

Once-daily mometasone furoate aqueous nasal spray (Nasonex™) in seasonal allergic rhinitis: an active- and placebo-controlled study

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Mometasone furoate aqueous nasal spray (Nasonex™) was compared with beclomethasone dipropionate (BDP) aqueous nasal spray in a double-blind, randomized, placebo-controlled, double-dummy, parallel-group study of adults with moderate to severe seasonal allergic rhinitis. Patients allergic to at least one tree and/or grass aeroallergen received one of the following regimens for up to 4 weeks: mometasone furoate 100 µg once daily [OD] ($n = 126$) or 200 µg OD ($n = 126$), BDP 200 µg twice daily ($n = 126$), or only placebo spray ($n = 123$). Physician-rated nasal and total symptom scores, and global evaluation of overall condition and therapeutic response by physicians and patients, showed that the three active treatments were equally effective, and all three were significantly superior to placebo at most time points. Overall, mometasone furoate 200 µg OD demonstrated somewhat greater numerical, but not statistical, superiority to mometasone furoate 100 µg OD at the earliest evaluation time point. At the end of treatment, complete or marked relief was obtained in 77% of patients with mometasone furoate 100 µg/day, 79% with mometasone furoate 200 µg/day, and 74% with BDP, compared with 54% of placebo vehicle control patients. Mometasone furoate and BDP were equally well tolerated. It was concluded that mometasone furoate adequately controls symptoms of moderate to severe seasonal allergic rhinitis, offers the advantage of OD treatment, and is well tolerated.

**J. R. Hebert¹, K. Nolop²,
B. N. Lutsky²**

¹Centre Hospitalier de l'Université Laval, Ste-Foy, Quebec, Canada; ²Schering-Plough Research Institute, Kenilworth, New Jersey, USA

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Jacques R. Hebert, MD
Department d'Immunologie
Centre Hospitalier de l'Université Laval
2705 boul Laurier
Bureau 9800, Ste-Foy
Quebec
Canada G1V 4G2

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Seasonal allergic rhinitis is a common condition, with an estimated prevalence reported by the International Rhinitis Management Working Group (1) of 6–19%. Susceptible patients experience a range of bothersome symptoms during pollen seasons, including nasal congestion, nasal itching, rhinorrhea, and sneezing. Nonnasal symptoms involving the eyes, throat, and palate may also be reported. The condition may have considerable negative impact on the patient's quality of life and can contribute to significant absenteeism from school and work (1).

Treatment strategies for seasonal allergic rhinitis are based on allergen avoidance and symptomatic drug therapy. Effective treatments include antihistamines, corticosteroids, and "mast-cell stabilizers",

such as cromoglycate (2). In recent years, topical nasal corticosteroids have been considered first-line therapy by many physicians (1, 3, 4). Controlled clinical trials have shown these agents to be well tolerated and especially effective against nasal symptoms of allergic rhinitis. The most widely used nasal corticosteroid is beclomethasone dipropionate (BDP, Beconase®), which is regarded as the standard comparator in controlled studies due to its well-documented clinical efficacy and safety profile (5–8).

Mometasone 17-furoate is a corticosteroid commercially available worldwide in a number of dermatologic formulations. It has been classified as a strong corticoid by EU guidelines. Clinical studies have demonstrated that, applied topically

to the skin, mometasone furoate has very low potential to cause systemic side-effects such as hypothalamic-pituitary-adrenal (HPA) axis suppression (9–12).

An aqueous suspension nasal spray formulation of mometasone furoate has recently been developed for use in acute and chronic rhinitis, based upon the prediction that this corticosteroid would be similarly devoid of potential for systemic activity when applied to the nose. In a recent clinical study, mometasone furoate applied to the nasal mucosa or administered orally, at doses up to 20 times the clinical dose, demonstrated no effect on plasma cortisol AUC, urinary free cortisol, and 8 a.m. plasma cortisol (13). Subsequent multicenter clinical trials have corroborated these findings (Schering-Plough Research Institute, unpublished data).

Moreover, administration of mometasone furoate to rodents and dogs results in exceedingly poor absorption via the oral route, and rapid and extensive metabolism (14). Oral bioavailability approaches zero. Over 30 different metabolites have been detected, many being moderately or highly polar; 6 β -hydroxylation is a major pathway for deactivation, but no single metabolite predominates (Schering-Plough Research Institute, unpublished data). The extensive and rapid metabolism of mometasone furoate to a multiplicity of metabolites and conjugates, via pathways known to deactivate other natural and synthetic corticosteroids (15–17), suggests that mometasone furoate should possess a desirable therapeutic ratio.

The present placebo-controlled study was designed to compare the efficacy and safety of two dose levels of mometasone furoate aqueous nasal spray, administered once daily, with that of placebo vehicle control nasal spray in the treatment of adults with seasonal allergic rhinitis and, secondarily, to compare mometasone furoate with BDP, which was administered in a b.i.d. dosing regimen.

Material and methods

Study design

This double-blind, randomized, placebo-controlled, double-dummy, parallel-group study was conducted at 19 centers across Canada and Europe during the spring and summer of 1993. The study protocol and statement of informed consent were approved by an institutional review board at each center. Written informed consent was obtained from each patient.

Patients eligible for inclusion were at least 18 years old, of either sex and any race, with a history of seasonal allergic rhinitis for at least 2 years and a positive skin test response to at least one aero-

allergen (i.e., tree and/or grass) relevant to each subject's participation in the study. Nasal and non-nasal symptoms were evaluated on a 4-point scale (Table 1) at the screening and baseline visits, which were held 2–7 days apart. At both screening and baseline, patients selected for the study had a combined nasal symptoms score of at least 6, and scores of at least 2 (moderate severity) for each of nasal congestion plus one other nasal symptom, with an overall disease rating of moderate or severe.

Patients were excluded from the study if they had asthma requiring therapy with inhaled or systemic corticosteroids, cromoglycate, or nedocromil; were known to be unresponsive to nasal corticosteroids; were dependent on systemic corticosteroids or nasal decongestants; had an allergy to corticosteroids; or had received potent corticosteroid treatment within the last month. Other exclusion criteria included chronic medication or a significant medical condition which could interfere with the study; asthenia or gross obesity; clinically relevant abnormal laboratory tests, vital signs, or electrocardiogram; patients on immunotherapy (unless on a stable regimen for at least 6 months); upper respiratory tract infection within the previous 4 weeks; use of any investigational drug within the previous 90 days; nasal polyps or significant nasal structural abnormality; or history of posterior subcapsular cataracts. Women who were pregnant, nursing, or at risk of pregnancy (in this study, women requiring birth control or of child-bearing potential) were also excluded.

At baseline (day 1), patients who met the entry criteria were randomly assigned to receive one of four treatments for 28 days: mometasone furoate aqueous nasal spray 100 or 200 μ g once daily in the morning, BDP aqueous nasal spray (Beconase) 200 μ g twice daily, or placebo vehicle control. Study medication was provided in metered, nasal pump spray bottles, providing 25 or 50 μ g/spray of mometasone furoate, 50 μ g/spray of BDP, or placebo vehicle control.

Since the mometasone furoate and BDP bottles differed in appearance, a double-dummy design was used to maintain blinding. Thus, subjects treated with mometasone furoate 100 or 200 μ g/day received, in the morning, two sprays per nostril of mometasone, 25 or 50 μ g/spray, plus two sprays per nostril of Beconase placebo and, in the evening, two sprays per nostril from each of mometasone and Beconase placebo bottles. Subjects in the BDP treatment arm received Beconase, two sprays per nostril, in the morning and again in the evening, plus mometasone placebo, two sprays per nostril, in the morning and evening. The placebo group was treated in the same fashion, using only the mometasone and BDP placebos in both the morning and

Table 1. Four-point scale used to evaluate severity of each nasal and nonnasal symptom of seasonal rhinitis*

Score	Description	
0	None	No signs or symptoms evident
1	Mild	Sign or symptom clearly present but minimal awareness; easily tolerated
2	Moderate	Definite awareness of sign or symptom which is bothersome but tolerable
3	Severe	Sign or symptom is hard to tolerate; causes interference with activities of daily living and/or sleeping

* Nasal symptoms: rhinorrhea, stuffiness/congestion, nasal itching, sneezing. Nonnasal symptoms: itching/burning eyes, tearing/watering eyes, redness of eyes, itching of ears or palate.

evening. Therefore, each subject received a total of 16 sprays per day; the sprays were to be administered randomly, with no waiting period between the two bottles in either the morning or the evening. The first dose of study medication was administered in the clinic under supervision of the physician or designee.

Loratadine 10-mg tablets were provided as rescue medication in case of intolerable symptoms, with a maximum permitted dosage of one tablet daily. Certain concomitant medications were restricted during the study, including corticosteroids (except for low-potency topical preparations such as hydrocortisone), mast-cell stabilizers, antihistamines (apart from rescue use of loratadine), decongestants, aspirin, nonsteroidal anti-inflammatory drugs, and systemic antibiotics. Efficacy and safety assessments were carried out on study days 4, 8, 15, 22, and 29.

Efficacy assessments

At each visit, the physician evaluated the severity of each nasal and nonnasal symptom by reviewing the patient’s diary for the appropriate time period, coupled with interview of the patient at the visit; the scoring scale in Table 1 was used throughout. Total nasal symptom score was defined as the combined total score of the four nasal symptoms. Total symptom score was defined as the combined total score for the four nasal and four nonnasal symptoms. Twice daily, after initiation of treatment, patients were asked to complete diary cards at home, on which they recorded the severity of each symptom, using the same scale as the one used by the physician. The physician and patient made a global evaluation of the overall condition of seasonal allergic rhinitis at each visit, using the same 4-point scale as was used for individual symptoms. At each visit, after initiation of treatment, the physician and patient made a global evaluation of response to treatment on a 5-point scale

(1 = complete relief, 2 = marked relief, 3 = moderate relief, 4 = slight relief, 5 = treatment failure). The physician was to refer to the patient’s diary cards in making all assessments.

Safety assessments

Details of all reported or observed adverse events were recorded throughout the study. The severity of each adverse event was graded as mild, moderate, or severe, and a relationship to treatment was assigned. At all visits, blood pressure, pulse, and body temperature were measured, and a routine (lamp and speculum) nasal examination was done by the physician. Clinical laboratory tests, urinalysis, an electrocardiogram, and a physical examination were carried out at screening and repeated at the end of the study.

Statistical methods

The primary efficacy variable was defined as the mean change in total nasal symptom score from baseline to day 8, as rated by the physician. An analysis of covariance was performed on the primary efficacy variable with baseline as a covariate; a repeated measures analysis was also performed. The remaining efficacy variables, including physician-evaluated individual nasal symptom scores and total symptom score, and physician and patient-evaluated overall condition and response to treatment, were analyzed by two-way analysis of variance. Run-in (prebaseline) patient diaries were not completed in this study; therefore, no analyses of diary data as change from baseline could be carried out. However, differences between active and placebo patients for each 15-day time period were calculated.

Results

Patients

A total of 501 patients was enrolled in the study: 497 patients were evaluated for safety (Table 2); four patients not evaluated did not receive any study medication. The efficacy analysis included 477 patients; the principal reasons for exclusion were insufficient medication, noncompliance, failure to meet entrance criteria, insufficient efficacy data, insufficient washout, and unacceptable concomitant medications. The treatment groups were comparable at baseline for demographic characteristics and symptom scores (Table 2). Most patients (mean of 78%) had moderate to severe seasonal allergic rhinitis, although the proportion with severe disease was slightly higher (28% compared

Table 2. Demographic data and baseline symptom scores for each treatment group (safety population)

	Treatment group			
	Mometasone 100 µg/day	Mometasone 200 µg/day	BDP 400 µg/day	Placebo vehicle control
Number of patients	126	125	125	121
Age (years)				
Mean	31	33	32	33
Range	18–67	18–73	18–71	18–67
Sex (n)				
M	117	115	111	112
F	9	10	14	9
Weight (kg)				
Mean	78	78	77	77
Range	48–121	54–116	48–103	49–111
Disease severity (%)				
Moderate	72	83	80	77
Severe	28	17	20	23
Mean total nasal symptom score ^a	8.1	8.1	7.9	8.0
Mean total symptom score ^b	12.7	12.2	12.4	12.8

^a Combined score of four nasal symptoms: score range 0 (no symptoms) to 12 (all symptoms severe).
^b Combined score of four nasal and four nonnasal symptoms: score range 0 (no symptoms) to 24 (all symptoms severe).

to 17–23%) in the mometasone furoate 100 µg/day group compared with the other treatment groups. Overall, 67/501 patients (13%) discontinued treatment before completing the study (Table 3). The proportion of patients discontinuing was greater in the placebo vehicle control group than in the active treatment groups, largely due to the number of treatment failures. Significantly more patients in the placebo group discontinued the study due to treatment failure than in the mometasone 200 µg or BDP groups ($P \leq 0.05$).

Physician-rated symptom scores

Total nasal symptom score improved in all groups during the treatment period. Mometasone furoate (100 and 200 µg/day) and BDP were significantly more effective than placebo vehicle control in reducing total nasal symptom score at all time points ($P \leq 0.01$), apart from the lower dose of mometasone furoate at day 4 (Fig. 1). Overall, the effects of mometasone furoate and BDP were similar. Mometasone furoate 200 µg/day was supe-

Table 3. Number (%) of patients who discontinued treatment (enrolled population)

Reason for discontinuation	Treatment group			
	Mometasone 100 µg/day (n = 126)	Mometasone 200 µg/day (n = 126)	BDP 400 µg/day (n = 126)	Placebo vehicle control (n = 123)
Treatment failure	9 (7%)	5 (4%)	4 (3%)	14 (11%)
Patient did not return	4 (3%)	4 (3%)	5 (4%)	5 (4%)
Adverse event	4 (3%)	5 (4%)	0	6 (5%)
Noncompliance	0	0	0	1 (1%)
Did not meet entry criteria	0	0	0	1 (1%)
Total	17 (13%)	14 (11%)	9 (7%)	27 (22%)

rior to BDP at day 15 ($P = 0.05$). At day 8, the mean improvements from baseline (decrease in total nasal symptom score) were 53%, 59%, and 59% for patients receiving mometasone furoate 100 µg/day, mometasone furoate 200 µg/day, and BDP, respectively, compared with a mean decrease of 34% in the placebo vehicle control group.

In general, all three active treatments were superior to placebo in relieving individual nasal symptoms (Table 4). At day 8, mean nasal stuffiness/congestion scores improved by 41–52% in patients receiving active treatment compared with a 28% improvement in placebo vehicle control patients ($P \leq 0.05$ for all active treatments compared with placebo). Similar results were seen for the other three nasal symptoms.

In a pattern similar to that seen for total nasal symptoms, all groups showed improvement in total symptom score over the treatment period. Mometasone furoate (100 and 200 µg/day) was significantly superior to placebo vehicle control in reducing total symptom score at all time points ($P < 0.05$), apart from day 4 when neither treatment was significantly different from placebo. BDP was significantly more effective than placebo vehicle control at all time points ($P \leq 0.02$). There were no significant differences between the two dose levels of mometasone furoate or between mometasone furoate 200 µg/day and BDP. BDP was superior to mometasone furoate 100 µg/day at day 4 ($P = 0.03$).

Global evaluation of overall condition

Physician-evaluated assessment of overall condition is shown in Fig. 2. According to the physician, at day 8, 66% and 71% of patients receiving mometasone furoate 100 µg/day and 200 µg/day,

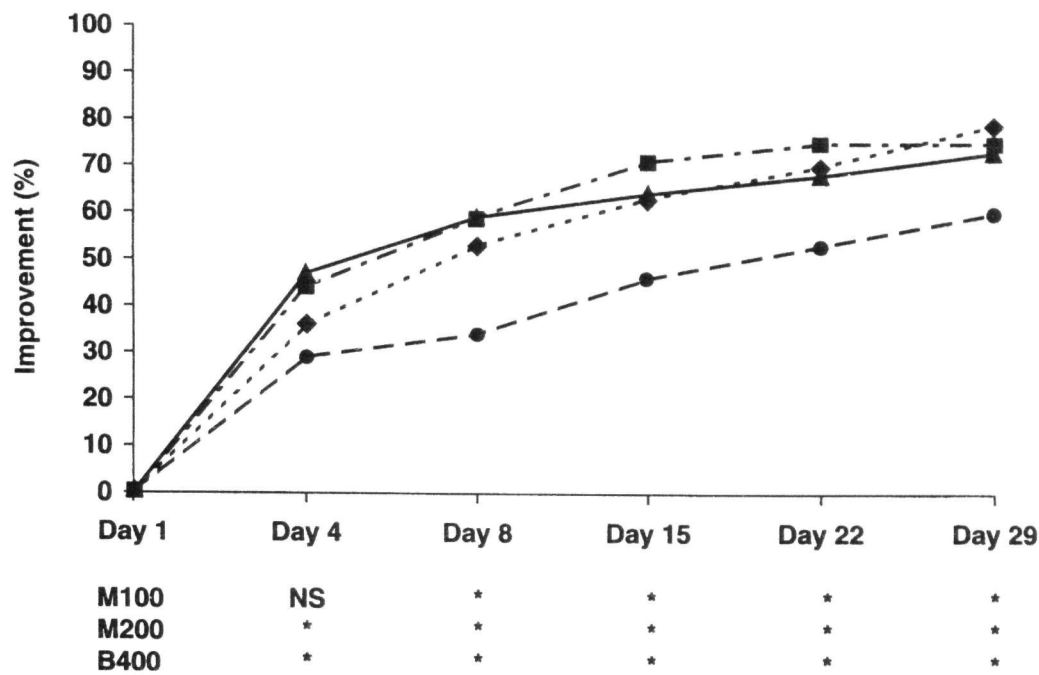


Fig. 1. Mean percentage improvement from baseline in total nasal symptom score evaluated by physician (efficacy population) for patients receiving mometasone 100 µg/day (M100; - - - ◆ - - -); mometasone 200 µg/day (M200; - - - ■ - - -); BDP 400 µg/day (B400; — — — ▲ — — —); or placebo vehicle control (- - - ● - - -). Combined total for four nasal symptoms (rhinorrhea, stuffiness/congestion, nasal itching, and sneezing). NS: not significant; * $P < 0.01$ compared with placebo vehicle control.

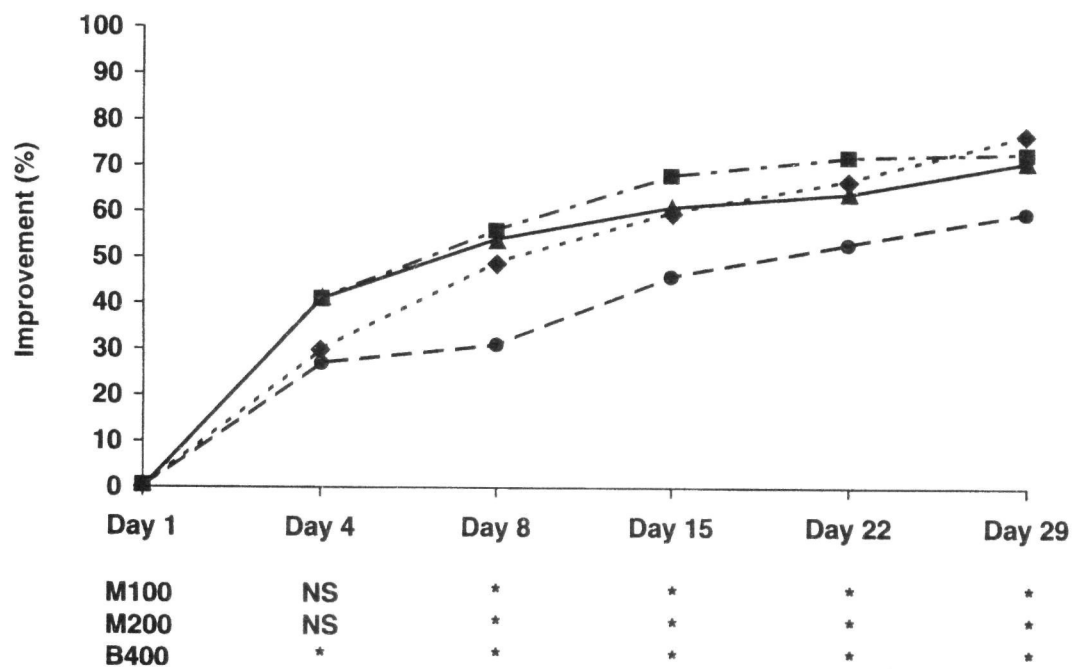


Fig. 2. Percentage of patients with no or mild symptoms evaluated by physician (efficacy population) for patients receiving mometasone 100 µg/day (M100; - - - ◆ - - -); mometasone 200 µg/day (M200; - - - ■ - - -); BDP 400 µg/day (B400; — — — ▲ — — —); or placebo vehicle control (- - - ● - - -). * $P < 0.05$ compared with placebo vehicle control.

respectively, had no or mild symptoms, compared with 75% of patients on BDP and 43% of placebo vehicle control patients. Inferences from patient-evaluated overall condition were very similar to those of the physician.

Physician-evaluated response to treatment

At the end of treatment (day 29), complete or marked relief was obtained in 77% of patients with mometasone furoate 100 mg/day, 79% with mometasone furoate 200 µg/day, and 74% with

BDP, compared with 54% of placebo vehicle control patients (Fig. 3). There were no significant differences between the mometasone furoate or BDP groups; all three active treatments were significantly superior to placebo vehicle control ($P \leq 0.01$). The patient's evaluation of therapeutic response essentially reflected that of the physician.

Use of rescue medication

Rescue medication (loratadine) was used during the study by significantly lower proportions of

Table 4. Mean percentage of improvement (change) from baseline in individual nasal symptom scores evaluated by physician (efficacy population)

		Mean improvement (change) from baseline (%)			
Symptom	Time point	Mometasone 100 µg/day	Mometasone 200 µg/day	BDP 400 µg/day	Placebo vehicle control
Rhinorrhea	Day 4	32	44**	47*	30
	Day 8	51*	55*	58*	26
	End point ^a	71*	75*	73*	49
Nasal stuffiness/ congestion	Day 4	27	36	43*	27
	Day 8	41*	352*	45*	28
	End point ^a	62*	67*	61*	45
Nasal itching	Day 4	35	38	41*	23
	Day 8	56*	59*	58*	31
	End point ^a	76*	77*	74*	52
Sneezing	Day 4	45*	49*	52*	20
	Day 8	63*	64*	71*	32
	End point ^a	80*	77*	80*	58

* $P \leq 0.01$ relative to placebo vehicle control group.
** $P \leq 0.05$ relative to placebo vehicle control group.
^a End point = last valid visit for each patient.

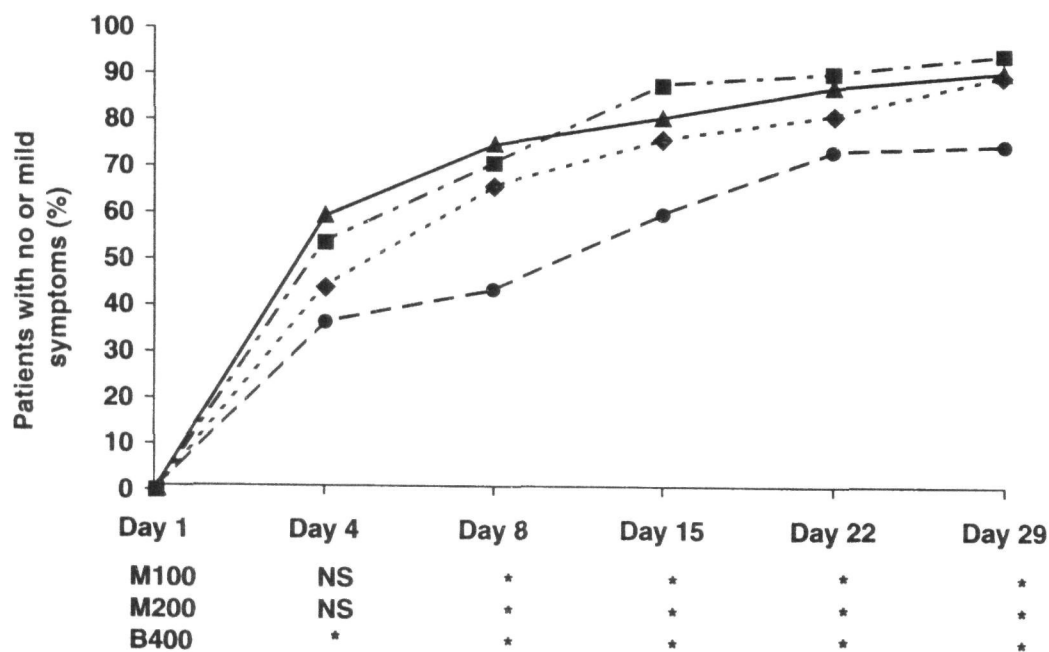


Fig. 3. Global evaluation of response to treatment by physician (efficacy population): cumulative frequency distribution of response. (M100; - - - ◆ - - -); mometasone 200 µg/day (M200; - - ■ - -); BDP 400 µg/day (B400; —▲—); or placebo vehicle control (- - - ● - -). * $P \leq 0.01$ active treatments compared with placebo vehicle control, percentage of patients with complete or marked relief.

patients in the active treatment groups than in the placebo vehicle control group (41% for mometasone furoate 100 µg/day, 34% for mometasone furoate 200 µg/day, and 35% for BDP, compared with 55% for placebo vehicle control; $P \leq 0.05$). There were no statistically significant differences between the active treatment groups in the use of rescue medication.

Patient diaries

Mean total nasal symptom scores recorded in patient diaries showed that all three active treatments were significantly ($P \leq 0.01$) more effective than placebo vehicle control throughout the study (Table 5). None of the active treatments differed from one another.

Table 5. Mean total nasal symptom scores from patient diaries (efficacy population)

	Treatment group							
	Mometasone 100 µg/day		Mometasone 200 µg/day		BDP 400 µg/day		Placebo vehicle control	
	<i>n</i>	mean	<i>n</i>	mean	<i>n</i>	mean	<i>n</i>	mean
Days 1–15	122	3.8*	122	3.4*	122	3.3*	110	5.2
Days 16–30	109	2.3*	112	2.0*	112	2.2*	98	3.6

Change from baseline score was not calculated due to inadequate baseline diary data (run-in diaries were not used). Means are adjusted for any rescue medication taken during study.
* $P \leq 0.01$ from placebo vehicle control.

Safety assessments

Adverse events were reported by a similar proportion of patients in each of the four treatment groups. Overall, the most commonly reported adverse events were headache, epistaxis, nasal burning, and pharyngitis. Most of the adverse events were of mild to moderate severity and of a short duration. Adverse events considered at least possibly related to treatment were reported by 25% of patients with mometasone furoate 100 µg/day, 26% with mometasone furoate 200 µg/day, 30% with BDP, and 28% with placebo vehicle control (Table 6); the same adverse events predominated. There were no clinically relevant changes in vital signs, electrocardiogram, or laboratory test results in any of the treatment groups.

Discussion

This study showed that mometasone furoate aqueous nasal spray, administered at a dosage of 100 or 200 µg once daily in the morning, was effective in relieving moderate to severe symptoms of seasonal allergic rhinitis in adults. Mometasone furoate 200 µg/day significantly ($P \leq 0.05$) improved individual nasal symptoms of congestion, rhinorrhea, sneezing, and nasal itch, compared with the placebo vehicle control group, at all time points except day 4 stuffiness and itch. The responses for mometasone 100 µg/day compared with placebo were very similar (Table 5); no statistical differences between the two mometasone doses were detected.

Progressive improvement was seen in the overall severity of the condition, as evaluated by both physicians and patients. Although placebo vehicle control patients showed some improvement in symptoms, as has been observed in other studies of similar design (18, 19), mometasone furoate was statistically significantly superior to placebo

Table 6. Adverse events reported as treatment-related^a during study by ≥4% patients (number and percentage) in any treatment group (safety population)

	Treatment group							
	Mometasone 100 µg/day (<i>n</i> = 126)		Mometasone 200 µg/day (<i>n</i> = 125)		BDP 400 µg/day (<i>n</i> = 125)		Placebo vehicle control (<i>n</i> = 121)	
Any adverse event	32	(25)	32	(26)	38	(30)	34	(28)
Headache	10	(8)	12	(10)	10	(8)	8	(7)
Epistaxis	4	(3)	8	(6)	6	(5)	4	(3)
Nasal burning	8	(6)	4	(3)	5	(4)	6	(5)
Pharyngitis	4	(3)	3	(2)	5	(4)	5	(4)
Sneezing	3	(2)	1	(<1)	5	(4)	6	(5)

^a Reported in at least 4% of patients in any treatment group; relationship possibly, probably, or definitely related to treatment.

throughout the study. At the end of the 4-week treatment period, fully 77–79% of patients who received mometasone furoate had obtained complete or marked symptomatic relief; i.e., had demonstrated clinically significant therapeutic response to treatment.

The active comparator in this study, BDP aqueous nasal spray, has well-documented clinical efficacy in patients with seasonal allergic rhinitis (5–8). In this study, mometasone furoate demonstrated comparable efficacy to BDP in terms of symptomatic relief. In general, there were no important differences between mometasone furoate and BDP in evaluations made by the physician (nasal and total symptom scores, overall condition [global assessment], response to treatment) or by the patient (global assessment, therapeutic response, symptom scores recorded in patient diaries). Taken together, these results suggest that mometasone furoate aqueous nasal spray, 100 or 200 µg administered once daily, is therapeutically equivalent to BDP aqueous nasal spray 200 µg administered twice daily. Mometasone furoate offers the benefit of once-daily dosing, and it is conceivable that simplification of the dosage regimen may enhance patient compliance.

Mometasone furoate and BDP were equally well tolerated in this study. The incidence and types of adverse events reported with each of the active treatments were similar to those observed in patients who received only placebo vehicle control. The incidence of adverse events (any adverse event, whether or not thought to be related to treatment) ranged from 41% to 46%; most of the reported symptoms were transient and of mild or moderate severity. Overall, only 15/501 patients (3%) discontinued treatment because of adverse events. Local reactions (e.g., nasal burning or stinging) are commonly associated with the administration of nasal

sprays in patients with rhinitis (7), but were seen infrequently in this study.

In conclusion, mometasone furoate aqueous nasal spray, administered at a dosage of 100 or 200 µg once daily, was significantly more effective than placebo vehicle control in relieving symptoms in adults with seasonal allergic rhinitis. Mometasone furoate had comparable efficacy to BDP aqueous nasal spray 200 µg twice daily and was equally well tolerated. These results suggest that mometasone furoate, which offers the convenience of once-daily dosing, should be an effective and well-tolerated alternative to corticosteroids labeled for twice-daily dosing, for treatment of seasonal allergic rhinitis in adults with moderate to severe symptoms.

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References

1. International Rhinitis Management Working Group. International consensus report on the diagnosis and management of rhinitis. *Eur J Allergy Clin Immunol* 1994;49 Suppl 19:1-34.
2. Horak F. Seasonal allergic rhinitis. Newer treatment approaches. *Drugs* 1993;45:518-27.
3. Meltzer EO. Treating allergic rhinitis. Overview and update. *Am J Asthma Allergy Pediatrician* 1992;6:13-17.
4. Mygind N. Glucocorticosteroids and rhinitis. *Allergy* 1993;48:476-90.
5. Delafuente JC, Davis TA, Davis JA. Pharmacotherapy of allergic rhinitis. *Clin Pharm* 1989;8:474-85.
6. Orgel HA, Meltzer EO, Kemp JP, Welch MJ. Clinical, rhinomanometric and cytologic evaluation of seasonal allergic rhinitis treated with beclomethasone dipropionate as aqueous nasal spray or pressurized aerosol. *J Allergy Clin Immunol* 1986;77:858-64.
7. Siegel SC. Topical intranasal corticosteroid therapy in rhinitis. *J Allergy Clin Immunol* 1988;81:984-91.
8. Siegel SC, Katz RM, Rachelefsky GS, et al. Multicentric study of beclomethasone dipropionate nasal aerosol in adults with seasonal allergic rhinitis. *J Allergy Clin Immunol* 1982;69:345-53.
9. Gip L, Lindberg L, Nordin P, Edwin AP. Clinical study of mometasone furoate cream 0.1% compared with hydrocortisone butyrate cream 0.1% in treatment of atopic and seborrheic dermatitis. *Today Ther Trends* 1988;5:21-34.
10. Medansky RS, Bressinck R, Cole GW. Mometasone furoate ointment and cream 0.1 percent in treatment of psoriasis: comparison with ointment and cream formulations of fluocinolone acetonide 0.025 percent and triamcinolone acetonide 0.1 percent. *Cutis* 1988;42:480-5.
11. Rosenthal D, Duke E. A clinical investigation of the efficacy and safety of mometasone furoate ointment 0.1% vs betamethasone valerate ointment 0.1% in the treatment of psoriasis. *Curr Ther Res* 1988;44:790-8.
12. Vernon HJ, Lane AT, Weston W. Comparison of mometasone furoate 0.1% cream and hydrocortisone 1.0% cream in treatment of childhood atopic dermatitis. *J Am Acad Dermatol* 1991;24:603-4.
13. Brannan MD, Seiberling M, Cutler DL, Cuss FM, Affrime MB. Lack of systemic activity with intranasal mometasone furoate. *J Allergy Clin Immunol* 1996;97:198.
14. Wirth MA, Nagabhushan N, Laudicina DC, Patrick J, Cayen M. Disposition of radiolabeled mometasone furoate in the mouse, rat and dog after oral and intravenous administration. *ISSX Proc* 1995;8:275.
15. Cope CL. Metabolic breakdown. In: Cope CL, editor. *Adrenal steroids and disease*. 2nd ed. Philadelphia: Lippincott, 1972.
16. Dorfman RJ, Ungar F. *Metabolism of steroid hormones*. New York: Academic Press, 1965.
17. Gerhards E, Nieuweboer B, Schulz G, Gibian H. Metabolism of flucortolon in man. *Acta Endocrinol* 1971;68:98-126.
18. Laforce CF, Dockhorn RJ, Findlay SR, et al. Fluticasone propionate: an effective alternative treatment for seasonal allergic rhinitis in adults and adolescents. *J Fam Pract* 1994;38:145-52.
19. van As A, Bronsky EA, Dockhorn RJ, et al. Once daily fluticasone propionate is as effective for perennial allergic rhinitis as twice daily beclomethasone dipropionate. *J Allergy Clin Immunol* 1993;91:1146-54.

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