

Comprehensive review of olopatadine: The molecule and its clinical entities

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ABSTRACT

Olopatadine is a tricyclic compound with antihistaminic, mast cell-stabilizing, and anti-inflammatory properties. In the United States olopatadine is approved as a b.i.d. ophthalmic solution, Patanol (Alcon Laboratories, Inc., Fort Worth, TX) to treat all signs and symptoms of allergic conjunctivitis and as a q.d. formulation, Pataday (Alcon Laboratories, Inc.), to treat itching associated with allergic conjunctivitis. A nasal spray, Patanase (Alcon Laboratories, Inc.), was approved in 2008 for treatment of the symptoms of seasonal allergic rhinitis. The available data on olopatadine was assessed with regard to future uses through a comprehensive literature review and a Roundtable Discussion held at the 2009 meeting of the American Academy of Allergy Asthma and Immunology. The unique mechanisms of action of olopatadine still under study include mast cell stabilization, potent H₁-antihistaminic activity, and anti-inflammatory effects. Data support consideration of nasal olopatadine for as-needed use for episodic symptoms of allergic rhinitis, for treatment of nonallergic rhinitis, and for use in combination with topical steroids for patients with moderate-to-severe allergy symptoms.

(Allergy Asthma Proc 31:112–119, 2010; doi: 10.2500/aap.2010.31.3317)

Key words: Allergic conjunctivitis, allergic rhinitis, antihistamine, mast cell stabilizer, nasal allergy, nasal antihistamine, ocular allergy, olopatadine

Olopatadine is a tricyclic compound (Fig. 1) with multiple mechanisms of action against multiple allergic conditions. It is a potent histamine H₁-receptor antagonist and a specific mast cell stabilizer, with additional anti-inflammatory properties. Olopatadine is approved as an ophthalmic solution in Europe, Japan, and the United States. In the United States, olopatadine as Patanol (Alcon Laboratories, Inc., Fort Worth, TX) is approved at a b.i.d. dose for the treatment of allergic conjunctivitis.¹ A q.d. formulation, Pataday (Alcon Laboratories, Inc.), is also available to treat itching associated with allergic conjunctivitis.² Additionally, a nasal spray, Patanase (Alcon Laboratories, Inc.), is available in the United States for relief of the symptoms of seasonal allergic rhinitis (SAR)³; and in Japan the molecule is available as an oral formulation (Allelock; Kyowa Hakko Kirin Co., Ltd., Tokyo, Japan) for treatment of allergic conditions.

A Roundtable Meeting of allergy experts was held in Washington, D.C., in March 2009 to review the history of olopatadine, from discovery of the molecule to its chemistry and pharmacology and, finally, to examine

clinical use for allergic conjunctivitis and allergic rhinitis. The meeting was chaired by Michael Kaliner, M.D., and the expert faculty included James Baraniuk, M.D.; Jonathan Bernstein, M.D.; Michael Blaiss, M.D.; Linda Cox, M.D.; Mark Dykewicz, M.D.; Michael Edwards, Ph.D.; Gary Gross, M.D.; Rohit Katial, M.D.; Phil Lieberman, M.D.; Eli Meltzer, M.D.; Robert Naclerio, M.D.; Anjuli Nyack, M.D.; John Oppenheimer, M.D.; Jay Portnoy, M.D.; Lanny Rosenwasser, M.D.; Russell Settipane, M.D.; Charles Siegel, M.D.; Peter Smith, M.D.; Dana Wallace, M.D., and John Yanni, Ph.D.

This article provides an overview of olopatadine based on a comprehensive review of the literature and material presented at that meeting. The critical discussion, including recommendations for future studies, is captured in supplemental online material.

PHARMACOLOGY

The pharmacologic properties of olopatadine have been extensively characterized. *In vitro* receptor binding studies have shown a high affinity and selectivity for the H₁-receptor, with a K_i value of 16 nmol/L in guinea pig cerebellum membranes and a lack of interaction with H₂- and H₃-histamine receptors.⁴ Olopatadine has also been shown to have a lack of interaction with α -adrenergic, dopaminergic, and muscarinic receptors.⁵

Anti-Inflammatory Activity

In relation to its activity as a histamine antagonist, olopatadine has been shown to inhibit the histamine-

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Development of this study was supported by Alcon Laboratories, Inc.
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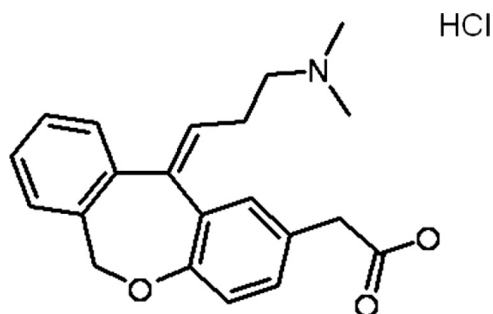


Figure 1. The chemical structure of olopatadine hydrochloride: 11-[(Z)-3-(dimethylamino)propylidene]-6,11-dihydrodibenz[b,e]oxepin-2-acetic acid monohydrochloride.

enhanced expression of intracellular adhesion molecule 1 and E-selectin at therapeutic doses.⁶ It is a potent inhibitor of cytokine secretion and has been shown to inhibit the histamine-induced secretion of IL-6 and IL-8 from human conjunctival epithelial cells with IC_{50} values of 5.5 and 1.7 nmol/L, respectively.^{7,8} Antigen-induced histamine release and anti-IgE-induced histamine release from human conjunctival tryptase/chymase-containing mast cells are also reduced by olopatadine.^{9,10} Unlike other H_1 -antagonists, olopatadine does not show a biphasic inhibition of histamine release *in vitro*, in which the inhibitory effect decreases as concentration increases. As shown in Fig. 2, most antihistamines exhibit a low-dose reduction in histamine release, thought to be caused by nonspecific membrane stabilization unrelated to the H_1 -receptor, and a high-dose induction of histamine release from mast cells attributed to a nonspecific effect causing cell membrane disruption.^{11,12} Olopatadine is unique among the antihistamines studied in that increasing concentration does not result in a nonspecific membrane effect on mast cells, leading to degranulation but results in a plateau of inhibition of histamine secretion (Fig. 2).^{11,12}

Olopatadine also has been shown to inhibit the production and release of various chemical mediators from different types of inflammatory cells in mechanisms unrelated to its activity at the histamine receptor. It inhibits the release of newly formed and preformed mediators from human conjunctival mast cells. Additionally, by reducing arachidonic acid release from membrane phospholipids, olopatadine has been shown to suppress leukotriene and thromboxane A_2 release and platelet-activating factor formation, important mediators of the late allergic reaction.⁹ It also inhibits anti-IgE antibody-mediated release of tumor necrosis factor (TNF- α), another mediator of the late reaction and through a TNF- α -specific mechanism, decreases anti-IgE mast cell-mediated up-regulation of intracellular adhesion molecule 1 on human conjunctival epithelial cells.^{13,14} The effects on mediators of the late response might contribute to the molecule's long

duration of antiallergic activity. Thus, for ocular use, olopatadine is a mast stabilizing agent with histamine receptor antagonism properties and shows effects on other mediators.

Oral administration of olopatadine also has been shown to block antigen-induced eosinophil influx in the nasal mucosa and bronchoalveolar lavage fluid and to decrease release of tachykinins from sensory nerve endings, inflammatory effects associated with expression of allergic symptoms in multiple conditions.⁸

Pharmacokinetics

In human subjects, olopatadine is highly and rapidly absorbed after oral administration, with a C_{max} of 0.5–2 hours,⁸ and a plasma elimination half-life ($t_{1/2}$) of 8–12 hours.^{1–3} Olopatadine is not extensively metabolized and is predominately (60–70%) excreted in the urine. Two active plasma metabolites (*N*-demethyl olopatadine and olopatadine *N*-oxide) have been identified at amounts of <10% of the parent compound after oral administration.^{1–3,8} Approximately 55% of olopatadine is protein bound in human serum, mostly to albumin, and independent of drug concentration over the range of 0.1–1000 ng/mL.^{1–3,8} Drug–drug interactions are unlikely to occur, and there has been no association with cardiac arrhythmias.^{1–3,8}

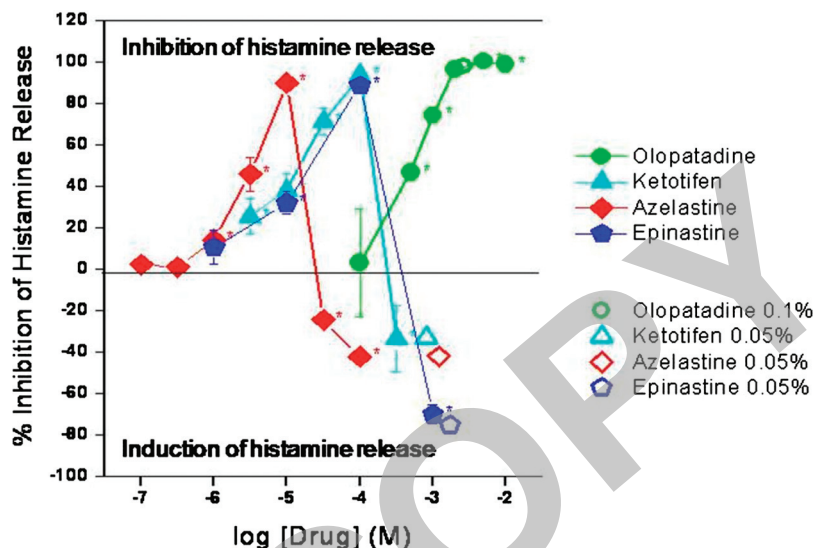
The pharmacokinetics of olopatadine nasal spray in pediatric SAR patients 6–11 years old was recently determined.¹⁵ Patients were dosed b.i.d. for 2 weeks with olopatadine at 0.8, 1.2, or 2.4 mg. Olopatadine and its active metabolites were dose proportional in pediatric patients and comparable with that observed in adult SAR patients.

Pharmacodynamics

The duration of action of olopatadine has been examined in a guinea pig model of histamine-induced conjunctival vascular permeability.¹⁶ A single topical application of olopatadine (0.1%) was significantly effective 16 hours after a single topical application, with an ED_{50} of 0.031%.¹⁷ In humans, preclinical pharmacologic studies showed a single topical dose of olopatadine (0.2%) to have significant antiallergy efficacy 24 hours after dosing.¹⁸ Receptor binding studies have indicated that histamine H_1 -receptor occupancy is 50% at 24 hours postdose.⁴ A clinical evaluation of olopatadine 0.2% solution confirmed the 24-hour duration of action, with statistically significant reductions in the signs and symptoms of allergic conjunctivitis induced by conjunctival antigen exposure 24 hours after administration.¹⁸

Studies in sensitized guinea pigs and rats showed that the oral administration of olopatadine at doses ≥ 3 mg/kg blocked allergic skin responses and symptoms of rhinoconjunctivitis and asthma.⁸ In patients with

Figure 2. Effects of H_1 -antagonists on histamine release in vitro. Most H_1 -antagonists reduce histamine release (shown by the upward inhibitory curves) at low doses, while inducing histamine release at high doses (shown by the downward histamine release curves). In contrast, olopatadine shows no induction of histamine release with increasing concentration, but rather a dose-related inhibitory curve followed by a plateau of inhibition.^{11,12}



SAR, olopatadine at oral doses of 2.5, 5, or 10 mg produced significantly greater inhibition of skin wheal responses to histamine ($p = 0.001$) and grass pollen ($p < 0.05$) than 60 mg of terfenadine.⁸

CLINICAL STUDIES: OPHTHALMIC FORMULATION

Olopatadine hydrochloride at a concentration of 0.1% (w/v) is the active ingredient in the topical ocular allergy medication, Patanol, which is indicated for b.i.d. administration.¹ A newer formulation, Pataday, contains olopatadine at a concentration of 0.2% (w/v) and is dosed q.d.² The Food and Drug Administration-approved indications are, Patanol, for the treatment of all signs and symptoms of allergic conjunctivitis; Pataday, for itching.^{1,2}

The treatment of allergic conjunctivitis has evolved from primarily systemic agents to topical ocular preparations. Current agents in the topical treatment of ocular allergy include vasoconstrictor and antihistamine eye drops, mast cell stabilizers, and corticosteroids. In general, antihistamines are effective in reducing conjunctival erythema and itching. Mast cell stabilizers are effective in reducing itching but are also effective in reducing other signs and symptoms of allergic conjunctivitis and can be used prophylactically.¹⁹ The side effects of topical corticosteroids limit their general use in the eye.

Clinical Experience with 0.1% Ophthalmic Solution (Patanol)

The efficacy of olopatadine 0.1% was compared with placebo in a contralateral eye comparison study using a conjunctival allergen challenge model.²⁰ Olopatadine solution was superior to placebo in preventing itching and redness, both immediately (within minutes) and 8 hours after drug administration. There were no serious or drug-related ocular or nonocular adverse events

reported.²⁰ The efficacy of olopatadine 0.1% treatment, administered b.i.d. for 10 weeks, was compared with placebo in the prevention and relief of the ocular and nasal symptoms of seasonal allergic conjunctivitis (SAC) and rhinoconjunctivitis.²¹ The proportion of patients with frequent ocular itching and hyperemia increased as a function of pollen level in the placebo group; the proportions remained low and virtually constant in patients in the olopatadine group.

A comparison with ketorolac ophthalmic solution (a nonsteroidal anti-inflammatory agent) in a clinical model of acute allergic conjunctivitis showed olopatadine 0.1% to be significantly ($p < 0.05$) more effective and more comfortable.²² Olopatadine 0.1% has also been compared with epinastine 0.5% ophthalmic solution, which is indicated for the ocular itching associated with allergic conjunctivitis.²³ In a conjunctival allergen challenge model olopatadine-treated eyes exhibited significantly lower mean itching and conjunctival redness scores than the contralateral epinastine-treated eyes ($p < 0.01$ and $p < 0.001$, respectively). Olopatadine-treated eyes also showed significantly less chemosis ($p < 0.001$), ciliary redness ($p < 0.001$), and episcleral redness ($p < 0.001$).²³ A *post hoc* analysis examining differences in the number of responders to treatment reported significantly more responders with olopatadine than epinastine at 7 minutes postchallenge for itching (27 versus 14, $p = 0.016$) and at 15 and 20 minutes after challenge for conjunctival redness (12 versus 1 and 10 versus 1, respectively, $p < 0.01$ for both).²⁴

The clinical benefit of using olopatadine 0.1% as an adjunctive treatment to systemic antihistamines for ocular symptoms has also been documented.^{25,26} Olopatadine b.i.d. given with loratadine, 10 mg q.d., for 7 days was compared with the use of loratadine alone in 94 patients with SAC. When used as adjunctive treat-

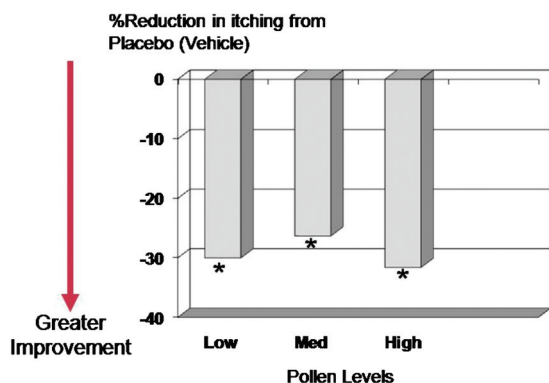


Figure 3. Effect of olopatadine 0.2%, ophthalmic solution q.d. on ocular itching induced by different grass pollen levels in a 10-week natural exposure study ($n = 260$ patients with seasonal allergic rhinoconjunctivitis to grass pollen). * $p < 0.05$ versus placebo (vehicle).²⁷

ment, olopatadine resulted in less ocular itching ($p < 0.05$), and patients rated their ocular symptoms as more improved compared with those receiving loratadine alone ($p < 0.05$).²⁶

Clinical Experience with 0.2% Ophthalmic Solution (Pataday)

The efficacy and safety of olopatadine 0.2% was compared with placebo in 260 patients with SAC and rhinoconjunctivitis in a 10-week “natural exposure” study conducted during the spring allergy season.²⁷ Olopatadine was associated with significant reductions in calculated mean scores for ocular itching relative to placebo, regardless of the level of allergen (Fig. 3). Similar results were obtained in a conjunctival allergen challenge in 90 patients, with significant differences favoring olopatadine 0.2% for both onset of action and protection from challenge at 16-hours postdosing (ocular itching, $p < 0.001$ at all time points).²⁸ Additionally, a modified conjunctival allergen challenge/environmental study showed that olopatadine significantly decreased the severity of nasal symptoms of rhinoconjunctivitis (sneezing, pruritus, and rhinorrhea) compared with placebo.²⁹

The efficacy and comfort of olopatadine 0.2% was compared with epinastine 0.05% in 92 patients with allergic conjunctivitis after conjunctival allergen challenge.³⁰ Olopatadine treatment was associated with significantly lower mean scores than epinastine for ocular itching at 5 and 7 minutes postchallenge ($p = 0.024$ and $p = 0.003$, respectively) and ocular redness at 7, 15, and 20 minutes ($p < 0.05$ for all). The patients rated olopatadine as significantly more comfortable than epinastine at 1-minute postdrop instillation ($p = 0.003$).³⁰

The body of clinical data indicates that olopatadine 0.1 and 0.2% ophthalmic solutions produce comparable

improvements in ocular allergy symptoms. The singular advantage of using the 0.2% solution would be the q.d. dosing. Whether the reduced dosing frequency improves adherence with treatment has not been directly studied. However, perception and quality of life (QOL) associated with the use of olopatadine 0.2% has been evaluated in patients with allergic conjunctivitis who previously used olopatadine 0.1% solution.³¹ Overall, more patients reported greater satisfaction with olopatadine 0.2% compared with olopatadine 0.1% ($p < 0.05$); and significant improvement in QOL, as assessed by the Rhinoconjunctivitis Quality of Life Questionnaire (RQLQ; $p < 0.0001$) was documented. The RQLQ, which includes specific questions about the impact of conjunctivitis symptoms on QOL, was used because there currently are no validated allergic conjunctivitis instruments to evaluate QOL.

The comfort and good tolerability of olopatadine 0.2% ophthalmic solution make it a useful option in the treatment of allergic conjunctivitis. Treatment-related adverse events are low.^{1,2} A recent retrospective analysis of 8 clinical trials reported ocular adverse events in 11 of 638 patients who received olopatadine 0.2% and 9 of 523 patients who received placebo—yielding identical rates of 1.7% for both.³² Olopatadine has also been shown to be safe for use in patients suffering from allergic conjunctivitis and mild-to-moderate dry eye.³³

The safety and tolerability of olopatadine 0.2% has been evaluated in 126 children and adolescents (3–17 years old).³⁴ No clinically relevant treatment-related changes in visual acuity, intraocular pressure, slit-lamp assessments, fundus examinations, or cardiovascular parameters were determined after 6 weeks of treatment, and other reported adverse events reported were mild or moderate in intensity. Once-daily use of olopatadine 0.2% has not been shown to affect wheal and flare responses during allergy testing; discontinuation of treatment is not necessary before skin-prick testing.³⁵

CLINICAL STUDIES: NASAL FORMULATION

At the time of the Roundtable Discussion, olopatadine nasal spray (Patanase) was indicated for the relief of symptoms of SAR in patients ≥ 12 years of age. It is dosed at 2 sprays/nostril b.i.d.³ Patanase is now indicated for the relief of the symptoms of SAR in adults and children 6 years of age and older. The recommended dosage in children 6–11 years of age is one spray per nostril twice daily.

In a nasal allergen challenge study, olopatadine nasal spray at concentrations of 0.1 and 0.2% was effective in suppressing allergen-induced nasal symptoms.³⁶ The onset and duration of action was evaluated for three different concentrations of olopatadine (0.2, 0.4, and 0.6%) in 320 patients with SAR exposed to ragweed allergen in an

% Change from Baseline in TNSS

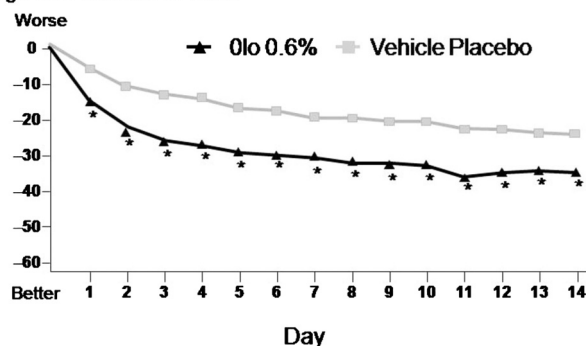


Figure 4. Change in total nasal symptom scores (TNSS) with olopatadine 0.6% nasal spray over a 2-week period in 677 patients with seasonal allergic rhinitis (SAR) to mountain cedar. Statistically significant reduction in TNSS was observed at all time points. * $p < 0.05$ compared with placebo (vehicle).³⁸

environmental exposure chamber (EEC).³⁷ Although all concentrations significantly reduced symptoms (sneezing, and runny, itchy, and stuffy nose) at 30 minutes compared with placebo ($p < 0.05$), olopatadine 0.6% nasal spray maintained effectiveness versus placebo for up to 12 hours after administration ($p < 0.05$).

These time points were separately verified in an EEC study examining the onset and duration of action of olopatadine 0.6% nasal spray in comparison with mometasone furoate, 50 μg , nasal spray and placebo in 425 SAR patients.³⁸ Significant reductions in the total nasal symptom score (TNSS; defined as the sum of the four major symptoms of allergic rhinitis: sneezing, runny nose, itchy nose, and stuffy nose) were observed with olopatadine compared with placebo ($p < 0.05$) starting at the first time point, 30 minutes posttreatment, and lasting throughout the 12-hour observation period. Olopatadine was statistically superior ($p < 0.05$) to mometasone at 13 of the 16 time points.³⁸

Two weeks of treatment with either olopatadine 0.4 or 0.6% nasal sprays produced significant improvements in overall reflective and instantaneous TNSS in a multicenter, randomized, placebo-controlled trial in 677 patients with SAR to mountain cedar (Fig. 4).³⁹ The 0.6% dose produced a 30.1% reduction in TNSS from baseline ($p < 0.001$) and statistical improvements in all nasal symptoms, including congestion ($p \leq 0.002$ for all; Fig. 5). Ocular symptoms were also improved with the higher concentration (reflective measurements: itchy eyes, $p < 0.001$; watery eyes, $p = 0.008$).³⁹ Similar efficacy results were obtained in a multicenter study examining olopatadine compared with placebo in 565 patients with fall allergies.⁴⁰ In this study, daily functioning also improved with olopatadine as measured by the RQLQ.

A pooled analysis of these two clinical trials was reported by Fairchild *et al.* in 2007, confirming that olopa-

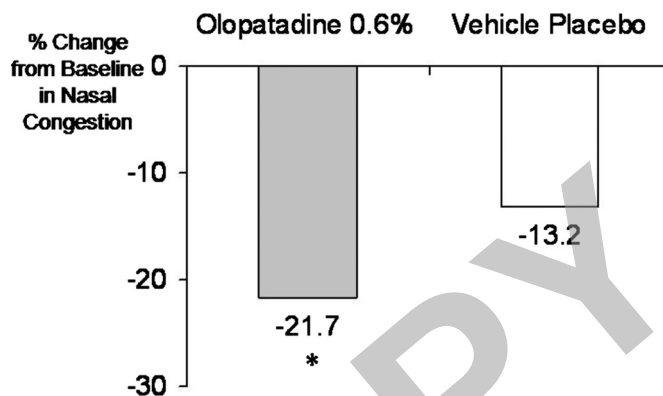


Figure 5. Overall reduction in nasal congestion with olopatadine 0.6% nasal spray over a 2-week period ($n = 677$ patients with seasonal allergic rhinitis [SAR] to mountain cedar). * $p = 0.002$ compared with placebo (vehicle).³⁸

dine improved nasal allergy symptoms during both the spring-summer and the fall-winter allergy seasons.⁴¹ Additionally, the relationship between health outcomes and daily functioning was examined using both the Work Productivity and Activity Impairment Questionnaire-Allergy Specific and the RQLQ. Significant correlations were determined between the improvements in TNSS with olopatadine 0.6% nasal spray and work impact ($r = 0.45$), activity impairment ($r = 0.55$), and overall RQLQ score ($r = 0.61$; all, $p < 0.0001$), indicating that symptom reduction with olopatadine was associated with improvements in function and QOL.^{41,42} Both concentrations of olopatadine resulted in significant improvements in RQLQ from baseline compared with placebo ($p < 0.05$ for both); and the observed improvements also were significantly correlated with the mean changes in TNSS: olopatadine 0.6%, $r = 0.66$, and olopatadine 0.4%, $r = 0.053$ ($p < 0.0001$), for both.

Olopatadine 0.6% nasal spray has been compared with azelastine 0.1% nasal spray, the other nasal antihistamine currently approved to treat symptoms of SAR in the United States. Active agent or a vehicle control was administered, 2 sprays/nostril b.i.d., for 16 days at the start of allergy season in a multicenter trial in 544 SAR patients.⁴³ Both nasal antihistamines produced significant and comparable reductions from baseline in reflective TNSS compared with placebo. Both agents also were similarly well tolerated. The most commonly reported treatment-related adverse event for both was bitter taste; the prevalence for azelastine was 19.7% compared with 12.2% for olopatadine ($p = 0.05$). Approximately 8% of the azelastine patients who reported bitter taste rated the taste as severe in comparison with none of the olopatadine patients ($p = 0.005$; Fig. 6). In the vehicle control group the most frequently reported treatment-related adverse events were bitter taste and nasal discomfort (1.7% for both).⁴³

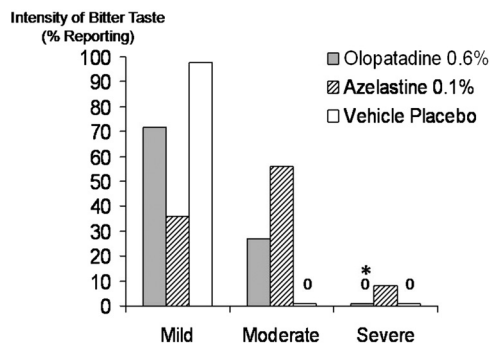


Figure 6. Prevalence and intensity of bitter taste reported by patients treated for 16 days with 2 sprays/nostril b.i.d. of olopatadine 0.6% ($n = 180$), azelastine 0.1% ($n = 188$), or vehicle placebo ($n = 176$). * $p = 0.005$, olopatadine versus azelastine.⁴²

The impact of sensory attributes on patient preference was examined in another comparison of olopatadine 0.6% nasal spray and azelastine 0.1% nasal spray.⁴⁴ This multicenter, double-blind, randomized, crossover study included 110 adult patients with at least a 2-year history of SAR who were symptomatic at time of study. Both treatments were well tolerated and effective. As in the earlier study, patients rated olopatadine as superior to azelastine in overall aftertaste (60.6% versus 30.3%; $p = 0.0005$).⁴⁴ Similar ratings were given for patient preference (62.4% versus 33.9%; $p = 0.0001$) and likelihood of extended use (60.9% versus 34.5%; $p = 0.0004$), important components of patient compliance.⁴⁴

A new formulation of azelastine 0.1% nasal spray was recently approved by the Food and Drug Administration that includes sucralose to mask the bitter taste that some patients experienced.⁴⁵ To date, no comparison of olopatadine and azelastine's new sucralose formulation have been reported.

Although intranasal steroids are cited as the "gold standard" for treating symptoms of allergic rhinitis, particularly nasal congestion, a recent study of olopatadine 0.6% nasal spray (2 sprays/nostril b.i.d.) and fluticasone propionate, 50 μ g, nasal spray (2 sprays/nostril q.d.) in patients with mild-to-moderate SAR symptoms showed noninferiority between the two.⁴⁶ This double-blind, randomized, parallel-group 2-week trial involved 130 patients with SAR. Both treatments reduced the reflective TNSS from baseline ($p < 0.05$), with reductions of 45.5% for olopatadine and 47.4% for fluticasone at end of treatment. No significant between-treatment differences in the magnitude of symptom reduction was observed for the average 2-week percentage changes from baseline for congestion, runny nose, sneezing, itchy nose, or ocular symptoms. However, greater reductions in all symptoms were consistently observed with olopatadine during the first 3 days of treatment, results that might be expected based on the quicker onset of action observed in the

EEC studies comparing olopatadine and mometasone.^{38,46} Statistical significance favoring olopatadine was shown for TNSS at day 1 ($p = 0.043$; Fig. 7). These results suggest that in a population of SAR patients with milder symptoms, the efficacies of a nasal antihistamine and an inhaled nasal steroid may be similar.

ORAL FORMULATION

Clinical studies with oral olopatadine have been conducted in Japan in patients with SAR, perennial allergic rhinitis, atopic asthma, chronic urticaria, and various pruritic dermatoses. All showed significant symptom reduction and at least comparable efficacy to other agents currently used in that country.⁸ In clinical trials in patients with perennial allergic rhinitis, oral olopatadine reduced nasal obstruction, unlike other oral antihistamines that have shown limited efficacy for nasal congestion. A comparison of published clinical data reported that olopatadine produced the greatest improvement in nasal obstruction compared with terfenadine, azelastine, ketotifen, ebastine, astemizole, epinastine, and emedastine.⁸ Olopatadine, 10 mg, also produced greater symptom reduction ($p < 0.05$) than ketotifen, 2 mg b.i.d., in urticaria patients, with fewer adverse events ($p < 0.001$).⁸ Oral olopatadine is well tolerated. The most common adverse effect is drowsiness, which has been reported at an incidence of ~11% at a dose of 10 mg b.i.d.⁸ No cardiac effects have been reported.

In Japan approved indications of the oral formulation (Allelock) are allergic rhinitis, urticaria, and itching resulting from skin diseases (eczema/dermatitis, prurigo, pruritus cutaneous, psoriasis vulgaris, and multiform exudative erythema). The approved oral doses are 2.5 and 5 mg b.i.d.

SUMMARY

Therapy for ocular and nasal allergies is generally focused on symptom control with a minimum impact on daily functioning and cognitive impairment. For SAR, a stepwise treatment approach is recommended, with nasal antihistamines, such as olopatadine, included as first-line pharmacotherapy.⁴⁷ These agents are differentiated from their oral counterparts by a clinically significant effect on nasal congestion, an annoying symptom that is often associated with other complications including sleep disturbance.⁴⁷ Additionally, current practice parameters note that the rapid onset of effect of these medications—30 minutes for olopatadine nasal spray—make them appropriate for as-needed use for episodic symptoms. The same guidelines recommend topical antihistamines/mast cell stabilizers such as olopatadine ophthalmic solution for both acute and long-term treatment of symptoms of allergic conjunctivitis.⁴⁷

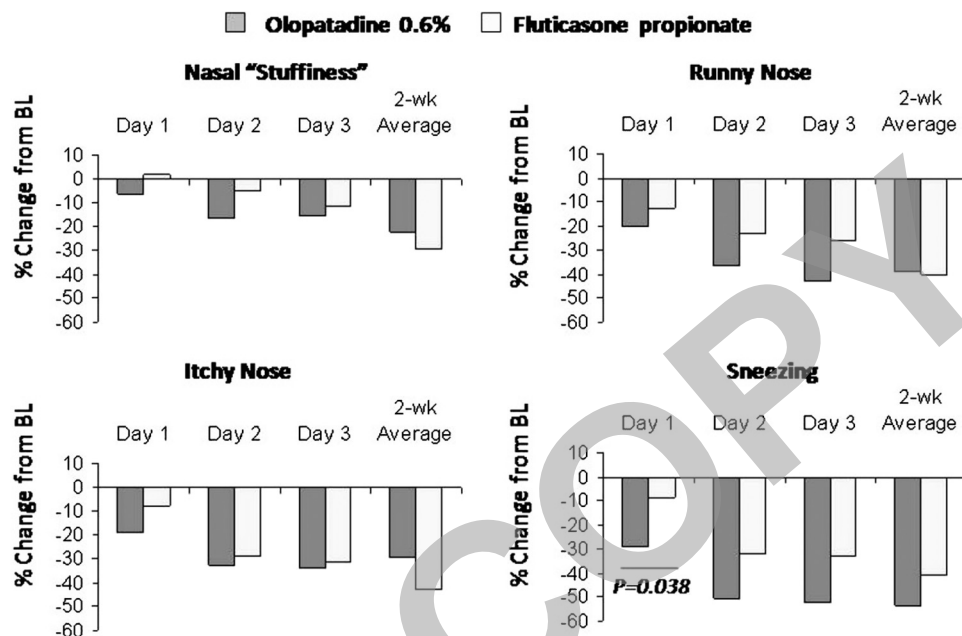


Figure 7. Effects of olopatadine 0.6% nasal spray and fluticasone propionate, 50 µg, nasal spray on nasal symptoms in 130 patients with mild-to-moderate SAR: onset of relief and overall change from baseline.⁴⁵ (Permission to reprint granted from Allergy and Asthma Proceedings.)

The molecule, olopatadine, is unique in its mechanism of action, still under study. The most comprehensive data to date are from studies in the ocular conjunctiva, which have shown that olopatadine has mast cell-stabilizing activity and anti-inflammatory effects in addition to its antihistaminic properties. It is likely that these effects account for the differentiating features of the molecule clinically. Discussion from the Roundtable Meeting can be found in supplemental online for this journal.

ACKNOWLEDGMENTS

The authors acknowledge the editorial and technical support of Sylvia Kolibol, Ph.D., in the development and writing of this article. Michael Edwards, Ph.D., and John Yanni, Ph.D., are employed by Alcon Research, Ltd. Their expert contribution to questions about science of olopatadine, including its development, is greatly appreciated.

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