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# Comparative Effects of Loratadine and Azatadine in the Treatment of Seasonal Allergic Rhinitis

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**SUMMARY** **The efficacy and safety of loratadine 10 mg once daily were compared with azatadine 1 mg twice daily in controlling symptoms of seasonal allergic rhinitis. The study was a randomized, double-blind, parallel-group design involving 34 patients receiving either loratadine or azatadine for 14 days. Both treatments were effective in relieving the histamine-mediated symptoms of seasonal allergic rhinitis. At baseline, 100% and 93% of the patients in the loratadine and azatadine treatment groups, respectively, had moderate or severe symptoms of disease; at endpoint of treatment 80% of the patients in the loratadine treatment group and 92% of those in the azatadine treatment group had mild or no disease symptoms. Sedation was reported by fewer patients in the loratadine treatment group than in the azatadine group. Thus loratadine is an effective and safe antihistamine when given once daily for the symptomatic relief of seasonal allergic rhinitis.**

There are currently many compounds which are known for their ability to selectively inhibit the action of histamine on $H_1$ receptors.[1] However, the antihistamine activity of many of these compounds is often accompanied by annoying side effects such as sedation and anticholinergic effects,[2] which in turn limit the clinical usefulness of these drugs in treatment of various allergic disorders.

Loratadine is a new selective peripheral histamine $H_1$-receptor antagonist. In preclinical studies this new antihistamine has had minimal central nervous system activity,[3] and thus, very limited potential for sedation. It also has negligible anticholinergic side effects. Clinical trials in patients have demonstrated the efficacy and rapid onset of action of loratadine when administered on a once-daily dosing basis in the treatment of seasonal allergic rhinitis.[4,5] Furthermore, loratadine has been shown to be comparable to two other non-sedating antihistamines, terfenadine and astemizole.[4,5]

The present study was conducted to compare the efficacy and safety of loratadine (10 mg once daily), with that of azatadine maleate (1 mg twice daily), when administered orally in patients with seasonal allergic rhinitis. Azatadine is an effective antihistamine, known to produce sedation and anticholinergic side effects.[6-9]

## MATERIALS AND METHODS

This was a randomized, double-blind, parallel-group study in patients with seasonal allergic rhinitis. An initial screening visit (within 14 days prior to treatment) was followed by a 14-day treatment period.

Informed consent was obtained at the initial screening visit, and the general health of each patient was assessed by a full history and physical examination. Full blood count, biochemical screen including liver function tests, serum creatinine, and electrolytes were performed. Urinalysis and an electrocardiogram were also performed. The allergic status of each patient was assessed by history, examination and skin prick tests with a battery of common environmental allergens. Patients with a history of asthma within the previous two years were excluded. Female patients were not to be pregnant or lactating and must have been using an acceptable form of contraception. Patients were also excluded if they had received immunotherapy with pollen extracts commenced with-

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in six months before enrolment in the study. Antihistamines or decongestants were ceased 24 hours before the onset of treatment. Any corticosteroid preparation or sodium cromoglycate were ceased two weeks before entry.

At the baseline screening visit. The following eight symptoms commonly associated with allergic rhinitis were evaluated:

*Nasal*

Nasal discharge (runny nose)
Nasal blockage
Nasal itching
Sneezing

*Nonnasal*

Itching or burning eyes
Tearing (watering) eyes
Redness of eyes
Itching of ears or palate

Symptoms were rated numerically on the scale: 0 = none, 1 = mild, 2 = moderate, 3 = severe. In order to initiate treatment, at least two of the nasal symptoms were to be moderate, and the total score of the nasal symptoms plus itching eyes was to be six or greater. The overall condition of rhinitis was also evaluated and rated numerically at baseline using the same scale as for individual symptoms.

Qualified subjects were randomly assigned (by a computer-generated random code) into one of two treatment groups; each group received orally either 10 mg loratadine once daily or 1 mg azatadine twice daily. Patients assigned to the loratadine treatment group received active drug in the morning and placebo in evening to maintain blinding. Evaluation of response to treatment was based on the following variables, which were rated daily by the patients and by the investigator on treatment days 3, 7, and 14: (1) nasal and nonnasal symptom scores, (2) the overall condition of rhinitis, and (3) therapeutic response to treatment (rated as excellent, good, fair, poor, or treatment failure). To compensate for invalid visits and early terminations, analyses were also performed on the data obtained from the last valid visit for each patient (ie, the "endpoint" of treatment for all patiets).

Safety evaluation included notation of any clinically meaningful changes from baseline laboratory test results. Patients were also questioned at each return visit about adverse experiences which might have occurred since the previous visit. Adverse experiences were graded as mild, moderate, or severe, and the investigator judged the relationship to treatment as probable, possible, or remote. An analysis of variance model was used to compare all efficacy parameters between treatment groups. Fisher's $2 \times 2$ Exact test was used to compare between treatment groups the number of patients reporting adverse experiences.

## RESULTS

### Patient population

Thirty-four patients (18 loratadine, 16 azatadine) with seasonal allergic rhinitis were enrolled for this study and received treatment. Six patients were excluded from the efficacy analysis; these patients were enrolled but did not have sufficient nasal symptom scores at baseline.

**Table 1.** Baseline demographic and epidemiologic characteristics of patients evaluated for efficacy

| Characteristics | Loratadine 10 mg OD | Azatadine 1 mg BID |
|---|---|---|
| Number of patients | 15 | 13 |
| Sex | | |
| Male | 8 | 8 |
| Female | 7 | 4 |
| Race | | |
| Caucasian | 14 | 13 |
| Other | 1 | 0 |
| Age (years) | | |
| Mean | 35 | 37 |
| Range (min, max) | 15–68 | 16–58 |
| Weight (kgs) | | |
| Mean | 69 | 75 |
| Range (min, max) | 57–83 | 59–105 |
| Duration of Allergic Condition (years) | | |
| Mean | 9 | 15 |
| Range (min, max) | 2–20 | 1–34 |
| Mean Symptom Severity* | | |
| Total nasal | 6.8 | 6.5 |
| Total nonnasal | 5.7 | 4.3 |

*Mean combined symptom scores for individual nasal (discharge, stuffiness, itching, and sneezing) and nonnasal symptoms (itching or burning and redness of eyes and itching of ears or palate); scale for individual scores: 0 = none (symptom not present), 1 = mild, 2 = moderate, 3 = severe.

thus 28 patients (15 loratadine, 13 azatadine) were included in the efficacy analysis. Demographic and epidemiologic data for patients included in the efficacy analysis are presented in Table 1. The two treatment groups were comparable in sex, age, weight, duration of allergic condition, and in total nasal and nonnasal symptom scores.

**Efficacy**

*Nasal Symptoms*

Figure 1 presents the percent improvement in the combined scores for the four nasal symptoms (discharge, blockage, itching, and sneezing) at the day 3 and endpoint analysis. At day 3 of treatment, the decrease from baseline in the mean total nasal symptom score (ie, improvement) was 72% in the loratadine treatment group and 65% in the azatadine treatment group. At endpoint analysis, nasal symptoms in the loratadine and azatadine treatment groups had improved 66% and 74%, respectively. There was no statistically significant difference in symptom improvement between the two treatment groups at day 3 or endpoint. The individual nasal symptom scores at endpoint indicated a degree of improvement similar to that observed in total nasal symptoms (Figure 2). However the degree of improvement in nasal blockage in both treatment groups was greater than that reported in similar studies.

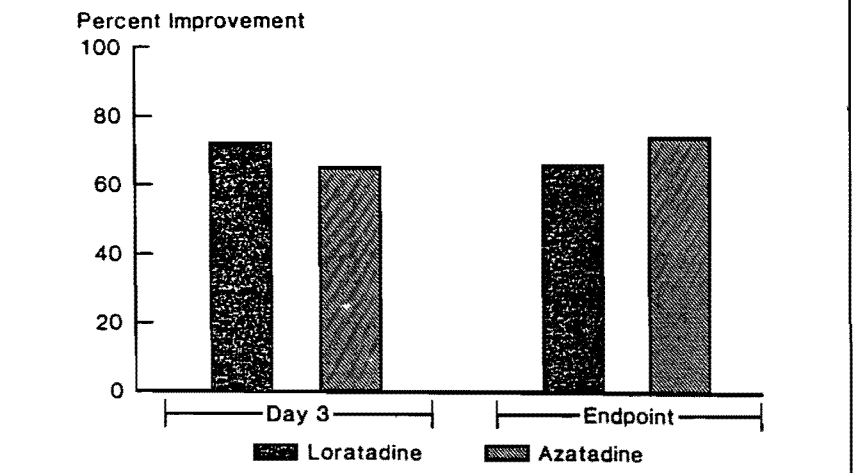


**Fig. 1** Percent improvement in combined nasal symptom scores in patients receiving loratadine or azatadine.

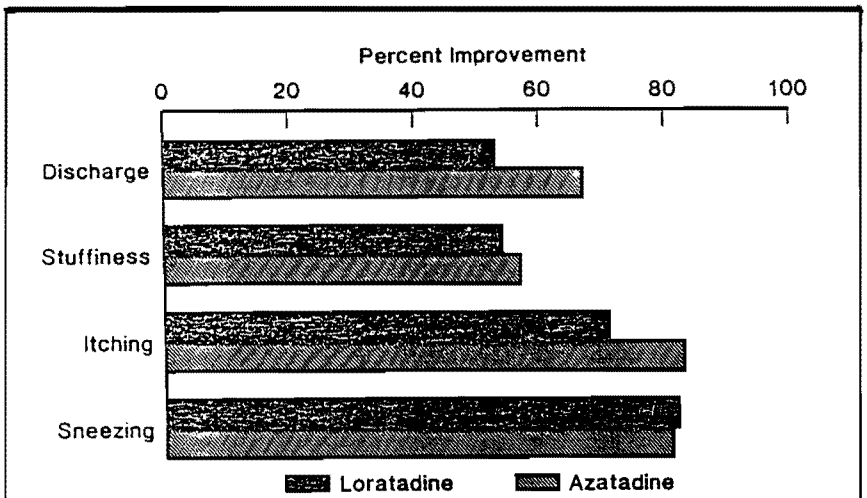


**Fig. 2** Percent improvement in individual nasal symptoms at endpoint in patients receiving loratadine or azatadine.

*Nonnasal Symptoms*

Figure 3 presents the percent improvement in the combined scores for the nonnasal symptoms (itching or burning, tearing, and redness of eyes, and itching of ears of palate). At day 3 of treatment, the mean total nonnasal symptom score had improved 88% in the loratadine treatment group compared to 58% in the azatadine group ($P = 0.02$). At endpoint analysis, the mean total nonnasal symptom score decreases were 82% for loratadine and 86% for azatadine ($p > 0.05$). Generally, this pattern of improvement observed in total nonnasal symptoms was also seen in the individual nonnasal symptoms.

*Overall Evaluation*

Table 2 presented the physician's overall evaluation of rhinitis symptoms. Following initiation of treatment, improvement in the overall condition of rhinitis was observed in both the loratadine and azatadine treatment groups as indicated by a lesser number of patients having moderate or severe rhinitis and a greater number of patients with mild symptoms or none at all as the study progressed.

*Therapeutic Response*

The physician's evaluation of therapeutic response to treatment also indicated a comparable response to treatment for loratadine and azatadine-treated patients (Table 3); by day 3, 94% or the loratadine-treated patients and 86% of the azatadine-treated patients had a good or excellent response to treatment. The endpoint analysis indicated that 80% of the

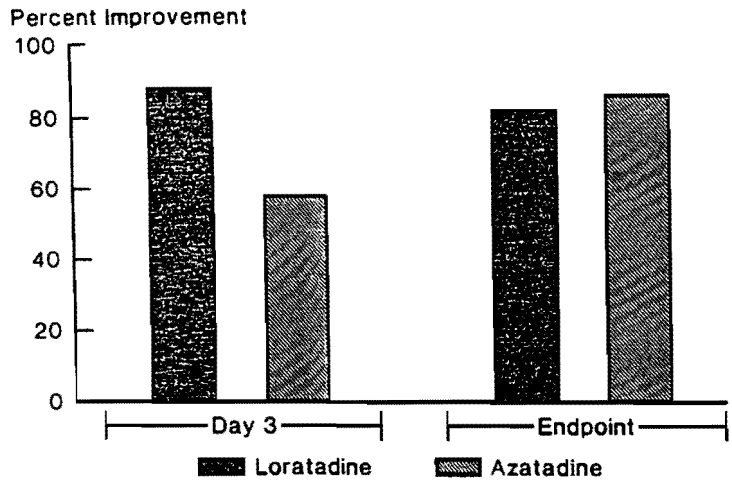


**Fig. 3** Percent improvement in combined nonnasal symptom scores in patients receiving loratadine or azatadine.

**Table 2.** Physician's evaluation of overall condition of rhinitis in patients receiving loratadine or azatadine.

| Treatment group | Rhinitis severity* | | | |
|---|---|---|---|---|
| | Severe | Moderate | Mild | None |
| Loratadine | | | | |
| Baseline | 27% | 73% | 0% | 0% |
| Day 3 | 0% | 7% | 53% | 40% |
| Endpoint | 0% | 20% | 40% | 40% |
| Azatadine | | | | |
| Baseline | 8% | 85% | 8% | 0% |
| Day 3 | 0% | 15% | 39% | 46% |
| Endpoint | 0% | 8% | 23% | 69% |

*Severe=significant/major interference with daily activities and/or sleep; Moderate=some interference with daily activities and/or sleep; Mild=symptoms did not interfere with daily activities and/or sleep; None=virtually no symptoms were present.

patients treated with loratadine had a good or excellent response to treatment, as did 85% of the azatadine-treated patients. No patient in either treatment group had a poor response to treatment or was considered a treatment failure.

*Safety*

There was no statistically significant difference between the treatment groups in the number of patients reporting adverse experiences, and the majority were mild or moderate in severity. However, there was a greater incidence of sedation in the azatadine patient population (8/16) than in the loratadine population (4/18). There were no reports on anticholinergic side effects in the loratadine-treated patients; two azatadine-treated patients reported dry mouth.

No patient had a clinically meaningful change in laboratory tests or ECG.

## DISCUSSION

In this 14-day study loratadine administered at a dose of 10 mg once daily was comparable to azatadine 1 mg twice daily in improving the symptoms of seasonal allergic rhinitis. The results of efficacy and safety analyses of azatadine were comparable to results reported in the literature for one to six week trials in which the efficacy and safety of azatadine were compared to other antihistamines and placebo.[6-9] Thus, azatadine displayed typical activity.

Improvement in allergy symptoms was observed by the first evaluation (day 3 of treatment) in both groups. However, the improvement in nonnasal symptoms at day 3 was significantly greater in the loratadine treatment group than in the azatadine group. The marked reduction in nasal blockage seen with both products probably reflects that for inclusion in the study patients had to be suffering at least two nasal symptoms of moderate severity. Thus there was a greater margin for improvement. Comparable results were seen in previous studies when loratadine was compared with astemizole, another nonsedating antihistamine that is known to have a delayed onset of action of several days.[5,10,11] Furthermore, the continued efficacy of loratadine throughout the two-week study period suggests that patients did not develop tolerance to the medication over the course of therapy.

The safety data show that loratadine is safe and well tolerated. The incidence of adverse experiences between loratadine and azatadine was not statistically different. However, a greater number of azatadine-treated patients reported sedation and dry mouth.

It can be concluded that loratadine is an effective and safe antihistamine when given once daily for the symptomatic relief of seasonal allergic rhinitis.

## ACKNOWLEDGEMENT

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**Table 3.** Physician's evaluation of therapeutic response to treatment in patients receiving loratadine or azatadine.

| Treatment Group | Response to treatment | | |
|---|---|---|---|
| | Excellent | Good | Fair |
| Loratadine | | | |
| Day 3 | 67% | 27% | 7% |
| Endpoint | 40% | 40% | 20% |
| Azatadine | | | |
| Day 3 | 39% | 47% | 15% |
| Endpoint | 77% | 8% | 15% |

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