Comparison of olopatadine 0.6% nasal spray versus fluticasone propionate 50 µg in the treatment of seasonal allergic rhinitis


ABSTRACT

The efficacy of nasal antihistamines (NAHs) for allergic rhinitis (AR) is comparable with or better than second-generation oral antihistamines, with faster onset of action and greater effect on congestion. Limited data suggest that NAHs may be equivalent to intranasal corticosteroids at reducing the full range of nasal seasonal AR (SAR) symptoms, including congestion. The efficacy of olopatadine 0.6% nasal spray (2 sprays/nostril b.i.d.) for symptoms of SAR was compared with fluticasone 50 microg nasal spray (2 sprays/nostril q.d.) in a double-blind, randomized, parallel-group, 2-week noninferiority trial. A total of 130 symptomatic patients were randomized to treatment and they recorded nasal and ocular allergy symptom scores b.i.d. (morning and evening) in a diary. Both treatments reduced reflective and instantaneous assessments of nasal and ocular symptoms from baseline throughout the 2-week study period (p < 0.05). The reflective total nasal symptom score (the primary efficacy variable) decreased by an average of ~45.4% for patients treated with olopatadine 0.6% and by ~47.4% for those treated with fluticasone; statistical significance favoring olopatadine was demonstrated at day 1. No significant between-treatment differences were determined for the average 2-week percent changes from baseline for congestion, runny nose, sneezing, itchy nose, and ocular symptoms, although olopatadine had a faster onset of action for reducing all symptoms. Both treatments were safe and well tolerated. Olopatadine and fluticasone nasal sprays both reduced nasal and ocular SAR symptoms with no significant between-treatment differences except for a faster and greater onset of action with olopatadine.


Key words: Allergic conjunctivitis, allergic rhinitis, allergy, antihistamines, fluticasone, intranasal steroids, nasal antihistamines, olopatadine, seasonal allergic rhinitis.

Allergic rhinitis (AR), one of the most common atopic diseases, afflicts an estimated 35–50 million people in the United States, up to 30% of the general population.1,2 Although often dismissed as a “nuisance disorder” by both clinicians and patients, the costs are substantial—both in terms of direct expenditures and societal costs related to absenteeism and presenteeism. AR represents a hyperactive immune system response to otherwise benign, noninfectious environmental aeroallergens (e.g., pollens, mites, and animal danders).2,3

The characteristic symptoms of AR are sneezing, rhinorrhea, nasal itching, nasal congestion, and itchy/red/watery eyes. Patients also frequently report headaches and/or facial pain, snoring, and sleep disturbance.1,2,4 Although generally not life-threatening, the symptoms can be annoying and debilitating—interfering with daily activities, performance and concentration, rest, and contributing to absenteeism and presenteeism.1,2,4 Rhinitis is often associated with other chronic conditions including asthma, eustachian tube dysfunction, otitis media, rhinosinusitis, atopic dermatitis, allergic conjunctivitis, and obstructive sleep apnea.1,4,5 Thus, early treatment of rhinitis symptoms can have significant clinical benefit.

Topical nasal antihistamines (NAHs) represent the latest addition to the armamentarium for treating AR. The efficacy of these topical agents is comparable with or better than second-generation oral antihistamines, with a much faster onset of action; and, unlike oral antihistamines, the NAHs also reduce nasal congestion. Limited data suggest that NAHs may be equivalent to intranasal corticosteroids (INSs) at reducing the full range of nasal AR symptoms, including congestion.6

From the *Institute for Allergy and Asthma, Chevy Chase, Maryland, #The William Storms Allergy Clinic, Colorado Springs, Colorado, §ASTHMA, INC, NW, Asthma and Allergy Center, Seattle, Washington, ¶California Allergy and Asthma Medical Group, Los Angeles, California, ‖Carolina Allergy and Asthma Consultants, Raleigh, North Carolina, **North Texas Institute for Clinical Trials, Fort Worth, Texas, and #Capital Allergy and Respiratory Disease Center, Sacramento, California

Funding for this research was supported by Alcon Laboratories, Inc., Fort Worth, Texas. W. Storms, M.A. Kaliner, and B. Chipps are consultants/speakers and receive grant support from Alcon Research Ltd. In addition, S. Tilles is a consultant/speaker for Alcon and C. LaForce and M. Kaliner are on the advisory board.

Address correspondence and reprint requests to Michael A. Kaliner, M.D., Institute for Allergy and Asthma, 5454 Wisconsin Avenue, Suite 1700, Chevy Chase, MD 20817

E-mail address: makaliner@ooc.com

Copyright © 2009, OceanSide Publications, Inc., U.S.A.
Olopatadine 0.6% nasal spray is the most recent NAH to reach the U.S. market. This mast cell stabilizing agent is also a potent topical H1-antagonist and has been available since 1996 as an ophthalmic solution to treat the signs and symptoms associated with allergic conjunctivitis. In 2008 the nasal formulation was approved by an institutional review board, and an informed consent document was signed by all of the patients or by the parent or legal guardian for patients ≤12 years of age.

In patients with SAR, olopatadine nasal spray has established an onset of action within 30 minutes and, when administered for 2 weeks, has shown significant efficacy in reducing nasal allergy symptoms, including congestion, when compared with placebo. Evaluations using the Rhinoconjunctivitis Quality of Life Questionnaire and the Work Productivity and Activity Impairment Questionnaire—Allergy Specific, have also shown significant positive health outcomes with treatment.

Antihistamines, including NAHs, are recommended by current guidelines and practice parameters as first-line therapy for SAR. However, INSs are considered “the gold standard” by some clinicians. On the other hand, many patients are concerned about potential INS side effects and also desire a product that works quickly to relieve symptoms.

A double-blinded parallel-group environmental exposure chamber study in 425 patients with SAR showed that a single dose of olopatadine nasal spray induced a significant reduction of allergy symptoms (p < 0.05) within 30 minutes and lasting for 12 hours when compared with an INS, mometasone furoate. However, the relative efficacies of the NAHs and INSs beyond 12 hours were not evaluated. The current study was undertaken to evaluate the comparative efficacy of olopatadine 0.6% nasal spray with that of an INS, fluticasone propionate, 50 μg/puff, in a 2-week SAR trial.

MATERIALS AND METHODS

Patients
Patients were ≥12 years of age with a ≥2-year history of spring/summer AR. All patients showed allergic sensitivity to a currently prevalent (at time of study) seasonal allergen within the past 5 years, defined by a positive reaction on skin-prick testing (a wheal size of ≥3 mm greater than the diluent) or intradermal testing (a wheal size of ≥7 mm greater than the diluent) within the past 5 years, and were symptomatic on trial entry. The study protocol was approved by an institutional review board, and an informed consent document was signed by all of the patients or by the parent or legal guardian for patients <18 years old.

Women of childbearing potential were enrolled if they agreed to use an acceptable method of contraception. Patients who had abnormal nasal anatomy, severe congestion, recent upper or lower respiratory infection or chronic sinusitis, or cardiovascular disease were excluded. Also excluded were smokers, known nonresponders to antihistamines, and patients with concurrent upper or lower airway disease that could interfere with successful nasal drug administration/absorption (e.g., rhinitis medicamentosa and asthma).

Medication washout times were 30 days for systemic corticosteroids and inhaled or ocular corticosteroids; 7 days for INSs, leukotriene inhibitors, anticholinergic agents, systemic antifungal agents, and systemic antibiotics; 3 days for ocular and nasal antiallergy agents, oral antihistamines, nonsteroidal anti-inflammatory drugs, decongestants, and over-the-counter cough/cold and sleep aids; and 1 day for nasal and ocular saline. Patients who were receiving immunotherapy were required to be stable for 30 days before and throughout the trial. Use of any prescription or over-the-counter nasal spray was not allowed.

Study Design
This was a 2-week, multicenter (seven sites in the United States), double-blind, randomized, two-arm parallel-group clinical trial of olopatadine 0.6% nasal spray and fluticasone propionate 50 μg nasal spray. Beginning with the screening visit and continuing to end of treatment, patients recorded in a diary the symptom severity of their itchy nose, runny nose, stuffy nose, sneezing, itching/burning eyes, tearing/watery eyes, and ocular redness using a 4-point scale (0 = absent, 1 = mild, 2 = moderate, and 3 = severe). The sum of scores for the four nasal symptoms was defined as the total nasal symptom score (TNSS), and the sum of the scores for the three ocular symptoms was defined as the total ocular symptom score (TOSS). Patients evaluated their symptoms as experienced at that moment (instantaneous) and in the hours since the last dose of study medication (reflective), in the morning before any other activity, and at bedtime.

The study design is shown in Fig. 1. For patients who did not require a medication washout period, the screening and randomization visits were combined. At
screening, patients had to have a minimum reflective TNSS of ≥4 with a maximum score of 10 and an individual score for congestion of ≤2. The patients were randomized to dose fluticasone propionate (50 μg) nasal spray q.d. and olopatadine 0.6% nasal spray b.i.d., 2 sprays of each per nostril for the 2-week treatment period. Because the olopatadine and fluticasone bottles were distinctly different, as were the treatment regimens, foil-wrapped bottles with appropriate dosing instructions were distributed to the patients in nontransparent envelopes. In this manner, the study staff, investigator, sponsor, monitors, and patients were unaware of any individual patient’s assigned treatment.

Diary scores, protocol compliance, medication changes, and reported adverse events were reviewed after each week of treatment. The exit visit (day 14) included physical and nasal examinations and measurement of vital signs.

Statistical Methods

Efficacy. The primary efficacy variable was the 2-week average percent change in reflective TNSS. Secondary efficacy variables included the percent changes in instantaneous TNSS and reflective/instantaneous TOSS. Individual symptoms (i.e., runny nose, itchy nose, sneezing, stuffy nose, watery/tearing eyes, itchy/burning eyes, and ocular redness) were also analyzed to explore onset of action.

Safety. Safety evaluation included nasal examination for significant anatomic abnormalities, evidence of infection, bleeding, and ulcerations of the mucosa; and physical examination of the head/eyes; ears, nose, throat, and neck; skin and extremities; cardiovascular and pulmonary systems; abdomen, lymph nodes and neurological signs. Unsolicited patient-reported adverse events were also recorded, regardless of relationship to treatment.

Sample Size Estimation. The study was powered based on the hypothesis that the differences in mean 2-week average reflective TNSS between the olopatadine 0.6% nasal spray and the fluticasone propionate 50 μg nasal spray would be within 2 points. Per sample size calculation, when the standard deviation is within 3 points and the nonevaluable rate is not >10%, a sample size of 65 patients/group would be sufficient to detect a 2-point (noninferiority margin) between-group difference with a 90% statistical power at 95% confidence level.

Data Analysis. All enrolled patients completed the study. Therefore, the intent-to-treatment population was the same as the per-protocol population. Comparability analysis with respect to baseline patient demographic and clinical characteristics was first performed to validate the between-group comparability. Between-group comparisons were conducted using the Student’s t-test for numeric variables or Pearson’s chi-square test for categorical variables.

Paired t-test was used for within-subject before-after comparisons. Analysis of covariance using age as the covariant and the repeated measures analysis of variance were further performed to adjust the potential impact of age difference between the treatment groups and the time effect on the primary outcome measure (TNSS). Statistical analysis was performed using SAS (PC-9.1.2; SAS Institute, Cary, NC) by an independent biostatistician. A 95% confidence level was set to all tests.

RESULTS

Of 132 patients screened at 7 U.S. centers, 130 met the study criteria and were randomized to treatment. All enrolled patients completed the study. There were 63 male and 64 female patients with ages ranging from 12 to 73 years (mean, 35.3 years; SD, 13.48). Fifty-six percent were white, 21% were African American, 13% were Hispanic/Latino, and 10% were Asian. The treatment groups were similar in terms of demographic characteristics (Table 1) except that the mean age was 5 years older in the olopatadine group. All patients had seasonal allergies to tree, grass, and/or weed allergens, documented by positive skin tests.

Primary Efficacy: Reflective TNSS

Pretreatment values for reflective TNSS were similar for both treatment groups (oloapatadine 0.6%, 6.72 ± 1.88 SD; fluticasone, 6.49 ± 1.66 SD; p = 0.4599). The mean 2-week average reflective TNSS was 3.52 ± 2.01 SD for olopatadine and 3.37 (±2.18 SD) for fluticasone, a 45.4 and 47.4% reduction from baseline, respectively (Fig. 2). Per t-test, the observed difference (fluticasone − olopatadine = -0.154) was not statistically significant (p = 0.6771). The 95% CI for treatment difference in mean 2-week average score was −0.886 to 0.577, which is within the defined noninferiority margin of 2. An analysis of covariance using age as the covariant indicated that the between-group age difference was not a significant factor in treatment outcome; the between-groups difference remained statistically insignificant after adjusting to age difference. The repeated measures analysis of variance with adjustments for time effect and time-by-treatment interaction confirmed the noninferiority conclusion (p = 0.7551).

Secondary Efficacy

TNSS during the 2-Week Period by Day. Per the within-subject before−after comparison using paired t-test, the
mean daily reflective TNSS decreased throughout the 2-week treatment period in both groups. No significant differences between treatments were noted using the magnitude of decrease per two-sample Student’s *t*-test. On day 1, the mean percent reduction from baseline was 26.7% for patients who received olopatadine compared with 13.6% for fluticasone (*p*/H11005 0.0432; Fig. 3A).

**Table 1** Comparison in patient baseline characteristics

<table>
<thead>
<tr>
<th>Variable</th>
<th>Total (n = 130)</th>
<th>Olopatadine 0.6% (n = 65)</th>
<th>Fluticasone Propionate (n = 65)</th>
<th><em>p</em> Value*</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (yr)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Mean (SD)</td>
<td>35.31 (13.48)</td>
<td>38.14 (15.25)</td>
<td>32.48 (10.83)</td>
<td>0.0163</td>
</tr>
<tr>
<td>Range</td>
<td>12–73</td>
<td>12–73</td>
<td>13–60</td>
<td></td>
</tr>
<tr>
<td>Gender#</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Male</td>
<td>63 (49.61%)</td>
<td>30 (46.88)</td>
<td>33 (52.38)</td>
<td>0.5349</td>
</tr>
<tr>
<td>Female</td>
<td>64 (50.39)</td>
<td>34 (53.13)</td>
<td>30 (47.62)</td>
<td></td>
</tr>
<tr>
<td>Race</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>White</td>
<td>72 (56.25)</td>
<td>36 (56.25)</td>
<td>36 (56.25)</td>
<td>0.8860</td>
</tr>
<tr>
<td>African-American</td>
<td>27 (21.09)</td>
<td>15 (23.44)</td>
<td>12 (18.75)</td>
<td></td>
</tr>
<tr>
<td>Hispanic/Latino</td>
<td>16 (12.50)</td>
<td>8 (1250)</td>
<td>8 (1250)</td>
<td></td>
</tr>
<tr>
<td>Asian</td>
<td>11 (8.59)</td>
<td>4 (6.25)</td>
<td>7 (10.94)</td>
<td></td>
</tr>
<tr>
<td>Other§</td>
<td>2 (1.56)</td>
<td>1 (1.56)</td>
<td>1 (1.56)</td>
<td></td>
</tr>
</tbody>
</table>

*The *p* values of between-group comparisons using Student’s *t*-test for numerical variables and Pearson *χ*²-test for categorical variables.

#Gender information not available for three patients.

§Other races are Indian in the olopatadine group, East Indian in the fluticasone group.

**Figure 2.** Mean average reflective total nasal symptom scores (TNSSs) at baseline and end of treatment (2 weeks).

Individual Reflective Nasal Symptoms Scores. Both olopatadine and fluticasone groups had significant reductions in the reflective scores for runny nose, itchy nose, sneezing, and stuffiness over the 2 weeks of treatment per paired *t*-test. No significant between-treatment differences in a specific mean 2-week average were detected (Fig. 4). A difference in onset of action was observed for all nasal symptoms, with greater percent reductions in patients treated with olopatadine in the first 72 hours, although because of the large variance observed, only the reflective sneezing score reached statistical significance (29.2% versus 8.76%; *p* = 0.0378; Fig. 4).

Reflective TOSS and Individual Ocular Symptoms Scores. Pretreatment values for reflective TOSS were similar for both treatment groups (oloapatadine 0.6%, 4.25 ± 2.05 SD; fluticasone propionate, 4.18 ± 1.84 SD; *p* = 0.8491), and both groups reported similar reductions over the course of the study: 38.5 and 40.6% for the olopatadine and fluticasone groups, respectively (*p* = 0.8402; Fig. 5). The mean 2-week average reflective individual ocular symptom scores for itching/burning eyes, tearing/watery eyes, and eye redness were also significantly reduced based on the within-patients analysis, with no between-treatment differences in the magnitude of reduction. However, again, a difference in onset of action was evident, with faster and greater relief for patients treated with olopatadine in the first 3 days (Fig. 6).

Instantaneous TNSS, TOSS, and Individual Symptoms Scores. Similar trends were observed for the instantaneous nasal and ocular symptom scores. Both olopatadine 0.6% and fluticasone propionate nasal sprays showed significant reductions in the mean instantaneous scores over the 2 weeks of treatment, with no significant between-treatment differences detected for any measurement (Table 2). Instantaneous TNSS decreased in similar manner to reflective TNSS on a day-to-day basis (Fig. 3B). Significant between-group
differences favored olopatadine on day 1 ($p = 0.0501$) and fluticasone on day 11 ($p = 0.0437$).

Safety

Both treatments were well tolerated. There also were no treatment-related changes in physical (including nasal) examination findings for either group. Eighteen patients (olopatadine, 11; fluticasone, 7) reported a total of 29 adverse events; 9 were determined to be related to treatment: epistaxis/nasal blood (3), bad/bitter taste (2), sore throat (1), cough (1), sleepiness (1), with olopatadine, and eyes mildly injected (1) with fluticasone. Adverse events were nonserious, did not

Figure 3. (A) Mean daily percent change in reflective total nasal symptom scores (TNSSs) from baseline during the 2-week treatment period. (B) Mean daily percent change in instantaneous TNSSs from baseline during the 2-week treatment period.

Nasal “Stuffiness”

Runny Nose

Itchy Nose

Sneezing

Figure 4. Mean percent changes from baseline in the reflective nasal symptom scores for days 1, 2, and 3 of treatment and the specific 2-week averages.

Figure 5. Mean average reflective total ocular symptom scores (TOSSs) at baseline and end of treatment (2 weeks).
interrupt treatment continuation in the study, and were resolved with or without treatment.

DISCUSSION

In this 2-week study, treatment with either olopatadine 0.6% nasal spray (2 sprays/nostril b.i.d.) or fluticasone propionate 50 μg nasal spray (2 sprays/nostril q.d.) provided relief from symptoms of SAR. Reductions in both nasal and ocular allergy symptoms were observed for both treatments with no significant between-treatment differences in the magnitude of reduction for specific parameters. The only difference observed was a faster and greater onset of action with olopatadine 0.6%. This finding was not surprising because the usual earliest onset of action for INSs is between 2 and 24 hours (for mometasone furoate, fluticasone propionate, budesonide, beclomethasone dipropionate, and triamcinolone acetonide).13–17 An environmental chamber study comparing olopatadine 0.6% nasal spray with the INS, mometasone furoate, reported an onset of action within 30 minutes for olopatadine versus 2.5 hours with mometasone.8

Figure 6. Mean percent changes from baseline in the reflective ocular symptom scores for days 1, 2, and 3 of treatment and the specific 2-week averages.

Table 2  Comparisons in 2-wk average percent changes from baseline in instantaneous assessments of symptoms

<table>
<thead>
<tr>
<th>Symptom Score</th>
<th>Olopatadine 0.6% (n = 65)</th>
<th>Fluticasone Propionate (n = 65)</th>
<th>p Value*</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Mean (SD)</td>
<td>Mean (SD)</td>
<td></td>
</tr>
<tr>
<td>TNSS</td>
<td>-45.26 (27.93)</td>
<td>-48.80 (30.10)</td>
<td>0.4895</td>
</tr>
<tr>
<td>Runny nose</td>
<td>-38.45 (49.62)</td>
<td>-38.30 (58.45)</td>
<td>0.9705</td>
</tr>
<tr>
<td>Itchy nose</td>
<td>-30.20 (60.54)</td>
<td>-42.57 (49.31)</td>
<td>0.2103</td>
</tr>
<tr>
<td>Stuffy nose</td>
<td>-16.49 (53.65)</td>
<td>-30.21 (42.69)</td>
<td>0.1109</td>
</tr>
<tr>
<td>Sneezing</td>
<td>-55.23 (48.75)</td>
<td>-42.88 (60.67)</td>
<td>0.2094</td>
</tr>
<tr>
<td>TOSS</td>
<td>-36.54 (60.26)</td>
<td>-41.63 (50.46)</td>
<td>0.6064</td>
</tr>
<tr>
<td>Itching/burning eyes</td>
<td>-38.36 (58.66)</td>
<td>-40.41 (50.53)</td>
<td>0.8346</td>
</tr>
<tr>
<td>Tearing/watering eyes</td>
<td>-27.14 (67.15)</td>
<td>-31.04 (69.16)</td>
<td>0.7545</td>
</tr>
<tr>
<td>Redness</td>
<td>-29.28 (64.91)</td>
<td>-26.25 (66.53)</td>
<td>0.8011</td>
</tr>
</tbody>
</table>

*The p values of between-group comparison using Student’s t-test.

TNSS = total nasal symptom score; TOSS = total ocular symptom score.
In this study, symptom reductions with olopatadine exceeded those with fluticasone by at least 10% for all reflective measures evaluated during one or more of the first 3 days of treatment. Statistical significance was attained on the 1st day of treatment for the primary efficacy variable, TNSS (olopatadine, −26.69%; fluticasone, −13.64%; p = 0.043), and also for sneezing (olopatadine, −29.17%; fluticasone, −8.76%; p = 0.038).

This is the first study directly comparing the efficacy of olopatadine 0.6% nasal spray to an INS, and it is of interest that both agents reduced nasal stuffiness to a similar degree. In this population of patients with active SAR, olopatadine reduced nasal congestion score by a 2-week average of 22.2% compared with 29.5% with fluticasone (p = 0.4035). Current guidelines and practice parameters for AR note that NAHs do reduce nasal congestion, but suggest that INSs are more potent. Additional studies may be required to confirm the observation of equal efficacy between olopatadine and INS.

The mean reduction in nasal congestion with olopatadine nasal spray observed here is comparable with that reported in other 2-week trials in patients with SAR. Individual studies with INSs (budesonide, triamcinolone acetonide, and fluticasone propionate) in patients with SAR have generally shown percentage reductions from baseline for nasal congestion of >30%, but it is difficult to compare studies because of differences in treatments and study protocols. Fluticasone propionate nasal spray (200 μg, q.d.) reduced nasal congestion by >40% when given to >20 patients with SAR for 15 days in two separate clinical trials. However, no screening data are available for congestion in those studies, and scores were reported on a visual analog scale (0–100).

Both olopatadine and fluticasone reduced ocular allergy symptoms to a similar degree. This might be expected because all allergy medications reduce ocular allergy symptoms to some extent. However, recently, there has been interest specifically in the effect of INSs on ocular allergy. The authors of a 2-week study of fluticasone furoate (110 μg q.d.) in patients with SAR suggested that this INS “might present a single treatment option for the nasal and ocular symptoms of SAR.” Over the 2-week treatment period, the reflective TOSS decreased by 33.8% in that study, which is in the range of the reductions observed in TOSS in this study (olopatadine, 38.5%; fluticasone, 40.6%). Obviously, the earlier article discounts the fact that most allergy medications provide some level of ocular protection. Of greater concern and as noted in the package inserts, is the potential for adverse ocular effects with INSs. In the present study, the only treatment-related ocular adverse event, mild eye injection, was reported by a fluticasone-treated patient. The best treatment for patients with more than mild ocular allergy symptoms is to target the allergic eyes directly with drops.

In conclusion, in patients with active SAR, olopatadine 0.6% nasal spray (2 sprays/nostril b.i.d.) and fluticasone propionate 50 μg (2 sprays/ nostril q.d.) given over 2 weeks provided comparable clinical benefit for nasal and ocular allergy symptoms. The study findings support olopatadine nasal spray as an effective first-line treatment for the rapid and sustained relief of the symptoms of SAR. More comparative data on the efficacy of INSs and NAHs are warranted in this patient population because both medications are considered to be first-line therapies for relieving the symptoms of SAR.1,4

ACKNOWLEDGMENTS

The editorial and technical expertise of Judith Farrar, Ph.D., is greatly appreciated. The authors also acknowledge the staff of the various offices in which data were collected. Dr. Chipps would like to specifically thank his study coordinator, Bryce Autret.

REFERENCES

dine HCl nasal spray 0.4% and olopatadine 0.6% compared with vehicle placebo. Allergy Asthma Proc 27:202–207, 2006.