

The health-related quality of life effects of once-daily cetirizine HCl in patients with seasonal allergic rhinitis: a randomized double-blind, placebo-controlled trial

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Summary

Background Seasonal allergic rhinitis (SAR) is characterized by subjectively irritating symptoms that can have a substantial impact on the patient's health-related quality of life (HRQL), adversely affecting physical and social or work activity, interpersonal relationships, and general psychological well-being. The objective of this study was to test the effect of cetirizine HCl 10 mg once daily on the HRQL of adult patients 18–65 years of age with SAR, concurrently assessing safety and efficacy.

Methods Randomized double-blind, placebo-controlled, parallel group trial conducted during the 1999 spring SAR season at 19 centers in the US. Following a 1-week placebo run-in period, qualified patients were randomized to cetirizine 10 mg, or placebo once daily for a 2-week treatment period. Change in Rhinoconjunctivitis Quality of Life Questionnaire (RQLQ) and Total Symptom Severity Complex (TSSC) scores from baseline were the primary outcomes of interest.

Results Of the 611 patients enrolled, 403 (66%) were randomized. Cetirizine-treated patients reported significantly greater improvement in overall HRQL ($P < 0.001$) and in each of the seven domains of the RQLQ at all time-points ($P < 0.05$ to < 0.001) than the placebo group. They also experienced significantly greater symptom relief ($P < 0.001$) and were more satisfied with treatment (65% vs. 44%) compared to the placebo group. Correlations between symptomatic relief and overall HRQL improvement were moderate to strong and statistically significant ($r = 0.49$ – 0.68 , $P < 0.01$).

Conclusions Results of this study are consistent with previous investigations, suggesting cetirizine HCl 10 mg taken once daily in the morning offers symptomatic relief that improves the HRQL of adults suffering from SAR.

Keywords cetirizine, health-related quality of life, seasonal allergic rhinitis

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Introduction

Allergic rhinitis is a common disorder affecting 35–50 million Americans, or as many as 24% of the US population [1, 2]. Seasonal allergic rhinitis (SAR), primarily caused by tree, grass and weed pollen, accounts for up to 60% of all diagnosed cases [3, 4]. The condition is characterized by repetitive sneezing, rhinorrhea, nasal congestion, watery eyes, itchy nose or eyes, post-nasal drip, and impaired taste or smell. These uncomfortable and subjectively irritating symptoms can be more than a minor nuisance. Research has shown that the symptoms of allergic rhinitis can have a substantial impact on patient's health-related quality of life (HRQL), that is, their physical, social and work activity, interpersonal relationships, and general psychological well-being [5–13]. Patients seek treatment because of the severity of their symptoms and the adverse effect

these symptoms have on HRQL. The condition accounts for an estimated 28 million days of restricted activity and more than 10 million physician office visits in the US each year [14, 15]. The direct and indirect costs of allergic rhinitis have been estimated to be \$US 3.4 billion (1993) [16].

The Rhinoconjunctivitis Quality of Life Questionnaire (RQLQ), developed by Juniper and Guyatt [17], assesses HRQL and treatment effectiveness among adults with SAR. The instrument addresses many of the questions clinicians ask patients during clinical evaluation: Have your symptoms led to problems with your usual activities? With your ability to get a sound night's sleep, with your work productivity? Are you having trouble concentrating? Feeling worn out? Feeling irritable [9]? Thus, the RQLQ extends traditional symptom severity assessment and queries patients about their tolerance and acceptance of symptoms, including the impact the symptoms have on day-to-day functioning and well-being [17]. Moderate correlations between symptom severity and the RQLQ support the complementary nature of the two outcomes [17–19].

Pharmacotherapy is the cornerstone of treatment, with second-generation antihistamines offering symptomatic relief with minimal to no sedating effects. Cetirizine, a

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second-generation H1-receptor blocker, has been shown to be safe and effective in relieving symptoms of SAR and perennial allergic rhinitis (PAR), including sneezing, rhinorrhea, nasal pruritis, ocular pruritis, post-nasal discharge, and tearing and redness of the eyes [6, 20–25]. Concomitant improvements in generic HRQL have been demonstrated in patients with PAR [6, 26] and in condition-specific HRQL in patients with SAR [1, 27]. The objective of the present study was to extend the work of Murray et al. [27] delineating the impact of treatment with cetirizine on patient self-reported HRQL in adults with SAR, while concurrently assessing conventional measures of drug safety and efficacy.

Methods

Study design

This was a randomized double-blind, placebo-controlled, parallel group, multi-centre trial conducted during the 1999 spring allergic rhinitis season. Eligible patients from 19 US centers were enrolled in a single-blind 1-week placebo run-in period and completed daily diary cards quantifying the severity of allergy-related symptoms.

Following this run-in period, diary cards were collected and symptom severity ratings assessed. Patients qualified for randomization at Visit 2 if they experienced at least two of five qualifying symptoms (sneezing, itchy nose, runny nose, watery eyes, and itchy eyes) of at least moderate severity (2 on a scale of 0–3) on at least 4 days between Visits 1 (screening) and 2 (randomization). In addition, patients must have recorded in their diary a total rhinoconjunctivitis score of at least 5 on any four days prior to Visit 2.

Qualified patients were randomized (1:1 ratio) to receive either cetirizine 10 mg or placebo once daily before 12:00 h for a 2-week treatment period. Patients completed a daily symptom diary throughout treatment, and the Rhinoconjunctivitis Quality of Life Questionnaire (RQLQ) at Visit 2 (baseline, post run-in), Visit 3 (end of Week 1) and Visit 4 (end of Week 2). The appropriate institutional review boards approved the study and signed patient consent was obtained prior to enrollment.

Patient population

Patients were eligible for the study if they were 18–65 years of age with a history and diagnosis of SAR to grass, with symptoms severe enough to require pharmacotherapy each year for the previous 2 years. SAR was confirmed by a prick, ID or Multi-test skin test performed within the previous year indicating sensitivity to grass [prick/puncture weal $\geq$ 3 mm, over the negative control; ID (up to concentration of 1:1000 w/v or 1000 protein nitrogen units (PNU)) weal $\geq$ 5 mm over the negative control].

Patients with impaired hematologic, renal, endocrine (except controlled diabetes mellitus, post-menopausal symptoms, or hypothyroidism) or gastrointestinal disease, neuropsychiatric disorders, history of malignancy (except basal cell carcinoma), epilepsy, clinically significant cardiovascular disease, excessive alcohol intake, or drug addiction were excluded. Patients were also excluded if they had history of chronic sinusitis, recent episode of acute sinusitis or upper respiratory tract infection, chronic use of anti-asthma medication within the last

24 months, or recent use of immunotherapy, corticosteroids, cromolyn, ipratropium bromide nasal spray, monoamine oxygenase inhibitors, reserpine, beta-blockers, tricyclic antidepressants, tranquilizers, or phenothiazine antiemetics. Patients using H1-receptor antagonists and/or H2-receptor antagonists within 7 days, or decongestants within 72 h of baseline were also excluded.

Study end-points

Changes in overall RQLQ score and Total Symptoms Severity Complex (TSSC) score from baseline to study conclusion served as the primary study end-points. Secondary end-points included change from baseline in the seven individual domains of the RQLQ; change in TSSC score after including nasal congestion symptom score; change from baseline in individual symptoms; change from baseline in the physician's assessment of patient symptoms (with and without nasal congestion); patient global evaluations, and physician global evaluations.

HRQL evaluation

The RQLQ was used to assess HRQL [10, 17]. The questionnaire included 28 questions in seven domains measuring patients' subjective experience of rhinoconjunctivitis symptoms and their effect on disease-specific HRQL. Symptoms were measured on a 7-point scale from 0 (not troubled or none of the time) to 6 (extremely troubled or all of the time). Domain-specific scores were expressed as a mean across items comprising the domain, with higher scores indicating poorer HRQL. Overall RQLQ score was computed by taking the mean of the 28 items comprising the instrument; scores therefore range from 0 to 7 with higher scores indicating poorer HRQL [10, 17, 28, 29]. Consistent with previous analyses, this study interpreted a change in score greater than 0.50 on the RQLQ domain and overall scores as the clinically meaningful 'minimal important difference' (MID) [19, 26, 30, 31].

Since the RQLQ first appeared, it has been used to evaluate HRQL outcomes in a number of clinical trials of allergic rhinitis and rhinoconjunctivitis [1, 18, 19, 27, 32–39]. The instrument has been linguistically and culturally translated into multiple languages, including Spanish, which was used at one site participating in the trial.

Symptom severity

Patients were instructed to complete symptom diaries each morning, immediately before taking the blinded medication, rating the severity of rhinoconjunctivitis symptoms over the 24 h since the last recording. Sneezing, runny nose, itchy nose, itchy eyes, watery eyes, post-nasal drip, and nasal congestion were each graded on a 4-point scale, from 0 (complete absence of symptoms) to 3 (severe, symptoms present day and night, impact on daily activities, as well as on ability to sleep). Individual scores for all symptoms but nasal congestion, were combined to form the TSSC score for the primary efficacy analyses. TSSC scores range from 0 to 18, with higher scores indicating more severe symptoms. Baseline TSSC score was defined as the mean of the scores at Visit 2 and on each of the 2 days prior to Visit 2. Patient-completed symptom diaries, including the TSSC, have been used in previous studies evaluating the efficacy of cetirizine [1, 20, 21, 25, 30] and other treatments [30–41] in SAR.

Physician assessment of symptom severity

Physicians assessed patient's rhinoconjunctivitis symptoms at baseline, midpoint and study conclusion, prior to review of the symptom diaries and after questionnaire administration, using the same 4-point scale as the symptom diaries.

Global evaluations

Patients and physicians provided a global assessment of treatment effectiveness at the conclusion of the study. The assessment was recorded on a 7-point scale, from 1 (major improvement; all signs/symptoms improved) to 7 (severe worsening; all signs/symptoms worsened). Patients also completed an appraisal of their personal satisfaction with treatment on a 4-point scale ranging from 1 (very satisfied) to 4 (very unsatisfied).

Safety

The incidence and severity of all observed or patient-reported adverse events (AEs) were recorded. Vital signs and physical examinations were also used to assess safety. Events involving adverse drug reactions, illnesses with onset during the study, or exacerbation of pre-existing illnesses were recorded. Treatment-emergent AEs were defined as those events that occurred for the first time in a patient during the active treatment period, or those that began during the placebo run-in period, but increased in severity during active treatment. Treatment-related AEs included events that in the investigator's judgement were most likely caused by the study drug (related), or for which causality was unknown.

Statistical methods

The study was powered (80%) to detect a mean change of at least 0.37 from baseline in overall RQLQ score between each cohort at the 5% significance level, assuming a pooled standard deviation of 1.30. Efficacy and HRQL analyses were performed on three efficacy populations: intent-to-treat (ITT), efficacy-analyzable, and completer, with the last observation carried forward defined as the end-point for the ITT and efficacy-analyzable cohorts. The ITT results served as the primary efficacy analysis. Analysis of safety data was performed on the safety-analyzable sample, i.e. all subjects randomized to double-blind treatment receiving at least one dose of study medication as determined by the study diary. All statistical tests were two-sided with statistical significance declared at the 0.05 probability level.

Baseline comparability of treatment groups was tested using two-way ANOVA models with terms for investigator, treatment, and investigator-by-treatment interaction and with main effects only. Treatment group comparisons were made using a two-way analysis of covariance (ANCOVA) model with main effects for treatment group and investigator, a treatment-by-investigator interaction effect, and the baseline value of the variable serving as the covariate. If the interaction effect was not statistically significant, a main effects ANCOVA model was used.

For the patient and physician global evaluation of treatment effectiveness, data were summarized and analyzed using a CMH test [42]. Pearson product-moment correlation coefficients and their respective *P*-values were used to characterize the relationship between symptom relief and improvement in HRQL. The incidence and severity of treatment-emergent and

treatment-related AEs were summarized, with treatment-emergent AEs summarized by body system and severity of event (mild, moderate, severe). All analyses were performed using Statistical Analysis System (SAS) software version 6.12 (SAS Institute Inc., Cary, NC, USA).

Results

Sample

A total of 611 patients enrolled in the study at Visit 1 (screening visit). Of these, 403 (66%) were randomized to treatment with cetirizine (*n* = 203) or placebo (*n* = 200). Three patients were lost to follow-up after randomization and prior to receiving the study drug. One patient from each treatment group voluntarily withdrew on the first day of treatment, leaving a final sample of 201 cetirizine patients and 197 placebo patients who had at least one follow-up visit.

During the study, two cetirizine patients and four placebo patients discontinued due to insufficient clinical response. One placebo-treated patient discontinued due to an adverse event related to the study medication. Therefore, 196 cetirizine-treated patients (97%) and 183 placebo patients (92%) completed the study.

There were no significant differences in the demographic characteristics of patients randomized to the two treatment groups (Table 1). Mean age of patients in the cetirizine cohort was 35.8 years versus 37.4 years in the placebo cohort (*P* = 0.38). A majority of all patients were between 18 and 44 years (80% cetirizine; 74% placebo); 88% were white (78% cetirizine; 82% placebo) and most were female (69% cetirizine; 64% placebo). The mean duration of SAR since first diagnosis was 19.3 years for the cetirizine group (range 2–54 years) and 20.9 years for the placebo group (range 2–55 years). Ninety percent of all patients required medications to treat SAR symptoms in the 3 months prior to study (89% cetirizine; 90% placebo).

HRQL

RQLQ scores for the two treatment groups were not significantly different at baseline. After 2 weeks of treatment, patients receiving cetirizine reported significantly greater improvement in HRQL, as measured by the RQLQ, compared to the placebo group (*P* = 0.001; Fig. 1). Similar results were seen at the overall time-point and at end-point. Cetirizine-treated patients also reported significantly greater improvement in each of the seven HRQL domains represented by the RQLQ at Week 2 (*P* < 0.05; Fig. 2). Similar findings were observed at all other time-points (*P* < 0.01).

Symptom severity

Significant baseline differences between the cetirizine and placebo-treated groups were observed for the TSSC and the TSSC plus nasal congestion scores, with those in the placebo group reporting more severe symptoms than those in the cetirizine group (Table 1). In the primary efficacy analysis, patients receiving cetirizine reported significantly greater symptom relief than patients receiving placebo at Week 2 (Visit 4/end of study), controlling for the observed differences at baseline (*P* < 0.001; Fig. 3). Similar results were seen at Week 1, overall, and at

Table 1. Demographic and clinical characteristics by treatment group

Characteristic	Cetirizine <i>n</i> = 202	Placebo <i>n</i> = 198	<i>P</i> -value
Age, years, mean $\pm$ SD	35.8 $\pm$ 10.6	37.4 $\pm$ 11.1	0.38*
Gender, <i>n</i> (% female)	139 (69%)	126 (64%)	0.31†
Race, <i>n</i> (% white)	158 (78%)	162 (82%)	0.33†
Duration since first diagnosis, years, mean $\pm$ SD (range)	19.3 (2–54)	20.9 (2–55)	0.67*
Past history of acute respiratory infections, <i>n</i> (%)	8 (4%)	15 (8%)	Not applicable
Past history of treatment for SAR (e.g. corticosteroids, sympathomimetics), <i>n</i> (%)	180 (89%)	178 (90%)	Not applicable
Baseline TSSC, mean $\pm$ SE	10.4 $\pm$ 0.2	11.0 $\pm$ 0.2	0.03‡
Baseline TSSC with nasal congestion, mean $\pm$ SE	12.4 $\pm$ 0.2	13.1 $\pm$ 0.2	0.04‡
Baseline RQLQ	3.3 $\pm$ 0.1	3.3 $\pm$ 0.1	0.5‡

**P*-value based on an ANOVA model with terms for investigator, treatment, and interaction effects with the treatment effect reported. †*P*-value based on CMH test, with investigator as the stratification variable. ‡*P*-value based on ANOVA with terms for investigator and treatment with the treatment effect reported for the intent-to-treat (ITT) sample. TSSC = Total Symptom Severity Complex; RQLQ = Rhinoconjunctivitis Quality of Life Questionnaire.

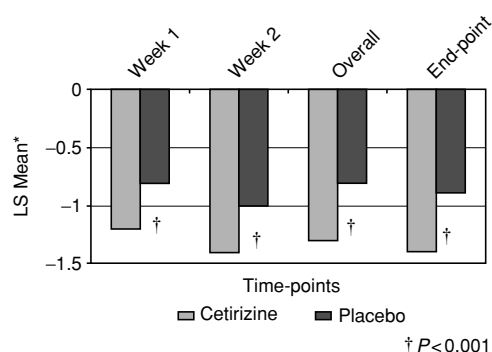


Fig. 1. Mean change from baseline for overall RQLQ. *Based on main effects models for intent-to-treat population. Mean baseline RQLQ scores were 3.3 for both the cetirizine and placebo cohorts. Week 2 was designated as the primary end-point. End-point = last post-baseline observation. †*P* < 0.001.

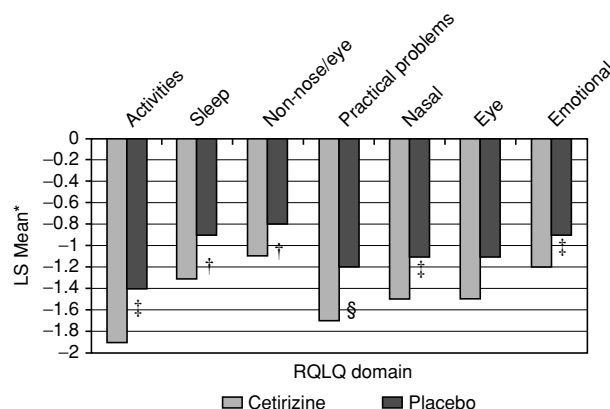


Fig. 2. Mean reduction from baseline to Week 2 in individual RQLQ domain scores. *Based on main effects models for intent-to-treat population. †*P* < 0.05; ‡*P* < 0.01; §*P* < 0.001.

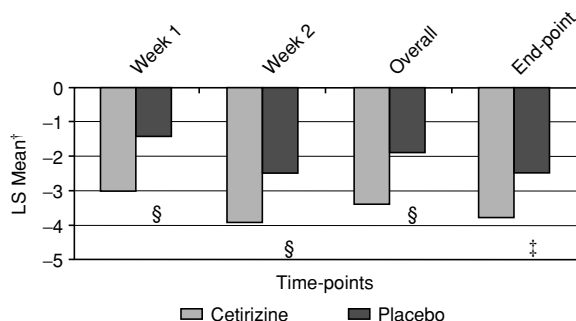


Fig. 3. Mean change from baseline in TSSC scores. *Includes sneezing, runny nose, itchy nose, itchy eyes, watery eyes, and post-nasal drip. †Based on main effects models for intent-to-treat population. Week 2 was designated as the primary end-point. End-point = last post-baseline observation. ‡*P* < 0.01; §*P* < 0.001.

end-point. When nasal congestion was added as a symptom to the TSSC score, cetirizine-treated patients again reported significantly greater reductions in symptoms (-4.4 , SE = 0.3) compared to placebo-treated patients (-2.8 , SE = 0.3) after 2 weeks of treatment, controlling for baseline differences ($P < 0.001$).

Change in symptoms by treatment group for the ITT sample at Week 2 are shown in Fig. 4. Significant differences were also observed for each individual symptom comprising the TSSC, with the exception of nasal congestion, at Week 1, overall, and end-point (data not shown).

The physician's assessment of patients' symptom severity at baseline was comparable for the two treatment groups. Mean change from baseline to Week 2 showed significantly greater improvement in patients treated with cetirizine compared with patients treated with placebo ($P \leq 0.01$). Similar results were seen for the Week 1 and end-point analyses.

HRQL – symptom relationship

The correlation between change in TSSC and change in overall RQLQ score was 0.68 at Week 2 ($P < 0.001$) (Table 2). Correlations between change in TSSC and change in the seven domain-specific RQLQ scores were also statistically significant ($P < 0.001$) and ranged from 0.52 (sleep) to 0.65 (practical problems). Correlations between specific TSSC symptoms and RQLQ overall ranged from 0.50 (post-nasal drip, watery eyes)

to 0.60 (runny nose, itchy nose); all were statistically significant ($P < 0.001$).

Perceived efficacy and patient satisfaction

Significant treatment group differences existed for the patient and clinician global evaluation of treatment effectiveness at the completion of the study. Eighty-two (41%) of the cetirizine-treated patients reported major or moderate improvement in symptoms as compared to 40 (20%) of placebo patients ($P < 0.001$). Similarly, clinicians determined that 87 (43%) of the cetirizine-treated patients had major or moderate improvement in their symptoms compared to 47 (23%) in the placebo group ($P < 0.001$). One hundred 30 (65%) cetirizine-treated patients reported being very satisfied or satisfied with treatment compared with 86 (44%) in the placebo group.

Safety

A total of 104 treatment-emergent AEs were reported by 83 (21%) patients during the treatment phase of the study. The incidence was similar between cohorts (19% vs. 23% for cetirizine and placebo, respectively). Somnolence and fatigue were the most frequently reported treatment-related AEs [1]. Thirteen (13%) were deemed treatment-related. Of these, six events were reported by five cetirizine-treated patients, and seven events were reported by six placebo patients. Three (1.5%) cetirizine patients and one (0.5%) placebo patient reported somnolence, and two (1.0%) patients in both groups reported

fatigue. One (0.5%) cetirizine patient and six (3%) placebo patients discontinued the study due to AEs; five of these seven discontinued due to AEs affecting the respiratory system.

Conclusions

The symptoms of seasonal allergic rhinitis are more than a nuisance as they can significantly impact patients' quality of life. This study examined the effect of cetirizine, 10 mg once daily, on the HRQL of adult patients with SAR while concurrently assessing symptomatic relief and safety. Both cetirizine-treated and placebo-treated patients experienced improvements in overall HRQL scores exceeding the clinically important 0.05 MID guideline. The mean change observed among cetirizine-treated patients exceeded the 'large change' of $1.18 (\pm 1.03)$ reported by Juniper et al. [30]. The HRQL improvement observed in the placebo group, however, is also noteworthy. Daily diary data as well as the global evaluations provided by patients and physicians suggests that a substantial proportion (20%) of placebo-treated patients experienced symptomatic improvement throughout the study. These improvements are consistent with previous studies of SAR [2], suggesting that the placebo response can run as high as 30–50% depending upon the study design. It is logical therefore that this response would extend to HRQL outcomes.

Between-cohort differences are central in determining the effect of active treatment as compared to placebo. In this study, cetirizine-treated patients had significantly greater improvements in overall RQLQ scores and in each of the seven HRQL domains. This effect was observed at Week 2, the primary time-point, as well as in the overall and end-point analyses. Interpreted conservatively, the magnitude of the mean between-group difference in overall RQLQ approached (0.4), but fell short of the 0.50 guideline at the primary end-point (Week 2). The 0.50 MID is a guideline, however, and should be considered in light of other available data. The 0.50 target was reached in the overall and end-point analyses, suggesting patients were experiencing clinically meaningful improvements in HRQL, beyond a placebo effect, by the end of the treatment period. The between-group differences observed in the activities and practical problems domains at Weeks 1 and 2, overall, and end-point are particularly noteworthy and indicate that

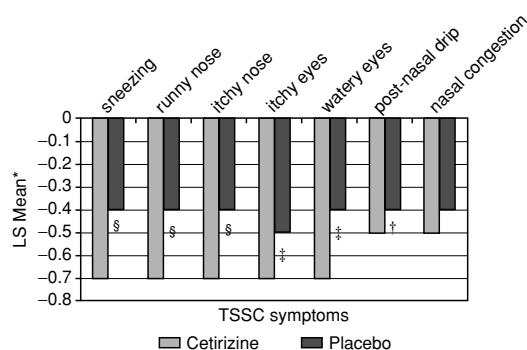


Fig. 4. Mean reduction from baseline to Week 2 in SAR symptoms scores. *Based on main effects models on intent-to-treat population. † $P < 0.05$; ‡ $P < 0.01$; \$ $P < 0.001$.

Table 2. Relationship between symptom relief and improvement in HRQL: Pearson correlation coefficients between TSSC and change scores (RQLQ) at Week 2*

Symptoms: TSSC	HRQL: RQLQ overall and domains							
	Overall	Activities	Non-nose/eye sleep	Practical symptoms	Nasal problems	Eye symptoms	Emotional symptoms	Function
Overall	0.68	0.64	0.52	0.51	0.63	0.64	0.60	0.54
Sneezing	0.55	0.54	0.44	0.40	0.54	0.57	0.43	0.44
Runny nose	0.58	0.55	0.42	0.44	0.58	0.62	0.43	0.48
Itchy nose	0.58	0.54	0.43	0.43	0.58	0.51	0.52	0.47
Itchy eyes	0.57	0.54	0.44	0.40	0.51	0.45	0.62	0.44
Watery eyes	0.49	0.47	0.37	0.37	0.42	0.39	0.55	0.40
Post-nasal drip	0.52	0.46	0.42	0.42	0.45	0.56	0.36	0.41

*All coefficients are statistically significant, $P < 0.01$. HRQL = Health-Related Quality of Life; TSSC = Total Symptom Severity Complex; RQLQ = Rhinitis Quality of Life Questionnaire.

cetirizine-treated patients experienced meaningful improvements in their ability to participate in valued activities, and experienced relief from SAR-related symptomology. Results of the end-point analyses indicate cetirizine-treated patients experienced clinically meaningful improvements in HRQL along six of the seven domains: activities, practical problems, symptom distress (nasal, eye), sleep problems, and emotional difficulties.

The HRQL effects of cetirizine seen in this study are consistent with those reported previously. Harvey et al. [1] compared the HRQL, efficacy, safety, and costs of cetirizine, chlorpheniramine, and terfenadine for the treatment of SAR in a two-phase, prospective, single-blind, randomized trial involving 131 patients undergoing treatment in a managed care setting. Mean RQLQ scores were significantly better among cetirizine-treated patients than those receiving terfenadine or chlorpheniramine at the end of phase I (week 2) and significantly better than terfenadine at the end of phase II (week 6). More patients were satisfied with cetirizine than terfenadine or chlorpheniramine (69%, 29%, and 50%, respectively). Other placebo-controlled studies investigating the impact of cetirizine on generic HRQL among patients with PAR further support the therapeutic benefit of cetirizine among allergy sufferers [6, 26].

Murray et al. [27] conducted a randomized double-blind, placebo-controlled multicentre trial of the efficacy, safety, and HRQL effects of cetirizine versus placebo in the treatment of SAR in adults. In this 3-week study, cetirizine-treated patients had significantly greater reductions in allergy-related symptoms (TSSC score) and improvements in HRQL (RQLQ overall score and in each of the seven domains) than placebo-treated patients at Week 1, Week 2, overall, and end-point ($P \leq 0.01$). Both groups experienced clinically meaningful improvements in RQLQ score at all time-points, with between-group differences exceeding the MID criterion at three of four observations (Week 1, overall, and end-points).

Other studies of second-generation, non-sedating antihistamines have also shown statistically significant HRQL effects, but have been less successful in approaching or exceeding Juniper's guideline for a clinically meaningful difference [31]. Meltzer et al. [36], for example, found that 180 mg fexofenadine each day over a 2-week treatment period had a significant HRQL effect compared with placebo, with statistically significant differences between active treatment and placebo in the overall RQLQ and each of the seven subscales ($P < 0.05$, $n = 845$). Tanner and colleagues [43] also reported significant within- and between-group effects in a pooled analysis of two placebo-controlled trials of 60 mg fexofenadine HCl twice daily. Improvement in overall RQLQ score in the active treatment group was significantly better than the placebo group at Weeks 1 and 2 of treatment ($P \leq 0.05$); between-group differences were significant for three of the seven subscales at Week 2. Between-group differences did not meet or exceed the MID in either study, however, and correlations between symptom relief and HRQL benefits were not reported.

Previous studies have shown that cetirizine effectively reduces the severity of symptoms associated with perennial and seasonal allergic rhinitis [19–25, 44–47]. In the present study, all patients exhibited improvements in HRQL and in symptom severity; however, those randomized to cetirizine experienced significantly more relief than the placebo group overall and in each

of the six symptoms represented by the TSSC. While baseline symptom scores were statistically different between groups, they were not clinically meaningful (0.6-point difference on an 18-point scale). These differences were controlled for, however, using statistical techniques and they did not impact the results (difference between groups at Weeks 1 and 2). The moderate to strong correlations between change in TSSC and change in RQLQ support the link between symptomatic relief and HRQL improvement in this population. In fact, nearly half (46%) of the variance in improved RQLQ overall scores can be attributed to symptom relief. It is reasonable to conclude therefore that the symptomatic relief experienced by patients in this study translated into improvements in HRQL.

The between-group differences in patient satisfaction with treatment are consistent with the differences observed in symptomatic relief and improvement in HRQL as well as with results reported by Harvey et al. [1]. In the present study, the majority of cetirizine-treated patients (65%) reported being satisfied or very-satisfied with treatment, compared with 44% in the placebo group. Harvey et al. [1] found that 69% of patients treated with cetirizine were satisfied with their therapy and chose not to switch to another medication. In addition, safety results suggested that cetirizine was well tolerated.

From a clinical management perspective, patients frequently seek treatment not for the symptoms *per se*, but because these symptoms are having an adverse effect on the quality of their lives. Patients and health care providers, in turn, evaluate the effectiveness of various treatments in terms of symptom relief and improvement in daily functioning and well-being [1, 5, 9, 30, 48]. Clearly, data on a drug's effectiveness in improving HRQL are central to the decision-making process. According to Blaiss [5], 'appraising the role of different pharmacologic agents in allergic rhinitis in improving the patient's quality of life is an important part of proving the medication's worth to the health care community' (p. 449). Meltzer and colleagues [48] suggest that 'the judicious treatment of rhinitis involves locating [the] "quality of life" issues within the continuum of quality and costs' (p. 1148). One could argue therefore that HRQL should be the standard against which empirical data on symptomatic change in SAR is measured.

The optimal treatment for SAR offers rapid, sustained relief from uncomfortable and irritating symptoms in the absence of undesirable side-effects, leading to improvements in patient functioning and well-being. The results of this study support those reported by Murray et al. [27] and suggest that once-daily treatment with cetirizine 10 mg offers adults suffering from SAR safe and effective symptomatic relief that translates into an improvement in their health-related quality of life.

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