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Short communication

Desloratadine reduces nasal congestion in patients with intermittent allergic rhinitis

Nasal congestion is among the most bothersome of the symptoms of intermittent allergic rhinitis (IAR). Decongestants such as pseudoephedrine are often accompanied by adverse effects and should be avoided by patients with hypertension, arrhythmia, and other medical conditions. Most of the currently available antihistamines are ineffective for nasal congestion. Oral desloratadine, a new, potent H_1-receptor antagonist, was examined for its ability to relieve nasal congestion/stuffiness in 346 patients (172 in the desloratadine group and 174 in the placebo group) with IAR. Desloratadine, administered once daily at a dose of 5 mg, demonstrated significant improvement in nasal congestion/stuffiness at all time points assessed in the study. This benefit was observed as early as the first patient evaluation on day 2 and continued throughout the 2 weeks of the study. Desloratadine is a new treatment option for patients with IAR and nasal congestion.

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Allergic rhinitis is a common disorder affecting an estimated 40 million people annually in the USA (1). Intermittent allergic rhinitis (IAR, also known as seasonal allergic rhinitis, and hay fever) is an inflammation of the nasal mucosa resulting from an IgE-mediated reaction to airborne allergens, such as pollens and molds, during specific seasons. Although the presentation may vary, IAR is characterized by symptoms of sneezing, itching, rhinorrhea, and nasal congestion (2). The nasal symptoms of IAR may be accompanied by symptoms involving the eyes, ears, throat, and sinuses; these include red, itchy, watery eyes; ear fullness and popping; itchy throat; pressure over the cheeks and forehead; and postnasal drainage (3).

Although IAR is often perceived to be a trivial disease, this condition is a cause of widespread morbidity that can result in fatigue, irritability, cognitive impairment, and other systemic dysfunction in addition to local symptoms (3–5). In addition, allergic rhinitis is associated with other disorders, including asthma, sinusitis, otitis media, nasal polyposis, and lower respiratory tract infections; effective treatment of IAR may be an important component of management for such coexisting or complicating conditions (6).

Histamine H_1-receptor antagonists have been used for more than 50 years and are the mainstay of therapy for allergic rhinitis (2). The newer nonsedating antihistamines are generally preferred because they have fewer sedative and anticholinergic side-effects than sedating antihistamines, such as diphenhydramine and chlorpheniramine (7). These agents are effective in suppressing histamine-mediated symptoms such as sneezing and nasal discharge, but are generally not effective in relieving symptoms of nasal congestion, which is driven by a number of vasoactive mediators in addition to histamine (8, 9). Consequently, most oral antihistamines must be used in combination with an oral decongestant to obtain symptomatic relief of nasal congestion. There is a need for agents that effectively reduce the signs and symptoms of IAR, including congestion, without significant side-effects.

Desloratadine is a new, nonsedating, peripheral H_1-receptor antagonist with antiallergic effects, and has been shown to be effective in the treatment of IAR and chronic idiopathic urticaria (10, 11). Evidence from *in vivo* animal studies and *in vitro* experiments has shown that desloratadine inhibits the release of inflammatory mediators, such as interleukins and other cytokines, in addition to its potent antihistaminic action (12–14). Proinflammatory responses such as these have the net effect of increasing vascular

permeability, which leads to nasal obstruction. These findings suggested the possibility of clinical decongestant activity and prompted evaluation of congestion during the development program for desloratadine. Results from one such trial are reported here, along with a brief review of the pathophysiology, complications, and management of congestion in patients with IAR.

Material and methods

Methods

The effect of desloratadine on nasal congestion was assessed in a randomized, placebo-controlled, double-blind study of IAR patients aged 12 years or older. In this trial, 172 patients received desloratadine 5 mg and 174 patients received placebo once daily in the morning for 2 weeks. Enrolled patients were required to be symptomatic at screening and baseline, experiencing both nasal and nonnasal IAR symptoms; they also had an overall allergy condition that was considered at least moderate, and had a minimum 2-year history of IAR. The allergic condition was documented by a positive skin test no more than 1 year prior to study entry. Patients had to be free of any clinically significant disease that would interfere with the study evaluation.

Exclusion criteria included asthma requiring chronic inhaled or systemic corticosteroids; dependency on nasal, oral, or ocular decongestants, nasal topical antihistamines, or nasal corticosteroids; rhinitis medicamentosa; and clinically significant sinusitis or chronic purulent postnasal drip. Sufficient washout time was required for previous IAR treatments before the study drug was administered (e.g., use of corticosteroids was prohibited for 1 month prior to screening; use of cromolyn or nedocromil was prohibited for 2 weeks; use of decongestants or topical anti-inflammatory agents was prohibited within 3 days; and use of antihistamines was prohibited from 12 h to 3 months prior to screening, depending on the antihistamine).

Patients recorded their assessment of nasal stuffiness/congestion in a diary twice daily (AM and PM) on a scale of 0 = none to 3 = severe (Table 1). Using similar scales, patients also assessed the severity of other symptoms of IAR, including rhinorrhea, nasal itching, sneezing, itching/burning eyes, tearing/watering eyes, redness of eyes, and itching of ears or palate. The primary efficacy variable was analyzed by a two-way analysis of variance (ANOVA) in order to identify sources of variation due to treatment and center. All patients receiving at least one dose of study drug were included in the efficacy analysis on an intent-to-treat basis. Confirmatory analyses were based on evaluable patients who had no protocol violations.

Results

The treatment groups were balanced at baseline (demographic characteristics are presented in Table 2): baseline scores for nasal congestion/stuffiness were 2.2 in both the desloratadine 5 mg and placebo groups, indicating that on average patients had moderate congestion that was considered bothersome.

Over the entire 2-week treatment period, patients receiving desloratadine 5 mg had a significant reduction in mean AM/PM nasal congestion scores compared with those receiving placebo ($P < 0.05$) (Fig. 1). Improvement in the nasal congestion scores for IAR was demonstrated for the full 24-h dosing interval following the first dose of desloratadine: nasal congestion was significantly reduced as compared with placebo on day 2, which was the first assessment time point. This reduction continued for days 3 and 4 and for the entire 2 weeks of the study (Fig. 1). Scores for other assessed nasal and nonnasal symptoms of IAR also were reduced significantly more with desloratadine than with placebo over the 2-week study. In addition, over days 2–15, there was a significantly greater decrease from baseline in the total symptom score (the sum of all nasal and nonnasal symptom scores) with desloratadine than with placebo (-4.3 *vs* -2.5, respectively; $P < 0.01$).

Safety data from this study demonstrate a placebo-like safety profile for desloratadine. The pattern and incidence of total and treatment-related adverse events were similar in both treatment groups. Treatment-related adverse events were reported in 19% and 14% of patients treated with desloratadine 5 mg and placebo, respectively. Most adverse events were mild to moderate in severity, and no serious adverse events were attributed to desloratadine. No unusual or unexpected adverse events were reported in either study. The most common adverse effect was headache, occurring in 6% and 5% of desloratadine- and placebo-treated patients, respectively. The incidence of somnolence was 2% in each group. In clinical trials, desloratadine has shown efficacy against the spectrum of IAR symptoms without evidence of CNS side-effects (no greater incidence of sedation or anticholinergic effects than placebo) or cardiovascular toxicity (10, 15–18).

Discussion

The mechanism of nasal congestion and other symptoms associated with IAR involves actions of a series of mediators, cytokines, and inflammatory cells (2, 7). The release of certain mediators (e.g., histamines, leukotrienes, kinins) in the early-phase allergic response causes vasodilation and increased vascular permeability of the blood vessels in the nasal mucosa, resulting in nasal obstruction and edema. During the late-phase allergic response, inflammatory cells migrate to the nasal mucosa, with subsequent release of mediators and cytokines that perpetuate the inflammatory response. Nasal obstruction is the predominant symptom at this stage.

For many patients, nasal obstruction is the most annoying or troublesome aspect of IAR. Nasal congestion, however, is far more than a simple annoyance: nighttime nasal congestion can disturb normal sleep patterns, leading to daytime fatigue, impaired cognitive function, mood disturbance, and irritability (3, 4). Exacerbations of sleep-disordered

Table 1. Scoring scale for symptoms of nasal congestion/stuffiness

Patients recorded their assessment of nasal stuffiness/congestion in a diary twice daily (AM and PM) on following scale		
Score	Classification	Description
0	None	No nasal congestion/stuffiness evident
1	Mild	Nasal congestion/stuffiness clearly present but easily tolerated
2	Moderate	Definite awareness of nasal congestion/stuffiness, which is bothersome but tolerable
3	Severe	Nasal congestion/stuffiness is difficult to tolerate and may cause interference with activities of daily living and/or sleep

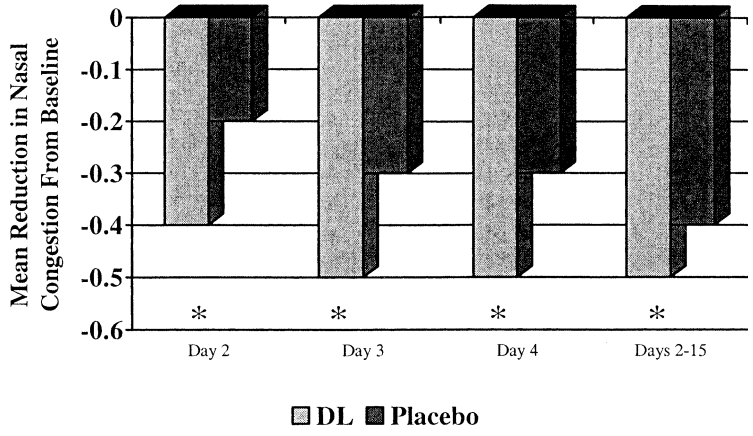
Table 2. Demographic characteristics

Characteristic	Desloratadine 5 mg ($n=172$)	Placebo ($n=174$)
Age group (years)		
12–17	26	22
18–65	143	152
>65	3	0
Sex		
M	68	81
F	104	93
Race		
White	129	131
Black	20	25
Asian	6	5
Hispanic	12	9
Other	5	4
Mean duration of IAR (years)	18	17

breathing, such as sleep apnea, and an increased risk of habitual snoring also have been attributed to nasal obstruction in individuals with allergic rhinitis (20). Furthermore, nasal inflammation and congestion associated with IAR can cause mouth-breathing, which can exacerbate seasonal symptoms of asthma and exercise-induced bronchospasm (6, 21). In children with chronic mouth-breathing because of nasal congestion, facial malformations – such as dental malocclusion (overbite), elevation of the upper lip, and high arched palate – have been observed (22, 23). Treatment of IAR to reduce nasal inflammation and blockage may avert many of the complications associated with nasal congestion.

Although the most common first-line agents for IAR manage other symptoms with relatively few side-effects, nasal congestion has been more difficult to treat because of the poor efficacy of antihistamines and the side-effects seen with decongestants (2, 11).

The addition of pseudoephedrine or other oral α-adrenergic agonists to a nonsedating antihistamine regimen, while improving congestion, commonly



* $P < 0.05$ versus placebo.

Figure 1. Mean change from baseline in nasal congestion scores for desloratadine 5 mg and placebo.

causes such adverse systemic effects as elevated blood pressure, palpitations, loss of appetite, tremor, insomnia, and headache. Because of these systemic effects, the use of decongestants should be avoided in patients with arrhythmia, hypertension, coronary heart disease, hyperthyroidism, glaucoma, diabetes, and urinary dysfunction. Oral decongestants should also be used with caution in children because of their stimulatory effects (2).

Desloratadine, a new, oral H_1-receptor antagonist, may help patients to relieve nasal congestion in addition to other symptoms of IAR, including rhinorrhea, nasal itching, sneezing, itching/burning eyes, tearing/watering eyes, redness of eyes, and itching of ears or palate. In all studies, desloratadine had a side-effect profile that was similar to placebo.

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