus, scaling and erythema (investigator's judgement) with mometasone applied once daily versus ketoconazole applied twice weekly in 49 patients with moderate to severe seborrhoeic dermatitis.[56] *Abbreviations and symbols:* KETO = ketoconazole; MOM = mometasone; * $p < 0.05$; ** $p \leq 0.01$ *vs* KETO.

Table VI. Comparative efficacy of mometasone (MOM) versus other topical glucocorticoids in the management of stable or worsening, moderate to severe psoriasis vulgaris[30,45,60-64] or scalp psoriasis[58,59]

Reference	Trial design	Treatment × duration (wk)	No. of patients treated (evaluated)	Treatment outcome	
				mean improvement in total sign and symptom scores at end-point (%)	% of patients successfully treated[a]
Compared with betamethasone valerate (BMV)					
Medansky et al.[62]	db	MOM 0.1% ung bid × 2	30 (30)	52**	
		BMV 0.1% ung bid × 2	30 (30)	40	
Svensson et al.[60]	sb,mc	MOM 0.1% ung od × 8	35 (32)	67*	
		BMV 0.1% ung bid × 8	37 (36)	51	
Vanderploeg et al.[59]	sb,mc	MOM 0.1% lo od × 3	(101)	85***	76
		BMV 0.1% lo bid × 3	(102)	70	55
Compared with diflucortolone valerate (DIF)					
De Panfilis et al.[63]b	r,eb,mc	MOM 0.1% ung od[c]	65	71	
		DIF 0.1% ung bid[c]	63	66	
Compared with fluocinolone acetonide (FLU)					
Medansky et al.[61]	sb,mc	MOM 0.1% ung od × 3	112 (112)	58**	35
		FLU 0.025% ung tid × 3	107 (107)	41	11
Medansky et al.[61]	sb,mc	MOM 0.1% cr od × 3	109 (109)	51***	25
		FLU 0.025% cr tid × 3	109 (109)	29	6
Compared with fluticasone propionate (FLUP)					
De Villez et al.[64]	r,eb,mc	MOM 0.1% ung od × ≤ 3	128 (122)	67**	
		FLUP 0.005% ung bid × ≤ 3	129 (121)	56	
Compared with hydrocortisone (HYD)					
Bressinck et al.[30]	db	MOM 0.1% ung 15g od × 3	24 (24)	47**	
		HYD 1.0% ung 15g od × 3	24 (24)	≤12	
Katz et al.[45]	bpc[d]	MOM 0.1% ung od × 6	51 (51)	60***	
		HYD 1.0% ung od × 6	51 (51)	38	
Compared with triamcinolone acetonide (TRI)					
Medansky et al.[61]	sb,mc	MOM 0.1% ung od × 3	98 (98)	60**	37
		TRI 0.1% ung bid × 3	97 (97)	37	8
Medansky et al.[61]	sb,mc	MOM 0.1% cr od × 3	66 (66)	54	39
		TRI 0.1% cr bid × 3	66 (66)	51	32
Swinehart et al.[58]	sb,mc	MOM 0.1% lo od × 3	103 (99)	78*	76
		TRI 0.1% lo bid × 3	99 (93)	73	62

a Successful treatment was defined as clearance or excellent or good (≥75%) improvement in the target area compared with baseline.

b Abstract.

c Duration not stated.

d Patients applied mometasone and hydrocortisone simultaneously to one of the two bilaterally symmetrical lesions (each approximately 10cm^2 in area) that were targeted for treatment evaluation.

Abbreviations and symbols: bid = twice daily; bpc = bilateral paired comparison; cr = cream; db = double-blind; eb = evaluator-blinded; lo = lotion; mc = multicentre; od = once daily; r = randomised; sb = single-blind; tid = 3 times daily; ung = ointment; * p≤ 0.05; ** p ≤ 0.01; *** p ≤ 0.001 *vs* comparator.

vulgaris,[30,45,60-64] exhibiting each of the 3 disease signs (erythema, induration and scaling) at the target area with a total disease severity score of ≥6 graded according to a scale of 0 to 3 (none to severe), were enrolled in the clinical studies (table VI). They had not used topical glucocorticoids for 2 weeks or taken systemic glucocorticoids for 6 weeks prior to enrolment. The efficacy of treatment was expressed as percentage improvement (i.e. difference between the total sign and symptom scores

at treatment and pretreatment divided by the total score at pretreatment, multiplied by 100) and as a change in patient categories (i.e. from not changed/exacerbated to cleared/markedly improved) according to the global evaluation scores based on an ordinal scale from 1 to 6 (cleared to exacerbated).

In general, mometasone (0.1% lotion, ointment or cream applied once or twice daily) was significantly superior to topical glucocorticoid preparations of similar and weaker potency (table VI). The ointment formulation of mometasone was significantly superior to once-daily hydrocortisone 1.0% ointment,[30,45] twice-daily betamethasone valerate 0.1% ointment,[60,62] triamcinolone acetonide 0.1% ointment,[61] fluticasone propionate 0.005% ointment[64] and 3 times daily fluocinolone acetonide 0.025% ointment (fig. 3).[61] The once-daily application of mometasone 0.1% ointment was as effective as twice-daily application of diflucortolone valerate 0.1% ointment.[63]

Alternate-day mometasone 0.1% ointment may be effective in maintenance therapy of psoriasis vulgaris. A randomised, double-blind, 3-week study in 48 adult patients with moderate psoriasis vulgaris evaluated the effects of alternate-day and once-daily application of mometasone 0.1% ointment. After 1 week (n = 48) of once-daily application of mometasone 0.1% ointment, patients either continued with daily application (n = 25) or applied mometasone 0.1% ointment on alternate days (n = 19) for 2 weeks. At the end of the study period both regimens were effective in treating disease signs and symptoms ($p < 0.01$ *vs* baseline) with no detectable difference between them ($p > 0.05$).[65]

Mometasone cream was reported to be as effective as twice-daily application of triamcinolone acetonide 0.1% cream, but significantly superior to 3 times daily application of fluocinolone acetonide 0.025% cream (fig. 3b).[61] In patients with scalp psoriasis, the effects of mometasone lotion were significantly superior to those of twice-daily application of betamethasone valerate 0.1% lotion or triamcinolone acetonide 0.1% lotion.[58,59]

A study in 24 patients with moderate to severe psoriasis evaluated the response to mometasone

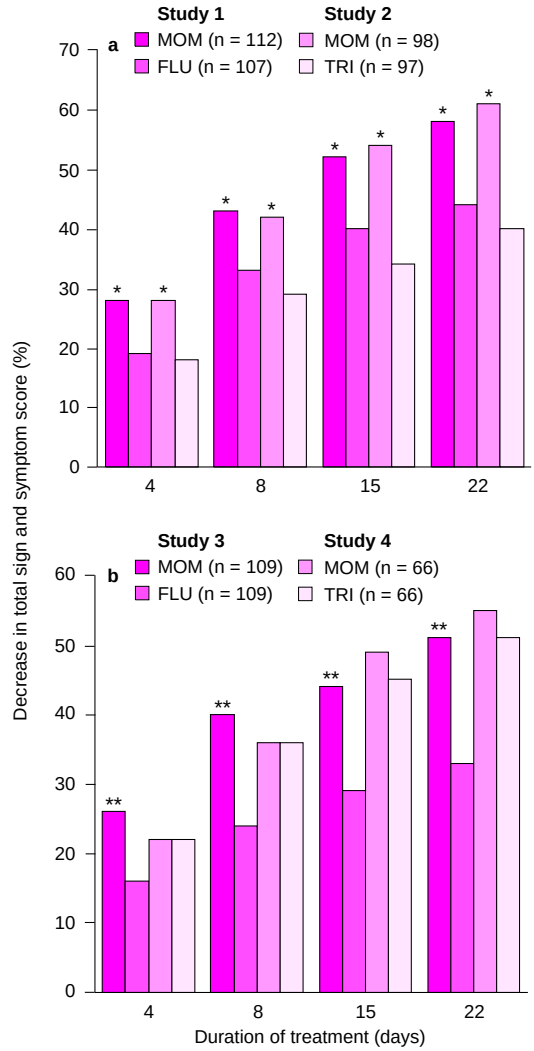

Fig. 3. Comparative efficacy of mometasome (MOM) ointment (**a**) and cream (**b**) in psoriasis. Effects of MOM 0.1% ointment or cream applied once daily versus those of flucinolone acetonide 0.025% (FLU) ointment or cream applied 3 times daily or triamcinolone acetonide 0.1% (TRI) ointment or cream applied twice daily in 4 studies in patients with moderate to severe psoriasis vulgaris. *Symbols:* * = $p < 0.01$; ** $p < 0.001$ *vs* comparator.

0.1% ointment applied once daily on the face and intertriginous areas (n = 15) and other affected body areas (n = 9).[66] At the start of therapy, both groups had similar severity of disease with a total disease severity score (values from graph) approx-

imately between 10.5 and 11. After 2 weeks, the face and intertriginous areas showed a quicker and significantly superior response to treatment as compared with other body areas (total disease severity score 1 *vs* 7, $p < 0.01$).[66]

2.4 Patients with Various Glucocorticoid-Sensitive Dermatoses

A number of studies have examined the efficacy of mometasone in patients with various glucocorticoid-responsive dermatoses. The majority of patients had atopic dermatitis, allergic contact dermatitis, seborrhoeic dermatitis, eczema or psoriasis. Other dermatoses, including neurodermatitis, endogenous eczema, discoid eczema, lichen planus, lichen simplex chronicus, guttate psoriasis, bullous pemphigoid, stasis dermatitis, superficial dermatitis, asteototic eczema and photodermatitis, were present in a few (1 to 4) patients.

Most trials were randomised, single-blind and compared the effects of mometasone 0.1% cream applied once daily with other topical glucocorticoids (table VII). Patients >15 years of age with a definite diagnosis of glucocorticoid-responsive dermatoses (i.e. lesions characterised by ≥3 of the following signs: erythema, induration, crusting, scaling or excoriation) were included. The severity of disease at a designated target area was scored according to an ordinal scale of 0 to 3 (none to severe) and efficacy was rated on a scale of 1 to 6 (cleared to exacerbated).

Mometasone 0.1% cream applied once daily displayed similar efficacy to other glucocorticoids with similar potency, such as methylprednisolone aceponate 0.1% cream applied once daily[67] and betamethasone valerate 0.1% cream[70,71] or betamethasone dipropionate 0.05% cream applied twice daily.[37] There were significant differences favouring mometasone 0.1% cream applied once daily for up to 3 weeks over other less potent glucocorticoids applied twice daily, such as hydrocortisone butyrate 0.1% cream[69] and clobetasone

Table VII. Comparative efficacy of mometasone versus other topical glucocorticoids in the treatment of various corticosteroid-responsive dermatoses. Summary of results from randomised, single-blind design trials. Unless stated otherwise, all studies were in patients≥15y of age and elderly patients were usually included

References	Diagnoses at entry (no. of patients)	Treatment × duration (wk)	No. of patients treated (evaluated)	Treatment outcome	
				mean decrease in target lesion score (%)	% of patients successfully treated[a]
Bianchi[67]b	ACD (57), ICD (58)	MOM 0.1% cr od × 15 days	58 (57)	85	84
		MPA 0.1% cr od × 15 days	57 (56)	82	76
Dominguez et al.[68]c	AD (46), SD (3), ACD (11), AP (1)	MOM 0.1% cr od × ≤3	31 (29)	91.9	93
		CLO 0.05% cr bid × ≤3	32 (32)	86.9	84
Gip et al.[69]	AD (205), SD (11)	MOM 0.1% cr od × ≤3	107 (107)	86*	89
		HYDB 0.1% cr bid × ≤3	109 (109)	77	69
Kelly et al.[37]	AD (10), SD (1), E (2), P (32), others (22)	MOM 0.1% cr od × ≤12	33 (22)	74.4	
		BMD 0.05% cr bid × ≤12	34 (30)	80.1	
Vigloglia et al.[70]	AD (18), SD (5), ACD (37), E (7), ND (2)	MOM 0.1% cr od × ≤3	39 (35)	93.6	
		BMV 0.1% cr bid × ≤3	38 (34)	96.5	
Wishart et al.[71]	AD (31), SD (3), ACD (2), E (15), P (6), NSD (1)	MOM 0.1% cr od × 4	29 (28)	93	89
		BMV 0.1% cr bid × 4	30 (30)	90	86

a Patients showing ≥ 75% improvement on physician's global evaluation score.

b Double-blind study.

c Study in children aged 6 to 12 years.

Abbreviations and symbols: ACD = allergic contact dermatitis; AD = atopic dermatitis; AP = actinic prurigo; bid = twice daily; BMD = betamethasone dipropionate; BMV = betamethasone valerate; CLO = clobetasone; cr = cream; E = eczema; HYDB = hydrocortisone butyrate; ICD = irritative contact dermatitis; MOM = mometasone; MPA = methylprednisolone aceponate; ND = neurodermatitis; NSD = nonspecific dermatitis; od = once daily; P = psoriasis; SD = seborrhoeic dermatitis; * $p < 0.01$ *vs* HYDB.

0.05% cream.[68] The end-point analysis indicated a significantly greater reduction in total disease sign/symptom scores in the mometasone group than in the hydrocortisone butyrate group (86 *vs* 77%; $p < 0.01$).[69] After 3 weeks, the reduction in induration severity score with mometasone was significantly superior ($p < 0.05$) to that achieved with clobetasone in a study in children (aged 6 to 12 years).[68]

3. Tolerability

Application of topical mometasone 0.1% cream in 319 adult and 74 paediatric patients was associated with local adverse effects in 1.6 and 7.0% of patients, respectively.[49] The adverse effects observed in studies reviewed in section 2 were usually transient, mild or mild to moderate, with an incidence that was either similar to or less than that observed with the comparator glucocorticoid.[34,35,52,57-61,67,72] Stinging, burning, pruritus, folliculitis, dryness, acneiform/erythematous eruptions, tenderness and signs of skin atrophy were the most frequently observed adverse events. The effects of mometasone on the HPA axis (section 1.2) and its atrophogenic potential (section 1.3) are discussed in previous sections. Uncommon local adverse effects reported in the manufacturer's product information are irritation, hypertrichosis, hypopigmentation, perioral dermatitis, allergic contact dermatitis, striae and miliaria. The manufacturers do not recommend the use of occlusive dressing with mometasone as it may increase the incidence of adverse effects.[49]

Preliminary clinical studies using patch tests have demonstrated negligible risk of primary sensitisation and cross-reactions with mometasone.[73-75] In a study designed to determine the frequency of positive reactions to mometasone among patients being routinely tested for contact allergy and those with known sensitivity to glucocorticoids, 40 of the 628 patients presented at least 1 positive patch-test reaction to the 14 glucocorticoids tested. However, none of them reacted to mometasone. Among another group of 38 glucocorticoid-sensitive patients, only 2 reacted to mometasone 0.5% in ethanol. However, both patients also reacted to ethanol alone.[73] Application of mometasone 1.0% in ethanol to 100 patients known to be allergic to glucocorticoids or suspected of glucocorticoid hypersensitivity, resulted in no positive reactions.[74] Patch testing in 15 female patients with glucocorticoid contact allergy also revealed no positive reactions to mometasone 1.0% in ethanol, although a 0.1% solution of the drug in ethanol elicited a positive reaction in 1 patient.[75]

Studies on cross-reaction patterns of glucocorticoids suggest that the C_{17} and/or C_{21} positions on the steroid ring are important.[76,77] Mometasone is chlorinated at position 21 and esterified with a cyclic furane ring at position 17. This could account for the lack of cross-reactions observed with mometasone.[73]

4. Dosage and Administration

Mometasone 0.1% cream, ointment or lotion is indicated for the relief of the inflammatory and pruritic symptoms of glucocorticoid-responsive dermatoses. A thin film of mometasone cream or ointment should be applied to the affected areas once daily. Mometasone lotion (a few drops) should be applied to the affected areas once daily, and massaged lightly until it disappears.[49] Like other glucocorticoids, mometasone should not be used for the treatment of acne, rosacea, perioral dermatitis, primary cutaneous viral, bacterial or fungal infections, or perianal or genital pruritus.

Paediatric patients may be more susceptible than adults to glucocorticoid-induced HPA axis suppression and skin atrophy, including striae. The tolerability and efficacy of mometasone treatment for periods >3 weeks have not been established in children; it is not recommended for children <2 years of age. Mometasone should not be applied with an occlusive dressing or in the diaper area of a child (if diapers or plastic pants are required), as these garments may increase the risk of adverse effects. Although the application of mometasone 0.1% ointment on the face and intertriginous areas has been evaluated,[66] use on the face, underarm,

or groin areas is not generally recommended.[49] Application of mometasone should be discontinued when control of symptoms is achieved or if no improvement is evident within 2 weeks.

5. Place of Mometasone in the Management of Dermatological Disorders

Both psoriasis and atopic dermatitis are common dermatological disorders with profound effects on patients, affecting their choice of occupation, leisure activities and dress and reducing their self-esteem. Personal and sexual relationships are also influenced by these diseases.[78]

Atopic dermatitis is a chronic inflammatory disease, the severity of which waxes and wanes with time. It usually manifests at an early age and is characterised by severe pruritus and a typical morphology and distribution of skin rash. One study found an increase in the prevalence of childhood atopic dermatitis from 5.1% in 1946 to 12.1% in 1970,[79] while another study in Taipei city found an increase from 1.43% in 1974 to 3.84% in 1991.[80] Although the disease tends to remit with time in 90% of cases, there are many adults with severe persisting chronic atopic dermatitis.[81]

Psoriasis is a chronic intractable skin disorder, usually of genetic origin, characterised by well demarcated scaly plaques which remit and relapse over time. Patients with psoriasis are usually treated with topical therapy such as glucocorticoids, dithranol, tar, vitamin D analogues or phototherapy (for review see Lebwohl et al.[82]). Systemic agents (e.g. immunosuppressive drugs such as methotrexate and cyclosporin) are reserved for patients with severe, refractory forms of the disease or those who are intolerant of other therapy.[83]

Treatment of patients with atopic dermatitis or psoriasis is aimed at containing the extent and reducing the severity of disease. Topical glucocorticoids are the most commonly used agents in these disorders. High potency glucocorticoids are associated with more local and systemic side effects than those with lower potency. However, research has focused on developing moderately to highly potent topical agents which show some dissociation between efficacy and risk of causing dermal atrophy or suppression of the HPA axis.

Mometasone is a potent topical agent with a chlorine-containing nucleus and a novel furoate ester side chain, which have both been suggested to confer high affinity for glucocorticoid receptors in the epidermis.[2] It is indicated for use in patients with atopic dermatitis, seborrhoeic dermatitis, psoriasis and other glucocorticoid-responsive dermatoses.

Cream and ointment formulations of mometasone demonstrated clinical efficacy in 3- to 6-week trials conducted in children and adults with moderate to severe atopic dermatitis. The results observed with mometasone were significantly superior to those observed with clobetasone, hydrocortisone, hydrocortisone butyrate and hydrocortisone valerate and similar to those observed with betamethasone dipropionate and methylprednisolone aceponate. In patients with seborrhoeic dermatitis, once-daily application of mometasone was as effective as ketoconazole applied twice weekly after 4 weeks, but exerted a quicker onset of action. Mometasone 0.1% cream was more effective than hydrocortisone 1.0% cream applied twice daily in the treatment of patients with seborrhoeic dermatitis. In most trials in patients with scalp psoriasis and psoriasis vulgaris, the efficacy of mometasone was significantly superior to that of most comparator glucocorticoids and similar to that of twice-daily triamcinolone acetonide and diflucortolone valerate.

Mometasone has been associated with few local adverse effects and little suppression of the HPA axis. The tolerability profile of mometasone was similar to that of other glucocorticoids with weaker and similar potency. It showed low potential for primary sensitisation or cross-reactivity in patch test studies and may prove to be an alternative for patients known to be sensitive to glucocorticoids. However, patch tests have a limited role in predicting the precise allergenic potential of any chemical and studies assessing the application of mometa-

sone over prolonged periods would be useful in defining the risk of primary sensitisation.

The once-daily mometasone regimen is likely to be more convenient and require less drug (by weight) than multiple daily administration regimens. This might result in improved compliance and lower treatment costs, particularly among patients requiring long term therapy. However, the cost-effectiveness of mometasone has not been assessed.

Clinical trials have shown topical mometasone to be an effective agent in the management of atopic dermatitis and seborrhoeic dermatitis. It is particularly effective in the treatment of patients with scalp psoriasis and psoriasis vulgaris. As yet, there are limited data comparing mometasone with other newer agents, such as fluticasone propionate (applied once or twice daily) or methylprednisolone aceponate (once daily) and its long term use has not been properly evaluated. Studies which address these issues would be valuable in attempting to position mometasone. Although patch test studies have found a low risk of primary sensitisation and cross-reactions with mometasone, data in patients are needed to confirm this potential advantage. Nevertheless, mometasone is an effective and well tolerated topical glucocorticoid which offers the advantage of once-daily administration.

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