

Treating acute rhinosinusitis: Comparing efficacy and safety of mometasone furoate nasal spray, amoxicillin, and placebo

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Background: Intranasal corticosteroids used with antibiotics are known to improve rhinosinusitis symptoms compared with antibiotic therapy alone. However, the efficacy of intranasal corticosteroid monotherapy for acute, uncomplicated rhinosinusitis is not established.

Objectives: To evaluate efficacy and safety of mometasone furoate nasal spray (MFNS) versus amoxicillin and placebo in patients with acute, uncomplicated rhinosinusitis.

Methods: In this double-blind, double-dummy trial, subjects (≥ 12 years; $N = 981$) were randomized to MFNS 200 μg once daily or twice daily for 15 days, amoxicillin 500 mg 3 times daily for 10 days, or respective placebo. Follow-up was 14 days. The primary efficacy endpoint was mean AM/PM major symptom score over the treatment phase. Secondary efficacy endpoints included total symptom score. Safety assessments included disease recurrence during follow-up and adverse event monitoring.

Results: Mometasone furoate nasal spray 200 μg twice daily was significantly superior to placebo ($P < .001$) and amoxicillin ($P = .002$) at improving major symptom score. Starting on day 2, MFNS 200 μg twice daily improved total symptom score throughout treatment versus amoxicillin ($P = .012$) and placebo ($P < .001$). Global response to treatment was significantly greater with MFNS 200 μg twice daily versus amoxicillin ($P = .013$) and placebo ($P = .001$). Although significantly superior to placebo, MFNS 200 μg once daily was not superior to amoxicillin for the primary or secondary efficacy endpoints. All treatments were well tolerated with a similar incidence of adverse events.

Conclusion: In patients with acute, uncomplicated rhinosinusitis, MFNS 200 μg twice daily produced significant symptom improvements versus amoxicillin and placebo, without predisposing the patient to disease recurrence or bacterial infection. (J Allergy Clin Immunol 2005;116:1289-95.)

Key words: Acute rhinosinusitis, amoxicillin, intranasal corticosteroid, mometasone furoate, symptoms

Acute rhinosinusitis, an upper respiratory tract inflammatory disorder, occurs mostly as a consequence of viral rhinitis, although bacterial infection can subsequently arise. Symptoms occurring from inflammation of the contiguous nasal and sinus mucosal membrane can last from several days to as long as 4 weeks. These include nasal congestion, purulent discharge, fever, headache, facial and dental pain, postnasal drip, cough, and tenderness around the sinus area.^{1,2} Data indicate that the prevalence of rhinosinusitis is rising: for example, in the United States, the frequency has increased by 18% since 1997.¹ Consequently, the economic significance is substantial: in 1992, the total estimated cost of rhinosinusitis in the United States was \$6 billion.¹

Currently, treatment of acute rhinosinusitis is largely directed at eliminating bacterial infection, because this can not be ruled out of any diagnosis. Antimicrobial therapy, most commonly amoxicillin, is used for severe or persistent symptoms of rhinosinusitis lasting for at least 7 days.² Although antibiotics are prescribed for an estimated 85% to 98% of cases treated in primary care,³ evidence suggests that most cases of acute rhinosinusitis resolve without antibiotic treatment.

In a meta-analysis of 6 studies in which patients with acute rhinosinusitis were randomized to receive an antibacterial agent versus placebo, 70% of placebo patients recovered spontaneously.⁴ In addition, data from 2 separate randomized, clinical trials showed no significant differences in the recovery rates of patients with acute rhinosinusitis who received placebo compared with antibiotics.^{5,6} Furthermore, the Cochrane Collaboration meta-analysis (including 32 randomized trials) conducted in patients with acute maxillary sinusitis supported the use of antibiotics but acknowledged that their use in general practice was debatable because the benefit afforded by antibiotics is relatively small.⁷ Notably, given the increasing prevalence of antibacterial-resistant respiratory pathogens,⁸ concern is growing about the overuse of antibiotics.¹ Consequently, a conservative approach to their use in patients with acute rhinosinusitis symptoms is recommended, and it is advised that mild acute rhinosinusitis cases be managed on a symptomatic basis.⁹

However, several studies suggest that intranasal corticosteroids in adjunct to antibiotics are effective for improving the symptoms of acute rhinosinusitis.¹⁰⁻¹² In

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Abbreviations used

MFNS: Mometasone furoate nasal spray
MSS: Major symptom score
TSS: Total symptom score

the Cefitin and Flonase for Sinusitis trial, patients with a history of recurrent rhinosinusitis receiving cefuroxime axetil with intranasal fluticasone propionate demonstrated greater improvement in their symptoms compared with patients receiving antibiotics alone.¹²

Recently, the efficacy of mometasone furoate nasal spray (MFNS) as an adjunctive therapy to antibiotics in the treatment of rhinosinusitis has been established. In 1 study of acute sinusitis, patients treated with amoxicillin potassium clavulanate were randomized to receive MFNS 400 µg twice daily or placebo. Data indicated that the inflammatory symptoms of headache, nasal congestion, and facial pain were significantly reduced with MFNS adjunctive therapy versus placebo.¹³ Data from a second study, in which patients with acute rhinosinusitis were treated with MFNS 200 µg twice daily or MFNS 400 µg twice daily as adjunctive therapy to amoxicillin potassium clavulanate, supported the findings from the first study.¹⁴

To date, there have been no studies of nasal steroids as monotherapy for acute rhinosinusitis. Mometasone furoate is a potent, topically active, anti-inflammatory corticosteroid prescribed for both therapeutic and prophylactic management of seasonal and perennial allergic rhinitis.¹⁵⁻¹⁹ This study evaluated the effectiveness of MFNS 200 µg twice daily and 200 µg once daily compared with amoxicillin and placebo in patients with acute, uncomplicated rhinosinusitis lasting for at least 7 days.

METHODS

Study design

This randomized, double-blind, double-dummy, placebo-controlled study was conducted at 71 medical centers in 14 countries from January to September 2003. The study compared the efficacy and safety of MFNS 200 µg once daily with MFNS 200 µg twice daily to establish the minimally effective MFNS dose.

The study was conducted in accordance with the Declaration of Helsinki and guidelines on Good Clinical Practice. Subjects who were eligible at the screening visit (visit 1) and baseline visit (visit 2) were randomized in a 1:1:1:1 ratio to 1 of 4 treatment arms: MFNS 200 µg in the morning (MFNS once daily) with placebo spray in the evening, MFNS 200 µg in the morning and evening (AM and PM, respectively, MFNS twice daily), amoxicillin 500 mg 3 times daily, or placebo. Those receiving MFNS received a matching placebo capsule 3 times daily, and those receiving amoxicillin a matching placebo nasal spray twice daily; patients randomized to placebo received placebo capsules 3 times daily and placebo nasal spray twice daily. Randomization was performed according to a computer-generated code, stratified on the basis of duration of rhinosinusitis symptoms before baseline (7-14 days and 15-28 days).

Nasal sprays were given for 15 days and capsules for the first 10 days. A 14-day, nontreatment, observational period followed. After the baseline visit, subjects were monitored by telephone on days 3 to 4, with treatment visits on days 8 (visit 3), 15 (visit 4), and 29 (visit 5). Subjects evaluated and recorded their rhinosinusitis symptoms over the period of the previous 12 hours in the AM and PM each day as 0 (none), 1 (mild), 2 (moderate), or 3 (severe). Major symptom score (MSS; sum of the scores for rhinorrhea, postnasal drip, nasal congestion/stuffiness, sinus headache, and facial pain/pressure/tenderness on palpation over the paranasal sinuses) and total symptom score (TSS; the sum of the MSS and cough score assessed on the same scale, ranging from 0 to 3) were evaluated. Treatment compliance was evaluated at visits 3 and 4 by questioning whether the study drug had been taken as instructed.

Subjects

Male and female subjects age ≥12 years with signs and symptoms of acute rhinosinusitis for ≥7 days but ≤28 days were eligible for inclusion. In addition, the MSS had to be ≥5 but ≤12 at screening and baseline visits (assessed jointly by the subject and investigator), with no more than 3 of the 5 symptoms rated severe.

Subjects were excluded if they had signs or symptoms suggestive of fulminant bacterial rhinosinusitis (fever ≥101°F/38.3°C, persistent severe unilateral facial or tooth pain, facial swelling, dental involvement, or a worsening of symptoms after initial improvement). Subjects were excluded if they had chronic rhinosinusitis (or sinus or nasal surgery for this condition within 6 months before screening), otitis or atrophic rhinitis, nasal polyps noted on anterior rhinoscopic examination, symptomatic seasonal allergic rhinitis (after pollen exposure during the study), an allergy to corticosteroids, or any other condition that would interfere with study evaluations. Subjects with asthma needed to be relatively stable with no history of exacerbations within 30 days before screening, and a FEV₁ ≥65% of predicted within 3 months before screening.

Concomitant medications that would interfere with study evaluations were not permitted, including nasal saline, nasal cromolyn sodium, ipratropium bromide, corticosteroids (excluding oral inhaled corticosteroids for mild to moderate persistent asthma), antihistamines, decongestants, and leukotriene pathway modifiers. Analgesics and nonsteroidal anti-inflammatory drugs were prohibited for the treatment of acute rhinosinusitis.

Efficacy endpoints

The primary efficacy endpoint was mean AM/PM MSS over days 2 to 15 of the treatment phase.

Secondary efficacy endpoints included mean MSS, TSS, and individual scores (average of AM/PM scores) for each symptom averaged weekly and for days 2 to 15 and 16 to 29. Time to onset of action was assessed and defined as the first day of active treatment on which MSS was statistically significantly different from placebo and sustained thereafter. Groups were compared for a global response to treatment at visit 4 or the last treatment visit (on a scale of 0 [complete relief] to 4 [no relief]). The subject's response to treatment was jointly evaluated by the investigator and the subject.

Subjects presenting with symptoms suggestive of fulminant bacterial rhinosinusitis or worsening or no improvement of symptoms by day 3 to 4 or thereafter were evaluated to determine whether they had failed to respond to treatment. The proportion of subjects who met the criteria for treatment failure was evaluated.

Safety assessments

Reported adverse events were recorded throughout the study, with severity graded as mild, moderate, severe, or life-threatening, and

TABLE I. Demographic details and baseline symptom scores for each treatment group (intent-to-treat population)

	MFNS 200 µg once daily AM (n = 243)	MFNS 200 µg twice daily (n = 235)	Amoxicillin 500 mg 3 times daily (n = 251)	Placebo (n = 252)
Mean age, y (range)	35.9 (12-76)	34.8 (12-66)	35.9 (12-69)	34.4 (12-68)
Male:female (%)	33:67	37:63	30:70	38:62
Mean weight, kg (range)	72.61 (41.7-153.0)*	71.48 (41.7-190.5)	69.05 (36.5-124.3)	71.05 (35.8-154.2)
History of seasonal allergic rhinitis, n (%)	40 (16)	50 (21)	40 (16)	44 (17)
History of perennial allergic rhinitis, n (%)	65 (27)	66 (28)	58 (23)	67 (27)
Duration of previous rhinosinusitis symptoms, n (%)				
6-14 d†	164 (67%)	153 (65%)	154 (61%)	147 (58%)
15-28 d	79 (33%)	82 (35%)	97 (39%)	105 (42%)
Mean AM/PM MSS	8.17	8.28	8.53	8.36

*Value for 1 subject missing. Summary statistics are based on the number of subjects who had nonmissing baseline values.

†Nine subjects were enrolled with 6 days' duration of symptoms instead of the originally specified minimum of 7 days.

a relationship to treatment was assigned by the investigator. At all visits, vital signs were measured, and a nasal examination was performed. Clinical laboratory tests and a physical examination were conducted at screening and the last treatment visit. The key safety variable was the proportion of subjects, as assessed by the physician, who met disease criteria for recurrence/relapse during the follow-up phase.

Statistical methods

All analyses and summaries were based on randomized subjects (intent-to-treat). A mean effects ANOVA was used to analyze responses for the primary endpoint with SAS software (Version 8 of the SAS System for Unix; SAS Institute Inc, Cary, NC). The primary and secondary treatment comparisons were MFNS 200 µg twice daily versus placebo and versus amoxicillin, respectively. These pairwise comparisons were based on the least-square means from the ANOVA model and were tested at a 2-sided α level of 0.05. If both were significant, then MFNS 200 µg once daily AM was compared with placebo and amoxicillin. A mean effects ANOVA was also used to analyze secondary endpoints: TSS, MSS, and individual symptom scores by week and at days 2 to 15 and 16 to 29; time to onset of action; and global response to treatment. Time to discontinuation was examined by using Kaplan-Meier estimates and tested for each pair of treatments by using the stratified log-rank test. Each MFNS treatment group was compared with the amoxicillin and placebo groups by using a Fisher exact test.

It was established that a total target sample size of ~940 subjects (235 subjects/treatment group) would provide 90% power at a 2-sided α level of 0.049 to detect a difference of ≥ 0.7 points in mean AM/PM MSS over days 1 to 15 between treatment groups. Joint power for detecting differences for MFNS 200 µg twice daily versus placebo and versus amoxicillin was at least 81%.

RESULTS

Subject disposition and characteristics

A total of 981 subjects were randomized to treatment. Each subject received at least 1 dose of study drug and was included in the efficacy and safety analyses. There were no clinically relevant differences in demographic characteristics between the treatment groups, and baseline symptom data were comparable (Table I). Mean MSS at baseline was 8.17 to 8.53 across the 4 treatment groups, indicating that most subjects had mild-to-moderate disease. Less than 22% and 29% of subjects had a history

of seasonal or perennial allergic rhinitis, respectively; this was comparable across the treatment groups.

Ninety-six subjects (10%) discontinued from treatment (days 1-15; Table II), 44 because of treatment failure and 10 after protocol noncompliance. A greater proportion of placebo recipients (13%) than treatment recipients (8% to 9%/group) discontinued. Although all subjects were expected to proceed to the follow-up phase (days 16-29), 30 did not. A further 6 subjects discontinued during follow-up, 3 because of noncompliance.

Efficacy endpoints

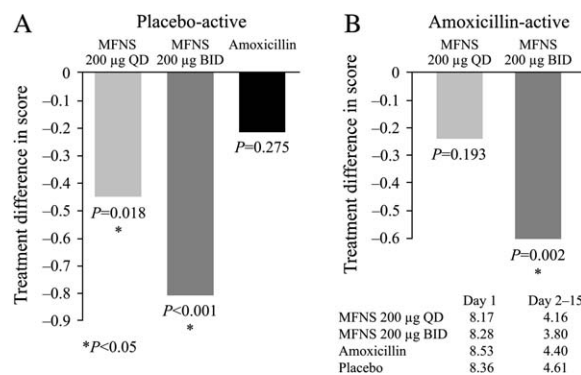
Mean AM/PM MSS. For the primary efficacy variable of mean MSS over the 15-day treatment phase, MFNS 200 µg twice daily was significantly superior to placebo ($P < .001$) and amoxicillin ($P = .002$; Fig 1). A treatment difference of 0.81 points for MFNS 200 µg twice daily versus placebo indicated a 9% relative improvement in MSS. Relative superiority to placebo was demonstrated each day during treatment and throughout follow-up (days 16-29; $P \leq .037$), and to amoxicillin at most time intervals.

Mean AM/PM TSS. The results of the analysis of the TSS were consistent with the analysis of the MSS, because the contribution of cough score to the TSS was minimal. MFNS 200 µg twice daily gave significant improvements in mean TSS over the 15-day treatment phase versus placebo ($P < .001$) and amoxicillin ($P = .012$). Although significantly superior to placebo ($P = .025$), MFNS 200 µg once daily AM was not shown to be superior to amoxicillin. No significant differences between the 2 doses of MFNS or between amoxicillin and placebo were noted.

Mean AM/PM individual symptom scores. The mean individual symptom scores over the 15-day treatment phase showed MFNS 200 µg twice daily as significantly superior to placebo and amoxicillin in 4 of the 6 symptom scores (rhinorrhea [$P \leq .001$], nasal congestion/stuffiness [$P \leq .001$], sinus headache [$P \leq .01$], and facial pain/pressure/tenderness [$P \leq .05$]). MFNS 200 µg once daily AM demonstrated significant improvement over placebo for rhinorrhea and nasal congestion/stuffiness scores ($P \leq .001$). No statistical differences for MFNS 200 µg once daily AM were observed relative to amoxicillin in

TABLE II. Number (%) of subjects who completed treatment/follow-up, number (%) of subjects who discontinued from treatment/follow-up, and reasons for discontinuation (intent-to-treat population)

	MFNS 200 µg once daily AM	MFNS 200 µg twice daily	Amoxicillin 500 mg 3 times daily	Placebo
Treatment phase (days 1-15)				
Subjects randomized	243 (100%)	235 (100%)	251 (100%)	252 (100%)
Subjects completed	220 (91%)	215 (91%)	231 (92%)	219 (87%)
Subjects discontinued	23 (9%)	20 (9%)	20 (8%)	33 (13%)
Reasons for discontinuation				
Adverse event	2 (1%)	7 (3%)	5 (2%)	6 (2%)
Treatment failure	13 (5%)	8 (3%)	9 (4%)	14 (6%)
Lost to follow-up	3 (1%)	1 (<1%)	1 (<1%)	4 (2%)
Did not wish to continue	1 (<1%)	2 (1%)	2 (1%)	2 (1%)
Noncompliance with protocol	2 (1%)	2 (1%)	3 (1%)	3 (1%)
Did not meet protocol criteria for entry	2 (1%)	0	0	4 (2%)
Follow-up phase (days 16-29)				
Subjects entered into follow-up	235 (100%)	230 (100%)	245 (100%)	241 (100%)
Subjects completed follow-up	232 (99%)	224 (97%)	242 (99%)	231 (96%)
Subjects discontinued	3 (1%)	6 (3%)	3 (1%)	10 (4%)
Reasons for discontinuation				
Adverse event	0	3 (1%)	0	0
Treatment failure	0	1 (<1%)	0	1 (<1%)
Lost to follow-up	1 (<1%)	2 (1%)	1 (<1%)	3 (1%)
Did not wish to continue	1 (<1%)	0	1 (<1%)	5 (2%)
Noncompliance with protocol	1 (<1%)	0	1 (<1%)	1 (<1%)
Missing	8	5	6	11

**FIG 1.** Difference in mean MSS (averaged daily for AM and PM assessments) over days 2 to 15. **A**, Active treatment groups compared with placebo. **B**, MFNS treatment groups compared with amoxicillin. Analyses are based on intent-to-treat population. BID, Twice daily; QD, once daily.

any of the individual symptom scores. MFNS 200 µg twice daily demonstrated significant superiority over MFNS 200 µg once daily AM in nasal congestion/stuffiness score ($P = .013$). Amoxicillin demonstrated a significant improvement over placebo in rhinorrhea, nasal congestion/stuffiness, and cough scores ($P \leq .032$; Table III).

Time to onset of action (MSS). The time to onset of action of MFNS 200 µg twice daily was shown to be day 2—that is, the day after the first dose of study medication (Fig 2).

Global response to treatment. At the last treatment visit (day 15, or earlier if subjects discontinued before this), MFNS 200 µg twice daily demonstrated a significant improvement over MFNS 200 µg once daily AM ($P = .002$), amoxicillin ($P = .013$), and placebo ($P = .001$) in terms of the patient-derived global response to treatment. No other pairwise treatment comparisons demonstrated significant between-treatment differences.

Treatment failure. A total of 81 subjects met criteria for treatment failure during the treatment phase. Fewer subjects treated with MFNS 200 µg twice daily had treatment failure ($n = 11$; 4.7%) compared with MFNS 200 µg once daily AM ($n = 25$; 10.3%; $P = .024$), amoxicillin ($n = 18$; 7.2%; $P = .258$), or placebo ($n = 27$; 10.7%; $P = .017$). Although not significant, fewer subjects treated with MFNS 200 µg twice daily discontinued treatment early because of treatment failure ($n = 8$; 3%) compared with MFNS 200 µg once daily AM ($n = 13$; 5%), placebo ($n = 14$; 6%), or amoxicillin ($n = 9$; 4%) subjects.

Safety assessments. Treatment with MFNS or amoxicillin was well tolerated with no unexpected events. Most adverse events were mild or moderate and were considered unlikely to be related to study treatment. The incidence of treatment-emergent adverse events was similar among the treatment groups: 36.2%, 35.4%, 33.5%, and 38.1% with MFNS 200 µg twice daily, MFNS 200 µg once daily AM, amoxicillin, and placebo, respectively. The most common treatment-emergent adverse events were headache and epistaxis (see Table E1 in the Online

TABLE III. Mean AM/PM individual symptom scores (least-squares means)*

	MFNS 200 µg once daily AM		MFNS 200 µg twice daily		Amoxicillin 500 mg 3 times daily		Placebo	
	n	Least-squares mean	n	Least-squares mean	n	Least-squares mean	n	Least-squares mean
Rhinorrhea								
Baseline	243	1.66	234	1.72	251	1.69	252	1.76
Days 2-15	240	0.89†	234	0.81†¶	249	0.92‡	247	1.04
Postnasal drip								
Baseline	243	1.80	234	1.88	251	1.87	252	1.84
Days 2-15	240	1.00	234	0.95	249	1.04	247	1.01
Nasal congestion/stuffiness								
Baseline	243	2.06	234	2.02	251	1.98	252	2.04
Days 2-15	240	1.06†#	234	0.94†	249	1.09†	247	1.25
Sinus headache								
Baseline	243	1.34	234	1.38	251	1.52	252	1.39
Days 2-15	240	0.63	234	0.57‡¶	249	0.71	247	0.68
Facial pain/pressure/tenderness								
Baseline	243	1.31	234	1.29	251	1.47	252	1.32
Days 2-15	240	0.57	234	0.52§¶	249	0.64	247	0.64
Cough								
Baseline	243	0.96	234	1.06	251	1.00	252	1.04
Days 2-15	240	0.57	234	0.55	249	0.50§	247	0.61

*Symptoms scored from 0 (none) to 3 (severe). Analyses are based on intent-to-treat population. Least-squares means were obtained from the ANOVA model with effects for treatment, site, and duration of symptoms (6-14 days or 15-28 days).

† $P \leq .001$ vs placebo; ‡ $P \leq .01$ vs placebo; § $P \leq .05$ vs placebo.

|| $P \leq .01$ vs amoxicillin; ¶ $P \leq .05$ vs amoxicillin.

$P \leq .05$ vs MFNS 200 µg twice daily.

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Nineteen subjects (1.9%) discontinued treatment because of adverse events (MFNS 200 µg once daily AM, $n = 1$; MFNS twice daily 200 µg, $n = 7$; amoxicillin, $n = 5$; placebo, $n = 6$). Sixty-three subjects entering follow-up exhibited prespecified disease criteria for recurrence. Fewer subjects on MFNS 200 µg once daily AM had recurrence ($n = 10$; 4.3%) versus MFNS 200 µg twice daily ($n = 16$; 7.0%), amoxicillin ($n = 20$; 8.2%), or placebo ($n = 17$; 7.1%). No significant differences were observed between treatment groups. No clinically meaningful changes in laboratory parameters, vital signs, or physical examinations were noted.

DISCUSSION

It has been shown that acute rhinosinusitis frequently resolves without medical intervention. This is most likely a result of the underlying viral and/or bacterial pathology of acute rhinosinusitis. Nevertheless, considering the host of symptoms associated with acute rhinosinusitis, recovery can take time and be of substantial discomfort to the affected patient. Although antibiotics have been the mainstay of therapy,^{20,21} recent evidence has suggested that intranasal corticosteroids can provide additional benefit when used as an adjunct.^{13,14} However, to date, there are no published data on the effectiveness of intranasal corticosteroid monotherapy for the treatment of rhinosinusitis.

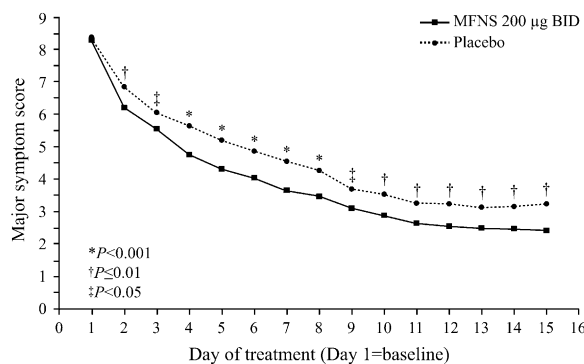


FIG 2. Change in MSS over time. Analyses are based on intent-to-treat population. BID, Twice daily.

The aim of this study was to evaluate the efficacy of MFNS monotherapy versus amoxicillin and placebo in the treatment of acute, uncomplicated rhinosinusitis.

In this trial, MFNS 200 µg twice daily monotherapy was significantly more effective than amoxicillin or placebo in relieving the symptoms of acute rhinosinusitis. This finding is consistent with the fact that intranasal corticosteroids act on the glucocorticoid receptor to inhibit transcription of proinflammatory mediators, which are upregulated during the inflammatory response.¹ Although a treatment difference of only 0.81 points was recorded for MFNS 200 µg twice daily versus placebo at the end of the treatment period, the change in the MSS represented a clinically significant reduction of approximately 46%

relative to baseline and 9% relative to placebo. This is a considerable improvement within the short treatment period of 15 days. These results are also comparable with those reported for intranasal corticosteroids used as adjunct to antibiotics in the treatment of acute rhinosinusitis.¹³ In this study, patients receiving MFNS in adjunct to amoxicillin clavulanate potassium showed a 0.82-point difference relative to placebo when recorded by using the same 4-point rating scale used in the current study. Interestingly, our data also correlate well with the results obtained in a further study on the efficacy of an antihistamine for the treatment of allergic rhinitis²²; a 1.2 total symptom score point difference between fexofenadine 120 mg once daily and placebo was reported when scored by using a 5-point rating scale.

The results from our study also showed that MFNS 200 µg twice daily provides rapid and sustained symptom relief from day 2. Although MFNS 200 µg once daily was significantly superior to placebo, MFNS 200 µg twice daily was more consistently superior across the endpoints and over amoxicillin. It was also at least numerically greater than the once-daily dose, suggesting that the higher dose of MFNS is required to treat rhinosinusitis effectively.

It is postulated that these study results will be achievable in practice, because the inclusion criteria of this study were designed to reflect the patient group seen in general practice; patients suggestive of signs/symptoms of fulminant bacterial rhinosinusitis requiring antibiotic treatment were excluded. However, despite these stringent exclusion criteria, one cannot fully rule out the possibility that subjects with a bacterial form of acute, uncomplicated rhinosinusitis may have been included in addition to those subjects with viral rhinosinusitis.^{2,23} In this trial, no differences between amoxicillin, a standard antibiotic in the care of acute rhinosinusitis,^{2,23} and placebo for overall MSS or TSS were observed. These data reflect results reported in other studies; for example, no significant differences in the length of time to cure between the 2 treatment groups were observed in subjects with acute rhinosinusitis who received either amoxicillin clavulanate potassium or placebo.²³ Such data reinforce the argument for decreasing antibiotic prescribing in acute rhinosinusitis. Furthermore, although laboratory confirmation was not obtained, this study suggests that it is likely that many of the patients recruited for this study in fact had the viral versus the bacterial form of acute, uncomplicated rhinosinusitis, similar to patients cared for in general practice.

Nasal congestion, which manifests as a blockage of the nostrils, is a critical symptom of diseases of the upper respiratory tract. Indeed, this symptom is reported to occur in 85% of patients with allergic rhinitis.²⁴ Furthermore, in a large internet survey conducted by Roper Public Affairs Group of NOP World, more than half of the respondents with allergic rhinitis considered nasal congestion to be the most bothersome symptom of their disease.²⁴ This result is not surprising considering data indicating that nasal congestion has severe implications for the patient: it affects the ability to sleep and perform daily activities, and

the state of emotional well being.²⁵ Although no such surveys have been conducted in patients with rhinosinusitis, given these data and the fact that allergic rhinitis is closely associated with rhinosinusitis, it is likely that nasal congestion has a major effect on patients with acute rhinosinusitis. Thus, the results of the current study showing MFNS 200 µg twice daily to be significantly superior to amoxicillin and placebo in 4 of the individual symptom scores, including nasal congestion/stuffiness, are of particular clinical relevance. Another clinically meaningful result was the patient-derived assessment of the global response to treatment. It was also significantly improved with MFNS 200 µg twice daily versus placebo and amoxicillin as reflective of the entire treatment period. This suggests that patients receiving MFNS 200 µg twice daily were more satisfied with their treatment, in terms of relieving symptoms, compared with patients administered amoxicillin or placebo.

From a safety standpoint, the 14-day follow-up observational period after the study medications were discontinued was important. It showed that there appeared to be no greater risk of bacterial infections and recurrence or exacerbation of rhinosinusitis after MFNS treatment compared with amoxicillin or placebo. These findings are of particular relevance considering the increasing prevalence and associated costs of rhinosinusitis.¹ Moreover, the percentage of patients reported with treatment failure was significantly lower for the MFNS 200 µg twice-daily recipients compared with placebo recipients. However, it should be noted that the short-term follow-up used in this study does not allow for prediction of recurrence rates over extended periods.

Both MFNS dosages were well tolerated. The 2 most common adverse events seen, headache and epistaxis, had a similar incidence between treatment groups and were consistent with clinical data for MFNS in the treatment of allergic rhinitis.¹⁴⁻¹⁸

In conclusion, this study is the first to demonstrate the efficacy of an intranasal corticosteroid as an effective monotherapy in acute rhinosinusitis. MFNS 200 µg twice daily monotherapy was well tolerated and induced significantly greater, sustained relief of most acute rhinosinusitis symptoms compared with amoxicillin and placebo. Furthermore, there was no evidence suggestive of rhinosinusitis recurrence or predisposition to bacterial infections after MFNS therapy cessation, supporting a recommendation to reduce prescribing of antibiotics for patients presenting with these clinical findings. These data indicate MFNS monotherapy is an effective treatment option for relieving the symptoms faced by patients of acute, uncomplicated rhinosinusitis in general practice.

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