Once daily mometasone furoate aqueous nasal spray is as effective as twice daily beclomethasone dipropionate for treating perennial allergic rhinitis patients

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Background: Perennial allergic rhinitis is chronic and persistent, may lead to a constellation of secondary complaints including sinusitis, mouth-breathing, and some symptoms resembling a permanent cold, and often requires constant medical intervention. Well-tolerated nasal corticosteroids, alone or in combination with antihistamines, have been found to be very effective in treating this condition.

Objective: To compare the effectiveness and tolerability of mometasone furoate aqueous suspension, a new once daily nasal spray, to placebo vehicle and to beclomethasone dipropionate, administered twice daily, in patients with perennial allergic rhinitis.

Methods: This was a randomized, double-blind, placebo-controlled, double-dummy, parallel group study, in 427 patients age 12 years and older at 24 centers in Canada and Europe. Patients allergic to at least one perennial allergen, confirmed by medical history, skin testing, and adequate symptomatology were eligible to receive one of the following regimens for 3 months: mometasone furoate, 200 μg once daily; beclomethasone dipropionate, 200 μg twice daily (400 μg total dose); or placebo vehicle control. The primary efficacy variable was the change from baseline in total AM plus PM diary nasal symptom score over the first 15 days of treatment.

Results: Three hundred eighty-seven patients were valid for efficacy. For the primary efficacy variable, mometasone furoate was significantly ($P \leq .01$) more effective than placebo and was indistinguishable from beclomethasone dipropionate. Similar trends were seen among individual symptoms, physician symptom evaluations, and therapeutic response. There was no evidence of tachyphylaxis. All treatments were well tolerated.

Conclusions: Mometasone furoate nasal spray adequately controls symptoms of perennial allergic rhinitis, offers the advantage of once daily treatment, and is well tolerated.

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INTRODUCTION

Allergic inflammation of the nasal mucosa has been estimated to occur chronically or recurrently in up to 10% of the population, making it the most common of rhinitic diseases.[1,2] The subset of individuals presenting with chronic symptoms due to exposure to perennial allergens such as dust mites, molds, mammals, and cockroach are said to suffer from perennial allergic rhinitis.[1] The disease is characterized by chronic nasal symptoms of congestion, rhinorrhea (including postnasal drip), sneezing, and nasal itching; these may be continuous or intermittent, present separately or together. Eye itching is less frequently a problem.[3]

The cardinal feature of patients with chronic symptoms is an inflammatory response in the nasal epithelium and submucosa, including an infiltrate of mast cells, eosinophils, basophils, T lymphocytes, and macrophages.[3–5] The intensity and persistence of the inflam-

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matory response explains why prolonged treatment with nasal corticosteroids is frequently required to control symptoms[3]; intranasal corticosteroid preparations alone or in combination with antihistamines are generally considered as a mainstay of treatment for patients with chronic rhinitis.[3,6] Nevertheless, chronic disease is more difficult to treat than simple hay fever; Tarlo et al previously reported[7] that only 54% of patients with perennial rhinitis achieved acceptable symptomatic improvement from intranasal corticoid treatment, suggesting that safe but more potent medications are still needed.

The most widely used nasal corticosteroid is beclomethasone dipropionate, which is regarded as the standard comparator in controlled studies due to its well documented clinical efficacy and safety profile.[5,8–10] Currently used corticosteroids may be absorbed through the gastrointestinal tract to a greater or lesser extent, and may not undergo rapid and complete biodeactivation, which can increase the risk of systemic effects; this may be particularly important in patients with allergic rhinitis who are chronically treated with higher doses of inhaled corticosteroids for asthma, or with potent topical corticosteroids for severe dermal conditions.[11,12] Clearly, there is a need for potent intranasal and inhaled corticosteroids with a reduced or absence of potential for systemic effects.

Mometasone 17-furoate is a corticosteroid that is commercially available worldwide in a number of dermatologic formulations. It has been classified as a strong corticoid by EUC guidelines. Clinical studies have demonstrated that when applied topically to the skin, mometasone furoate has very low potential to cause systemic side effects such as hypothalamic-pituitary-adrenal (HPA) axis suppression.[13–16]

An aqueous suspension nasal spray formulation of mometasone furoate has been developed recently for use in acute and chronic rhinitis, based upon the assumption that this corticosteroid would be similarly devoid of systemic potential when applied to the nose. In recent clinical studies, mometasone furoate applied to the nasal mucosa or administered orally, at doses up to 20 times the clinical dose, demonstrates no effect on plasma cortisol AUC, urinary free cortisol, and 8 AM plasma cortisol.[17] Further, mometasone furoate is poorly absorbed following oral administration and is rapidly and extensively metabolized following intravenous or oral administration. Furthermore, mometasone furoate has the advantage of once daily dosing, which may improve patient compliance over corticosteroids requiring more frequent dosing.

The objective of this study was to compare the effectiveness and tolerability in patients with moderate to severe symptoms of perennial allergic rhinitis, of mometasone furoate aqueous nasal spray (200 μg once daily) to placebo, and to beclomethasone dipropionate (200 μg twice daily) when patients were treated for up to 3 months.

MATERIALS AND METHODS

Patients

Adults and adolescents (individuals at least 12 years of age) were eligible to participate who presented with at least a 2-year history of moderate to severe perennial allergic rhinitis sufficient to warrant chronic use of intranasal corticoids to control symptoms, and who demonstrated sufficient symptoms of active disease at both screening and baseline visits. If skin testing had not been conducted within the last 2 years, the patient's hypersensitivity to at least one perennial allergen to which he or she had had continuous exposure was confirmed by a positive skin test. Wheals induced by skin prick or intradermal injection must have been $\geq$3mm or $\geq$7mm, respectively, larger than diluent control.

Patients were excluded who were expected to have a clinically significant exacerbation of symptoms due to seasonal aeroallergens by history and skin testing, at any time over the course of this study. Females were postmenopausal, surgically sterilized or, if of childbearing potential, were using a medically acceptable form of birth control for at least 3 months prior to screening; no female was pregnant, breast feeding, or premenarchal. Patients were subject to exclusion on the basis of a number of criteria, including requirement for treatment with inhaled or systemic corticosteroids, upper respiratory tract or sinus infection requiring antibiotic therapy within the previous 2 weeks, dependency upon decongestants, history or evidence of posterior subcapsular cataracts, or any significant disorder that could interfere with the study or require treatment that could interfere with the study. Patients were also excluded who, prior to screening received nasal or ocular corticoids within 2 weeks, inhaled, oral, or intravenous corticoids within 1 month, intramuscular or intra-articular corticoids within 3 months, or high potency topical corticoids within one month of initiation of the study.

STUDY DESIGN

This was a randomized, double-blind, placebo-controlled, double-dummy, parallel group design study carried out at 24 centers in Europe and Canada. The study was conducted in accord with the Declaration of Helsinki. The investigators agreed to comply with US Federal Regulations concerning written informed consent and the rights of human subjects, as outlined in 21 CFR 50. Prior to study initiation the protocol and amendments, and site-specific consent forms, were approved by The European Ethical Review Committee for all centers; relevant documents were also approved by individual institutional review boards governing activities at each center and by the Canadian Health Protection Branch (HPB) for centers in Canada. Written informed consent was obtained from all patients (or from the patient and parent/guardian for patients younger than 18 years of age).

Patients attended the research center for seven visits: Pretreatment screening and baseline visits, and assessments after 1, 2, 4, 8, and 12 weeks of

treatment. Patients were screened by medical history, general physical examination, vital signs, electrocardiogram, routine clinical laboratory tests including pregnancy test for all potential female subjects, nasal examination, and nasal/non-nasal symptoms assessment. In order to qualify for randomization into the study, a patient must have demonstrated at least moderate (score of 2 on a 4-point scale of 0 to 3, none to severe) rhinorrhea and/or congestion, and a total nasal symptoms score (sum of scores for rhinorrhea, congestion, sneezing, and nasal itching) of at least 5, at both screening and baseline visits, as rated by the physicians. Patients were provided with loratadine, 10 mg once daily, as rescue medication for treatment of intolerable symptoms. Usage of rescue medication was recorded on a separate diary card.

In addition, patients kept individual daily symptom and rescue medication usage diaries between the screening and baseline visits. In order to qualify for the study, patients were required to demonstrate at least moderate nasal rhinorrhea and/or congestion (diary scores of at least 2), for four of the last seven days just prior to the baseline visit.

At the baseline visit, qualified patients were assigned to one of three double-blind treatment groups by a computer-generated random code: mometasone furoate, 200 μg once daily in the morning; beclomethasone dipropionate, 200 μg twice daily, in the morning, and in the evening (total daily dose of 400 μg); or placebo. Four hundred micrograms of beclomethasone dipropionate is the usual daily dose outside the United States. The placebo nasal sprays were formulated as the vehicle without active ingredients. Each active comparator and its corresponding placebo formulation was indistinguishable in appearance, smell, and taste; however, the mometasone furoate and beclomethasone dipropionate bottles were of different appearance, hence the double-dummy design.

At randomization and at monthly intervals thereafter, patients were provided with four bottles, two labeled for morning use and two labeled for evening use. Patients in the mometasone furoate group administered two sprays per nostril of mometasone furoate and two sprays of beclomethasone dipropionate placebo in the morning, and two sprays per nostril of each placebo in the evening. Patients in the beclomethasone dipropionate group administered two sprays per nostril in the AM and in the PM from each of the beclomethasone dipropionate active and mometasone furoate placebo bottles. Patients in the placebo group administered two sprays per nostril of each of the two placebos in the morning and again in the evening. Each patient therefore received a total of 16 sprays per day. The order of spray with regards to the AM and PM treatment bottles was random. In addition, loratadine (10-mg) tablets were distributed for use once daily, as needed for relief of intolerable rhinitis symptoms. Compliance regarding use of all study medications was monitored throughout the study by tablet and bottle count, examination of spray bottles to confirm use, and thorough review of records of use kept in diaries and case report forms. Patients were questioned at every visit to ensure compliance with the protocol and use of study medications.

Patients were trained in the use of daily diaries, in which they were to record, twice daily in the morning and evening, their nasal symptoms (sneezing, rhinorrhea, nasal itch, and congestion) and non-nasal symptoms (ocular itch/burning, tearing/watering, or redness, and ear/palate itch) on the same scale of 0 to 3 as used by physicians. All diary entries were to be made before dosing. Patients requiring the use of loratadine as rescue medication were to record time of dosing, primary reason for use, and symptoms rating just prior to loratadine use, in a separate rescue medications diary.

EFFICACY EVALUATIONS

In addition to diary assessments, at each visit to the clinic the physician assessed the patient's nasal and non-nasal symptoms and evaluated the presence or severity of each symptom on the same 4-point scale as was used for the diaries. The scores were combined to yield a total nasal symptom score, and a total symptom score which reflected the overall condition of rhinitis. Both the patient and the investigator also assessed the patient's overall response to therapy, based upon the investigator's observations at the time of each visit, as well as the patient's diary entries. The overall response to therapy was assessed on a global assessment scale of 1 (excellent) to 5 (treatment failure).

The primary efficacy comparison was the comparison of mometasone furoate to placebo with respect to the primary efficacy variable, which was the patient's average change from baseline in total AM plus PM diary nasal symptom score over the first 15 days of treatment. Secondary efficacy variables consisted of total diary nasal symptom scores averaged over 15-day intervals beyond day 15. Supplementary efficacy variables included all other composite total and individual diary symptom scores, physician-evaluated perennial rhinitis symptoms, as well as physician and patient evaluations of therapeutic response. Pairwise comparisons between beclomethasone dipropionate and placebo, and between beclomethasone dipropionate and mometasone furoate were also conducted. Efficacy data in this report are derived from the valid-for-efficacy population.

SAFETY EVALUATIONS

Routine safety laboratory tests, urinalysis, pregnancy test (for all female subjects) and electrocardiogram were carried out at screening and at week 12, or at the patient's final visit. Vital signs, body weight, and use of any concomitant medications were recorded at each visit. Adverse events were solicited at each treatment visit and the date, time of onset, and duration were recorded for each event. The severity of each adverse event was defined as mild (did not cause patient any real problem), moderate (was a problem to the patient but did not interfere significantly with daily activities or the clinical status of the patient) or severe

(caused significant interference with normal daily activities or the clinical status of the patient). The investigator assigned each adverse event as unrelated, possibly, probably or related to the study drug.

STATISTICAL ANALYSIS

With a sample size of 125 patients per treatment group, an alpha-level of 0.05, differences of approximately 0.41 standardized units among treatment means were calculated to be detectable with a power of 90% (derived from in-house studies of similar design). That is, with a pooled standard deviation of 3.5 points on change from baseline in total nasal symptom score, differences of approximately 1.43 points or more would be detectable with a power of 90%. A change from baseline of this magnitude was considered clinically significant.

The presence of a treatment effect with respect to the primary efficacy variable, average change in total nasal symptom score over the initial 15-day study period using diary entries, was tabulated and analyzed using a two-way analysis of variance model with terms for treatment, investigator, and treatment by investigator interaction.

Since the primary analysis was based upon daily symptom diary data, it was important to account for the effect of the use of rescue medication on diary symptom scores. As per the protocol, for patients who took loratadine as rescue medication between the screening and final visits, the last symptom score recorded in their rescue diary prior to using rescue medication was considered the valid score of the symptoms for the following 24-hour period. In the statistical analyses and summaries of results, the daily symptom diary scores that were recorded during the 24-hour period after the dose of rescue medication was taken were therefore replaced by the rescue diary scores recorded immediately prior to using the rescue medication.

In the analysis of other efficacy and safety parameters, raw means and changes from baseline were analyzed via two-way analysis of variance/covariance models with terms for treatment, investigator, and treatment by investigator interaction. Possible influence of baseline values on subsequent response was accounted for by its inclusion as a grouping factor or covariate, where appropriate (with non-null homogeneous slopes for treatments), in corresponding analyses of covariance. Discrete variables were analyzed using linear categorical models with similar terms via CATMOD, or by the Fisher's exact test.

The poolability of the multicentric data was evaluated by examining the demographic information, entry level nasal and total symptom score, and treatment by investigator interaction during the treatment period. The total nasal symptom scores were analyzed separately for each investigator to assess uniformity of results across centers. All other composite total and individual diary symptoms scores, physician-evaluated perennial rhinitis symptoms, and physician and patient evaluations of therapeutic response were analyzed using the same two-way ANOVA described for the primary analysis. Each comparison was performed at the .05 (two-sided) level of significance with no adjustment for multiple comparisons. Prior to unblinding the study, patients or individual patient visits not meeting conditions of compliance established prestudy were eliminated from efficacy evaluations (valid for efficacy population), except as intent-to-treat.

Adverse events and patient discontinuation were summarized and tabulated for the intent-to-treat population.

Table 1. Demographic Characteristics at Baseline (Safety Population)

Characteristic	Treatment Group		
	Mometasone Furoate	Beclomethasone Dipropionate	Placebo
Patients enrolled	143	146	138
Sex			
Male	88	73	72
Female	55	73	66
Age, yrs			
Mean (SD)	33 (12)	31 (10)	31 (11)
Range	13–65	12–58	12–67
Weight, kg			
Mean (SD)	74 (14)	71 (15)	72 (15)
Range	47–108	47–126	34–117
Duration of condition, yrs			
Mean (SD)	12 (10)	11 (8)	11 (8)
Range	2–60	2–52	2–36
Asthma			
With	34	27	26
Without	108	117	111
Seasonal allergic rhinitis			
With	69	66	74
Without	74	80	64
Total nasal symptom score, mean (SD) (Investigator Evaluated)	7.1 (1.7)	7.1 (1.8)	7.0 (1.7)

RESULTS

Patient Disposition

A total of 427 patients was enrolled in the study. There were no significant differences in demographic characteristics among the three treatment groups, including physician-evaluated total nasal symptom score at baseline, which was approximately 7 out of a maximum possible score of 12. The mean duration of perennial allergic rhinitis among all patients was 11 years (Table 1). All of the enrolled patients valid for efficacy had a positive skin test reaction to at least one perennial allergen; individuals were usually sen-

Table 2. Number of Patients Who Discontinued the Study

Reason for Discontinuance	Treatment Group		
	Mometasone Furoate	Beclomethasone Dipropionate	Placebo
Adverse Event	8	6	2
Treatment Failure	15	14	26
Lost to Follow-up	4	4	6
Noncompliance	1	2	3
Did not meet entry criteria	4	3	2
Total	**32**	**29**	**39**

sitive to more than one allergen (household dust, unspecified, 100 patients; specific dust mite, 368 patients; molds, 217 patients; household pets, 247 patients; other, 32 patients).

Of the 427 patients enrolled, 387 patients (129 in the mometasone furoate group, 134 in the beclomethasone dipropionate group, and 124 in the placebo group) were included in the efficacy population (Table 2); reasons for exclusion from analysis for efficacy included premature withdrawal due to treatment failure, an adverse event, noncompliance, failure to meet entrance criteria, or individuals lost to follow-up (Table 2). Certain patient visits were also invalidated, primarily due to intercurrent illness, improper use of non-study medications, and improper visit spacing.

A total of 328 patients (77%) completed the entire 12 week study; 111 were in the mometasone furoate group, 116 patients were in the beclomethasone dipropionate group, and 101 were in the placebo group. Fifty-five patients withdrew early due to treatment failure: 26 patients were in the placebo group, and 15 and 14 patients were in the mometasone furoate and beclomethasone dipropionate groups, respectively. A total of 16 individuals were withdrawn from the study due to adverse events, eight in the mometasone furoate group, six in the beclomethasone dipropionate group, and two in the placebo group.

Efficacy Evaluations

The mean diary total nasal symptom score at baseline was approximately 7 out of a maximum possible score of 12; however, 76 of the patients enrolled presented with severe rhinitis.

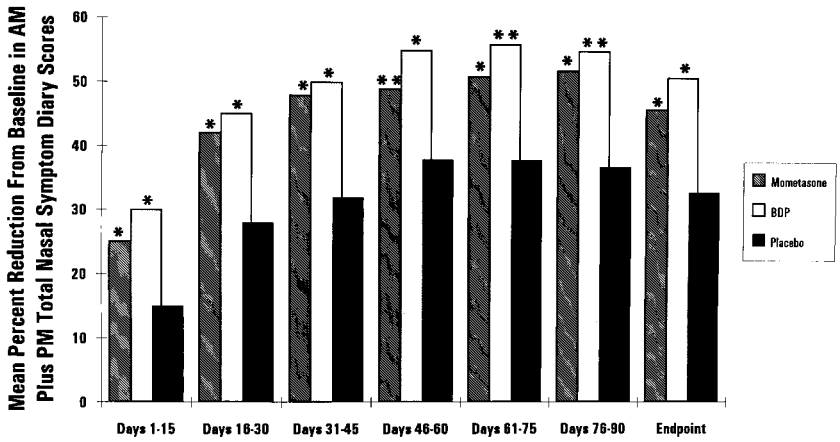

Figure 1. Patient-rated (from diaries) mean total nasal AM plus PM symptom score changes from baseline, averaged over 15-day intervals. Combined total of four nasal symptoms (rhinorrhea, congestion, sneezing, itch). Percent reductions from baseline are given in parentheses. * $P \leq .01$ relative to placebo vehicle control. ** $P \leq .03$ relative to placebo vehicle control.

The mean percent reductions from baseline in total combined AM plus PM diary nasal symptom score ranged, for each 15-day period of treatment, from 25% to 52% for the mometasone furoate treatment arm compared with 30% to 56% for the beclomethasone dipropionate group, and 15% to 38% for the placebo group.

For the primary efficacy variable, which was the average change from baseline in total (AM plus PM averaged scores) diary total nasal symptoms (congestion, rhinorrhea, sneezing, and itching) over the first 15 days, both the mometasone furoate and the beclomethasone dipropionate treatment groups produced a significantly ($P \leq .01$) greater improvement (reduction in severity scores) than the placebo group at all time periods (Fig 1). The difference between mometasone furoate and beclomethasone dipropionate treatment groups was not statistically different ($P \geq .32$) at any time point. Trends for the individual nasal symptom scores, as recorded on diary cards, generally followed the pattern seen for the total of the four symptoms, for most time points.

To assess whether once daily (morning) treatment with mometasone furoate would provide 24 hour coverage, patients were instructed to record symptoms each morning *before* taking study medication. Patients in both active treatment groups demonstrated significant improvement in morning nasal symptoms compared with the placebo-treated patients at all time periods (Fig 2). Mometasone furoate and beclomethasone dipropionate were indistinguishable in this regard. The reductions in AM scores were very nearly identical to PM diary scores.

In general, results for the physician-evaluated individual nasal symptoms and total nasal symptom scores at scheduled visits were consistent with patterns of improvement derived from patient diaries. The mean reduction from baseline in total nasal symptom score assessed by physicians at office visits (Fig 3) ranged from 34% to 58% for the mometasone furoate treatment group, 40% to 64% in the beclometha-

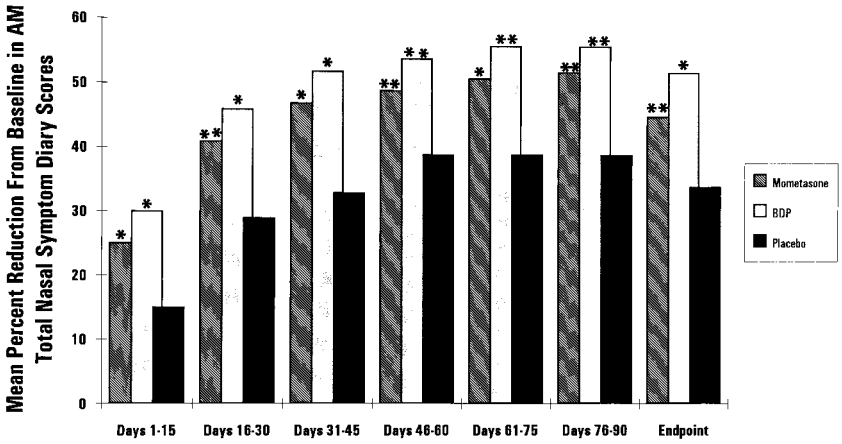

Figure 2. Patient-rated (from diaries) morning (AM) mean total nasal symptom score changes from baseline, averaged over 15-day intervals. Combined total of four nasal symptoms. Percent reductions from baseline are given in parentheses. * $P \leq .01$ relative to placebo vehicle control. ** $P \leq .03$ relative to placebo vehicle control.

sone dipropionate group, and 20% to 47% for the placebo group. The mometasone furoate response was statistically superior to placebo at visit days 8, 15, and week 12 while the beclomethasone dipropionate response was statistically greater than placebo at all visits. The beclomethasone dipropionate and mometasone furoate results, however, were not statistically different from each other at any time point. Individual nasal symptoms rated by the physician were similar to trends derived from diary scores.

Results of physician's evaluation of patient's response to treatment were very similar to results of symptoms evaluation. Patients treated with either mometasone furoate or beclomethasone dipropionate showed a more favorable response to treatment than did those receiving placebo. While numerical superiority to placebo for both active treatments was evident at each time period, statistical superiority was not always achieved. Mometasone furoate was statistically superior to placebo on days 8, 15, and week 12 ($P \leq .05$); beclomethasone dipropionate was superior to placebo on days 8, 15, and 29 ($P < .01$). Mometasone furoate and beclomethasone dipropionate were not statistically different from each other at any time point.

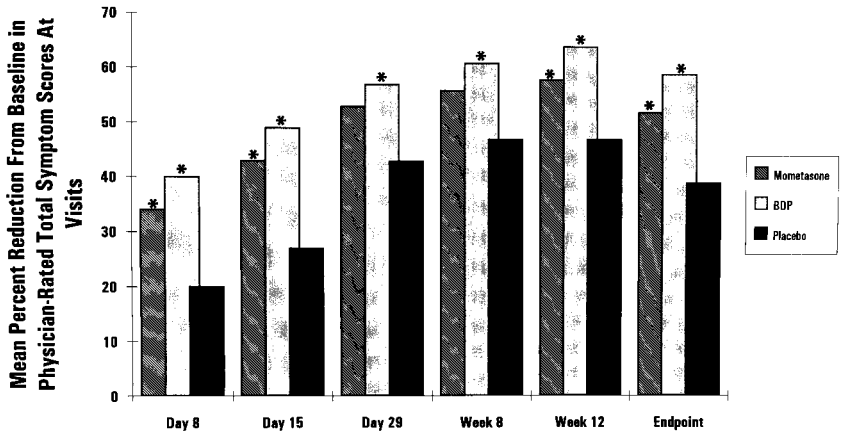

Figure 3. Physician-rated total nasal symptom score changes from baseline, at visits. Percent reductions from baseline are given in parentheses. * $P \leq .01$ relative to placebo vehicle control.

Similarly, expressed as numbers of patients demonstrating complete or marked relief of symptoms, mometasone furoate and beclomethasone dipropionate appeared similarly effective, especially at the later time periods (eg, 53% versus 53% at week 8 and 54% versus 53% at week 12 for mometasone furoate and beclomethasone dipropionate, respectively). In comparison, the highest percentage of placebo patients demonstrating complete or marked relief was 37% at the 1-month evaluation time point. The patient's evaluations of response to treatment showed trends similar to those of the physicians.

In this study, 50% of evaluable patients (192 of 387 total) used loratadine rescue medication at least once; the rates were 48%, 46%, and 56% for the mometasone furoate, beclomethasone dipropionate, and placebo groups, respectively. These differences were not statistically significant.

Safety Evaluations

A total of 427 patients were included in the safety population; three patients were excluded from any analysis as they dropped out immediately after enrollment, before receiving any study medication. Overall, safety data collected during the study indicated that all treatments were well tolerated.

The incidence of treatment-related adverse events was similar among the three groups (Table 3). Forty-three percent, 42%, and 36% of patients treated with mometasone furoate, beclomethasone dipropionate or placebo, respectively, reported an adverse event which was possibly, probably, or definitely related to study drug.

The most frequently reported adverse events with at least a possible relationship to study medication were epistaxis (nasal bleeding and/or blood in nasal secretions) followed by headache (Table 3). Twenty percent of patients receiving mometasone furoate reported epistaxis at least once compared with 23% and 11% in the beclomethasone dipropionate and placebo groups, respectively. Headache was reported by 10% of patients re-

Table 3. Number (Percent) of Patients with Adverse Events Reported as Treatment-Related.*

Adverse Event	Treatment Group		
	Mometasone Furoate	Beclomethasone Dipropionate	Placebo
All	59 (41)	62 (42)	49 (36)
Epistaxis/Blood in Nasal Discharge	27 (19)	34 (23)	15 (11)
Headache	14 (10)	10 (7)	9 (7)
Pharyngitis	6 (4)	9 (6)	5 (4)
Coughing	4 (3)	4 (3)	1 (<1)
Rhinitis	1 (<1)	5 (3)	5 (4)
Nasal Irritation	4 (3)	5 (3)	8 (6)
Nasal Burning	4 (3)	4 (3)	5 (4)
Sneezing	1 (<1)	4 (3)	5 (4)
Infection, viral	0	1 (<1)	6 (4)
Pruritus	0	0	5 (4)

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

ceiving mometasone furoate compared with 7% for each of the beclomethasone dipropionate and placebo groups. The majority of events were considered mild to moderate in severity, and resolved over the course of the study.

A total of 16 patients discontinued the study because of adverse events (eight treated with mometasone furoate, six treated with beclomethasone dipropionate, and two treated with placebo). All of these adverse events save for one patient (in the mometasone furoate group, reporting lower back pain) were considered to be treatment-related. The most prevalent adverse event leading to discontinuance was epistaxis (three patients receiving mometasone furoate and five patients receiving beclomethasone dipropionate).

There were no clinically relevant changes in vital signs, electrocardiograms, or laboratory tests results, nor were there any reports of oropharyngeal candidiasis.

DISCUSSION

The active comparator in this study, beclomethasone dipropionate aqueous nasal spray, has well documented clinical efficacy in patients with perennial allergic rhinitis.[8–10] Results from this study indicate that an aqueous suspension of mometasone furoate, 200 μg administered intranasally once daily in the morning, is as effective as intranasal beclomethasone dipropionate, 200 μg administered twice daily, for the treatment of moderate to severe perennial allergic rhinitis.

In the present study, mometasone furoate demonstrated efficacy comparable to beclomethasone dipropionate in terms of symptomatic relief. In general, there were no significant differences between mometasone furoate and beclomethasone dipropionate in evaluations made by the patient (nasal symptom scores recorded in patient diaries and response to treatment) and by the physician (nasal symptom scores at visits and therapeutic response). This finding was generally consistent across both patient-rated and clinician-rated efficacy measures; physician-rated activity of mometasone furoate at the 1-month and 2-month timepoints was numerically but not statistically superior to placebo, but was only modestly different from values for beclomethasone dipropionate (which was statistically different from placebo). Presumably as a consequence of these modest numerical differences between the mometasone furoate and beclomethasone dipropionate responses, there was no statistical difference between the two at any time point. Further, treatment failures were equivalent for the two active comparators, and were roughly half the number seen in the placebo treatment group.

Compared with placebo, significant improvement in nasal symptoms by mometasone furoate was noted at the first office evaluation, following seven days of treatment; activity was sustained throughout the 3-month treatment period, indicative of a lack of tolerance or tachyphylaxis.

At most time points, mometasone furoate significantly improved all individual nasal symptoms, composed of rhinorrhea, congestion, sneezing and itch, compared with placebo control; in this regard, the trends followed the same pattern as demonstrated by the overall sum of the four symptoms.

Several factors should be considered in judging the success of a therapeutic regimen, including effectiveness, ease of administration and patient compliance. As demonstrated in this study, pooled AM diary data derived from patient evaluations *prior* to their morning dose of corticosteroid indicate that once daily treatment with mometasone furoate successfully controls symptoms throughout the entire dosing interval. Mean reductions from baseline using morning diary scores were very similar to those derived from evening diary scores (not shown), suggesting that mometasone furoate provides 24-hour coverage. These observations further support the overall effectiveness of mometasone considering that, in the majority of patients with allergic rhinitis, their nasal symptoms are most severe in the morning.[19] Once daily medication, which is effective throughout a 24-hour period and which is simple to administer, should significantly bolster patient compliance and acceptance of treatment.

Mometasone furoate and beclomethasone dipropionate were equally well tolerated in this study and were similar to placebo. The total drug-related incidence of adverse events reported, as well as the incidence and type of individual adverse events associated with each active treatment, was similar to the adverse event profile of patients who received placebo control, with local effects predominating. In this regard, the incidence and nature of the adverse event profile for mometa-

sone furoate is consistent with adverse events recently reported for other corticosteroids.[19] Although some local adverse events, such as epistaxis, have been associated with the chronic use of placebo nasal sprays,[11] in the present study slightly more patients receiving either corticosteroid developed blood in nasal mucous or nasal bleeding than did patients in the placebo group. It would be expected that, after prolonged treatment as in this study, incidence of epistaxis would be higher than that observed in patients receiving intranasal corticoid for shorter periods of time, for example in treatment of seasonal allergic rhinitis.

CONCLUSIONS

Mometasone furoate aqueous suspension nasal spray, administered at a dosage of 200 μg once daily, was significantly more effective than placebo vehicle control in relieving symptoms of patients 12 years of age and older with perennial allergic rhinitis. Efficacy was observed early during the course of treatment and was maintained throughout the study. Mometasone furoate demonstrated comparable efficacy to beclomethasone dipropionate 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, is an effective and well-tolerated alternative to intranasal corticoids requiring twice daily administration for treatment of moderate to severe symptoms of perennial allergic rhinitis.

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