Advances In Therapy® | *Volume 17 No. 3*
May/June 2000

Efficacy and Acceptability of Nedocromil Sodium 2% and Olopatadine Hydrochloride 0.1% in Perennial Allergic Conjunctivitis

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ABSTRACT

In this 2-week, randomized, crossover study, ophthalmic solutions of nedocromil sodium 2% and olopatadine hydrochloride 0.1% were compared for effectiveness and acceptability in 28 patients with perennial allergic conjunctivitis and previous olopatadine experience. Patients received nedocromil twice daily or olopatadine twice daily for 1 week, then were crossed over to the alternate medication for 1 week. Outcome measures were patient satisfaction (questionnaire), severity of ocular symptoms (daily diary scores), clinical signs (physician assessments), quality of life (questionnaire), and global assessments of effectiveness. Both medications were well accepted. Of the 28 patients, 16 (57.1%) would request a nedocromil prescription, 10 (35.7%) an olopatadine prescription ($P = .157$); 22 patients (78.6%) would recommend nedocromil to other allergy sufferers, while 18 (64.3%) would recommend olopatadine ($P = .480$). Light sensitivity scores were significantly lower with nedocromil ($P = .0125$); other symptom scores were comparable between medications. Both drugs significantly ($P<.01$) and comparably decreased erythema, conjunctival injection, and overall conjunctival signs from baseline. Comparable improvement also occurred in quality-of-life scores. Both physicians and patients judged nedocromil and olopatadine to be similarly effective in preventing signs and symptoms. Nedocromil sodium 2% is an effective treatment for perennial allergic conjunctivitis. Patients receiving olopatadine can be switched to nedocromil with no loss in efficacy or satisfaction, but with a reduction in cost.

Keywords: allergic conjunctivitis; nedocromil; olopatadine; cost-effectiveness

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INTRODUCTION

Allergic conjunctivitis affects an estimated 20% of the population in temperate climates.[1] The characteristic symptoms of itching, burning, tearing, and redness occur year round in perennial allergic conjunctivitis, because the causative allergens (dust mites, pet dander, mold, air pollutants) are always present. Although allergic conjunctivitis does not generally threaten vision, its symptoms are bothersome and can interfere with daily activities.[1]

When allergen exposure cannot be avoided, pharmacologic intervention may be needed to control symptoms. Current therapies include topical formulations of the traditional mast-cell stabilizer sodium cromoglycate, antihistamines (eg, levocabastine and olopatadine), the corticosteroid loteprednol, and the nonsteroidal anti-inflammatory drug ketorolac.

Nedocromil sodium is a mast-cell stabilizer with additional anti-inflammatory actions on other cells involved in the allergic response, including eosinophils, neutrophils, and macrophages.[2] The first member of the pyranoquinoline class indicated for topical ophthalmologic application, nedocromil sodium has recently been approved for the treatment of itch associated with allergic conjunctivitis. Nedocromil sodium eyedrops have proved to be safe and significantly more effective than placebo in both adults and children,[3-6] substantially reducing the rescue use of oral antihistamines.[7]

Although a wealth of comparative data attest to the superiority of nedocromil sodium to placebo, few head-to-head comparisons with other active treatments have been published. In particular, a comparison with a topical antihistamine has, until now, been lacking. This study was conducted to compare ophthalmic solutions of nedocromil sodium 2% (Alocril™*) and olopatadine hydrochloride 0.1% (Patanol®†) for effectiveness and patient acceptance in the treatment of perennial allergic conjunctivitis.

PATIENTS AND METHODS

Patients

This 2-week, open-label, randomized, crossover study involved 28 patients, at least 7 years old, who had perennial allergic conjunctivitis with sensitivity to dogs, cats, or dust mites. Inclusion criteria were use of olopatadine within the previous 12 months; a minimum baseline ocular itch score of 1 (on a scale of 0 = none to 6 = severe); positive results of skin-prick test to dog, cat, or dust mite extract within 2 years prior to randomization; and confirmed cohabitation with the allergen source. Patients receiving immunotherapy were eligible if the dose had been stable for at least 3 months. Exclusion criteria were use of systemic, nasal, or ophthalmic steroids within 1 week of enrollment; use of systemic or ophthalmic antihistamines (except olopatadine) within 1 week of enrollment; any comorbid ophthalmic disease; diagnosis of an upper respiratory tract infection within 2 weeks of enrollment; renal or hepatic disease, or serious illness that could impair quality of life; history of allergy or sensitivity to either study medication; anticipated use of contact lenses during the study; and current or antici-

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†Registered trademark of Alcon Laboratories, Inc, Fort Worth, Tex.

pated use of any other topical ocular medication during the study. All patients provided signed informed consent prior to enrollment.

Intervention and Timing

Visits were scheduled at baseline (day 0), day 7, and day 14. At baseline, patients were randomly assigned to one of two treatment groups and received either nedocromil sodium 2% or olopatadine hydrochloride 0.1%, with instructions to instill one drop of the medication into each eye twice daily for 1 week. At a follow-up visit on day 7, the alternate study medication was dispensed for use twice daily during the next 7 days. The last follow-up visit and study exit occurred on day 14.

Outcome Measures

During the 24 hours prior to the office visits at the end of each study week, patients completed a questionnaire in which they indicated their willingness to use the study medications (if available) after completion of the trial, to recommend the medications to others, and to use the medications for the duration of the allergy season.

Patients kept a daily record of their medication use and rated itching, burning, stinging, redness, tearing, photophobia, and swelling on a seven-point scale (0 = none to 6 = severe). In addition, at the weekly visits, physicians assessed erythema, conjunctival injection (hyperemia), and edema on a five-point scale (0 = none to 4 = severe), and patients filled out the modified rhinoconjunctivitis quality-of-life questionnaire with standardized activities (RQLQ[S]).[8] This validated vehicle evaluates ability to participate in activities (regular, social, outdoor), sleep disturbances, affect, practical problems in daily living, and symptoms (ocular, nasal, and other) on a scale of 0 (never experience problems) to 6 (always experience problems). Also at the study visits, physicians and patients assessed the overall effectiveness of the eyedrops in preventing allergic signs and symptoms.

Data Analysis

Results of the questionnaire probing patient acceptance of medications were compared by means of McNemar's test. Within-subject analysis of variance (ANOVA) was used for diary card symptom scores, scores for clinical signs, treatment effectiveness ratings, and RQLQ(S) scores. Between-drug comparisons of improvement in clinical signs were carried out with a matched-pairs signed rank test. The improvement in RQLQ(S) scores from baseline was analyzed with ANOVA for repeated measures. The level for significance was set at .05.

RESULTS

Demographics

All 28 enrolled patients reported experiencing symptoms of allergic conjunctivitis during each month of the year; 27 had received a minimum of 5 days of olopatadine therapy immediately prior to the baseline visit, and 1 patient had received olopatadine for 150 days 6 months prior to the study. All 28 patients completed this 2-week study (Table 1).

Table 1. Patient Demographics

	Enrolled Patients (n = 28)
Age, y (range)	33 (14–58)
Sex	
Male	5
Female	23
Previous olopatadine use, d* (range)	43 (5–298)
Duration of conjunctivitis, y (range)	18 (2–40)
Atopic disease, no. (%)	
Rhinitis	27 (96.4)
Asthma	10 (35.7)
Eczema	0 (0)
Dermatitis	1 (3.6)
Family history of atopic disease, no. (%)	24 (85.7)

*Within the 12 months prior to the study.

Acceptability of Study Medications

After 1 week of treatment, there was a trend for greater patient acceptance of nedocromil, although the differences between medications were not statistically significant (Fig 1). Sixteen of the 28 patients (57.1%) would request a prescription for nedocromil, while 10 (35.7%) reported that they would request a prescription for olopatadine ($P = .157$). Similarly, 22 patients (78.6%) would recommend nedocromil to other allergy sufferers, while 18 (64.3%) would recommend olopatadine ($P = .480$). Fifteen patients (53.6%) would be willing to use nedocromil for the entire allergy season, and 12 (42.9%) would be willing to use olopatadine ($P = .617$).

Diary Card Symptom Scores

Mean symptom scores for seven ocular symptoms generally were comparable with nedocromil and olopatadine (Table 2) except that light sensitivity was significantly lower with nedocromil ($P = .012$), while redness scores tended to be lower with olopatadine ($P = .093$).

Clinical Signs

In the physicians' evaluations, both medications caused comparable, significant decreases from baseline ($P<.01$) in erythema, conjunctival injection, and overall conjunctival signs (Fig 2). Improvement in edema was not statistically significant with either drug. Mean scores for discharge tended to increase with olopatadine and decrease with nedocromil, but the difference between groups was not statistically significant ($P = .31$).

Fig 1. Patient acceptance of nedocromil and olopatadine. Acceptability was evaluated by the number of patients willing to request a prescription, recommend the study medication to others, and use it throughout periods of active allergies.

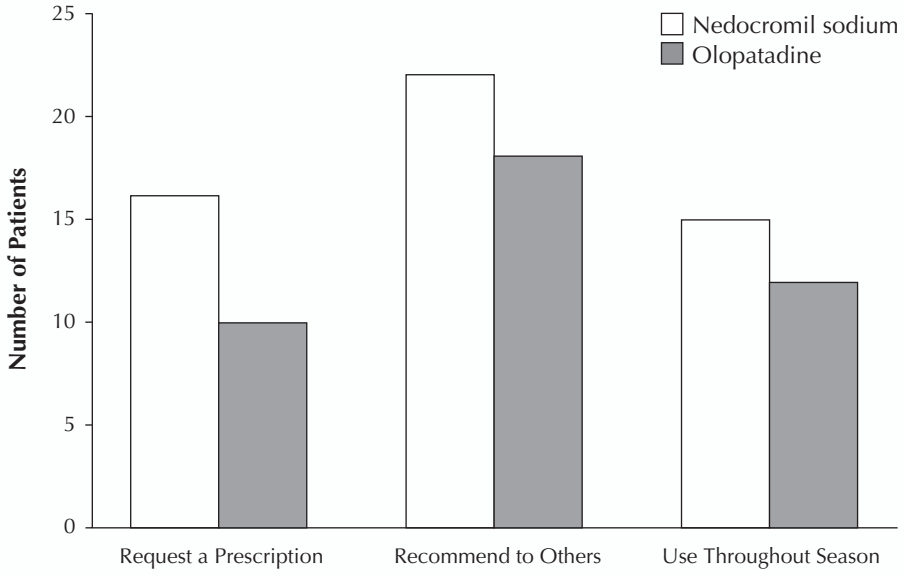
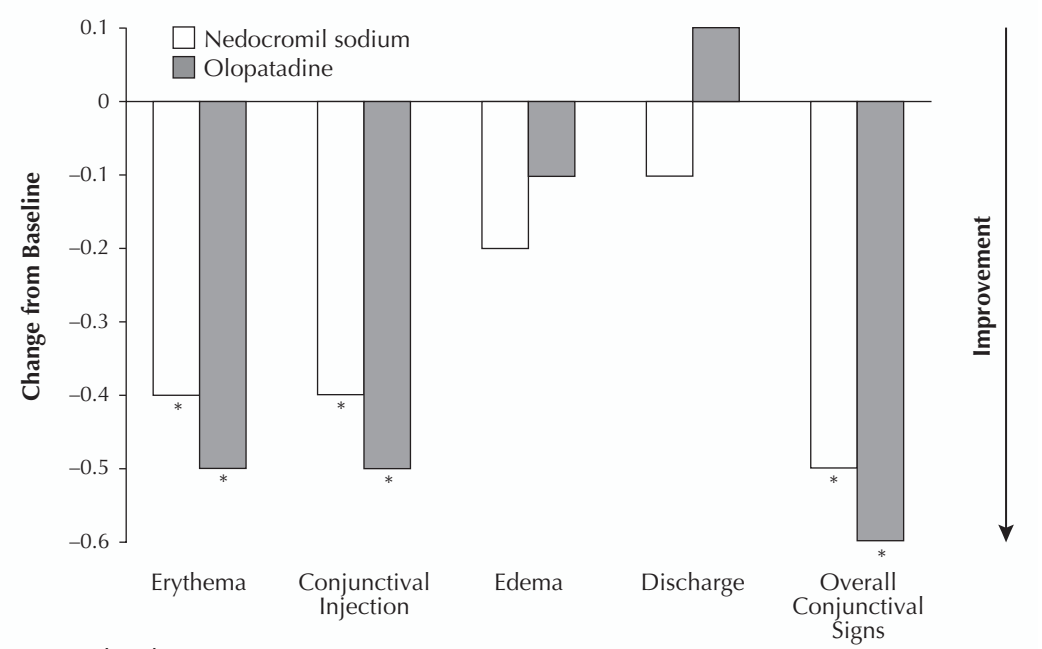


Table 2. Mean Symptom Summary Scores from Patients' Diary Cards*

	Nedocromil	Olopatadine	*P* Value
Itching	1.87	1.94	.750
Burning	2.00	1.84	.232
Grittiness	1.45	1.49	.794
Tearing	1.29	1.26	.810
Redness	2.27	1.90	.093
Light sensitivity	1.43†	1.70	.012
Discharge	1.31	1.38	.593
Swelling	1.67	1.53	.354

*Recorded during the 7 days of treatment.
†Statistically superior to olopatadine.

Fig 2. Physician-evaluated clinical signs following 1 week of treatment with nedocromil or olopatadine. Clinical signs were rated on a scale of 0 (none) to 4 (severe). Data shown are changes in mean scores from baseline (n = 28).



*P<.01 vs baseline.

Quality-of-Life-Scores

RQLQ(S) scores improved following treatment with nedocromil (change from baseline –1.02; P = .0001) and olopatadine (change from baseline –0.90; P = .0001). The improvement was comparable with the two drugs (P = .603).

Treatment Effectiveness

Nedocromil and olopatadine were similarly effective in preventing onset of allergic signs and symptoms. Both physicians and patients rated nedocromil as moderately or completely effective in 18 patients and olopatadine as moderately or completely effective in 17 patients.

DISCUSSION

In this study, nedocromil sodium 2% was as effective and provided as much satisfaction as olopatadine hydrochloride 0.1% in patients with perennial allergic conjunctivitis. Many patients with allergic conjunctivitis have had experience with antiallergy medications. In our patients, who had been treated previously with olopatadine, nedocromil sodium was comparable to olopatadine on all measures of

efficacy with the exception of control of photosensitivity, which was significantly better with nedocromil. Notably, the comparable scores for burning suggested that nedocromil eyedrops were as comfortable as olopatadine eyedrops. Acceptability of both drugs was good, but a trend toward greater acceptance favored nedocromil: 10 patients would request a prescription for olopatadine, while 16 patients would request a nedocromil prescription.

Many placebo-controlled studies have demonstrated the effectiveness of nedocromil sodium in allergic conjunctivitis,[3-7] but few published reports have involved head-to-head comparisons with other active treatments. Three environmental studies[9-11] compared nedocromil sodium with other oral and topical therapies for seasonal allergic conjunctivitis. Nedocromil and sodium cromoglycate were both effective, but during the peak pollen season when allergen levels were highest, nedocromil sodium twice daily provided better symptom control than sodium cromoglycate four times daily,[9] suggesting that the efficacy of nedocromil is superior to that of traditional mast-cell stabilizers. Nedocromil sodium eyedrops were as fast and effective as levocabastine eyedrops in controlling ocular symptoms associated with allergic rhinoconjunctivitis[10] and controlled the symptoms of seasonal allergic conjunctivitis more rapidly than the oral antihistamine terfenadine.[11] Our results demonstrate that nedocromil sodium is as effective and well tolerated as olopatadine, the topical antihistamine most frequently prescribed for allergic conjunctivitis.

The number of prescriptions for ocular antiallergy medications has increased precipitously since olopatadine was indicated for the prevention of ocular itching associated with allergic conjunctivitis, and this drug is now the most frequently prescribed medication for this condition. Olopatadine is also relatively expensive, however. The current average wholesale price of 5 mL of nedocromil sodium 2% ophthalmic solution is $53.75, compared with $56.88 for olopatadine hydrochloride 0.1%. In addition to its reduced cost, nedocromil sodium may represent the most comprehensive treatment available for allergic conjunctivitis, because its mechanism of action combines mast-cell stabilization with additional anti-inflammatory activities.[2] The results of this study, demonstrating comparable effectiveness and patient satisfaction with both medications, suggest that nedocromil sodium 2% may be more cost-effective than olopatadine 0.1% as therapy for perennial allergic conjunctivitis.

Because patients who have used antiallergy medications might be best able to discern differences in effectiveness and comfort, those with no prior olopatadine experience were excluded from this study. Future studies, however, will determine whether nedocromil also provides effectiveness and satisfaction at least as great as those afforded by olopatadine in newly diagnosed patients and in patients naïve to olopatadine use.

In summary, nedocromil sodium 2% ophthalmic solution is an effective and well-accepted treatment of allergic conjunctivitis. Switching patients from olopatadine to nedocromil sodium produced no loss in efficacy or patient satisfaction yet lowered the cost of treatment. Nedocromil sodium 2% ophthalmic solution has great potential as a cost-effective, patient-satisfying treatment for allergic conjunctivitis.

ACKNOWLEDGMENT

The authors thank Dr. E. F. Juniper for providing the RQLQ(S) questionnaire.

None of the authors has any proprietary interest in the drugs used in this study. This study was supported in part by an unrestricted grant from Allergan, Inc.

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