

Symptom Suppression in Subjects with Perennial Allergic Rhinitis Treated with Mometasone Furoate Nasal Spray

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Key Words

Allergic rhinitis • Intranasal corticosteroids • Quality of life • Total nasal symptom score

Abstract

Background: Allergic rhinitis (AR) carries a high symptom burden and impact on quality of life. The ability of an AR treatment to achieve and sustain symptom suppression would be expected to enhance quality of life and improve long-term outcomes. **Methods:** In this ad hoc analysis of data from 4 phase 3 clinical trials of mometasone furoate nasal spray (MFNS), subjects with perennial AR recorded the severity of nasal symptoms twice daily for 12 weeks on a 4-point scale to determine the total nasal symptom score. **Results:** In the pooled sample of 1,149 subjects, 580 received MFNS 200 µg per day and 569 received placebo. Significantly more subjects receiving MFNS achieved symptom suppression versus those receiving placebo: 63.3% (n = 367) versus 51.0% (n = 290; p < 0.001). Median time to suppression was significantly shorter with MFNS versus placebo (29 vs. 59 days; p < 0.001). Total suppression was achieved in a significantly greater percentage of patients receiving MFNS versus placebo (36.0 vs. 25.5%; p < 0.001). **Conclusions:** A high level

of symptom relief is attained faster and sustained longer with MFNS. This analysis validates the importance of treatment adherence to achieve optimal, sustained symptom relief.

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Introduction

Allergic rhinitis (AR) is a widespread (affecting more than 500 million persons worldwide) [1] and increasing health issue that imposes a marked, yet often underappreciated, impact on individual quality of life (QOL). Its burden is particularly great among those with perennial AR (PAR), whose symptom load is comparatively higher than that of subjects suffering from seasonal AR and for whom there is no seasonal variation [2, 3].

Recent 'real-world' survey data suggest that many patients with AR fail to achieve adequate symptom control, even with multiple medications [2, 3]. The ability of a

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Table 1. Details of studies included in the pooled analysis

	Study 92-280	Study 92-293	Study 94-078	Study 94-079
Duration	12 weeks	12 weeks	3 months	12 weeks
Run-in period	7–14 days	7–14 days	7–14 days	7–14 days
Timing	Aug.–May 1994	Oct.–June 1994	Jan. 1995–Sep. 1995	Dec. 1994–June 1995
Location	19 centers in the US	24 centers in Canada, Belgium, Finland, Germany, The Netherlands, Norway, Sweden, Switzerland, UK	25 centers in Canada, Argentina, Chile, Venezuela, Mexico, Columbia, Guatemala, Austria, Portugal, UK	25 centers in Canada, Argentina, Chile, Venezuela, Mexico, Columbia, Guatemala, Austria, Portugal, UK
Allergen testing	Skin test for dust mite, cockroach, molds or animal dander (if daily exposure to animal was present)	Skin test for dust mite, cockroach, molds or animal dander (if daily exposure to animal was present)	Skin test for perennial allergen (not specified) or NARES ¹ Patients allergic to animal dander were required to be subject to daily exposure	Skin test for perennial allergen (not specified) or NARES ¹

¹ Only subjects with positive skin prick tests were included in the present analysis. NARES = Nonallergic rhinitis eosinophilia syndrome.

treatment to achieve and sustain symptom suppression would be expected to provide enhanced QOL, prevent symptom recurrence and improve long-term outcomes. In addition, QOL in AR patients has been shown to correlate with the number of symptom-free days [2, 3]. Symptom improvement is commonly reported in AR clinical trials, yet there are relatively few data on time to suppression and duration of suppression. These concepts prompted us to propose an analysis not simply of the degree of symptom improvement, as is commonly reported, but also to measure the dynamics of overall symptom suppression, including the time until suppression is achieved and the length of time it can be maintained.

Material and Methods

We performed an ad hoc analysis of data from 4 similarly designed phase 3 clinical trials of mometasone furoate nasal spray (MFNS) in subjects with PAR, with a particular interest in time to symptom suppression and to symptom recurrence [4–6]. Details of the studies are shown in table 1. Subjects in the pooled study sample were aged ≥ 12 years, with at least a 2-year history of PAR symptoms. Although subjects with nonallergic rhinitis eosinophilia syndrome were also enrolled in 2 of the 4 studies, they were excluded from this analysis by including only those with positive skin test results.

Subjects scored the severity of individual nasal symptoms (congestion, itching, sneezing, rhinorrhea) in diaries twice daily (AM and PM, reflective over the previous 12 h), using a 4-point scale from 0 (none) to 3 (severe) over a period of 12 weeks. A total nasal symptom score (TNSS) was determined as the sum of the averaged AM/PM individual scores (maximum TNSS = 12). Eli-

gible participants were required to be sufficiently symptomatic, with a baseline congestion score severity ≥ 2 and a TNSS ≥ 5 .

For this analysis, we defined symptom suppression as a $\geq 75\%$ decrease in TNSS from baseline. A suppressed week was defined as a week in which TNSS was 0 on at least 1 day. Symptom recurrence was defined as a return to TNSS $\geq 50\%$ of baseline after achieving suppression. Minimal-symptom days were defined as days on which all individual symptom scores were ≤ 1 and TNSS was ≤ 2 . Total suppression was defined as a TNSS = 0.

Results

Among the 1,149 qualifying subjects, 580 received MFNS 200 μg and 569 received placebo (vehicle minus mometasone furoate) once daily over the study period. Mean baseline TNSS were similar between groups (MFNS = 6.35, placebo = 6.32). The median time to symptom suppression was significantly shorter with MFNS compared with placebo, by a difference of about 4 weeks (29 vs. 59 days; $p < 0.001$). Furthermore, the percentage of subjects who achieved symptom suppression at any point was significantly greater in the MFNS group compared with the placebo group: 63.3% (367/580) versus 51.0% (290/569; $p < 0.001$). Total suppression (TNSS = 0) was achieved in a significantly greater percentage of patients receiving MFNS versus placebo: 36.0% ($n = 209$) versus 25.5% ($n = 145$; $p < 0.001$).

Following initial suppression, treatment with MFNS resulted in a significantly higher proportion of minimal-symptom days compared with placebo (72.3 vs. 54.2%;

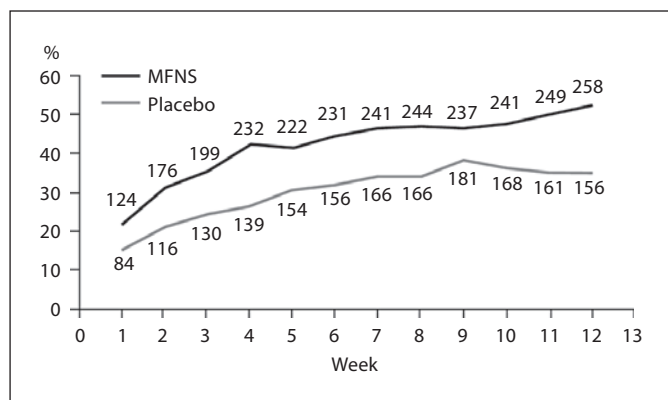


Fig. 1. Number of patients experiencing suppressed weeks (weeks in which subjects reported TNSS = 0 on at least 1 day) with MFNS and placebo. Data from 4 pooled PAR studies. MFNS = Mometasone furoate nasal spray; PAR = perennial allergic rhinitis; TNSS = total nasal symptom score.

$p < 0.001$). Once achieved, symptom suppression was maintained for 8 days with MFNS versus 5 days with placebo ($p = 0.003$). Additionally, subjects in the MFNS group had more suppressed weeks (2,654/6,395 patient-weeks, 41.5%) than did those in the placebo group (1,777/6,059 patient-weeks, 29.3%; odds ratio 1.710; $p < 0.001$) (fig. 1). The number of patients receiving MFNS experiencing suppressed weeks was notably higher versus the placebo group as early as week 1. Among subjects who achieved symptom suppression, significantly more in the MFNS group were still without recurrence (TNSS $\geq 50\%$ of baseline) at both 30 days (28.1 vs. 20.0%; $p = 0.017$) and 60 days (21.8 vs. 15.5%; $p = 0.042$). Figure 2 shows the percentage of patients with no recurrence of symptoms after achieving suppression, indicating the consistently greater proportion of MFNS patients with sustained symptom relief throughout the study period.

Discussion

While MFNS demonstrated clear statistical advantage compared with placebo, the numerical differences between the 2 treatments may be perceived as less dramatic. However, it is likely that saline nasal spray (the placebo intervention) may provide some degree of physiologic benefit in PAR. Saline irrigation has been reported to reduce levels of some inflammatory mediators (histamine, leukotriene C₄, soluble intercellular adhesion molecule-1) in nasal secretions [7, 8] and has been shown to have mea-

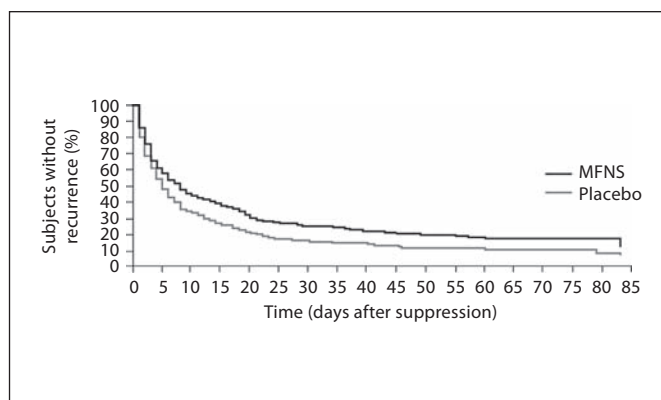


Fig. 2. Time to recurrence of symptoms in subjects who achieved initial symptom suppression at any time. In the MFNS and placebo groups, 367 and 290 subjects, respectively ($p < 0.001$), achieved initial symptom suppression ($p = 0.003$ for difference vs. placebo in time to recurrence). MFNS = Mometasone furoate nasal spray.

surable clinical benefits in relieving/preventing nasal symptoms [8, 9]. As a result, a true 'placebo effect' is difficult to study with an intranasal preparation.

Furthermore, we defined a decrease in TNSS of $\geq 75\%$ as the benchmark for symptom suppression. A prior study comparing MFNS and fluticasone propionate nasal spray in subjects with PAR reported mean reductions from baseline in TNSS ranging from 37 to 63% during different 15-day segments [5], indicating that an improvement in $\geq 75\%$ is an aggressive target indicative of robust symptom relief. The current analysis confirmed that this high level of symptom relief was attained significantly faster and sustained significantly longer among subjects using MFNS. This is important as QOL scores have been shown to correlate with symptom-free days [2]. The high level of symptom relief was also indicated by the greater percentage of minimal-symptom days and suppressed weeks among patients receiving MFNS.

These findings indicate that MFNS can achieve substantial and sustained symptom relief in AR in a controlled study environment. Unfortunately, outside the clinical study setting, adherence issues may preclude the achievement of maximum efficacy with MFNS and other intranasal steroids (INSs) [10]. It is not uncommon for AR patients to stop using medications after their symptoms have been sufficiently relieved. A small Canadian survey of pediatric patients with AR reported that only about half of respondents used INSs daily as directed by their physician [11]. In a survey of 2,500 adult allergy sufferers,

37% reported stopping their allergy medication because of perceived ineffectiveness [12]; in a study of 63 adults, over 75% reported forgetfulness [10]. In PAR, symptoms wax and wane, and treatment lags behind symptoms. In a downward cycle, the reduced efficacy attendant upon nonadherence may further hinder adherence because of perceived lack of benefit.

With regular, consistent use, almost two thirds of subjects using MFNS in this analysis experienced suppression of symptoms at some point during 12 weeks of treatment. Patients who are well counseled on the expected time frame of symptom improvement and the impor-

tance of regular, daily INS administration even after experiencing initial symptom relief are more likely to attain maximal symptom suppression and better QOL.

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