

Effect of desloratadine on the control of morning symptoms in patients with seasonal and perennial allergic rhinitis

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ABSTRACT

The symptoms of allergic rhinitis vary in severity over the course of the day and often are worse in the morning. This review focuses on data from clinical studies of the antihistamine desloratadine to establish whether it effectively controls the morning symptoms of allergic rhinitis. Studies of desloratadine in patients with allergic rhinitis that used instantaneous scoring to assess the severity of morning symptoms were selected for inclusion from published literature (peer-reviewed articles and abstracts presented at professional meetings). When administered once daily, desloratadine is effective in alleviating the morning symptoms of allergic rhinitis, including nasal congestion. Its action is sustained over the 24-hour dosing interval. A comparison of morning and evening dosing of desloratadine revealed equivalent relief of morning symptoms, illustrating that the effect of desloratadine is independent of the time of dosing. Clinical studies indicate that desloratadine is nonsedating and well tolerated, with no evidence of adverse cardiac effects. For many patients with allergic rhinitis, symptoms are most severe in the morning. To maximize the benefits for patients, pharmacologic agents used in the management of allergic rhinitis should be effective in controlling these peak morning symptoms. The sustained 24-hour action of desloratadine and its effective control of morning symptoms make it a valuable tool for improving the quality of life of patients with allergic rhinitis.

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Allergic rhinitis is the most common form of chronic rhinitis or inflammation of the nasal mucous membranes. Allergic rhinitis is thought to affect up to 40% of the worldwide population, depending on geographical area and age,¹ and its prevalence has increased over the past 30–40 years.^{2,3} Recent estimates suggest that up to 40 million people in the United States⁴ and 23% of the population in Europe⁵ suffer from allergic rhinitis, with a higher incidence in children than in adults.⁴ The condition has a considerable negative impact, both on individuals' (QOL) quality of life and in terms of the economic costs to society. For example, it has been estimated that >\$6 billion was spent on prescription medications for allergic rhinitis in the United States in the year 2000.⁶

Seasonal allergic rhinitis (SAR) occurs in response to seasonal allergens, such as grass, weeds, and tree pollen. Perennial allergic rhinitis (PAR) is caused by allergens that are present year-round, such as house-dust mites, cockroaches, mold, and animal dander, but may be exacerbated by seasonal allergens.⁷ Overall, it is thought that ~20% of all cases of allergic rhinitis are seasonal, ~40% of cases are perennial, and the remain-

ing 40% are mixed (perennial symptoms with seasonal exacerbations).⁷

This review outlines the impact of allergic rhinitis symptoms and discusses the variation in symptom severity over the course of the day. Data from studies investigating the use of the antihistamine desloratadine in the management of allergic rhinitis are presented to assess the drug's control of morning symptoms.

SYMPTOMS OF ALLERGIC RHINITIS

Overview of Symptoms

Allergic rhinitis is an inflammatory condition. In an allergic individual, exposure of the respiratory mucosal epithelium to allergens triggers an immunoglobulin E-mediated allergic cascade, which releases mediators such as histamine and leukotrienes from mast cells (Fig. 1; The Allergy Report. American Academy of Allergy, Asthma and Immunology, Inc. 2000: www.aaaai.org/ar/default.stm. last accessed Oct. 10, 2006). This "early" phase of the allergic response occurs within minutes of allergen exposure and results in mucosal edema, the dilation of blood vessels, and stimulation of the sensory nerves.⁷ These physiological changes lead to copious clear rhinorrhea, sneezing, nasal itching, and some degree of nasal congestion.⁷ The "late" phase of the allergic response occurs 4–8 hours after allergen exposure.⁷ During this phase, inflammatory mediators are released in the nasal mucosa, reactivating many of the proinflammatory reactions seen earlier in the allergic response.⁷ The late-phase response is accompanied

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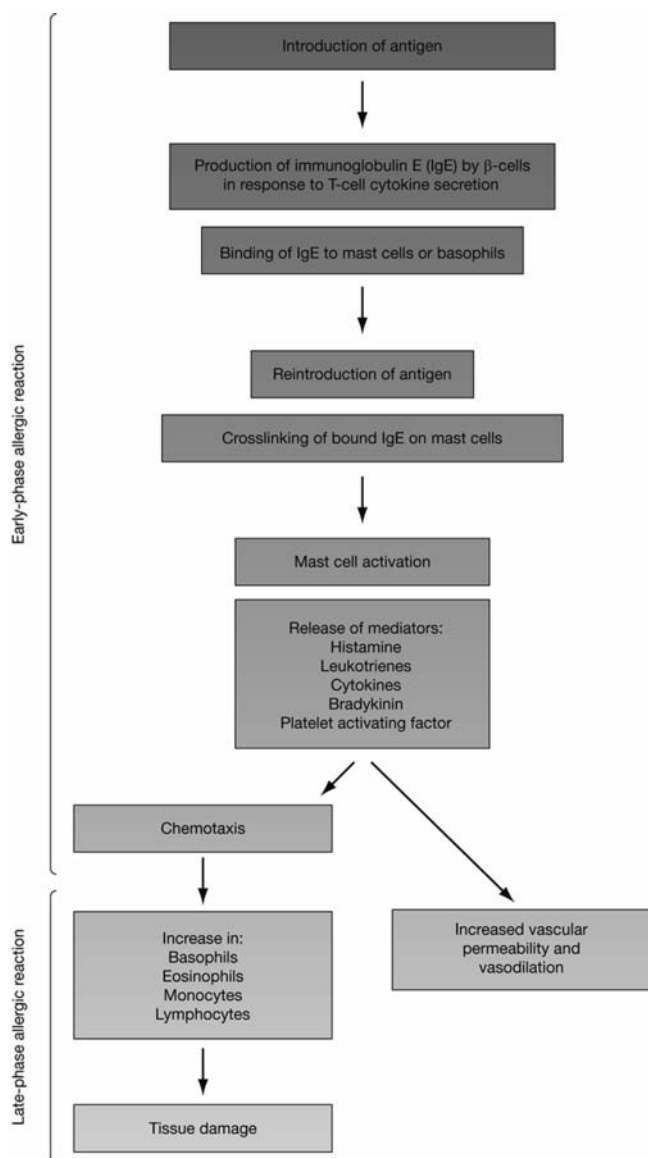


Figure 1. Illustration of the allergic cascade. (Adapted from The Allergy Report. American Academy of Allergy, Asthma and Immunology, Inc. 2000: www.aaaai.org/ar/default.stm. last accessed Oct. 10, 2006.)

by nasal congestion, fatigue, malaise, irritability, and possibly neurocognitive defects.⁷ Although clinically similar to the earlier stages of allergic response, congestion tends to be the predominant feature of this phase.⁸

The specific symptoms experienced by patients vary depending on whether they suffer from the seasonal or perennial form of allergic rhinitis. In SAR, the most typical clinical symptoms are profuse watery rhinorrhea, itching, sneezing, and allergic ocular symptoms.⁷ Although nasal congestion does occur in patients with SAR, it may not be the primary symptom. In contrast, in PAR, nasal congestion and mucus production tend

to be the dominant symptoms; sneezing, itching, and rhinorrhea may be minimal.⁷

Impact on QOL

Health-related QOL (HRQOL) can be severely affected by allergic rhinitis. Patients report impairment of certain aspects associated with mental health⁹ and may experience emotional strain as a result of the condition.¹⁰ Sleep disturbance is common, resulting in daytime fatigue and exhaustion, decreased alertness, and poor concentration.^{10,11} In addition, the symptoms of allergic rhinitis can directly impact both productive work and school learning performance,^{12,13} and this negative impact may be further exacerbated by sleep impairment.¹¹ A recent online survey in the United States asked >2000 people who either suffered from allergic rhinitis or were the parent of a child with allergic rhinitis about their experience of nasal congestion, a key symptom of the condition.¹⁴ Of those respondents who were employed, 59% said that their congestion affected their work, and 61% of parents said that congestion affected their child's school performance. Furthermore, 35% of respondents felt that nasal congestion frequently impacted daily activities, such as household chores, outdoor activities, or exercise and sports.¹⁴

Several clinical studies have attempted to quantify the impact of allergic rhinitis on HRQOL. Using a generic QOL instrument (the Medical Outcomes Study Short-Form Health Survey [SF-36]), significant impairment was observed in subjects with moderate-to-severe PAR compared with matched controls.¹⁵ Of the nine health concepts evaluated by the SF-36 (covering physical and social functioning, role limitation in physical and emotional problems, mental health, energy/fatigue, pain, general perception of health, and change of health), all except one (change of health) showed a significant impairment in patients with PAR ($p < 0.001$). The detrimental impact of the symptoms of allergic rhinitis also has been shown using a disease-specific instrument, the Juniper Rhinoconjunctivitis Quality of Life Questionnaire.¹⁶ Aggregate scores for all seven dimensions covered by the Rhinoconjunctivitis Quality of Life Questionnaire (sleep, nonallergic rhinitis symptoms, practical problems, nasal symptoms, ocular symptoms, specific activities limited by symptoms in the previous week, and emotional function) were significantly higher in patients with allergic rhinitis than in controls ($p < 0.01$), indicating poorer health status. These findings reinforce the need for effective management of the symptoms of allergic rhinitis to optimize patients' HRQOL.

Diurnal Variation in Symptom Severity

As in many conditions, circadian rhythms influence the course of allergic rhinitis, with the most severe

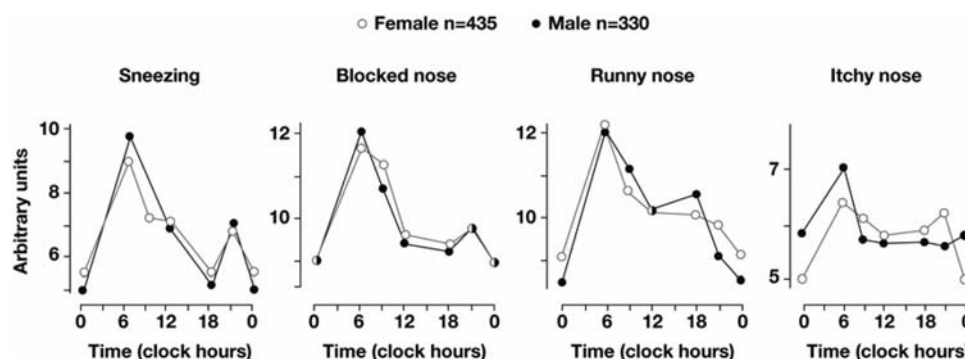


Figure 2. Circadian rhythms in allergic rhinitis symptoms. Peak-to-trough differences were statistically significant for sneezing, blocked nasal passages, and runny nose ($p < 0.008$). (Reproduced, with permission from the American Academy of Allergy, Asthma and Immunology, from Ref. 19.)

symptoms often occurring during the morning hours. For example, in the online survey described previously, when asked to specify at what time of day nasal congestion was most bothersome, approximately one-third of respondents reported that this symptom was particularly problematic in the morning, on awakening; ~15% reported late morning, afternoon, or early evening (5% for each); 26% reported throughout the day; 9% reported just before bed; and 17% reported during the night.¹⁴

Another recent online survey of 1000 adults in the United States with allergic rhinitis found that 49% felt that their allergy symptoms were most severe during the morning period (either on awakening or at other times of the morning).¹⁷ This is consistent with results from an early Finnish study of 770 patients with allergic rhinitis, where more than one-half reported that their symptoms were most severe in the morning.¹⁸ This was true both for patients with seasonal symptoms alone (55.9%) and for those with perennial symptoms (65.7%), although it is noteworthy that those with PAR reported worse symptoms in the morning significantly more often than those with SAR ($p < 0.01$).¹⁸ Similarly, another large study of 765 French patients with allergic rhinitis found a clear, large-amplitude, circadian variation, with peaks in the early morning (at ~6 A.M.) for the symptoms of sneezing, blocked nasal passages, and runny nose (Fig. 2).¹⁹ Overall, these three main symptoms were worse in the morning on awakening in ~60–70% of patients. Itchiness of the nose did not display statistically significant daily variations but was still worse in the morning in 56% of patients.¹⁹ It is hypothesized that this variation in symptom severity reflects underlying circadian rhythms in both allergen levels and the mechanisms contributing to the body's allergic response.¹⁹ Thus, approaches to the management of allergic rhinitis should be effective in targeting morning symptoms.

MANAGEMENT OF ALLERGIC RHINITIS

The Role of Antihistamines

Antihistamines act by blocking the histamine-mediated elements of the allergic cascade and are a mainstay of the pharmacologic management of allergic rhinitis (The Allergy Report. American Academy of Allergy, Asthma and Immunology, Inc. 2000: www.aaaai.org/ar/default.stm. last accessed Oct. 10, 2006). They have a rapid onset of action and alleviate the majority of nasal rhinitis and ocular allergy symptoms (The Allergy Report. American Academy of Allergy, Asthma and Immunology, Inc. 2000: www.aaaai.org/ar/default.stm. last accessed Oct. 10, 2006). A recent review of agents used in the management of allergic rhinitis concluded that, in addition to controlling symptoms, antihistamines improve patients' QOL.²⁰ It is important to note that the newer, nonsedating antihistamines are not associated with the detrimental side effects that occurred with first-generation antihistamines, such as daytime somnolence and anticholinergic effects (The Allergy Report. American Academy of Allergy, Asthma and Immunology, Inc. 2000: www.aaaai.org/ar/default.stm. last accessed Oct. 10, 2006).¹

Desloratadine: An Overview

Desloratadine (Clarinet; Schering-Plough Corp., Kenilworth, NJ) is a potent, orally active, nonsedating, peripheral histamine H₁-receptor antagonist indicated for the relief of the symptoms of SAR, PAR, and chronic idiopathic urticaria.²¹ It has an elimination half-life of 27 hours, allowing once-daily dosing.^{22,23} Using this regimen, oral desloratadine has been shown to be effective for the relief of the symptoms of SAR and PAR in a range of clinical trials.^{24–28} Studies have also shown that, in addition to improving other nasal symptoms, desloratadine reduces nasal congestion in SAR,^{26,27,29–31} and recent data have confirmed that this effect is seen also in PAR.³² The impact of deslorata-

dine on congestion appears to be caused by its anti-inflammatory activity; *in vitro* studies have shown that it inhibits the allergic response at various points,³³ and thus may act to retard the mechanisms that lead to edema and swelling of the nasal passages. Although there are no head-to-head clinical studies specifically comparing the effects on nasal congestion of desloratadine and its parent compound, loratadine, Kreutner *et al.*³⁴ found that desloratadine is 10-fold more potent than loratadine in reducing guinea pig nasal response to histamine challenge.

Treatment with desloratadine has been shown to enhance QOL in SAR,³⁵ PAR,³⁶ and chronic urticaria,^{37,38} restoring patients' ability to perform the tasks of daily living. For example, a recent study involving task simulation showed that, compared with placebo, desloratadine improves the performance and decision-making ability of patients with SAR during the allergy season.³⁹

CONTROL OF MORNING SYMPTOMS OF ALLERGIC RHINITIS WITH DESLORATADINE

Improvement in Morning Symptoms in Patients with SAR

As outlined previously, the symptoms of allergic rhinitis tend to be worse in the morning, when patients first awake. Data from a range of studies establish the effectiveness of desloratadine once daily in controlling these morning symptoms. In two double-blind studies, one conducted in the spring and one in the fall, 346 and 328 patients with SAR, respectively, were randomly assigned to receive desloratadine, 5 mg, or placebo once daily, in the morning, for 14 days.²⁴ Patients assessed their allergic rhinitis symptoms each morning before dosing and each evening, scoring both nasal (itching of the nose, stuffiness/congestion, rhinorrhea, and sneezing) and nonnasal (itching or burning eyes, itching of the ears or palate, eye redness, and eye tearing) symptoms on a scale of 0 (no symptoms) to 3 (severe symptoms). At each time point, two symptom scores were obtained, one based on how the patients had felt over the previous 12 hours (reflective) and one based on how they felt at the time of the evaluation (instantaneous). The morning instantaneous symptom assessment provided valuable information on whether desloratadine was effective for the full 24-hour period between doses.

In the study performed during the spring allergy season,²⁴ at the earliest morning instantaneous symptom assessment after the first dose (day 2), the total symptom score (TSS; sum of all individual symptom scores) was significantly reduced in patients receiving desloratadine compared with those receiving placebo (−2.9 versus −1.5; $p < 0.01$). Thus, desloratadine was still effective 24 hours after dosing and reduced pa-

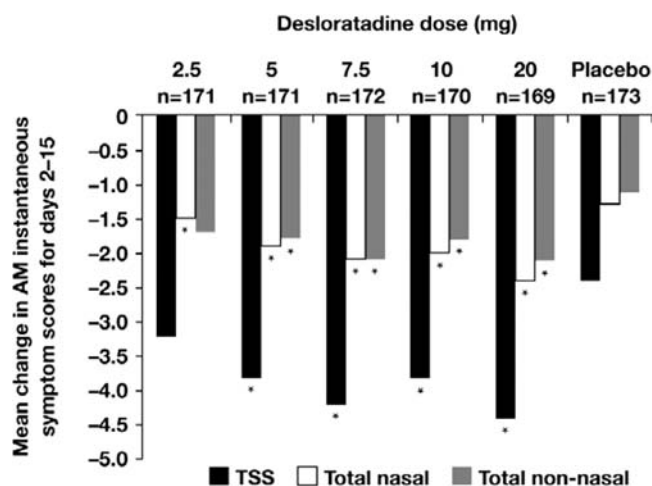


Figure 3. Mean change in morning instantaneous symptom scores in patients with SAR for desloratadine 2.5, 5, 7.5, 10, and 20 mg compared with placebo for days 2–15. Mean changes from baseline are least-squares means based on an ANOVA model with treatment and center effects. TSS indicates nasal plus nonnasal scores (* $p < 0.01$ versus placebo). (Reproduced, with permission from BioMed Central, from Ref. 25.)

tients' morning symptoms. Similar results were seen in the parallel study conducted in the fall.²⁴

The 24-hour efficacy of desloratadine and improvement in morning symptoms after administration were further shown in a dose-ranging study conducted in patients with SAR.²⁵ As in the aforementioned studies, patients ($n = 1026$) were randomly assigned to receive desloratadine or placebo once daily, in the morning, for 14 days. In this study, desloratadine was administered at a dose of 2.5, 5, 7.5, 10, or 20 mg. Patients assessed the severity of their nasal (itching of the nose, stuffiness/congestion, rhinorrhea, and sneezing) and nonnasal (itching or burning eyes, itching of the ears or palate, eye redness, and tearing) symptoms in the morning before dosing and again in the evening. Scores measured how patients had felt over the previous 12 hours (reflective) and how they felt at the time of assessment (instantaneous), on a scale of 0 (no symptoms) to 3 (severe symptoms). To evaluate the 24-hour efficacy of desloratadine, the primary outcome of the study was the 2-week average morning instantaneous TSS, expressed as a mean change from baseline.

All desloratadine doses except for the 2.5-mg dose were statistically significantly superior to placebo for the primary end point ($p < 0.01$; Fig. 3). The 2.5-mg dose was numerically superior to placebo. Efficacy was maintained 24 hours after the first dose: by day 2, patients receiving desloratadine 5, 7.5, 10, and 20 mg experienced a significant reduction in morning instantaneous TSS, compared with those receiving placebo ($p < 0.01$).

The findings of a study of 331 patients with SAR and mild seasonal allergic asthma also support the effec-

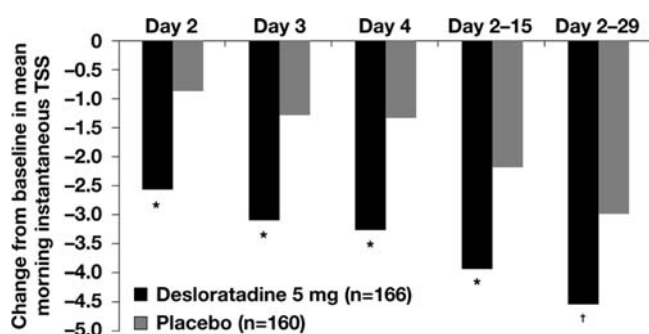


Figure 4. Change from baseline in mean morning instantaneous TSS for days 2, 3, and 4, and days 2-15 and 2-29 in desloratadine- and placebo-treated patients (* $p < 0.001$; † $p = 0.002$). (Adapted from Ref. 27.)

tiveness of desloratadine in controlling morning symptoms.²⁷ Patients were randomly assigned to once-daily desloratadine, 5 mg, administered in the morning or placebo for 4 weeks. They scored the severity of individual SAR and asthma symptoms on a scale of 0 (no symptoms) to 3 (severe symptoms) each morning (before taking medication) and evening, using both reflective and instantaneous assessments. Desloratadine significantly reduced the mean instantaneous morning TSS compared with placebo at the first study time point ($p < 0.001$). This reduction was maintained throughout the study period (Fig. 4), showing the effectiveness of desloratadine in controlling the morning symptoms of both SAR and asthma, even at trough plasma concentrations. The finding that desloratadine alleviates both allergic rhinitis and asthma symptoms is noteworthy in light of the increasing evidence that the two conditions often coexist and may even be linked.⁴⁰

Given the known daily variation in severity of allergic rhinitis symptoms, a recent study of desloratadine was designed to establish whether the timing of the daily dose affects overall efficacy (Haye R, Høye K, Berg O, et al. Clin Mol Allergy 3:3, 2005; www.clinicalmolecularallergy.com/content/3/1/3, last accessed Oct. 10, 2006). A total of 663 patients with SAR were assigned randomly to receive desloratadine, 5 mg, once daily either in the morning (7-9 A.M.) or in the evening (7-9 P.M.) for 14 days. Both nasal and nonnasal symptoms were assessed on a scale of 0 (no symptoms) to 3 (severe symptoms) each morning and evening before dosing. Scores were based on both the previous 12 hours (reflective evaluation) and the last hour before the assessment. The primary efficacy variable was the mean change from baseline in the morning "last-hour" TSS over the 2-week treatment period (sum of scores for rhinorrhea, nasal stuffiness/congestion, sneezing, and eye symptoms, with a maximum score of 12).

There was no statistically significant difference between the two treatment groups for the primary effi-

cacy variable, indicating the effectiveness of desloratadine in alleviating symptoms throughout the day, irrespective of the time of dosing. The mean ($\pm$ SE) reduction in morning last-hour TSS was 1.63 ± 0.17 for the morning dosing group (30% reduction from baseline) compared with 1.80 ± 0.17 for the evening dosing group (35% reduction). In both groups, the circadian variation in symptoms seen at baseline was much less apparent during treatment. However, it is interesting that although 32% of patients reported more severe symptoms in the morning at the start of treatment (based on last-hour assessment scores), as expected for this population, 37% experienced more severe symptoms in the evening. This may, in part, be a result of the individual characteristics of those selected for the study: diaries showed that patients spent an average of 3.5 hours outside each day during the pollen season, which would be likely to aggravate SAR symptoms during the later part of the day. However, confirming the overall findings of the study, an analysis of these two subgroups of patients did not show a difference in treatment efficacy with either morning or evening dosing.

Improvement in Morning Symptoms in Patients with PAR

The effectiveness of desloratadine in alleviating morning symptoms has been shown in patients with PAR in a large, randomized, placebo-controlled study of once-daily desloratadine, 5 mg ($n = 676$).²⁸ As in the SAR studies, patients evaluated their symptoms (rhinorrhea, nasal itching, sneezing, postnasal drip/drainage, itchy/burning eyes, tearing/watering eyes, and itching of ears or palate) each morning, before dosing and each evening during the 4-week treatment period. Symptoms were measured on a scale of 0-3 (from least to most severe), both reflectively (for the previous 12 hours) and instantaneously.

Desloratadine was significantly more effective than placebo in reducing the 4-week average morning-evening instantaneous TSS (the primary efficacy variable), with a mean reduction of 35% compared with 27.4% for placebo ($p = 0.005$). A significant difference between the treatment groups was noted after the first dose on day 2 ($p = 0.001$), and this persisted throughout the study. Morning instantaneous scores alone were also analyzed and showed a similar pattern to those seen for the combined morning-evening instantaneous scores. Thus, desloratadine was effective in alleviating morning symptoms and established sustained efficacy throughout the 24-hour dosing interval.

Effect on Congestion

As noted previously, in addition to its effectiveness in alleviating other symptoms of allergic rhinitis, deslo-

ratadine has been shown to reduce the severity of nasal congestion. This symptom may be particularly troublesome for patients on awakening, and a recent study has indicated that once-daily desloratadine is effective in reducing the severity of congestion during the morning period.⁴¹ Patients with SAR ($n = 1018$) were randomly assigned to receive once-daily desloratadine (5 mg), pseudoephedrine (240 mg), or desloratadine plus pseudoephedrine (5 mg/240 mg) each morning for 15 days. Symptoms, including nasal congestion, were scored in the morning and evening, both reflectively and instantaneously, on a scale of 0 (no symptoms) to 3 (severe symptoms). Desloratadine showed effectiveness comparable with pseudoephedrine in reducing morning instantaneous congestion scores (reduction of 0.59 [21.1%] for desloratadine, compared with 0.61 [22.3%] for pseudoephedrine), with no significant difference in the reduction in nasal congestion observed between treatments. Furthermore, when desloratadine was administered in combination with pseudoephedrine, the reduction in morning symptoms was significantly greater than with either treatment alone (reduction in score of 0.75 [27.6%]; $p < 0.01$ versus desloratadine or pseudoephedrine monotherapy). This additive effect suggests that the two treatments act on congestion *via* different mechanisms.

SAFETY AND TOLERABILITY OF DESLORATADINE

Clinical data show desloratadine to be well-tolerated in patients with SAR^{24–27,30,31} and PAR,²⁸ with an incidence of adverse events comparable with that observed in patients receiving placebo. It is important to note that given the association with ventricular arrhythmia that has been seen with some antihistamines,^{42,43} desloratadine has not been found to result in any deleterious cardiac effects in clinical trials.^{24,25,27,28} No adverse interactions with food or other drugs have been observed.²³ Finally, evaluation of desloratadine in healthy subjects has confirmed that it is not associated with sedation or psychomotor effects. At the recommended adult dose of 5 mg, desloratadine did not impair driving skills or performance in a range of psychomotor tests.⁴⁴

DISCUSSION

The symptoms of allergic rhinitis can have damaging effects on sufferers' HRQOL and impose a considerable economic burden on society through both direct costs and lost productivity. There is, therefore, a need for effective management of this condition. A recent systematic review of available data concluded that the efficacy, safety, and pharmacology of desloratadine broadly meet the criteria outlined by the Allergic Rhinitis and Its Impact on Asthma/European Academy of

Allergy and Clinical Immunology requirements for medications used in the management of allergic rhinitis.⁴⁵ Desloratadine is nonsedating and well tolerated and is not associated with neurocognitive impairment or cardiovascular adverse events.⁴⁵

The symptoms of allergic rhinitis vary in severity over the course of the day and often are worse in the morning. Therefore, to maximize the benefits for patients and to maintain a good overall efficacy and safety profile, any pharmacologic agent used in the management of allergic rhinitis should be effective in controlling these peak morning symptoms. The 27-hour elimination half-life of desloratadine allows convenient once-daily dosing. Studies show that the action of desloratadine is sustained over the 24-hour dosing interval and that it effectively controls morning symptoms in patients with allergic rhinitis (Haye R, Høye K, Berg O, et al. Clin Mol Allergy 3:3, 2005: www.clinicalmolecularallergy.com/content/3/1/3. last accessed Oct. 10, 2006).^{24,25,27,28} In general, antihistamines would be expected to exert their maximum effect near or shortly after peak serum levels are reached. Because desloratadine reaches its peak serum levels ~3 hours after dosing,²² evening dosing might be expected to give the most relief from morning symptoms. However, this did not appear to be the case when morning and evening dosing were compared. Overall relief of symptoms was equivalent for morning and evening dosing (Haye R, Høye K, Berg O, et al. Clin Mol Allergy 3:3, 2005: www.clinicalmolecularallergy.com/content/3/1/3. last accessed Oct. 10, 2006), indicating that the sustained 24-hour effect of desloratadine is independent of the time of dosing.

Nasal congestion is a particularly troublesome symptom of allergic rhinitis and often is cited by patients as the most bothersome symptom.¹⁴ In a series of allergen-exposure studies, desloratadine has been shown to reduce effectively nasal congestion in patients with SAR, whether this is measured objectively, in terms of nasal airflow, or subjectively, in terms of symptoms.^{26,31} Clinical data confirm that desloratadine also results in a clear improvement in nasal congestion in patients with PAR.³² Again, desloratadine is effective in alleviating this symptom during the morning period, when congestion often is the worst, with efficacy comparable with that of the nasal decongestant pseudoephedrine.⁴¹

In summary, desloratadine, with its broad action against a range of symptoms and its excellent safety profile, has an important place in the range of pharmacologic options available for the management of allergic rhinitis. In particular, its sustained 24-hour action and effective control of morning symptoms make it a valuable tool for improving the QOL of patients with allergic rhinitis.

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REFERENCES

1. Bousquet J, van Cauwenberge P, and Khaltaev N, and the World Health Organization. Allergic Rhinitis and its Impact on Asthma (ARIA) in collaboration with the World Health Organization. Executive summary of the workshop report, 7–10 December 1999, Geneva, Switzerland. *Allergy* 57:841–855, 2002 (Erratum in *Allergy* 57:1208).
2. Lundback B. Epidemiology of rhinitis and asthma. *Clin Exp Allergy* 28(suppl 2):3–10, 1998.
3. Butland BK, Strachan DP, Lewis S, et al. Investigation into the increase in hay fever and eczema at age 16 observed between the 1958 and 1970 British birth cohorts. *BMJ* 315:717–721, 1997.
4. Dykewicz MS, Fineman S, Skoner DP, et al. Diagnosis and management of rhinitis: Complete guidelines of the Joint Task Force on Practice Parameters in Allergy, Asthma and Immunology. *American Academy of Allergy, Asthma, and Immunology. Ann Allergy Asthma Immunol* 81:478–518, 1998.
5. Bauchau V, and Durham SR. Prevalence and rate of diagnosis of allergic rhinitis in Europe. *Eur Respir J* 24:758–764, 2004.
6. Stempel DA, and Woolf R. The cost of treating allergic rhinitis. *Curr Allergy Asthma Rep* 2:223–230, 2002.
7. Skoner DP. Allergic rhinitis: Definition, epidemiology, pathophysiology, detection, and diagnosis. *J Allergy Clin Immunol* 108(suppl 1):S2–S8, 2001.
8. Skoner D, Doyle W, Boehm S, and Fireman P. Late phase eustachian tube and nasal allergic responses associated with inflammatory mediator elaboration. *Am J Rhinol* 2:155–161, 1988.
9. Leynaert B, Neukirch C, Liard R, et al. Quality of life in allergic rhinitis and asthma. A population-based study of young adults. *Am J Respir Crit Care Med* 162:1391–1396, 2000.
10. Juniper E. Quality of life in adults and children with asthma and rhinitis. *Allergy* 52:971–977, 1997.
11. Ferguson BJ. Influences of allergic rhinitis on sleep. *Otolaryngol Head Neck Surg* 130:617–629, 2004.
12. Kessler RC, Almeida DM, Berglund P, and Stang P. Pollen and mold exposure impairs the work performance of employees with allergic rhinitis. *Ann Allergy Asthma Immunol* 87:289–295, 2001.
13. Vuurman EF, van Veggel LM, Uiterwijk MM, et al. Seasonal allergic rhinitis and antihistamine effects on children's learning. *Ann Allergy* 71:121–126, 1993.
14. Roper Public Affairs Group of NOP World. Impact of nasal congestion among allergic rhinitis sufferers. May–June 2004.
15. Bousquet J, Bullinger M, Fayol C, et al. Assessment of quality of life in patients with perennial allergic rhinitis with the French version of the SF-36 Health Status Questionnaire. *J Allergy Clin Immunol* 94:182–188, 1994.
16. Meltzer EO. The prevalence and medical and economic impact of allergic rhinitis in the United States. *J Allergy Clin Immunol* 99:S805–S828, 1997.
17. Roper Public Affairs Group of NOP World. Impact of morning symptoms on allergy sufferers. An internet survey of 1000 adults, January 2005.
18. Binder E, Holopainen E, Malmberg H, and Salo O. Anamnestic data in allergic rhinitis. *Allergy* 37:389–396, 1982.
19. Reinberg A, Gervais P, Levi F, et al. Circadian and circannual rhythms of allergic rhinitis: An epidemiologic study involving chronobiologic methods. *J Allergy Clin Immunol* 81:51–62, 1988.
20. Tripathi A, and Patterson R. Impact of allergic rhinitis treatment on quality of life. *Pharmacoeconomics* 19:891–899, 2001.
21. Murdoch D, Goa KL, and Kream SJ. Desloratadine: An update of its efficacy in the management of allergic disorders. *Drugs* 63:2051–2077, 2003.
22. Affrime M, Gupta S, Banfield C, and Cohen A. A pharmacokinetic profile of desloratadine in healthy adults, including elderly. *Clin Pharmacokinet* 41(suppl 1):13–19, 2002.
23. Schering Corporation. Clarinex (desloratadine) tablets, syrup, Reditabs tablets package insert. Kenilworth, NJ; March 2005.
24. Meltzer EO, Prenner BM, and Nayak A, and the Desloratadine Study Group. Efficacy and tolerability of once-daily 5mg desloratadine, an H1-receptor antagonist, in patients with seasonal allergic rhinitis. Assessment during the spring and fall allergy seasons. *Clin Drug Invest* 21:25–32, 2001.
25. Salmun LM, and Lorber R. 24-hour efficacy of once-daily desloratadine therapy in patients with seasonal allergic rhinitis (IS-RCTN32042139). *BMC Fam Pract* 3:14, 2002.
26. Horak F, Stübner P, Zieglmayer R, and Harris AG. Comparison of the effects of desloratadine 5-mg daily and placebo on nasal airflow and seasonal allergic rhinitis symptoms induced by grass pollen exposure. *Allergy* 58:481–485, 2003.
27. Berger WE, Schenkel EJ, and Mansfield LE, and the Desloratadine Study Group. Safety and efficacy of desloratadine 5 mg in asthma patients with seasonal allergic rhinitis and nasal congestion. *Ann Allergy Asthma Immunol* 89:485–491, 2002.
28. Simons FE, Prenner BM, and Finn A Jr, and the Desloratadine Study Group. Efficacy and safety of desloratadine in the treatment of perennial allergic rhinitis. *J Allergy Clin Immunol* 111:617–622, 2003.
29. Bachert C. Decongestant efficacy of desloratadine in patients with seasonal allergic rhinitis. *Allergy* 56(suppl 65):14–20, 2001.
30. Nayak AS, and Schenkel E. Desloratadine reduces nasal congestion in patients with intermittent allergic rhinitis. *Allergy* 56:1077–1080, 2001.
31. Horak F, Stübner UP, Zieglmayer R, and Harris AG. Effect of desloratadine versus placebo on nasal airflow and subjective measures of nasal obstruction in subjects with grass pollen-induced allergic rhinitis in an allergen-exposure unit. *J Allergy Clin Immunol* 109:956–961, 2002.
32. Holmberg K, Tonnel AB, Dreyfus I, and Gustafsson E. Desloratadine reduces nasal congestion and other symptoms of perennial allergic rhinitis. Presented at the XXIII European Academy of Allergology and Clinical Immunology Congress, Amsterdam, The Netherlands, June 12–16, 2004 (Abs 261).
33. Agrawal DK. Anti-inflammatory properties of desloratadine. *Clin Exp Allergy* 34:1342–1348, 2004.
34. Kreutner W, Hey JA, Anthes J, et al. Preclinical pharmacology of desloratadine, a selective and nonsedating histamine H1 receptor antagonist. 1st communication: Receptor selectivity, antihistaminic activity, and antiallergenic effects. *Arzneimittelforschung* 50:345–352, 2000.
35. Heithoff K, Meltzer EO, Mellars L, and Salmun LM. Desloratadine improves quality of life in patients with seasonal allergic rhinitis. *J Allergy Clin Immunol* 105:1121, 2000 (Abs 1121).
36. Tonnel AB, Holmberg K, Sauvage N, and Enander I. Desloratadine improves the health-related quality of life in persistent allergic rhinitis. Presented at the XXIII European Academy of Allergology and Clinical Immunology Congress, Amsterdam, The Netherlands, June 12–16, 2004 (Abs 260).
37. Monroe E, Finn A, Patel P, et al. Efficacy and safety of desloratadine 5 mg once daily in the treatment of chronic idiopathic urticaria: A double-blind, randomized, placebo-controlled trial. *J Am Acad Dermatol* 48:535–541, 2003.
38. Ring J, Hein R, Gauger A, et al. Once-daily desloratadine improves the signs and symptoms of chronic idiopathic urticaria: A randomized, double-blind, placebo-controlled study. *Int J*

- Dermatol 40:72–76, 2001.
39. Satish U, Streufert S, Dewan M, and Voort SV. Improvements in simulated real-world relevant performance for patients with seasonal allergic rhinitis: Impact of desloratadine. Allergy 59: 415–420, 2004.
40. Togias A. Unique mechanistic features of allergic rhinitis. J Allergy Clin Immunol 105:S599–S604, 2000.
41. Schenkel E, Corren J, and Murray JJ. Efficacy of once-daily desloratadine/pseudoephedrine for relief of nasal congestion. Allergy Asthma Proc 23:325–330, 2002.
42. DuBuske LM. Second-generation antihistamines: The risk of ventricular arrhythmias. Clin Ther 21:281–295, 1999.
43. van Cauwenberge P, Bachert C, Passalacqua G, et al. Consensus statement on the treatment of allergic rhinitis. European Academy of Allergology and Clinical Immunology. Allergy 55:116–134, 2000.
44. Vuurman EF, Rikken G, Muntjewerff ND, et al. Effects of desloratadine, diphenhydramine, and placebo on driving performance and psychomotor performance measurements. Eur J Clin Pharmacol 60:307–313, 2004.
45. Bousquet J, Bindslev-Jensen C, Canonica GW, et al. The ARIA/EAACI criteria for antihistamines: An assessment of the efficacy, safety, and pharmacology of desloratadine. Allergy 59(suppl 77):4–16, 2004. □

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