

Efficacy and safety of mometasone furoate nasal spray in nasal polyposis

Catherine Butkus Small, MD,^a Jaime Hernandez, MD,^b Antonio Reyes, MD,^c Eric Schenkel, MD,^d Angela Damiano, MD,^e Paul Stryszak, PhD,^f Heribert Staudinger, MD,^f and Melvyn Danzig, PhD^f Valhalla, NY, Medellin and Cali, Colombia, Philadelphia, Pa, and Kenilworth, NJ

Background: Studies have suggested that topical corticosteroids are effective in the treatment of nasal polyps; however, this has yet to be confirmed in a large, robust clinical trial.

Objective: To evaluate the efficacy and safety of mometasone furoate nasal spray (MFNS) for nasal polyposis.

Methods: A total of 354 subjects with bilateral nasal polyps and clinically significant congestion/obstruction participated in this multinational, randomized, double-blind, placebo-controlled study. Subjects received MFNS 200 µg once or twice daily or placebo for 4 months. Coprimary endpoints were (1) change from baseline to last assessment in physician-evaluated bilateral polyp grade score and (2) change from baseline averaged over month 1 in subject-assessed nasal congestion/obstruction. ANOVA was used for all efficacy endpoints, except for change in bilateral polyp grade score, for which baseline polyp grade was added as a covariate.

Results: Compared with placebo, MFNS 200 µg administered once or twice daily produced significantly greater reductions in bilateral polyp grade score ($P < .001$, $P = .010$, respectively) and congestion/obstruction ($P = .001$, $P < .001$), as well as improvement in loss of smell ($P < .001$, $P = .036$), anterior rhinorrhea ($P < .001$ for both), and postnasal drip ($P < .001$, $P = .001$) over month 1. MFNS 200 µg twice daily was superior to MFNS 200 µg once daily in reducing congestion/obstruction ($P = .039$), and there were more improvers in the MFNS 200 µg

twice daily group ($P = .035$). MFNS was well tolerated in both groups.

Conclusion: MFNS 200 µg, once or twice daily, was safe and significantly superior to placebo in reducing polyp grade (size and extent) and improving congestion/obstruction and return of sense of smell. MFNS is an effective medical treatment for nasal polyposis and may reduce or delay the need for surgery. (J Allergy Clin Immunol 2005;116:1275-81.)

Key words: Congestion, corticosteroid, clinical trial, intranasal, mometasone furoate, nasal polyps

Nasal polyposis is estimated to affect approximately 4% of the population.¹ Symptoms include nasal obstruction, congestion, nasal discharge, purulence, and postnasal drip.² More than 75% of patients have impaired sense of smell or loss of sense of smell.³ Nasal polyposis is characterized by eosinophil-dominated inflammation of unknown cause and is often associated with asthma, aspirin sensitivity, or cystic fibrosis.² One possible mechanism for the development of nasal polyposis involves bacterial colonization of the nasal cavity, causing synthesis and release of enterotoxins that act as superantigens to stimulate the local immune system.⁴ A hallmark of bilateral nasal polyposis, which is observed in approximately 90% of adults with the condition, is a mixed cellular infiltrate with predominant eosinophilia.⁵ Increased levels of inflammatory mediators, such as IL-5,⁶ eotaxin,⁷ and eosinophilic cationic protein,⁸ are also present.

Topical nasal corticosteroids reduce the eosinophil-associated inflammation associated with polyposis⁹ and are therefore a rational choice for the management of this condition.^{9,10} The literature contains several small studies showing the positive effects of topical nasal corticosteroids on nasal polyps;¹¹⁻¹⁷ however, these are limited by small patient numbers or short duration of treatment. Therefore, a large, appropriately powered trial was initiated to establish the benefits of the corticosteroid mometasone furoate on nasal polyp grade and the symptoms associated with nasal polyps.

This study evaluated the efficacy and safety of mometasone furoate nasal spray (MFNS) 200 µg administered once daily (QD) or twice daily (BID) as monotherapy, compared with placebo, in the treatment of patients with nasal polyposis.

From ^aDivision of Infectious Diseases, New York Medical College; ^bMedellin Clinic; ^cOtorrinolaringologo, Centro Médico Imbanaco, Cali; ^dthe Drexel University School of Medicine, Philadelphia; ^eDivision of Otolaryngology, New York Medical College; and ^fSchering-Plough Research Institute, Kenilworth.

Supported by a grant from the Schering-Plough Research Institute.

Disclosure of potential conflict of interest: Dr Small received research support from PO 1998 SAR Study, PO 1925 Polyp Study, PO 2573 Follow-Up to Polyp Study, PO 2683 Acute Rhinosinusitis, and PO 2692 Acute Rhinosinusitis. Dr Stryszak, Dr Staudinger, and Dr Danzig are employed by Schering-Plough. Dr Schenkel has consultant arrangements with Schering-Plough and Sanofi-Aventis; receives research support from Schering-Plough, Sanofi-Aventis, and Glaxo; and is on the speakers bureau for Schering-Plough, Sanofi-Aventis, and Glaxo. All other authors have no conflict of interest to disclose.

Received for publication April 1, 2005; revised June 28, 2005; accepted for publication July 5, 2005.

Available online September 27, 2005.

Reprint requests: Catherine Butkus Small, MD, Division of Infectious Diseases, Munger Pavilion Rm. 245, Valhalla, NY 10595. E-mail: Catherine.Small@nymc.edu.

0091-6749/\$30.00

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doi:10.1016/j.jaci.2005.07.027

Abbreviations used

ANCOVA: Analysis of covariance
 BID: Twice daily
 LS: Least squares
 MFNS: Mometasone furoate nasal spray
 PNIF: Peak nasal inspiratory flow
 QD: Once daily

METHODS**Study design**

A randomized, double-blind, double-dummy, placebo-controlled study was carried out in 44 medical centers worldwide in accordance with the Declaration of Helsinki and guidelines on Good Clinical Practices. The study protocol and statement of informed consent were reviewed and approved by an Institutional Review Board and Independent Ethics Committee.

Subjects who met eligibility criteria at the screening visit (day –14, visit 1) underwent a 14-day, single-blind, placebo run-in period to help exclude placebo responders and identify subjects with stable disease. Subjects who met eligibility criteria at the baseline visit (visit 2) were randomized in a 1:1:1 ratio to 3 treatment arms: MFNS 200 µg QD in the morning (AM) with matching placebo nasal spray in the evening; MFNS 200 µg BID in the morning and evening; or matching placebo nasal spray BID. MFNS was supplied as commercial Nasonex (Schering-Plough Corp, Kenilworth, NJ) in a metered-dose manual pump spray unit containing an aqueous suspension of mometasone furoate monohydrate equivalent to 0.05% wt/wt mometasone furoate calculated on the anhydrous basis. The aqueous medium contained glycerin, microcrystalline cellulose and carboxymethylcellulose sodium, sodium citrate, 0.25% wt/wt phenylethyl alcohol, citric acid, benzalkonium chloride, and polysorbate 80.

Treatment duration was 4 months, with study visits at day 8 (visit 3) and months 1, 2, 3, and 4 (visits 4, 5, 6, and 7, respectively). A nasal examination by endoscopy was performed by the investigator at each visit except visit 3, and polyps were graded by size and extent in both the left and right nasal fossa on a scale of 0 to 3 (0 = no polyps; 1 = polyp in middle meatus, not reaching below the inferior border of the middle turbinate; 2 = polyp reaching below the inferior border of the middle turbinate but not the inferior border of the inferior turbinate; and 3 = large polyp reaching to or below the lower border of the inferior turbinate or polyps medial to the middle turbinate). The sum of the left and right nasal fossa polyp scores gave the total bilateral polyp grade. Investigators also evaluated subjects' therapeutic response at each visit on a qualitative scale ranging from complete relief of symptoms to no relief.

Subjects evaluated their symptoms (congestion/obstruction, loss of sense of smell, anterior rhinorrhea, and postnasal drip) each morning on a diary card immediately before dosing. Symptoms were scored on a scale of 0 to 3 (0 = none; 1 = mild; 2 = moderate; 3 = severe) to reflect the subject's condition at the time of scoring. After this symptom assessment, subjects also measured their peak nasal inspiratory flow (PNIF) each morning by using a PNIF meter (Clement Clarke International Ltd, Harlow, United Kingdom). Subjects were trained in using the meter at the baseline visit. Treatment compliance was evaluated at visits 3 through 7 by weighing study drug bottles without the subjects' knowledge. Compliance was defined as use of 59% to 138% of the reference study drug bottle weight. (Compliance is normally defined as the use of 70% to 120% of study drug bottle weight, but because the reference bottle weight could vary by 15%, the range was increased to account for this variability.)

Subjects

Subjects ≥ 18 years with a diagnosis of bilateral nasal polyps (graded ≥ 1 on each side) and clinically significant nasal congestion/obstruction (average morning score ≥ 2 for each of the last 7 days of the 14-day run-in period) were eligible for study entry. Subjects with asthma were included if they had a documented FEV₁ $\geq 80\%$ of the predicted value within the 6 months before screening and no asthma exacerbations within 30 days before screening. Those treated with inhaled corticosteroids were required to be on a moderate, stable regimen of beclomethasone dipropionate ≤ 800 µg/d or equivalent for ≥ 1 month before screening and to remain on a stable regimen throughout the study period.

Subjects were not included in the study if they had a history of seasonal allergic rhinitis within the past 2 years, sinus or nasal surgery within the previous 6 months or ≥ 3 nasal surgeries (or any surgical procedure preventing an accurate grading of polyps), presumed fibrotic nasal polyposis, or complete or near complete nasal obstruction. Subjects with the following diagnoses were also excluded: nasal septal deviation requiring corrective surgery; nasal septal perforation; acute sinusitis, nasal infection, or upper respiratory tract infection at screening or in the 2 weeks before screening; ongoing rhinitis medicamentosa; Churg-Strauss syndrome; dyskinetic ciliary syndromes; cystic fibrosis; glaucoma or a history of posterior subcapsular cataracts; allergies to corticosteroids or aspirin; or any other clinically significant disease that would interfere with the evaluation of therapy.

Concomitant medications that would interfere with study evaluations were not permitted, including nasal sodium cromolyn; nasal atropine or ipratropium bromide; corticosteroids (except oral inhaled corticosteroids for asthma or mild-strength or mid-strength topical corticosteroids for dermatologic purposes); antihistamines; decongestants; topical, oral, or ocular anti-inflammatory drugs; or topical nasal or oral antifungal agents. Acetaminophen (paracetamol) was encouraged for analgesic purposes, with the use of nonsteroidal anti-inflammatory drugs limited to 5 consecutive days if alternative analgesia was required. Antibiotics were administered for any bacterial infections that occurred during the study, at the discretion of the principal investigator.

Efficacy endpoints

The study had 2 primary efficacy endpoints: (1) change from baseline to endpoint (at 4 months or last study visit) in bilateral polyp grade score, and (2) change from baseline in congestion/obstruction score averaged over the first month of treatment.

Secondary endpoints included change from baseline in loss of smell, anterior rhinorrhea, and postnasal drip score averaged over each month of treatment. Other assessments were change from baseline in PNIF at months 1, 2, 3, and 4, the proportion of subjects demonstrating an improvement (defined as a reduction in bilateral polyp grade score of ≥ 1.0 from baseline and a reduction in congestion/obstruction score of ≥ 0.5 from baseline) at the endpoint, and the investigators' evaluation of symptomatic therapeutic response at day 8 and months 1, 2, 3, and 4.

Safety assessments

Safety assessments included adverse event reporting, laboratory tests, vital signs, and physical examination. Details of all reported adverse events were recorded throughout the study, with severity graded as mild, moderate, severe, or life-threatening, and a relationship to treatment assigned. At all visits, vital signs were measured. Clinical laboratory tests and a physical examination were performed at the screening visit (visit 1) and the last treatment visit (visit 7). Change from baseline to the endpoint in 24-hour urinary cortisol levels (corrected for creatinine) was measured in a subset of subjects at 28 centers.

TABLE I. Demographic details and baseline polyp grade scores and symptom scores for each treatment group*

	MFNS 200 µg QD AM (n = 115)	MFNS 200 µg BID (n = 122)	Placebo (n = 117)
Mean age, y (range)	46.7 (18.0-80.0)	48.3 (18.0-77.0)	47.5 (18.0-81.0)
Age subgroup, n (%)			
18 to <65 y	99 (86)	104 (85)	102 (87)
≥65 y	16 (14)	18 (15)	15 (13)
Male/female, %	66:34	61:39	61:39
Mean weight, kg (range)	74.4 (48.0-118.0)	73.2 (48.0-136.1)	75.0 (41.0-127.4)
Asthma history, n (%)	21 (18)	26 (21)	25 (21)
Perennial allergic rhinitis history, n (%)	23 (20)	30 (25)	20 (17)
Bilateral polyp grade score, LS mean	4.21	4.27	4.25
Congestion/obstruction, LS mean	2.29	2.35	2.28
Loss of smell, LS mean	2.27	2.14	2.32
Anterior rhinorrhea, LS mean	1.66	1.62	1.58
Postnasal drip, LS mean	1.55	1.43	1.48
PNIF, L/min, LS mean	87.6	92.7	83.9

*LS means were obtained from ANOVA with treatment, baseline asthma status, and site effects.

TABLE II. Number (%) of randomized subjects who completed treatment and discontinued treatment, and reasons for discontinuation*

	MFNS 200 µg QD AM	MFNS 200 µg BID	Placebo
Subjects randomized to treatment	115 (100)	122 (100)	117 (100)
Subjects completed treatment	101 (88)	109 (89)	95 (81)
Subjects discontinued treatment	14 (12)	13 (11)	22 (19)
Reasons for discontinuation			
Adverse event	2 (2)	4 (3)	4 (3)
Treatment failure	3 (3)	1 (1)	6 (5)
Lost to follow-up	2 (2)	1 (1)	3 (3)
Did not wish to continue	4 (3)	4 (3)	3 (3)
Noncompliance with protocol	2 (2)	2 (2)	2 (2)
Did not meet protocol criteria for entry	1 (1)	1 (1)	4 (3)

*Subjects who were randomized but never treated are included in the discontinued treatment category.

Statistical methods

Analyses and summaries were based on all randomized subjects (intent-to-treat principle) and were performed by using SAS software, Version 8 (SAS Institute Inc, Cary, NC). An effects ANOVA was used to analyze responses for the efficacy endpoints. The ANOVA included sources of variability because of treatment, site effects, and asthma status. Baseline bilateral polyp grade was added as a covariate to the ANOVA model for analysis of the change from baseline in bilateral polyp grade score (analysis of covariance; ANCOVA) to account for any between-group baseline differences in this variable. Comparisons between treatment groups were based on differences in mean estimates from the ANOVA or ANCOVA models. All tests were performed at the unadjusted significance level of $\alpha = 0.05$.

It was determined that a total target sample size of 100 subjects per treatment group would provide 90% simultaneous power at a 2-sided α level of 0.05 to detect a difference of ≥ 1.0 point in change from baseline to the endpoint in bilateral polyp grade score (assuming a SD of 1.44) and ≥ 0.37 point in change from baseline in average congestion/obstruction over the first month of treatment (assuming a SD of 0.8). With 100 subjects per treatment group, a difference of 0.66 in bilateral polyp grade score would be detectable with 90% individual power. With 30 subjects per treatment group, differences

between treatment means of 32.3 nmol/mmol in urinary free cortisol levels would be detectable with 90% power and 5% significance (2-sided), assuming a SD of 37.9.

RESULTS

Subject disposition and characteristics

A total of 354 subjects were randomized. No clinically relevant differences in demographic characteristics among the 3 treatment groups were observed, with $\leq 25\%$ of subjects having a history of mild asthma or perennial allergic rhinitis (Table I). Small differences in baseline bilateral polyp grade score were observed between treatment groups, with the majority of subjects having a total bilateral polyp grade score of 4 to 6. More than 90% of subjects had a moderate to severe baseline congestion/obstruction score, and baseline mean PNIF was below the normal range (100-300 L/min) in all treatment groups.

A total of 305 subjects (86%) completed the 4-month treatment period, with a greater proportion of placebo recipients discontinuing the treatment phase than MFNS recipients (Table II). The majority of subjects ($n = 331$;

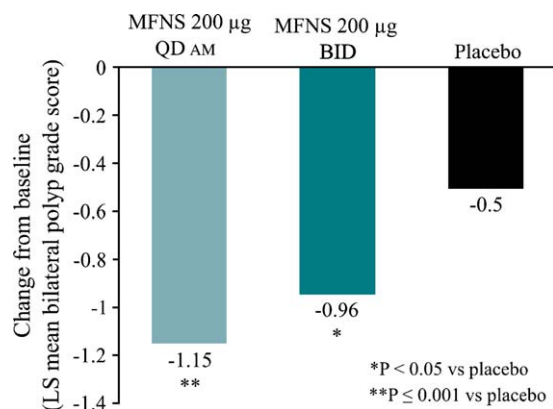


FIG 1. Change in bilateral polyp grade score from baseline to the endpoint. LS means and pairwise comparison *P* values were obtained from ANCOVA, with treatment, baseline asthma status, site effects, and baseline bilateral polyp grade score. Endpoint was defined as the last nonmissing reading for the subject. Baseline bilateral polyp grade scores were 4.21, 4.27, and 4.25 in the MFNS 200 µg QD, MFNS 200 µg BID, and placebo groups, respectively.

93.5%) were considered to be compliant with the dosing regimen.

Efficacy endpoints

Bilateral polyp grade score. Greater reductions in bilateral polyp grade scores were observed with MFNS 200 µg QD (1.15 points; $P \leq .001$) and MFNS 200 µg BID (0.96 points; $P = .010$) compared with placebo (0.50 points) at the endpoint (Fig 1). Polyp grade scores decreased over time, with the differential between placebo and active treatment greater at the endpoint than at month 1. For example, the least squares (LS) mean change from baseline in polyp score (ANOVA results) at month 1 was -0.61 for MFNS 200 µg BID ($P < .05$) compared with -0.33 for placebo, reflecting a score differential of 0.28, whereas the change from baseline at month 3 was -0.93 for MFNS 200 µg BID ($P < .05$) compared with -0.56 for placebo, reflecting a score differential of 0.37 and a greater than 32% increase in the differential after an additional 2 months of treatment. No statistically significant differences between the MFNS treatment groups were observed at any time point during the study.

Congestion/obstruction score. Significantly greater reductions in congestion/obstruction scores were observed with MFNS 200 µg QD or BID over the primary time interval of 1 month compared with placebo ($P = .001$ and $P < .001$, respectively), with a significant difference also observed between active treatment groups in favor of MFNS 200 µg BID ($P = .039$; Fig 2). MFNS 200 µg BID was also significantly superior to placebo at each study visit over the entire 4 months of treatment ($P \leq .001$) and superior to MFNS 200 µg QD at the 3-month and 4-month study visits ($P = .027$ and $P = .024$, respectively; Fig 2). Congestion/obstruction scores progressively decreased from baseline over the course of the

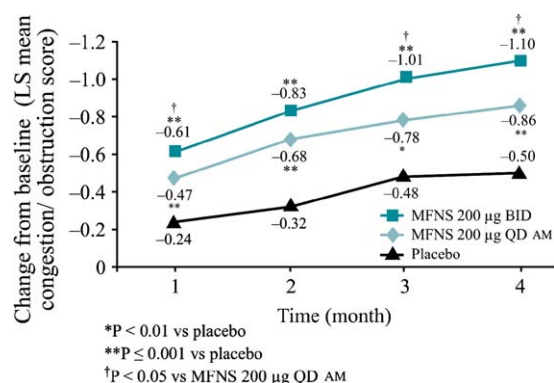


FIG 2. Change from baseline in congestion/obstruction score during the treatment period. LS means and pairwise comparison *P* values were obtained from ANOVA with treatment, baseline asthma status, and site effects. Baseline congestion/obstruction scores were 2.29, 2.35, and 2.28 in the MFNS 200 µg QD, MFNS 200 µg BID, and placebo groups, respectively.

study in the treatment groups (Fig 2), demonstrating a continuing effect of active treatment over time.

Individual symptom scores. Both MFNS 200 µg QD AM and BID produced significantly greater improvements compared with placebo over month 1 in individual symptom scores (Fig 3, A), which were sustained over the 4-month treatment period (Fig 3, B).

PNIF rate. Statistically significant superiority over placebo was observed for change in PNIF with MFNS 200 µg QD AM and MFNS 200 µg BID at months 1, 2, 3, and 4 ($P \leq .003$ and $P < .001$, respectively; Fig 4). No statistically significant differences in change in PNIF were observed between the active treatment groups during the study, with the exception of week 1, when MFNS 200 µg BID demonstrated a greater improvement relative to MFNS 200 µg QD AM ($P = .038$).

Proportion of subjects with improvement. A significantly greater proportion of MFNS 200 µg BID recipients (57%) were classed as improvers at the endpoint compared with either MFNS 200 µg QD AM recipients (43%; $P = .035$) or placebo recipients (34%; $P < .001$).

Investigators' assessment of therapeutic response. Both active treatment groups were associated with a significantly greater improvement in therapeutic response as assessed by investigators at all time intervals compared with placebo ($P \leq .003$). No statistically significant differences were observed between MFNS treatment groups in the therapeutic response.

Safety assessments

Treatment with MFNS was well tolerated, with no unusual or unexpected events. Most adverse events reported during the study were of mild or moderate intensity and were considered by investigators to be unrelated to study treatment. The overall incidence of treatment-emergent adverse events, the majority of which were considered unlikely related to study drug, was similar among the 3 treatment groups: 49%, 49%, and 55% in subjects receiving MFNS 200 µg QD AM, MFNS 200 µg BID, and

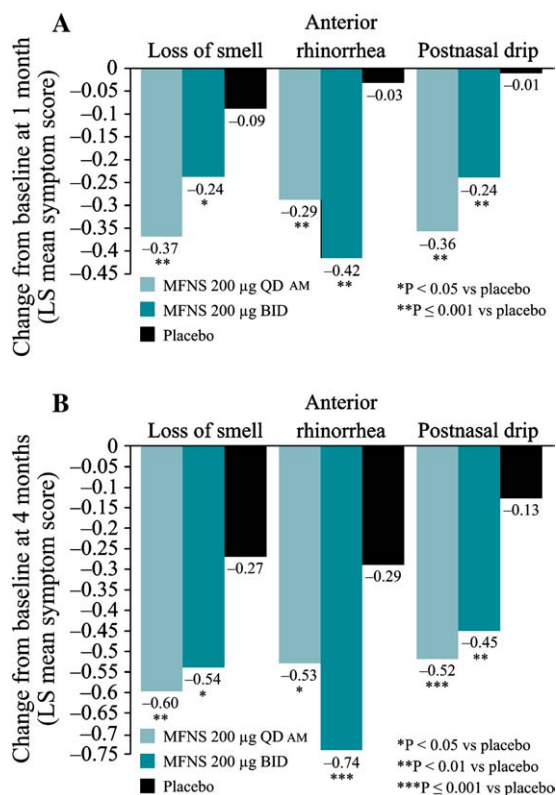


FIG 3. Change from baseline in individual symptom scores (loss of smell, anterior rhinorrhea, and postnasal drip) at month 1 of treatment (**A**) and month 4 of treatment (**B**). LS means and pairwise comparison *P* values were obtained from ANOVA with treatment, baseline asthma status, and site effects. Baseline individual symptom scores were 2.27, 2.14, and 2.32 for loss of smell, 1.66, 1.62, and 1.58 for anterior rhinorrhea, and 1.55, 1.43, and 1.48 for postnasal drip in the MFNS 200 µg QD, MFNS 200 µg BID, and placebo groups, respectively.

placebo, respectively. The most common adverse events considered to be possibly related to treatment were epistaxis (defined to include a wide range of bleeding episodes, from frank bleeding to bloody nasal discharge to flecks of blood in the mucus) and headache (Table III).

No deaths or life-threatening adverse events were reported during the study. Two subjects were reported to have serious adverse events during the treatment period, neither of which was considered to be related to the study drug. Ten subjects discontinued treatment because of adverse events (Table II), and 7 subjects interrupted randomized treatment because of an adverse event (MFNS 200 µg QD AM, 2 subjects; MFNS BID 200 µg, 3 subjects; placebo, 2 subjects). The majority of these events were considered mild or moderate in intensity and unrelated to study treatment.

No clinically meaningful changes in laboratory parameters, vital signs, or physical examination were noted in any treatment group. In the subset of subjects in whom 24-hour urinary free cortisol was measured (*n* = 164), no significant differences between treatment groups were noted for this parameter.

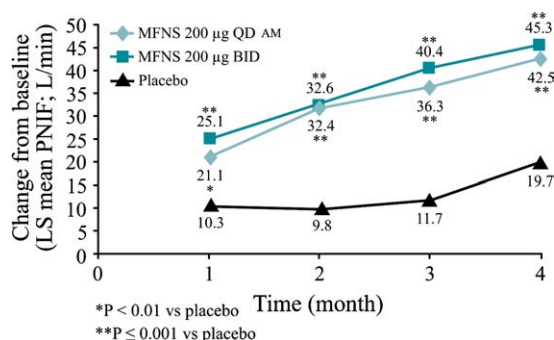


FIG 4. Change from baseline in PNIF during the treatment period. LS means and pairwise comparison *P* values were obtained from ANOVA with treatment, baseline asthma status, and site effects. Baseline PNIF rates were 87.6 L/min, 92.7 L/min, and 83.9 L/min in the MFNS 200 µg QD, MFNS 200 µg BID, and placebo groups, respectively.

TABLE III. Number of subjects (%) with adverse events considered to be related to treatment: Events occurring in ≥2% of subjects in any group

	MFNS 200 µg QD AM (n = 115)	MFNS 200 µg BID (n = 122)	Placebo (n = 117)
Epistaxis	7 (6)	15 (12)	5 (4)
Headache	3 (3)	5 (4)	7 (6)
Nasal dryness	2 (2)	2 (2)	3 (3)
Nasal irritation	2 (2)	2 (2)	2 (2)
Nasal burning	1 (1)	0 (0)	2 (2)
Dizziness	0 (0)	1 (1)	2 (2)
Sinusitis	0 (0)	0 (0)	3 (3)
Throat irritation	0 (0)	2 (2)	0 (0)
Hypertension	0 (0)	0 (0)	2 (2)

DISCUSSION

The objectives of medical therapy for nasal polyposis are to reduce or eliminate polyps, open the nasal airway, improve or restore the sense of smell, and prevent recurrence.^{9,10} Although endoscopic sinus surgery has been shown to be effective in reducing polyp size and nasal blockage, at least temporarily,¹⁸ a randomized controlled study evaluating medical treatment (oral and topical corticosteroids) with or without surgical treatment in subjects with symptomatic nasal polyposis found that medical treatment alone appeared to be sufficient to treat most of the symptoms.¹⁹

This study was designed to assess the efficacy and safety of 2 different doses of MFNS in the treatment of nasal polyposis over a 4-month period. Mometasone furoate is a potent, topically active, synthetic corticosteroid with anti-inflammatory activity. The nasal spray formulation of mometasone furoate is used therapeutically and prophylactically in seasonal allergic rhinitis and therapeutically in perennial allergic rhinitis.²⁰⁻²² Furthermore, MFNS is the first intranasal corticosteroid to be approved by the US

Food and Drug Administration for the medical treatment of nasal polyposis.

Subjects in this study had endoscopically verified bilateral nasal polyps, with a mean total bilateral grade score of approximately 4 and a relatively large polyp size, reaching below the inferior border of the middle turbinate. Baseline symptom scores indicated that subjects found congestion/obstruction and loss of smell more serious than other nasal symptoms, as in other studies of nasal polyposis.^{23,24}

Both dosage regimens were significantly more effective than placebo in substantially reducing polyp size and extent over the course of the study, with no statistically significant differences observed between the 2 active treatment groups. At the end of the treatment period, the change in bilateral polyp grade score overall with MFNS treatment represented a clinically significant reduction of approximately 30% relative to baseline score. Given that reducing nasal polyp size is generally thought to be a slow process, this degree of improvement in 4 months is noteworthy. Incremental improvements in polyp grade score continued throughout the course of the study, suggesting that treatment should be continued in patients to achieve full response. Furthermore, the observation that both doses produced statistically significant reductions in polyp size suggests that the intranasal spray formulation can be adequately delivered to the inflamed tissue in the upper part of the nasal cavity. Finally, a post hoc analysis of baseline polyp size suggests that the response to MFNS does not vary with the size of polyps. This result was confirmed by testing the treatment by polyp size (at baseline) interaction term in the ANOVA model. The test was not statistically significant ($P = .691$), suggesting that the response to treatment was not dependent on the size of the polyp.

Highly significant reductions in levels of congestion/obstruction were also observed relative to placebo at the first month of treatment and were sustained throughout the course of the study, with BID dosing showing statistical superiority to QD dosing at the first, third, and fourth month of treatment. Furthermore, when considering the effect on polyp grade and severity of congestion/obstruction together, 57% of MFNS 200 μ g BID recipients were considered to be improved, compared with 43% of MFNS 200 μ g QD and 34% of placebo recipients. This is an important indicator of the clinical significance of this treatment, particularly because the definition of response is based on individual subject changes. In addition, this response rate suggests that MFNS may offer patients a therapy option that can reduce or delay the need for nasal polyp surgery and relieve the symptoms of polyposis.

This concept is also supported by the ability of MFNS to relieve other symptoms of nasal polyposis, in particular loss of smell. Comparisons between medical and surgical treatment indicate that surgery has very little effect on hyposmia or anosmia,¹⁹ supporting the importance of medical therapy in treating this symptom.

Finally, this study also offered an opportunity to compare the relative effectiveness of the 2 dosing regimens

of MFNS. Interestingly, no statistically significant differences were observed between the 2 regimens for most parameters, except for the congestion/obstruction score, for which BID dosing was superior at months 1, 3, and 4, and the proportion of improvers at endpoint. These data suggest that QD dosing is as effective as BID dosing across the study population as a whole; however, it is likely that some patients will respond better to BID dosing, whereas QD dosing is sufficient in others.

Confirming its known safety profile in the treatment of allergic rhinitis, both MFNS dosing regimens were well tolerated during the study, with the most common adverse events consistent with those seen in previous clinical trials of MFNS in allergic rhinitis.^{20-22,25} Although hypothalamic-pituitary-adrenal axis suppression is often a concern for corticosteroids in general, there was no indication in this study of an effect of MFNS on this parameter, as indicated by lack of change in 24-hour urinary free cortisol over the treatment period. This surrogate measure of hypothalamic-pituitary-adrenal axis suppression is sensitive to the presence of systemic corticosteroids, even after short-term use of the medications.²⁶

In conclusion, the results of this multicenter, randomized, placebo-controlled trial demonstrate that MFNS is well tolerated and able to significantly reduce nasal polyp grade score and improve congestion/obstruction over a 4-month treatment period. Treatment with MFNS is also associated with improvements in loss of smell, anterior rhinorrhea, postnasal drip, and peak nasal inspiratory flow. Individual patient response is likely to determine whether once-daily or twice-daily dosing is appropriate. Therefore, treatment with MFNS is a useful management approach for patients with nasal polyposis and may reduce or delay the need for nasal polyp surgery while improving nasal symptoms.

Editorial assistance was provided by Thomson Gardiner-Caldwell London.

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