A Review of the Evidence from Comparative Studies of Levocetirizine and Desloratadine for the Symptoms of Allergic Rhinitis

Giovanni Passalacqua, MD, and Giorgio Walter Canonica, MD

Allergy and Respiratory Diseases, Department of Internal Medicine, University of Genoa, Genoa, Italy

ABSTRACT

Background: Levocetirizine and desloratadine are newer antihistamines indicated for the treatment of allergic rhinitis and chronic idiopathic urticaria.

Objective: This article discusses the pharmacokinetics and pharmacodynamics of levocetirizine and desloratadine and reviews studies that have directly compared the effects of these 2 drugs in allergic rhinitis and urticaria.

Methods: Relevant articles were identified through a search of MEDLINE from 1999 through 2004 using the main search terms *levocetirizine* and *desloratadine*.

Results: Levocetirizine is absorbed rapidly and reaches a steady-state plasma concentration more quickly than does desloratadine. It is also metabolized to a lesser extent than desloratadine, has a lower V_d, and has higher specificity for histamine$_1$ receptors. Eight well-controlled trials were identified that directly compared the effects of levocetirizine and desloratadine in the skin and nose of healthy individuals and patients with allergic rhinitis. Drug activity was measured in terms of wheal, flare, and itch reactions; nasal symptoms or symptom scores; increases in concentrations of inflammatory markers; or facial thermography. In most of these trials, levocetirizine had a faster onset and greater consistency of effect than desloratadine. The differences in the pharmacokinetic and pharmacodynamic profiles of the 2 drugs may partially explain these clinical findings.

Conclusions: Levocetirizine may be preferred to desloratadine as a treatment option for allergic rhinitis because of its faster onset of action and greater consistency of effect. Although comparative studies in chronic idiopathic urticaria are not available, data from histamine-induced wheal and flare studies in healthy volunteers suggest that levocetirizine may be more effective in preventing itching than desloratadine. (*Clin Ther.* 2005;27:979–992) Copyright © 2005 Excerpta Medica, Inc.

Key words: antihistamines, levocetirizine, desloratadine, pharmacokinetic and pharmacodynamic properties.

INTRODUCTION

Histamine, a primary amine synthesized and released predominantly by immunologic/nonimmunologic stimulation of mast cells and basophils, plays a key role in the pathogenesis of allergic diseases, in particular rhinitis and urticaria.[1] Allergen challenge studies have demonstrated that concentrations of histamine are increased in the nasal secretions of patients with allergic rhinitis and in plasma and skin lesions of patients with urticaria.[1] Several studies have found that histamine contributes to nasal obstruction, sneezing, and rhinorrhea in rhinitis and to itchy skin, wheals, and flares in urticaria.[1] There is also increasing evidence that histamine influences the maturation and/or activity of several inflammatory, effector, and immunologic cell types (including neutrophils, eosinophils, macrophages, monocytes, T-cells, epithelial cells, and endothelial cells) and therefore directly or indirectly elicits proinflammatory and immunomodulatory effects.[1–3]

It is now understood that histamine exerts its effects in allergic disease by interacting mainly with 1 of the 4 histamine-receptor subtypes—H_1, H_2, H_3, and H_4. These receptor subtypes belong to the superfamily of G-protein–coupled receptors[4] and differ in their location, second messengers, and histamine-binding properties.[5] The H_1 receptor has been shown to exist in both active and inactive isoforms that are in equilibrium on the cellular surface and respond to the ag-

Accepted for publication May 24, 2005.
doi:10.1016/j.clinthera.2005.07.011
0149-2918/05/$19.00

onist (histamine) and "inverse agonists" (antihistamines), respectively.[4] Interaction of histamine with the $G_{q/11}$-coupled H_1 receptor, in particular, leads to initiation of intracellular signaling pathways and activation of the transcription factor nuclear factor–κB, ultimately resulting in expression of many of the classic symptoms of allergic rhinitis and of itching in urticaria.[4] A greater understanding of the mechanisms underlying histamine and H_1-receptor activation has led to the development of several efficacious and well-tolerated H_1-receptor antagonists (H_1 antihistamines), which are currently considered first-line therapy for the management of allergic rhinitis and urticaria.[6–8] Levocetirizine* and desloratadine,† derivatives of cetirizine and loratadine, respectively, are indicated for the treatment of allergic rhinitis and urticaria and have been commercially available in many countries since 2001 (levocetirizine) and 2002 (desloratadine). Their dosing is summarized in Table I.

Several trials in rhinitis and urticaria have documented the clinical efficacy and tolerability of levocetirizine and desloratadine. In a randomized trial including >600 patients with perennial allergic rhinitis (PAR), patients who received desloratadine 5 mg for 4 weeks had significantly lower total symptom scores ($P = 0.005$) and nonnasal symptom scores ($P = 0.023$) compared with those who received placebo.[9] Similarly, 47 patients with seasonal allergic rhinitis (SAR) receiving desloratadine 5 mg for 1 week had a significantly lower total symptom score, less nasal congestion, and better nasal airflow compared with those receiving placebo (all, $P < 0.02$).[10] A 6-week randomized trial in 226 patients with chronic idiopathic urticaria (CIU) found that desloratadine significantly reduced all symptoms of urticaria compared with placebo ($P < 0.05$).[11] In a randomized study including 294 patients with PAR,[12] levocetirizine was associated with a relative improvement from baseline in total symptom scores as high as 47% over an 8-week period.[12] A randomized trial involving >400 patients with SAR found that levocetirizine significantly reduced symptom scores compared with placebo ($P < 0.01$).[13] In a study in patients with CIU, 70, 65, and 59 patients who received levocetirizine 2.5, 5, and 10 mg, respectively, for 4 weeks had significant reductions in mean pruritus severity scores, compared with 63 with placebo ($P < 0.001$).[14] This finding was duplicated in a subsequent 4-week study, in which 166 patients were randomized to receive levocetirizine 5 mg or placebo.[14]

Table I. Recommended dosing of levocetirizine and desloratadine.

	Children	Adults
Levocetirizine	Age >6 y: 5 mg/d	5 mg/d
Desloratadine	Age 2–5 y: 1.5 mg/d Age 6–11 y: 2.5 mg/d	5 mg/d

This article discusses the pharmacokinetics and pharmacodynamics of levocetirizine and desloratadine and reviews studies that have directly compared the effects of these 2 drugs in allergic rhinitis and urticaria.

METHODS

Relevant clinical trials and studies dealing with the pharmacokinetics and pharmacodynamics of the 2 drugs were identified through a search of MEDLINE from 1999 through 2004 using the main search terms *levocetirizine* and *desloratadine*. An additional search was conducted to identify clinical studies possibly comparing desloratadine with other antihistamines. Studies directly comparing the activity of levocetirizine with that of loratadine and/or desloratadine are discussed in detail, and consideration is given to the possible contribution of the drugs' pharmacokinetic and pharmacodynamic characteristics to the study findings.

PHARMACOLOGY OF LEVOCETIRIZINE AND DESLORATADINE

Differences that have been observed in the onset of effect and variability in the response to levocetirizine and desloratadine may be related, at least in part, to differences in the chemical structures of the 2 compounds, which in turn result in differences in their pharmacokinetic and pharmacodynamic properties. Levocetirizine, unlike desloratadine, can exist as a zwitterion (due to the presence of both carboxylic acid and amine residues)[15,16] and therefore has an overall decreased lipophilicity compared with desloratadine.

Pharmacokinetics

Although the pharmacokinetic properties of levocetirizine and desloratadine have been investigated

*Trademark: Xyzal® (UCB Pharma, Brussels, Belgium).

†Trademark: Clarinex® (Schering Corporation, Kenilworth, New Jersey).