
Ocular symptom reduction in patients with seasonal allergic rhinitis treated with the intranasal corticosteroid mometasone furoate

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Background: Allergic rhinitis (AR) is more appropriately termed *allergic rhinoconjunctivitis* owing to the equally bothersome nasal and ocular symptoms. Extensive evidence supports the ability of intranasal corticosteroids to reduce nasal symptoms of AR, although less evidence is available to define clearly their impact on allergic conjunctivitis.

Objective: To determine the effect of the intranasal corticosteroid mometasone furoate nasal spray (NS) on the ocular symptoms of seasonal AR.

Methods: This retrospective pooled analysis of 4 placebo-controlled clinical studies randomized patients 12 years and older with symptomatic seasonal AR to receive mometasone furoate NS, 200 µg once daily (n = 491), or placebo (n = 492). Ocular symptom (eye tearing [epiphora], itching [pruritus], and redness [erythema]) severity was rated by patients twice daily on a 4-point scale (0 = none to 3 = severe) in the morning and evening, with scores averaged to obtain a daily mean score. Efficacy variables were the pooled mean change from baseline in the averaged morning and evening total ocular symptom score (TOSS) and the individual ocular symptom scores.

Results: The change in mean TOSS from baseline to days 1 to 15 was −1.33 (−19.8%) with mometasone furoate NS and −0.93 (−5.6%) with placebo ($P < .001$). Improvements in individual symptoms were significantly better with mometasone furoate NS than with placebo on days 2 (tearing) and 4 (itching and redness). A slightly greater reduction in TOSS was seen with mometasone furoate NS treatment in the evening than in the morning.

Conclusions: This detailed analysis of an intranasal corticosteroid on individual ocular symptoms supports the positive impact of mometasone furoate NS on ocular symptoms.

Ann Allergy Asthma Immunol. 2008;100:272–279.

INTRODUCTION

Allergic rhinitis (AR), more appropriately termed *allergic rhinoconjunctivitis* in many patients, affects at least 10%, and perhaps up to 25%, of the general population.^{1,2} The incidence of ocular allergic symptoms of AR has not been well studied, but recent studies have indicated a larger impact than previously suggested. Data from the Third National Health and Nutrition Examination Survey show that approximately 40% of adults in various regions of the United States expe-

rience ocular symptoms associated with AR during a 12-month period, and after nasal congestion, ocular symptoms are a major concern of people with AR.^{3–5} The actual burden of AR is much higher because not all patients recognize AR as a disease, and approximately 80% decide to self-medicate their illness with 1 or more over-the-counter treatments.⁶ Nevertheless, many people with AR are bothered enough to seek the advice of a physician, making it 1 of the top 10 most common reasons for primary care clinic visits.⁷ Ocular symptoms, such as tearing (epiphora), itching (pruritus), and redness (erythema), are also known to be underappreciated and have been shown to be bothersome enough to interfere with quality of life.^{3,8,9} In addition, the costs allocated to allergic conjunctivitis may be more than those associated with AR, and people with seasonal allergic conjunctivitis are more likely than those without the condition to have other allergies, nasal symptoms, asthma, perennial allergic conjunctivitis, and a diminished quality of life.^{8,10}

The treatment options for managing ocular symptoms include topical formulations of antihistamines, vasoconstrictors, mast cell stabilizers, and nonsteroidal anti-inflammatory drugs. These topical treatments are generally used to supplement oral or intranasal therapies in patients who commonly have nasal and ocular symptoms, necessitating the use of multiple treatments. Oral nonsedating antihistamines reduce the ocular symptoms of seasonal AR (SAR), but they are not

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Disclosures: Dr Bielory owns stock in Pfizer, Novartis, Genentech, APPI, and Ocusense; has been a consultant to Forest, Schering-Plough, GlaxoSmithKline, Merck, Novartis, UCB-Pharma, Alcon, Medpointe, Ciba-Vision, Santen, Eyetech Pharmaceuticals, and Ocusense; is on the advisory board at Schering-Plough, GlaxoSmithKline, Novartis, Medpointe, Inspire, Eyetech Pharmaceuticals, Genentech, and Ocusense; has been on the speaker's bureau for Schering-Plough, Alcon, Medpointe, and Inspire; has received honoraria from Schering-Plough, GlaxoSmithKline, Alcon, Medpointe, and Inspire; and has received research support from Abbott Laboratories, Dyax, Novartis, Fujisawa, Sepracor, Genentech, and Lev Pharmaceuticals.

Funding Source: This study was funded by a grant from Schering-Plough Corp.

Received for publication June 29, 2007; Received in revised form August 17, 2007; Accepted for publication September 17, 2007.

as effective as intranasal corticosteroids for the control of nasal symptoms, especially congestion.² Emerging evidence^{11–13} suggests that intranasal corticosteroids, considered one of the most effective treatments for nasal allergy symptoms, are equivalent to oral antihistamines in reducing ocular symptoms.

Mometasone furoate nasal spray (NS) is a once-daily intranasal corticosteroid with minimal systemic absorption and well-documented efficacy in the treatment and prophylaxis of the symptoms of SAR.^{14–18} Pooled data from 4 studies regarding the treatment of nasal congestion with mometasone furoate NS were analyzed and described elsewhere.¹⁹ The effect of mometasone furoate NS in reducing the ocular symptoms of SAR across days 1 to 15 was also analyzed from data in the 4 studies and reported.²⁰ The objectives of this analysis are to (1) evaluate the efficacy of mometasone furoate NS in improving the total and individual ocular symptoms of tearing, redness, and itching of SAR; (2) identify the time to onset of statistical significance with mometasone furoate NS compared with placebo; and (3) examine the impact of mometasone furoate NS in the morning and evening through an analysis of data pooled from the same 4 clinical trials. Analyses included patients with all degrees of symptom severity (eg, patients with no symptoms at baseline to those with the most severe symptoms).

METHODS

Study Design

Four phase 3 clinical studies were selected and analyzed based on the following design considerations: randomized, double-masked, placebo-controlled studies with mometasone furoate NS, 200 µg once daily, administered in the morning on arising in patients with the nasal and nonnasal symptoms of SAR. All the studies were conducted in accordance with the Declaration of Helsinki or the guidelines on Good Clinical Practice that were current when the studies were conducted and were approved by local institutional review boards at clinical study centers in the United States and Canada. Written informed consent was obtained from all the participants or parents or legal guardians in the case of minors. The studies were conducted in the mid-1990s during the fall and spring allergy seasons at 41 medical centers in the United States and Canada.

To participate in any of the studies, patients must have been at least 12 years of age with a minimum 2-year history of SAR documented by a positive skin prick test reaction (a wheal diameter ≥3 mm larger than the diluent control) to a prevailing aeroallergen. Patients were also required to be symptomatic at screening and at baseline, with a nasal symptom score of at least 6 of 12 points, with congestion being 2 points or greater, so that it was appropriate (ie, physician evaluations concluded that patients exhibited symptoms that could be reduced with treatment) to initiate treatment with mometasone furoate NS. Although the 4 studies also collected data on nonnasal symptoms (ie, ocular symptoms and

ear and palate itching), the analysis of nasal symptoms was the primary focus. Patients were excluded for any clinically significant concomitant disease that could interfere with the study schedule or the evaluation of SAR, pregnancy, asthma requiring the use of inhaled or systemic corticosteroids, or clinically significant upper respiratory tract or sinus infection. The present pooled analysis included all the patients from the 4 studies with ocular symptom severity data from baseline to days 1 to 15, regardless of baseline ocular symptom score.

The 4 source studies followed similar designs. After a 3-day run-in period without treatment, patients were randomly assigned on day 1 to receive mometasone furoate NS, 200 µg once daily, or matching placebo spray consisting of the inactive ingredients of mometasone furoate NS but not the active ingredient (mometasone furoate monohydrate). Treatment was continued for 15 days in 3 of the studies and for 29 days in the fourth study, and only data from the first 15 treatment days of the latter study were included in this analysis.

In the source studies, patients were asked on day 15 to evaluate their therapeutic response to treatment using a 5-point scale from 1 (complete response) to 5 (no response). The outcome of this evaluation considers all symptoms, not just ocular symptoms. Pollen counts for ragweed and other weeds were obtained at each study center during the spring allergy season (March to June) for 2 pooled studies and during the autumn allergy season (August to October) for the other 2 studies.

Post hoc Evaluations

During the run-in and treatment periods, patients rated the severity of their ocular symptoms (itching, redness, and tearing) on a 4-point scale from 0 (none) to 3 (severe). Patients recorded symptom scores each morning on arising and before administration of mometasone furoate NS and approximately 12 hours later in the evening in a diary for investigator review. In effect, the evening diary recorded daytime symptoms and the morning diary recorded nighttime symptoms. The daily total ocular symptom score (TOSS) was defined by averaging morning and evening scores for the individual symptoms during the 2-week period. Changes in mean morning and evening scores were also analyzed separately. The baseline score was defined as the average of the morning and evening severity scores recorded during the 3-day run-in period plus the morning score on day 1, before the first dose of study medication, which was generally within 1 hour of awakening. For efficacy analyses, day 1 symptom scores consisted of the evening diary entries only (ie, the first 12 hours after the first dose).

Post hoc Statistical Analysis

The variables in this post hoc analysis were (1) the pooled mean change from baseline in the average morning and evening individual ocular symptom scores, (2) TOSS, and (3) improvements in ocular symptoms between mometasone furoate NS and placebo on a daily basis. Daily symptom se-

verity values were calculated as the mean of the morning and evening scores. Patients without a postbaseline ocular symptom evaluation were excluded. The source studies were not originally powered to detect differences in ocular symptom severity on a daily basis. Although it would be expected that a pooled data analysis should be capable of detecting day-to-day differences on the composite symptom severity rating (TOSS), it may still be difficult to consistently detect treatment differences among individual symptoms.

Daily and day 1 to 15 changes from baseline in ocular symptom scores (individual symptoms and TOSS) were analyzed using an analysis of covariance model, with treatment and study site as fixed effects. Baseline ocular symptom score was included as a covariate to account for differences in baseline scores. The average for days 1 to 15 was determined by taking the mean of all nonmissing days across the 15-day interval.

As an AR trial, these studies required a minimum nasal symptom score of 6 of 12 points to enter the clinical trial but did not require a baseline minimum severity of ocular symptoms for participation, thus creating a bias to demonstrate intranasal corticosteroid impact on nasal symptoms. Therefore, some patients with very low ocular symptom scores (eg, <1 point) at baseline might generate large percentage increases with only small score improvements, making it difficult to demonstrate reliable estimates of percentage changes from baseline. For this reason, separate subgroups, including patients with minimum baseline scores of 1 to less than 2 points and at least 4 points, are also analyzed. The 4-point minimum subgroup represents patients with more severe allergic conjunctivitis symptoms who would have been included in a study specifically designed for the evaluation of ocular symptoms.

RESULTS

The pooled population from the 4 studies included 991 patients randomized to receive mometasone furoate NS, 200 μ g once daily (n = 494), or matching placebo spray (n = 497), of whom 491 in the mometasone furoate NS group and 492 in the placebo group were included in the efficacy analysis. Eight patients did not meet the requirement of having baseline and follow-up ocular symptom data and were excluded. Baseline demographics and mean TOSS and individual symptom scores were similar for the 2 groups (Table 1). The distribution of patients within the TOSS severity categories of none, mild, moderate, and severe was also similar between groups. The greatest proportion of patients in each group had moderate or mild ocular symptoms at baseline.

All Patients

Overall ocular symptom analysis. For the entire pooled population during the 15 days of the analysis, mometasone furoate NS was associated with a mean change in TOSS of -1.33 (-19.8%) compared with -0.93 (-5.6%) with placebo ($P < .001$) (Fig 1A). As early as day 2 of treatment, the first day in which morning and evening data were analyzed,

Table 1. Baseline Demographic and Clinical Characteristics of the Study Groups

Characteristics	MFNS, 200 μ g once daily	Placebo
All patients		
No.	494	497
Age, mean (range), y	30.1 (12–71)	30.2 (12–71)
Sex, % male	49.4	50.1
Race, No. (%)		
White	429 (86.8)	438 (88.1)
African American	40 (8.1)	31 (6.2)
Hispanic	12 (2.4)	17 (3.4)
Asian	11 (2.2)	9 (1.8)
Other	2 (0.4)	2 (0.4)
Baseline scores, mean (SD)		
TOSS	4.42 (2.06)	4.57 (2.13)
Itching (pruritus)	1.68 (0.74)	1.72 (0.77)
Redness (erythema)	1.35 (0.81)	1.40 (0.79)
Tearing (epiphora)	1.39 (0.77)	1.45 (0.81)
Symptom severity subgroups		
Severity by baseline TOSS, No. (%)		
None (<1)	28 (5.7)	25 (5.0)
Mild (1 to <4)	166 (33.7)	165 (33.2)
Moderate (4 to <7)	239 (48.6)	236 (47.5)
Severe (≥ 7)	59 (12.0)	71 (14.3)

Abbreviations: MFNS, mometasone furoate nasal spray; TOSS, total ocular symptom score.

improvements in TOSS and all individual symptom scores were numerically greater with mometasone furoate NS than with placebo. By day 3, the decrease in TOSS was significantly greater with mometasone furoate NS than with placebo (-0.92 [-8.9%] vs -0.65 [-1.1%]; $P = .02$) and was significantly better than placebo on all subsequent study days.

Individual ocular symptom analyses. For eye tearing, a significantly greater reduction was seen with mometasone furoate NS than with placebo as early as day 2 of treatment (-0.26 [-9.8%] vs -0.17 [-4.8%]; $P = .03$) and on all subsequent days (Fig 1B). Treatment with mometasone furoate NS was statistically superior to placebo by day 4 for improvements in mean eye itching (-0.39 [-10.0%] vs -0.3 [-7.8%]; $P = .047$) (Fig 1C) and mean eye redness (-0.34 [-14.5%] vs -0.19 [-3.2%]; $P < .001$) (Fig 1D). In general, tearing was one of the first symptoms to improve and itching one of the last.

Morning and evening symptoms. When morning and evening symptom scores were analyzed separately, similar reductions in severity were observed with mometasone furoate NS, although a slightly greater decrease in TOSS was observed in the evening (-1.44) than in the morning (-1.23) assessments. However, the differences between mometasone furoate NS and placebo in the morning (0.43 difference in improvement) and evening (0.36 difference) TOSS were minor and favored the morning score. During the 15-day treatment period, mometasone furoate NS produced significantly

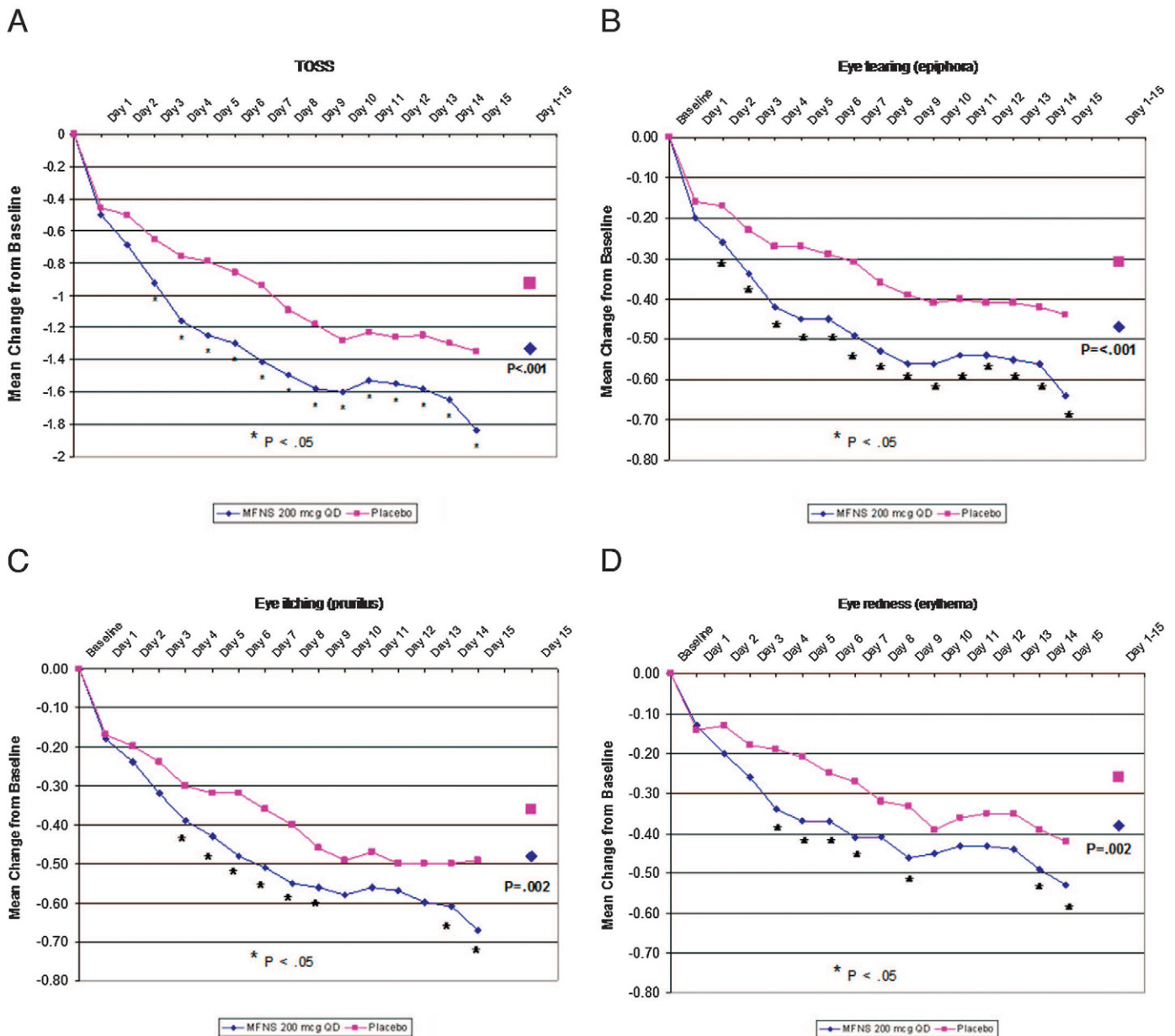


Figure 1. Mean changes from baseline in ocular symptom severity scores across 15 days of treatment for total ocular symptom score (A), eye tearing (epiphora) (B), eye itching (pruritus) (C), and eye redness (erythema) (D). Data are shown for all patients (mometasone furoate nasal spray [MFNS]; $n = 491$; placebo; $n = 492$) and represent the daily average of morning and evening scores. QD indicates once daily.

greater reductions for overall ocular symptoms and all individual ocular symptom scores compared with placebo nasal spray for morning and evening assessments (Table 2).

Severity Subgroup Analyses

Figure 2 illustrates the percentage changes from baseline in TOSS for patients with mild (TOSS 1 to <4 ; $n = 384$) and moderate-to-severe (TOSS ≥ 4 ; $n = 605$) baseline ocular symptoms compared with the entire population. The greatest reduction in symptom severity was noted in patients with the

highest initial symptom burden. Among patients with moderate-to-severe baseline ocular symptoms, MFNS was associated with a significantly greater improvement in symptom scores compared with placebo (-1.97 [-32.0%] vs -1.51 [-25.0%]; $P = .002$). A numerically greater reduction in symptoms was observed in patients with mild baseline ocular symptoms treated with mometasone furoate NS vs placebo (-0.42 [-12.6%] vs -0.12 [1.3%]). Owing to the smaller sample size, this difference did not achieve statistical significance.

Table 2. Comparative Analyses of Morning and Evening Total and Individual Symptom Score Severity Reductions for MFNS vs Placebo, Days 1 to 15

	Change from baseline, least squares mean (%) ^a					
	Morning scores			Evening scores		
	MFNS	Placebo	P value	MFNS	Placebo	P value
All patients						
TOSS	-1.23 (-18.4)	-0.80 (-3.4)	<.001	-1.44 (-23.3)	-1.08 (-13.7)	.001
Itching	-0.44 (-17.4)	-0.31 (-9.3)	.001	-0.53 (-23.1)	-0.41 (-19.5)	.006
Redness	-0.35 (-16.4)	-0.22 (-10.0)	<.001	-0.41 (-26.3)	-0.30 (-17.1)	.005
Tearing	-0.44 (-23.1)	-0.26 (-8.1)	<.001	-0.50 (-29.1)	-0.36 (-18.3)	<.001
Patients with baseline TOSS ≥4						
TOSS	-1.93 (-32.1)	-1.41 (-23.4)	<.001	-2.13 (-33.9)	-1.69 (-26.9)	.003
Itching	-0.68 (-29.4)	-0.53 (-22.7)	.005	-0.76 (-30.8)	-0.62 (-25.8)	.01
Redness	-0.58 (-30.0)	-0.43 (-20.1)	.002	-0.64 (-30.5)	-0.51 (-25.1)	.02
Tearing	-0.67 (-33.9)	-0.45 (-21.4)	<.001	-0.74 (-34.9)	-0.56 (-25.4)	<.001

Abbreviations: MFNS, mometasone furoate nasal spray; TOSS, total ocular symptom score.

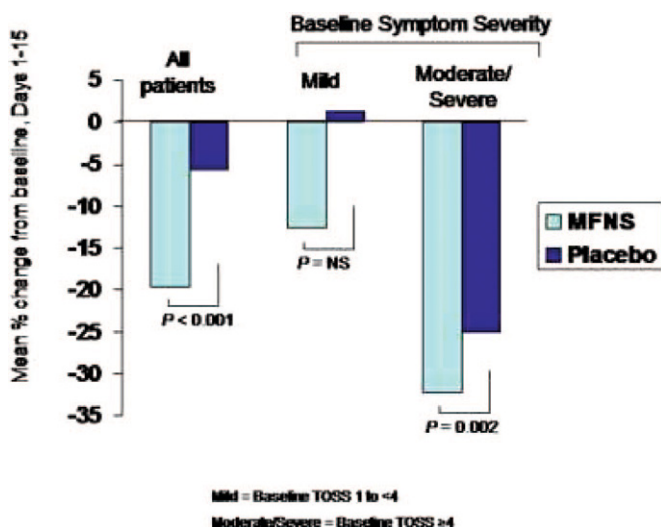


Figure 2. Mean percentage changes from baseline in total ocular symptom score (TOSS) for all patients and those with mild (TOSS 1 to <4) or moderate-to-severe (TOSS ≥4) ocular symptoms at baseline using mometasone furoate nasal spray (MFNS) or placebo nasal spray.

In patients with moderate-to-severe baseline ocular symptoms, the overall pattern of improvement was similar to that seen in the total pooled population (Fig 3). Improvements in tearing and itching symptoms were delayed by 1 day in these patients relative to the total pooled population, whereas improvement in redness occurred 1 day sooner. Overall, statistical superiority of mometasone furoate NS over placebo for improvement in TOSS was observed by day 4 in this subgroup (-1.71 [-28.2%] vs -1.33 [-21.9%]; $P = .02$). As early as day 3, significantly greater improvements were seen in the mometasone furoate NS group vs the placebo group for eye redness (-0.44 [-22.0%] vs -0.32 [-14.6%]; $P = .04$) and eye tearing (-0.53 [-27.3%] vs -0.39 [-18.8%]; $P =$

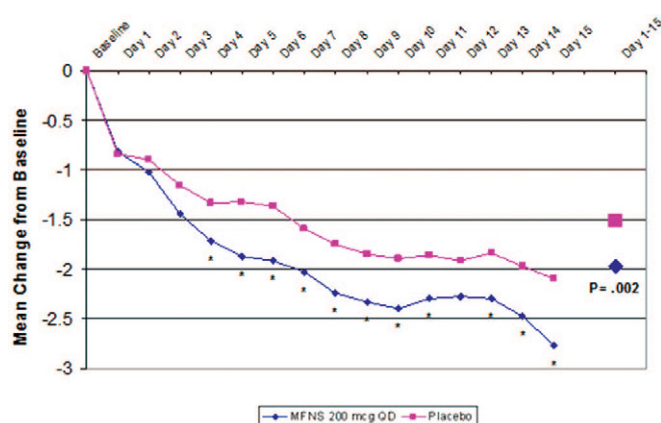


Figure 3. Mean changes from baseline in total ocular symptom score (TOSS) (daily averages of morning and evening scores) across 15 days of treatment in patients with moderate-to-severe ocular symptoms (baseline TOSS ≥4). MFNS indicates mometasone furoate nasal spray; QD, once daily.

.02). The improvement in eye itching was significantly greater with mometasone furoate NS by day 5 (-0.63 [-22.5%] vs -0.50 [-21.3%]; $P = .045$). Mometasone furoate NS maintained statistical superiority over placebo on most subsequent study days in patients with moderate-to-severe symptoms.

A separate analysis of individual symptom scores also was conducted for patients with a baseline TOSS of 1 to less than 2. Among these patients, a significant improvement with mometasone furoate NS vs placebo was attained on day 3 in eye tearing (-0.35 [-24.3%] vs -0.22 [-14.3%]; $P = .42$) and on day 4 in redness (-0.36 [-23.6%] vs -0.21 [-13.7%]; $P = .02$), with significance maintained across days 1 to 15 ($P < .001$ and $P = .004$, respectively). Improvements in eye itching were numerically but not statistically

significantly greater with mometasone furoate NS than with placebo.

In most patients, those with a baseline TOSS of at least 2, mometasone furoate NS led to significantly greater improvements than placebo across days 1 to 15 in all individual symptoms: eye redness (-0.79 [-34.0%] vs -0.64 [-27.6%]; $P = .05$), itching (-0.85 [-33.6%] vs -0.63 [-25.4%]; $P < .001$), and tearing (-0.83 [-35.3%] vs -0.67 [-28.3%]; $P = .047$). Significance for eye redness was reached on day 3 (-0.62 [-27.7%] vs -0.43 [-19.3%]; $P = .02$), for itching on day 5 (-0.81 [-31.3%] vs -0.60 [-23.9%]; $P = .008$), and for tearing on day 5 (-0.85 [-36.1%] vs -0.64 [-26.7%]; $P = .03$).

The group with baseline ocular symptom severity categorized as “none” (TOSS <1) was too small to analyze with sufficient statistical power, especially in light of very low baseline TOSS scores and the potential for disproportionately large percentage changes with only minor score improvements. Similarly, the group with baseline ocular symptoms categorized as “severe” (TOSS ≥ 7) was relatively small, and results for this group were pooled with the moderate severity group to preserve sufficient power to detect relevant differences.

DISCUSSION

This retrospective analysis of pooled data from almost 1,000 patients with SAR demonstrated that an intranasal corticosteroid, mometasone furoate NS, at a dose of $200\text{ }\mu\text{g}$ once daily, provided significant reductions in overall and individual ocular symptom severity scores. Although morning and evening symptom severity scores were combined to obtain daily mean scores, they were also analyzed independently. Reductions in symptom scores with mometasone furoate NS were generally similar for morning and evening evaluations. Differences between morning and evening scores may be related to the increased open eye exposure to allergens during the day. The morning score represents limited ocular exposure to allergens because patients usually have approximately 8 hours of sleep during the 12 hours before they record symptoms. The slightly better improvement in the evening score may reflect the greater daytime allergen exposure during the 12 hours before recording of symptoms.

The results of this analysis corroborate a growing body of evidence supporting the use of intranasal corticosteroids to reduce ocular symptoms of AR. Initial evidence of this therapeutic benefit was revealed during placebo-controlled clinical trials of the effects of intranasal corticosteroids on a spectrum of AR symptoms.^{21–23} More recently, studies designed specifically to investigate effects on ocular symptoms have reinforced those observations.^{11,12} In a pooled analysis¹¹ of data from 7 randomized, placebo-controlled clinical trials of intranasal fluticasone propionate in SAR, patient and physician ratings of ocular symptom severity on study days 7 and 14 also favored intranasal fluticasone.

Intranasal corticosteroids have been shown to be superior to placebo for reducing ocular symptoms of AR and to have

a comparable or possibly greater positive effect than oral antihistamines. A meta-analysis¹³ of 11 randomized controlled trials found no significant difference between intranasal corticosteroids and oral antihistamines regarding improvement in eye symptoms, indicating that corticosteroids are as effective as antihistamines in treating ocular symptoms. A similar meta-analysis²⁴ of 10 randomized clinical trials did not identify any significant difference in ocular symptom relief between intranasal corticosteroids and nonsedating antihistamines.

The mechanism by which an intranasal corticosteroid affects ocular allergy symptoms is not yet fully understood, although several explanations have been postulated. Allergen exposure in the nose has been shown to stimulate inflammatory mediators and, subsequently, the trigeminal ganglion, a phenomenon known as the naso-ocular reflex (or oculonasal reflex). This process produces ocular symptoms of vasodilation, erythema, and tearing.²⁵ Therefore, it follows that use of an intranasal corticosteroid could alter or normalize this heightened reflex neural activity, with carryover effects on ocular irritation.^{12,26–28} A nasal allergen challenge study²⁹ concluded that histamine released at the site of the challenge caused nasonasal and naso-ocular reflexes, indicating that the ocular symptoms associated with AR are at least partially due to a naso-ocular reflex. In fact, our findings indicated that the earliest effects of mometasone furoate NS were on the ocular symptoms of tearing and redness, with somewhat delayed relief in itching, at least in patients with the greatest symptom burden.

Another theory proposes that intranasal corticosteroids, through their anti-inflammatory properties, act to improve nasolacrimal drainage, which, in turn, reduces conjunctival retention of allergens and mediators.^{11,12,30} Bernstein et al¹² give credence to this theory based on their observation that patterns of ocular symptom relief followed those for reductions in nasal congestion. However, this result may also reflect the possibility that nasal neural stimulation is linked to congestion, and as nasal congestion improves, ocular symptoms are reduced.³⁰ Systemically mediated pharmacologic activity on the eye is considered unlikely for intranasal corticosteroids as a class, although in a study³¹ of patients with glaucoma, intranasal corticosteroid use was associated with reversible increases in intraocular pressure when baseline ocular pressures were compared with those recorded during intranasal corticosteroid treatment and after intranasal corticosteroid treatment discontinuation. A 12-week study³² of fluticasone furoate in 558 children (2–11 years old) did not find evidence of glaucoma or cataracts after slitlamp examination, funduscopy, and tonometry. In a study³³ evaluating orally and intranasally administered budesonide, a corticosteroid with a high systemic bioavailability (34%), intranasal administration produced greater ocular symptom relief than oral administration, despite higher plasma levels of budesonide with oral administration. In contrast, mometasone furoate NS has almost undetectable systemic bioavailability.³⁴

Another putative reason for the positive effects of intranasal corticosteroids on ocular symptoms is the systemic effects of these locally administered agents. For example, intranasal corticosteroids have been shown in clinical and in vivo studies to decrease levels of glucocorticoid receptor messenger RNA in peripheral lymphocytes.³⁵ Intranasal corticosteroids also improve the symptoms of asthma by reducing the pathologic signs of inflammation in patients with asthma and AR.³⁶ Their positive effect on asthma symptoms is thought to be due to their ability to reduce the presence of eosinophils, which mediate inflammation in the airway by recruiting basophils, eosinophils, and progenitor cells from bone marrow in the airways of asthmatic patients. This improvement in asthma symptoms with intranasal corticosteroids also further supports the validity of the "1-airway, 1-disease" concept.³⁶

The beneficial reductions in ocular symptoms associated with placebo nasal spray in this study also warrant consideration. The pattern of improvement in patients using placebo nasal spray followed a pattern observed in patients using mometasone furoate NS, although improvements with placebo were not as robust and were delayed by 2 to 3 days. This substantiates a pharmacologic effect of intranasal administration, with the faster onset and greater impact likely related to additional anti-inflammatory effects on the accentuated neuronal impulse.

A major limitation of this pooled analysis is that a minimum degree of ocular symptom severity was not a prerequisite for participation in the source studies because these studies were designed to detect the signal in nasal allergic symptoms. For the present analysis, the degree of ocular symptom severity was not a criterion for patient inclusion or exclusion. The absence of a minimum severity standard raises the likelihood that a certain percentage of patients would have had minimal ocular symptoms at baseline, and the reporting of percentage changes in symptom scores can be misleading when baseline scores are near zero. The actual percentage of patients with baseline TOSS less than 1 was small (5.7%), suggesting that this subgroup should not have had a significant impact on overall findings. Furthermore, significant benefits of mometasone furoate NS compared with placebo were noted regarding absolute decreases in symptom scores, not only percentage reductions. To further address this limitation, patients were grouped and analyzed separately based on baseline ocular symptom severity. The trends in improvement observed in patients with the greatest ocular symptom burden were generally similar to those seen in the overall group, albeit with greater percentage reductions in severity ratings, as might be expected in patients with more severe symptoms at baseline.

The retrospective nature of this study represents an additional limitation. A prospective study should be conducted to confirm the findings of this analysis, with inclusion criteria that focus on the ocular domain. Finally, this analysis was not designed to evaluate quality-of-life issues, although the deleterious impact of ocular symptoms on quality of life has been well demonstrated. The presence of ocular symptoms,

such as itchy, watery, swollen, and sore eyes, has been shown to correlate with impaired sleep, limitations in daily activities, and emotional distress.³⁷ Therefore, the significant improvement in ocular symptoms would be expected to be clinically relevant to patients given the negative effect on quality of life attributed to ocular symptoms.⁸

Traditionally held perceptions about the limited scope of the positive effect of intranasal corticosteroids on the treatment of SAR continue to evolve in light of emerging data. A heightened appreciation for their potential impact beyond the nasal mucosa may give them even greater prominence in the care of patients with allergic rhinoconjunctivitis or perhaps in some patients better described as having "conjunctivorhinitis."³⁸ The present analysis confirms that the intranasal corticosteroid mometasone furoate reduces ocular symptoms of SAR in 1 to 3 days. Given the well-established role of mometasone furoate NS in treating nasal allergy symptoms, corroboration of these results through future prospective studies may position mometasone furoate NS and other intranasal corticosteroids as effective and safe monotherapy for the nasal and ocular symptoms of SAR. It also provides a platform for future development of intranasal corticosteroid compounds that will have an improved impact on ocular allergy symptoms.

ACKNOWLEDGMENTS

Editorial assistance in the preparation of this manuscript was provided by Adelphi Eden Health Communications.

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