Effectiveness of Azelastine Nasal Spray Compared with Oral Cetirizine in Patients with Seasonal Allergic Rhinitis

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ABSTRACT

Background: Azelastine nasal spray and oral cetirizine are selective histamine H_1-receptor antagonists that are approved in the United States for the treatment of seasonal allergic rhinitis (SAR).

Objective: The objective of the present study was to compare the efficacy and tolerability of azelastine nasal spray administered at the recommended dosage of 2 sprays per nostril twice daily with those of cetirizine in the treatment of moderate to severe SAR.

Methods: This multicenter, randomized, double-blind, parallel-group, 2-week comparative study was conducted during the 2004 fall allergy season in patients with moderate to severe SAR. After a 1-week placebo lead-in period, patients were randomized to receive azelastine nasal spray 2 sprays per nostril twice daily plus placebo tablets or cetirizine 10-mg tablets once daily plus a placebo saline nasal spray for the 2-week double-blind treatment period. The primary efficacy variables were (1) change from baseline to day 14 in the 12-hour reflective total nasal symptom score (TNSS), which combines scores for rhinorrhea, sneezing, itchy nose, and nasal congestion, and (2) onset of action, based on the instantaneous TNSS over 4 hours after the first dose of study drug. During the double-blind treatment period, patients recorded their symptom scores on diary cards twice daily (morning and evening). Patients aged ≥18 years also completed the Rhinoconjunctivitis Quality of Life Questionnaire (RQLQ) at baseline and on day 14.

Results: Three hundred seven patients were randomized to treatment, and 299 completed 2 weeks of study treatment. The age of the population ranged from 12 to 74 years (mean, 35 years), 62.9% were female, and 69.6% were white. Over 2 weeks of treatment, both groups had significant improvements in the TNSS compared with baseline ($P < 0.001$). The overall change in TNSS was significantly greater with azelastine nasal spray compared with cetirizine (29.3% vs 23.0% improvement, respectively; $P = 0.015$). In terms of onset of action, azelastine nasal spray significantly improved the instantaneous TNSS compared with cetirizine at 60 and 240 minutes after the initial dose (both, $P = 0.040$). Scores on each domain of the RQLQ were significantly improved in both groups compared with baseline ($P < 0.001$); the overall RQLQ score was significantly improved with azelastine nasal spray compared with cetirizine ($P = 0.049$). Both treatments were well tolerated.

Conclusion: In this 2-week study in patients with moderate to severe SAR, azelastine nasal spray was well tolerated and produced significantly greater improvements in TNSS and total RQLQ score compared with cetirizine. (*Clin Ther.* 2005;27:543–553) Copyright © 2005 Excerpta Medica, Inc.

Key words: azelastine nasal spray, cetirizine, allergic rhinitis, double-blind clinical trial.

INTRODUCTION

Azelastine nasal spray† is a topical second-generation antihistamine indicated for the treatment of seasonal

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†Trademark: Astelin® (MedPointe Pharmaceuticals, Somerset, New Jersey).

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allergic rhinitis (SAR) and nonallergic vasomotor rhinitis. The active ingredient, azelastine hydrochloride, is a high-affinity histamine H_1-receptor antagonist with potency at the H_1-receptor site ~10 times greater than that of chlorpheniramine.[1] In addition to histamine antagonism, azelastine has been shown in clinical studies to have inhibitory effects on leukotrienes,[2] bradykinin and substance P,[2,3] cytokines,[4] intercellular adhesion molecule–1 (ICAM-1) expression,[5] and eosinophil chemotaxis.[5] Cetirizine hydrochloride* is an oral second-generation antihistamine indicated for the treatment of SAR, perennial allergic rhinitis, and chronic urticaria. It is a selective H_1-receptor antagonist[6] that has been shown to inhibit leukotriene[7] and prostaglandin production,[8] as well as ICAM-1 expression and eosinophil chemotaxis.[9]

In clinical studies, cetirizine has been compared with other oral second-generation antihistamines, including loratadine and fexofenadine. In two 2-day, placebo-controlled studies in an environmental exposure unit[10,11] and in a 2-day outdoor study,[12] cetirizine 10 mg once daily was more effective than loratadine in improving nasal symptoms in patients with SAR ($P \leq 0.05$). In two 2-week, multicenter studies comparing cetirizine 10 mg once daily with fexofenadine 120 and 180 mg once daily, there were no significant differences in efficacy between cetirizine and the 2 fexofenadine doses.[13,14] However, in another environmental exposure unit study,[15] cetirizine was significantly more effective than fexofenadine during the 24-hour interval after initial administration ($P < 0.001$).

Comparative studies of azelastine nasal spray have been carried out in Europe at a dosage of 1 spray per nostril twice daily, one half the recommended adult dosage in the United States. In a 2-week, double-blind study of azelastine nasal spray and intranasal beclomethasone in patients with SAR,[16] both treatments significantly improved symptom scores compared with placebo ($P < 0.001$), and there were no significant differences between treatment groups. In a 2-week, double-blind study in patients with SAR, azelastine nasal spray and cetirizine decreased nasal symptom scores by 60% and 63%, respectively, with no significant differences between treatments.[17] In addition, the results of placebo-controlled studies have indicated that azelastine nasal spray at a dosage of 2 sprays per nostril twice daily was effective in patients who remained symptomatic after treatment with loratadine[18] or fexofenadine.[19]

Given the preceding findings, the objective of the present study was to directly compare the efficacy and tolerability of azelastine nasal spray administered at the US recommended dosage of 2 sprays per nostril twice daily with those of cetirizine in the treatment of moderate to severe SAR.

PATIENTS AND METHODS

This was a randomized, double-blind, parallel-group, 2-week comparative trial conducted during the 2004 fall allergy season at 20 investigational research centers distributed throughout the major geographic regions of the United States.

Inclusion and Exclusion Criteria

Study investigators selected patients from their practices and/or recruited volunteers to participate in the study. Eligible patients were male and female patients aged ≥12 years with at least a 2-year history of SAR and a documented positive allergy skin test, either intradermal or epicutaneous, during the previous year. Patients were excluded for the following reasons: use of concomitant medication(s) that could affect the assessment of efficacy of study treatment; any medical or surgical condition that could affect the metabolism of study medications; clinically significant nasal disease (other than SAR) or significant nasal structural abnormalities; respiratory infection or other infection requiring antibiotic therapy within 2 weeks of the single-blind placebo lead-in period; past or current alcohol or drug abuse; and significant pulmonary disease, including persistent asthma requiring use of controller medication. Women of childbearing potential not using an accepted method of contraception and women who were pregnant or nursing also were excluded.

Study Design

This was a randomized, double-blind, parallel-group clinical trial designed to be consistent with a draft guidance from the US Food and Drug Administration for the conduct of clinical trials in allergic rhinitis.[20] A computer-generated randomization schedule was used to assign eligible patients to the 2 treatment groups in blocks of 4. The randomization schedule was provided by a biostatistical group employed by the sponsor, and access to the code was confidential and accessible only to authorized persons not involved in the study.

*Trademark: Zyrtec® (Pfizer Inc., New York, New York).