

Comparative outdoor study of the efficacy, onset and duration of action, and safety of cetirizine, loratadine, and placebo for seasonal allergic rhinitis

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Background: Cetirizine, a new once-daily highly specific H_1 -antagonist, has been shown in conventional studies to be efficacious in the treatment of seasonal and perennial allergic rhinitis and chronic idiopathic urticaria.

Objective: The efficacy, duration and onset of action, and safety of cetirizine, 10 mg once daily, was compared with that of loratadine, 10 mg once daily, and placebo in a field study of patients with seasonal allergic rhinitis.

Methods: This was a randomized, double-blind, parallel, double-dummy study conducted over 2 days in spring allergy season at outdoor parks in San Diego and Iowa City. Study medication was administered at 10:00 AM on both days. After screening, eligible patients completed rhinitis symptom diaries in the park hourly from 7:30 to 9:30 AM (baseline); at 10:30 AM and hourly from 11:00 AM to 4:00 PM (period I); at 6:00, 8:00, and 10:00 PM at home (period II); and the next day in the park hourly from 8:00 to 10:00 AM (period III), and from 11:00 AM to 4:00 PM (period IV). Major and total symptom complex scores, global efficacy and overall satisfaction, and adverse events were assessed.

Results: Of the 279 patients (140 men and 139 women; mean age, 29 years) randomized to treatment, 278 were included in the efficacy analysis. Cetirizine produced significantly greater mean reductions than loratadine or placebo in major symptom complex severity scores at all periods ($p \leq 0.05$), except period I for placebo. Cetirizine also produced mean reductions in total symptom complex severity scores that were superior to loratadine at every evaluation period ($p < 0.05$) and were statistically different from placebo at period II ($p < 0.01$). A rapid onset of action was observed with cetirizine, as was a better response pattern in the patient global assessment of efficacy compared with loratadine. Study medications were well tolerated; no patient stopped treatment because of side effects. The incidence of somnolence with cetirizine was 13% versus 2% with placebo ($p < 0.05$); headache occurred more frequently with loratadine (23%) than with cetirizine (11%, $p = 0.03$).

Conclusion: Cetirizine relieved rhinitis symptoms more effectively and quickly than loratadine and placebo in this field study of seasonal allergic rhinitis. Both active agents were generally well tolerated. (*J ALLERGY CLIN IMMUNOL* 1996;97:617-26.)

Key words: Allergic rhinitis, cetirizine, park study, loratadine, placebo, seasonal allergic rhinitis

Allergic rhinitis is one of the most prevalent chronic conditions in the United States, affecting

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Abbreviations used

MSC: Major symptom complex

TSC: Total symptom complex

as many as one in five Americans.¹ Antihistamines are a mainstay of treatment for seasonal allergic rhinitis, providing relief from symptoms such as sneezing, pruritus, and rhinorrhea. However, the usefulness of the first generation of such agents has been limited by untoward activity-restraining side

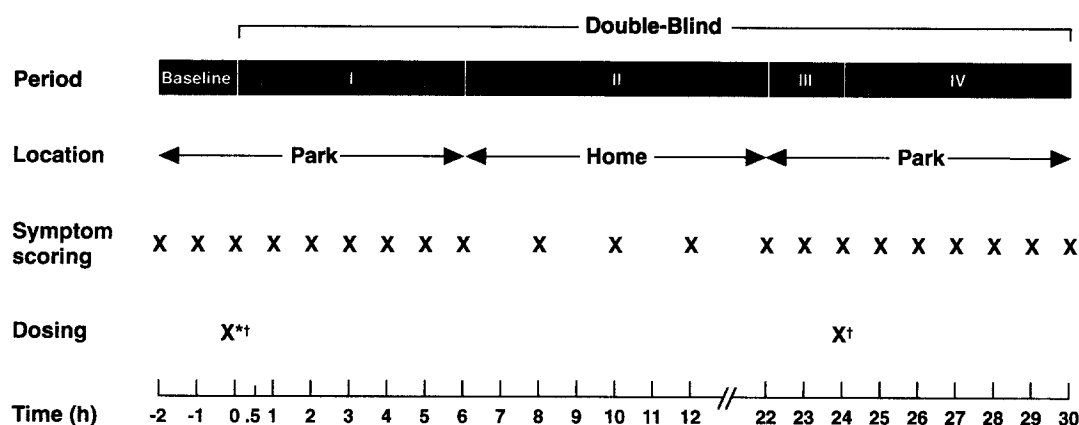


FIG. 1. Study sequence. *Only patients with qualifying baseline symptom scores were randomized to treatment. †Study medication was administered after the symptom diary entry for this time point was completed.

effects. The advent of newer, more specific H_1 -antagonists has prompted renewed interest in the clinical utility of antihistamines in treating a diverse population of patients with allergy.²

Cetirizine is a new once-daily oral antihistamine with high specificity for the H_1 -receptor and a rapid onset of action.³ Cetirizine, the principal metabolite of hydroxyzine, is minimally metabolized and has a low rate of penetration of the blood-brain barrier. This agent has been shown, in conventional studies, to be efficacious and well tolerated in the treatment of seasonal and perennial allergic rhinitis and chronic idiopathic urticaria.⁴⁻⁷ Cetirizine has also been shown to provide efficacy that is at least comparable with that of other newer H_1 -antagonists including terfenadine^{8,9} and astemizole.^{10,11}

Although the newer H_1 -receptor antagonists have been widely tested against older agents, less is known about their direct comparative effects outside the laboratory in patients with seasonal allergies. Therefore using a well-controlled park-study design, we compared the efficacy, duration and onset of action, and safety of cetirizine with that of loratadine, a widely used newer antihistamine, and placebo in patients with established allergic rhinitis during spring allergy season.

METHODS

Study design

This investigation was a randomized, double-blind, parallel, double-dummy study conducted over 2 days in spring allergy season (May 1994) at two sites—Balboa Park in San Diego, California, and City Park in Iowa City, Iowa. The study protocol and patient consent forms were approved by the appropriate institutional review boards.

Patients

Informed consent was obtained from each patient before entry into the study; patients under the age of 18 years were accompanied by an adult. Patients were male and female 12 years of age or older, who had a history of seasonal allergic rhinitis for at least 2 years and who were confirmed within the previous year to be sensitive to an allergen prevalent at the time of the study according to a recognized skin test. All patients underwent physical examinations at the time of screening and were required to be free of major diseases. Women were either not of childbearing potential or agreed to use acceptable methods of birth control to avoid pregnancy, had a negative pregnancy test result at the time of the screening visit, and were not nursing mothers.

Patients with significant nasal anatomic deformities causing more than 50% obstruction and those who had experienced an episode of acute sinusitis within 30 days of the study were excluded. Also excluded were patients who had used medications to treat allergies or other chronic or acute upper respiratory tract disease at intervals predetermined to be unacceptable.

Study sequence

The study sequence is outlined in Fig. 1. Participants were initially screened during office visits, 3 to 21 days before the first day of the study. All eligible patients reported to the park site on the same day; were questioned concerning adverse events, concomitant medications, and concurrent illness; and then completed rhinitis symptom diaries at 7:30, 8:30, and 9:30 AM during a baseline period. Those with qualifying symptom scores were assigned in randomized, blinded fashion to receive either cetirizine, 10 mg once daily; loratadine, 10 mg once daily; or placebo and were given the first dose of study medication at 10:00 AM. Separate symptom diaries were completed at 10:30 AM and hourly from 11:00 AM to 4:00 PM (period I) in the park; and at 6:00, 8:00, and 10:00 PM at home (period II).

The next morning, patients returned to the park and completed symptom diaries at 8:00, 9:00, and 10:00 AM (period III), after which they were administered the second dose of study medication. Patients resumed symptom diary evaluations hourly from 11:00 AM to 4:00 PM (period IV). At the end of the study, patients provided overall assessments of the efficacy of treatment and their personal satisfaction with it.

Patients were seen in the clinic at a follow-up visit within 7 days of the study and underwent a physical examination and laboratory evaluation (including a pregnancy test for all women). Adverse experiences, concurrent medications, and concurrent illnesses were noted.

Daily average pollen and total mold counts were obtained near each park site from 2 days before until 2 days after each park study.

Study medications

At approximately 10:00 AM each morning in the park, patients randomized to therapy were given in blinded fashion either a 10 mg cetirizine tablet once daily plus a loratadine placebo capsule, a 10 mg loratadine tablet in a capsule once daily plus a cetirizine placebo tablet, or both a placebo tablet and placebo capsule. Any concomitant medication use was recorded. Patients were instructed not to use chronic asthma medications (with the exception of a β -agonist aerosol for exercise-induced asthma), antibiotics, H_1 -antagonists, or decongestants for the duration of the study.

Symptom assessments

Patients rated their rhinitis symptoms throughout the study on diary cards. The cards were collected in the park after each assessment; diary cards completed at home on day 1 were collected at the beginning of the second day. All patients, regardless of age, were monitored in the park. Stuffy nose was evaluated individually on the right and left sides by using a scale of 0 (clear) to 4 (blocked, i.e., cannot move any air through nostril) to denote the degree of noticeable blockage of air passage. Nose blows and sneezes were scored by using the actual number for the first five occurrences, then the number 6 for six to nine occurrences, 7 for 10 to 15 occurrences, and 8 for more than 15 occurrences. A score of 0 (none) to 5 (very severe, i.e., very bothersome and disabling) was used to assess itchy nose and runny nose individually on each side, sniffles, postnasal drip, watery eyes, itchy eyes or ears, itchy throat, and cough. Patients qualified for randomization to therapy if the sum of the three hourly pretreatment scores for nose blows, sneezes, right and left itchy nose, right and left runny nose, sniffles, postnasal drip, watery eyes, itchy eyes or ears, itchy throat, and cough was 18 or greater.

At the end of the study (or at time of discontinuation), patients were asked to rate the global efficacy of treatment on a scale of 1 (excellent) to 5 (poor). In addition, they were asked to appraise their personal satisfaction

with treatment on a scale of 1 (exceptionally satisfied) to 5 (unsatisfied).

Symptom diary data entry

Each hour, symptom diary cards were scanned into an IBM-compatible computer with a card reader and SymptomCardReader software (CompleWare Corporation, Iowa City, Iowa). Data entered into the computer were automatically checked for missing or inappropriate entries; cards requiring corrections were returned immediately to patients for clarification. The software program also enabled investigators to determine on site whether or not patients met the qualifying minimum symptom severity sum of 18 or greater after the 9:30 AM data entry. Case-report forms completed by each investigator were also scanned into the database with ScanCRF (CompleWare Corporation).

Efficacy measures

Two predetermined composite variables, major symptom complex (MSC) and total symptom complex (TSC) severity scores, were used as primary end points to assess clinical effectiveness. Six individual symptoms most dominant in the rhinitis profile—runny nose, sniffles, itchy nose, nose blows, sneezes, and watery eyes—formed the MSC. Four additional symptoms—itchy eyes or ears, itchy throat, cough, and postnasal drip—were added to the MSC to form the TSC. For symptoms requiring ratings on both the left and right sides, scores from the two sides were first averaged to form an hourly mean. Two similar symptoms, runny nose and sniffles, were combined and included as one symptom in the MSC and TSC.

Secondary efficacy end points included TSC scores with the inclusion of nasal congestion, individual rhinitis symptoms, global efficacy scores, and overall satisfaction scores.

Safety

Safety was assessed by comparing results of physical examinations and laboratory evaluations before administration of study medications and within 7 days of completing the study. Investigators assessed the nature, severity, number of all observed or volunteered adverse experiences, and their relation to treatment.

Statistical analysis

Demographic characteristics were summarized by frequency distributions for categorical variables and by means and ranges for continuous variables.

Pretreatment baseline comparability among groups for MSC and TSC severity scores was assessed by two-way analysis of variance,¹² incorporating terms for treatment, investigator, and their respective interactions. For both the MSC and TSC, the absolute reduction from baseline was assessed. Of note, in computing period averages, only hourly scores were used; thus, the first half-hour measurement in period I was not included in

TABLE I. Patient demographics

	Group			Total
	Cetirizine	Loratadine	Placebo	
No. of patients	93	93	93	279
Gender (no.)				
Male	52 (56%)	42 (45%)	46 (49%)	140 (50%)
Female	41 (44%)	51 (55%)	47 (51%)	139 (50%)
Race (no.)				
White	82 (88%)	77 (83%)	80 (86%)	239 (86%)
Black	6 (7%)	5 (5%)	2 (2%)	13 (5%)
Other	5 (5%)	11 (12%)	11 (12%)	27 (9%)
Age (yr)				
Mean	27.7	30.1	28.6	28.8
Range	14-57	13-62	13-60	13-62
Weight (lb)				
Mean	163.1	160.3	155.8	159.8
Range	104-248	100-268	81-275	81-275
Rhinitis history (yr)				
Mean	16.6	18.7	16.5	17.3
Range	2-53	3-60	2-48	2-60
Baseline symptom score				
MSC severity	12.8	12.3	11.4	—
TSC severity	21.1	20.5	18.6	—

this calculation. However, the MSC and TSC severity scores were also compared at each of the 19 time points in a separate analysis.

To account for the possibility that score reductions could be a function of baseline values, comparability of treatment groups was assessed by an analysis of covariance,¹² incorporating terms for treatment, investigator, treatment-by-investigator interaction, and baseline as a covariate. The underlying assumptions necessary to perform parametric analysis of covariance were satisfied for MSC and TSC severity scores; therefore, efficacy was assessed with this tool. Similar analyses were performed for the secondary variable, TSC-plus-nasal congestion, and for the absolute change in each individual rhinitis symptom.

Treatment effects at each period for each efficacy variable were analyzed, as were treatment effects for the primary variable at each time point. To minimize bias caused by omission of data from patients who withdrew from the study early, analyses were done for overall and end-point responses. An additional end-point analysis, based on period III, was performed for the primary efficacy variables to assess the sustained effect of the first dose of study medication over the first 24 hours. Onset of action was determined by comparing the primary MSC and TSC response variables between groups during the first 6 hours in period I; duration of effect was assessed by comparing responses during period III (hours 22, 23, and 24). Global improvement ratings for each treatment group were summarized and analyzed with the Mantel-Haenszel mean score test.¹³

All patients who received at least one dose of study

medication were included in the safety evaluations. Differences between groups were compared by chi square tests.¹⁴

Statistical significance was defined for all tests at $p \leq 0.05$. For $0.05 < p \leq 0.01$, statistical trends or suggestive differences were noted. All comparisons were based on two-sided tests. The p values for drug effects were based on comparisons of adjusted or least-squares means obtained from the statistical analyses.

RESULTS

Patients

Of 316 patients screened, 279 met the randomization criteria and were assigned to treatment groups ($n = 93$ in each group). Demographic characteristics of the patients randomized to treatment are described in Table I. Approximately 50% were men and 50% were women. The mean age was 29 years; there were no patients 12 years of age, and there were 32 patients (11.4%) 13 to 17 years of age, with the majority (21 patients) being 15 to 17 years old. The mean weight was 160 pounds, and mean duration of allergic rhinitis was 17 years. Most patients were white (86%). These characteristics did not differ significantly among groups.

Six patients randomized to therapy did not complete the study: three withdrew consent, two were lost to follow-up, and one was discontinued early because of noncompliance with the protocol. The

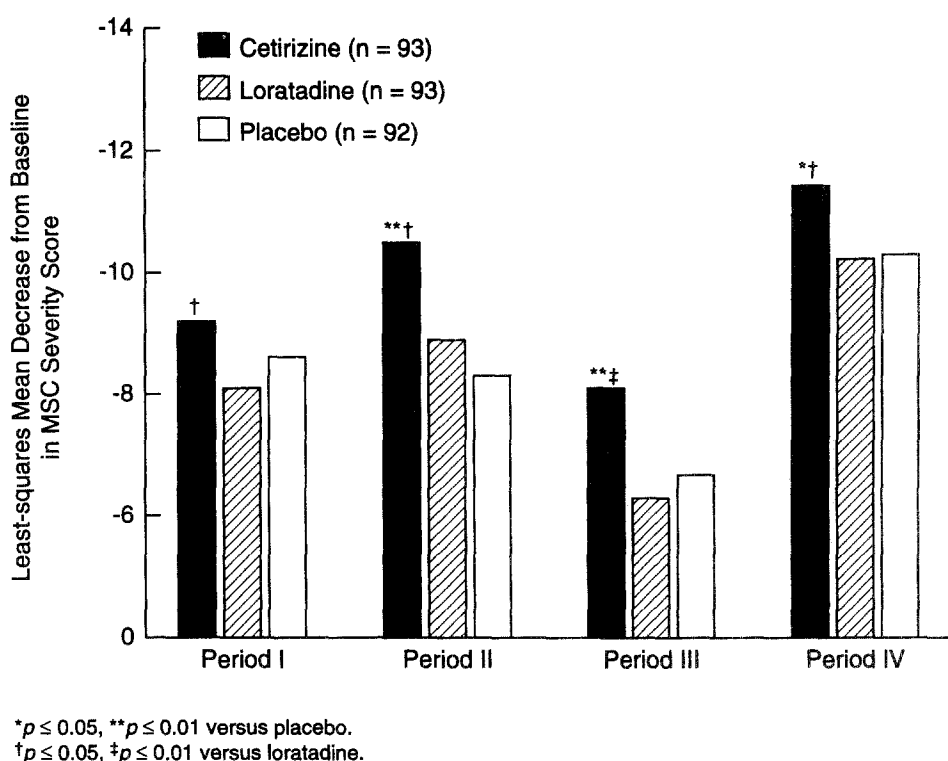


FIG. 2. Mean reductions from baseline in MSC severity scores for each period during treatment.

number of patients completing the study was 91 in the cetirizine group, 92 in the loratadine group, and 90 in the placebo group.

Pollen counts

The average daily pollen count in City Park, Iowa City, was $186.3/\text{m}^3$, ranging from 113 to $227/\text{m}^3$ over a 7-day period encompassing the study. The mean over the 2-day study period itself was $210/\text{m}^3$. Respective values in Balboa Park, San Diego, were an average of $37.3/\text{m}^3$, ranging from 26 to $59/\text{m}^3$ over the course of 7 days, with a mean over the 2-day study period of $34/\text{m}^3$.

MSC severity scores

The mean MSC severity scores at baseline were comparable among groups (Table I). Mean reductions from baseline in the MSC scores for each period during treatment are shown in Fig. 2. Cetirizine produced significantly greater reductions than loratadine at all periods ($p \leq 0.05$). The MSC score reductions observed in the cetirizine group were significantly greater than those in the placebo group at all periods except period I; the loratadine group did not differ from the placebo group at any period. Reductions in MSC severity scores overall were comparable between study

TABLE II. Least-squares mean overall and end-point reductions in MSC severity scores for each treatment group

	Group		
	Cetirizine (n = 93)	Loratadine (n = 93)	Placebo (n = 92)
Overall	5.9* [†]	4.4	4.4
First 24 hours	4.1* [†]	2.3	2.6
Last period	7.5 ^{‡§}	6.2	6.3

* $p \leq 0.01$ versus placebo.

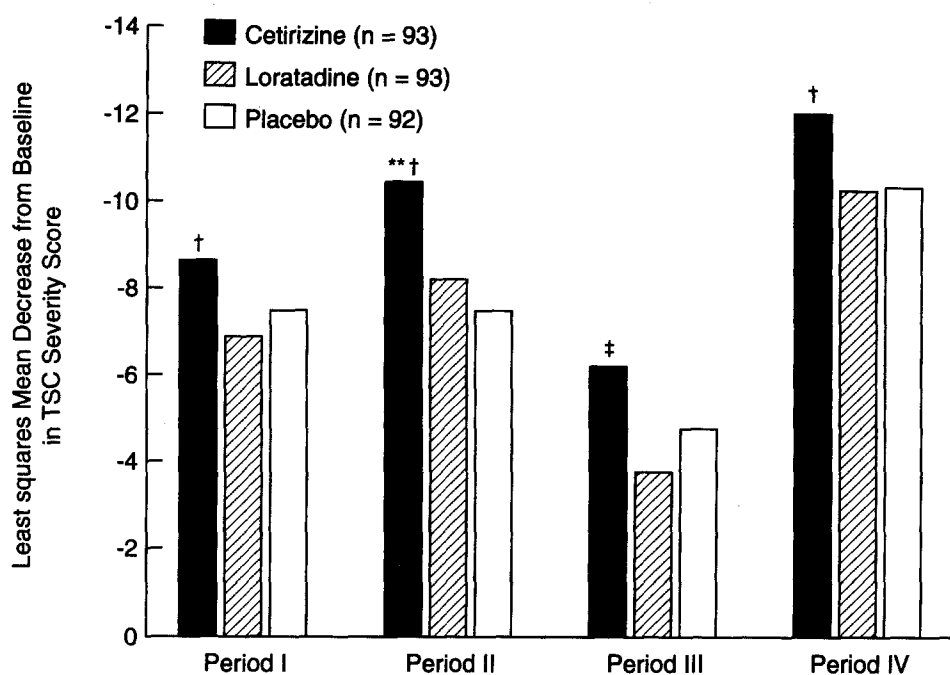
[†] $p \leq 0.01$ versus loratadine.

[‡] $p \leq 0.05$ versus placebo.

[§] $p \leq 0.05$ versus loratadine.

centers ($p = 0.91$) when tested for treatment-by-investigator interactions.

Mean overall and end-point reductions in MSC severity scores for each treatment group are shown in Table II. The overall reductions from baseline with cetirizine were significantly greater than those of loratadine ($p \leq 0.01$) or placebo ($p \leq 0.01$). Similarly, the reductions observed in the cetirizine group were superior to those of either the loratadine or the placebo group when considering the



^{**} $p \leq 0.01$ versus placebo.

[†] $p \leq 0.05$, [‡] $p \leq 0.01$ versus loratadine.

FIG. 3. Mean reductions from baseline in TSC severity scores for each period during treatment.

TABLE III. Least-squares mean overall and end-point reductions in TSC severity scores for each treatment group

	Group		
	Cetirizine (n = 93)	Loratadine (n = 93)	Placebo (n = 92)
Overall	9.4 ^{*†}	7.3	7.5
First 24 hours	6.3 ^{‡§}	3.8	4.7
Last period	11.9 [§]	10.1	10.3

^{*} $p \leq 0.01$ versus placebo.

[†] $p \leq 0.01$ versus loratadine.

[‡] $0.05 < p \leq 0.10$ versus placebo.

[§] $p \leq 0.05$ versus placebo.

^{||} $p \leq 0.05$ versus loratadine.

mean over the first 24 hours of treatment ($p \leq 0.01$) or the data during the last period ($p \leq 0.05$).

TSC severity scores

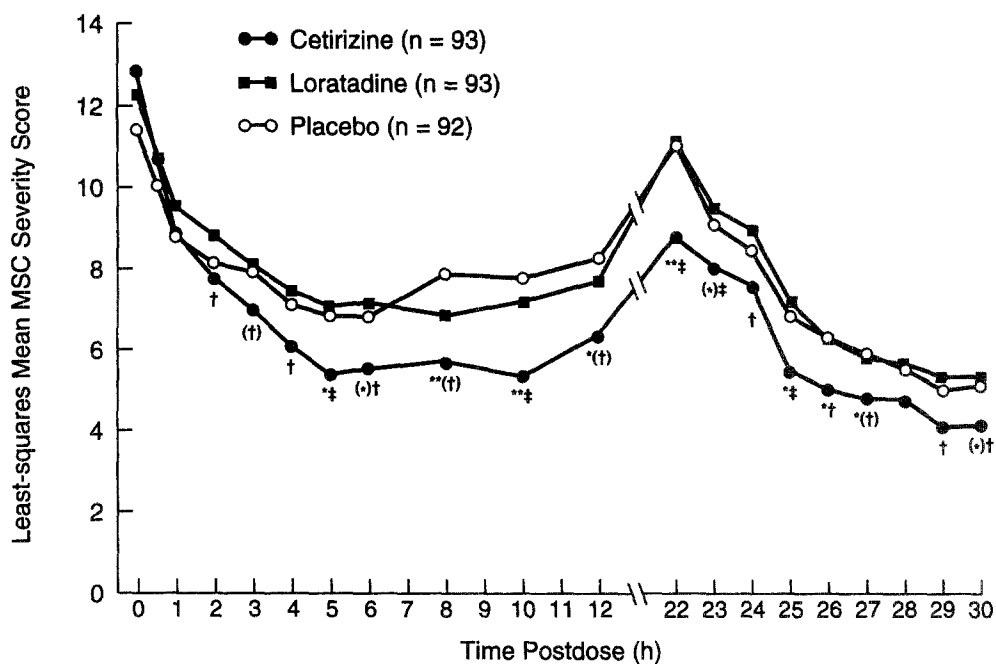
Mean baseline TSC scores were comparable among groups (Table I). As shown in Fig. 3, cetirizine produced mean reductions in TSC severity scores that were superior to loratadine at every evaluation period ($p \leq 0.05$). Cetirizine afforded a reduction in TSC score that was statistically differ-

ent from placebo at period II ($p \leq 0.01$). Reductions in TSC severity scores overall were comparable between study centers ($p = 0.77$).

Mean overall and end-point reductions in TSC severity scores for each treatment group are shown in Table III. The mean reduction in TSC score over all four evaluation periods was significantly greater with cetirizine than with either loratadine or placebo ($p \leq 0.01$). When changes over the first 24 hours were assessed, the cetirizine group was found to have a significantly greater reduction in TSC scores compared with the loratadine group ($p \leq 0.01$). The end-point analysis encompassing data from the last treatment period revealed significantly greater reductions in TSC scores in the cetirizine group than in either the loratadine group or the placebo group ($p \leq 0.05$).

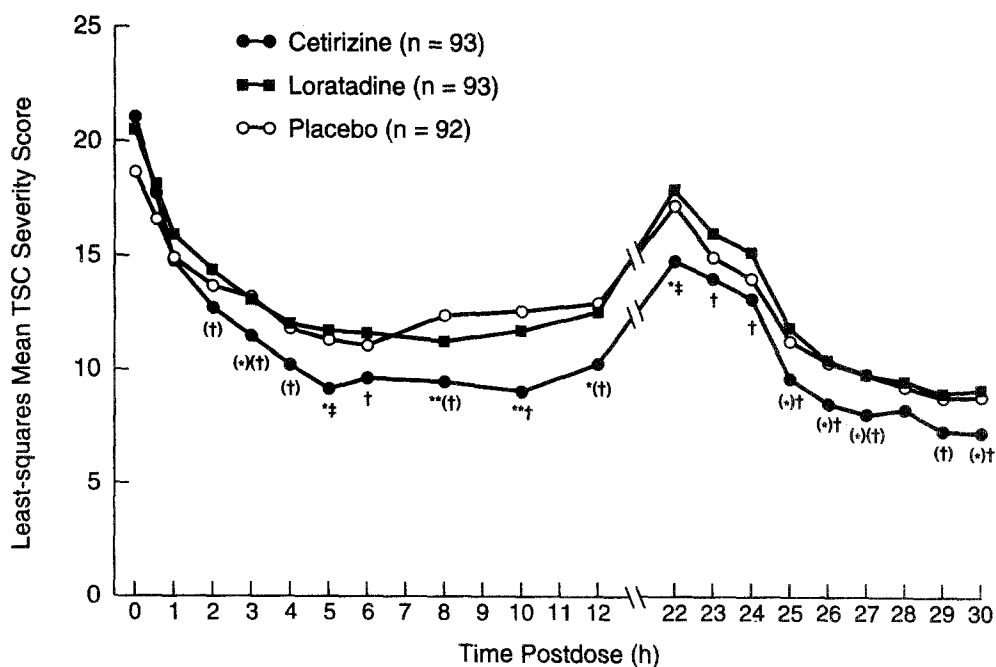
Onset and duration of action

The onset and duration of action of the study medications were assessed by comparing mean hourly symptom scores. The mean MSC and TSC severity scores for each group at each evaluation point are shown in Figs. 4 and 5, respectively. The onset of action of cetirizine was apparent within 2 hours of administration. Statistically significant reductions in both symptom scores for cetirizine



* $p \leq 0.05$, ** $p \leq 0.01$, (*) $0.05 < p \leq 0.10$ versus placebo.
 † $p \leq 0.05$, ‡ $p \leq 0.01$, (†) $0.05 < p \leq 0.10$ versus loratadine.

FIG. 4. Mean MSC severity scores for each group at each evaluation point.



* $p \leq 0.05$, ** $p \leq 0.01$, (*) $0.05 < p \leq 0.10$ versus placebo.
 † $p \leq 0.05$, ‡ $p \leq 0.01$, (†) $0.05 < p \leq 0.10$ versus loratadine.

FIG. 5. Mean TSC severity scores for each group at each evaluation point.

TABLE IV. Patient assessment of global efficacy

	Group					
	Cetirizine (n = 91)		Loratadine (n = 92)		Placebo (n = 91)	
	No.	%	No.	%	No.	%
Improved	67	73.6	52	56.5	54	59.3
Fair	20	22.0	31	33.7	27	29.7
Poor	4	4.4	9	9.8	10	12.0
<i>p</i> Value*			0.05		0.08	

*Compared with cetirizine.

TABLE V. Patient appraisal of personal satisfaction with treatment

	Group					
	Cetirizine (n = 91)		Loratadine (n = 92)		Placebo (n = 91)	
	No.	%	No.	%	No.	%
Satisfied	60	65.9	56	60.9	56	61.5
Neutral	21	23.1	25	27.1	26	28.6
Unsatisfied	10	11.0	11	12.0	9	9.9
<i>p</i> Value*			0.77		0.70	

*Compared with cetirizine.

compared with either loratadine or placebo were evident by 5 hours and were sustained compared with loratadine for 24 hours ($p \leq 0.05$). No differences in MSC or TSC scores were detected between the loratadine group and the placebo group.

Effects on TSC severity scores plus nasal congestion

An overall analysis of changes in the TSC-plus-nasal congestion (stuffiness) score demonstrated a statistically greater mean reduction in the cetirizine group compared with either the loratadine group or the placebo group ($p \leq 0.01$). When analyzed according to period, the mean reductions in the TSC-plus-stuffiness scores observed with cetirizine were all statistically superior ($p \leq 0.04$) to the means noted with loratadine in all four periods. The differences between cetirizine and placebo were significant at period II ($p = 0.01$) and suggestive at period IV ($p = 0.07$).

Individual symptoms

Compared with loratadine, statistically significantly ($p \leq 0.05$) greater reductions for cetirizine were seen for nose blows in periods I and III; for sneezes in all periods; for runny nose or sniffles in period IV; for itchy eyes or ears in period I; and for itchy nose in periods I, II, and IV. Statistically

significant differences ($p \leq 0.05$) between cetirizine and placebo were seen for nose blows in all periods; for sneezes in periods II, III, and IV; for runny nose or sniffles in periods II and IV; for itchy nose in periods II and III; for itchy eyes or ears in period II; and for cough in period I.

Overall and global assessments

Treatment with cetirizine resulted in a better response pattern ($p = 0.05$) compared with loratadine in patients' global assessment of efficacy, as shown in Table IV. Seventy-four percent of patients receiving cetirizine assessed showed improved global efficacy compared with 57% and 59% of patients receiving loratadine and placebo, respectively. Although the percentage of patients satisfied with treatment was higher in the cetirizine group, none of the treatment differences were statistically significant, as shown in Table V.

Adverse events

Study medications were well tolerated. No patient stopped treatment because of side effects or intercurrent illness. Treatment-emergent adverse events (i.e., events noted during the double-blind treatment period but not during the baseline period), which occurred in more than 2% of patients are reported in Table VI. The most common side

TABLE VI. Treatment-emergent adverse events occurring in more than 2% of patients for each treatment group

	Group					
	Cetirizine (n = 93)		Loratadine (n = 93)		Placebo (n = 93)	
	No.	%	No.	%	No.	%
Headache	10	10.8	21	22.6	15	16.1
Somnolence	12	12.9	5	5.4	2	2.2
Pharyngitis	3	3.2	4	4.3	4	4.3
Dizziness	2	2.2	1	1.1	2	2.2
Abdominal pain	0	0	0	0	4	4.3
Dyspepsia	1	1.1	0	0	2	2.2
Nausea	0	0	1	1.1	2	2.2
Fatigue	0	0	2	2.2	0	0

effects in each group were somnolence and headache for cetirizine; headache, somnolence, and pharyngitis for loratadine; and headache, pharyngitis, and abdominal pain for placebo. Significantly more patients in the loratadine group reported headache compared with those in the cetirizine group ($p = 0.03$). More patients in the cetirizine group reported somnolence compared with those in the placebo group ($p = 0.05$). No other statistically significant treatment differences were observed.

DISCUSSION

The design of this park study, based on methods first described by Connell,¹⁵ allowed a tightly controlled direct comparison of the response to cetirizine, 10 mg once daily, loratadine, 10 mg once daily, or placebo therapy in a setting in which many potential variables, such as exposure to allergen during the day, were standardized. The design accommodated randomization and double-blind, parallel-group treatment in an environment closely aligned with that seen in the real lives of patients. In this setting cetirizine provided greater relief of allergic rhinitis symptoms caused by outdoor allergens compared with both loratadine and placebo. Furthermore, the onset of action was quick with cetirizine, and symptomatic relief was sustained for a full 24 hours after dosing. Unexpectedly, the overall efficacy profile of loratadine was similar to that of placebo. The beneficial response observed with cetirizine compared with placebo is consistent with other studies of placebo-controlled studies of this agent in patients with seasonal allergic rhinitis.¹⁶⁻¹⁸

This is the first full report of a study directly comparing the symptomatic effects of cetirizine and loratadine in patients with seasonal allergic rhinitis in a clinical setting. Cetirizine produced greater reductions in aggregate symptom scores than loratadine

for each defined period of active treatment and according to hourly assessments. Cetirizine also appeared to have a rapid onset of action. These clinical findings are consistent with effects observed in several laboratory-based studies.¹⁹⁻²¹ For example, in a single-dose study comparing antihistaminic effects of a number of H₁-receptor antagonists, cetirizine was the most effective and loratadine was among the least effective in suppressing histamine-induced wheals and flares.¹⁹ In that study cetirizine had a rapid onset and sustained duration of activity, beginning in less than an hour and lasting 24 hours after administration, whereas loratadine appeared to have a relatively slow onset, 4 hours after dosing, and a duration of effect that was significant at 24 hours compared with placebo but not with baseline measurements. Longer-term studies of cetirizine therapy in patients with allergic rhinitis have shown a relatively rapid onset of action and sustained relief of symptoms.^{4, 8-10, 18}

The finding that loratadine lacked significant symptomatic effects compared with placebo differs from results of many other reported studies of this agent in patients with seasonal allergic rhinitis, including those that involved active control groups.²²⁻³⁰ Most of these studies extended over a period of many weeks, and it is possible that the full effects of loratadine had not yet emerged in the 2-day study period. However, the findings are consistent in part with effects observed in one long-term, double-blind, parallel-group study of loratadine, 10 mg once daily, versus placebo as prophylactic therapy for seasonal allergic rhinitis.³¹ In that 6-week study of 118 patients, the differences between groups in actual symptom scores did not differ significantly, although patients receiving loratadine had more symptom-free days.

Both cetirizine and loratadine were well tolerated in this study. Most patients (i.e., 74% of the cetirizine

group, 67% of the loratadine group, and 70% of the placebo group) were free of treatment-related side effects, and no patient stopped treatment because of adverse events. In the cetirizine group somnolence was the most common side effect, occurring more frequently than in the placebo group. Headache was the side effect most common among patients treated with loratadine, occurring more frequently than in the cetirizine group.

In conclusion, in this park study investigating the antiallergic effects of the specific H_1 -antagonist cetirizine, this agent relieved rhinitis symptoms rapidly and more effectively than loratadine, another H_1 -antagonist, and placebo in patients with seasonal allergic rhinitis. Both active agents were well tolerated. The acute outdoor exposure of subjects with allergy to aeroallergens is an efficient method for studying the efficacy, onset and duration of action, and safety of pharmacologic agents.

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