Original Article

Effect of fexofenadine on the quality of life of Japanese cedar pollinosis patients

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ABSTRACT

Background: The aim of the present survey was to investigate the changes associated with fexofenadine administration in the quality of life (QOL) of Japanese cedar pollinosis patients.

Methods: After obtaining informed consent, volunteers suffering from Japanese cedar pollinosis were divided into two groups: (i) the fexofenadine group (2 × 60 mg/day); and (ii) the placebo group. Changes in QOL were examined after administration for 14 days (randomized, double-blind comparison study). The study period was from 27 February to 13 March 2003. Subjects were recruited from the Tokyo metropolitan area; 104 were randomized to the fexofenadine group and 103 were randomized to the placebo group. The QOL was evaluated using the Japanese Allergic Rhinitis Standard QOL Questionnaire (JRQLQ no. 1). The JRQLQ is structured to evaluate six domains of usual daily activities, outdoor activities, social functioning, sleep problems, general physical problems and emotional function, as well as the overall QOL.

Results: On the 14th day after the start of fexofenadine or placebo administration, the QOL was improved in all domains of the JRQLQ in the fexofenadine group, whereas it had worsened in all domains, except outdoor activities, in the placebo group. The overall evaluation of QOL was significantly more favorable in the fexofenadine group on the 14th day after the start of administration.

Conclusions: The present study showed that fexofenadine administration suppressed the deterioration of overall QOL and alleviated the interference with daily life in patients suffering from Japanese cedar pollinosis.

Key words: allergic rhinitis, cedar pollinosis, daily life, fexofenadine, quality of life.

INTRODUCTION

Allergic rhinitis does not threaten life directly, but it has a significant impact on the quality of life (QOL) and sometimes restricts the daily activity of patients. Furthermore, allergic rhinitis symptoms influence study and work conditions, inflicting a significant burden socially and economically. In Japan, approximately 15% of the population nationwide suffers from cedar pollinosis.1

Many types of therapy are used for the treatment of allergies, including pollinosis. Among the most frequently used pharmacotherapies, antihistamines are often the drugs of choice. Antihistamines relieve symptoms, but they do not cure the disease. With antihistamines, patients can spend their daily life more comfortably and productively.

Fexofenadine HCl was approved as an antihistamine against allergies in September 2000 in Japan and it is currently used widely. Abroad, it has been approved in 102 countries, including the US, UK, France and Germany, and, as of March 2000, fexofenadine HCl was marketed in 57 countries.
In the present study, the QOL of Japanese cedar pollinosis patients was evaluated, in comparison with a placebo control, using the ‘Japanese Allergic Rhinitis QOL Standard Questionnaire’ (JRQLQ) after administration of 60 mg fexofenadine HCl, twice daily for 14 days.

METHODS

Patients

The present study was a randomized, double-blind comparison study against a placebo control, performed at a single institution.

After obtaining patient consent, screening was performed to confirm compliance with the subject selection and exclusion criteria and to examine the physical condition of each individual. Screening included patient background, physician’s examination, clinical laboratory analysis (hematology, blood biochemistry, serology and urinalysis), physical examination, and electrocardiogram (12 lead electrocardiogram). The physician-in-charge determined the eligibility of each patient as a subject in the present study based on the results of screening. The pre-observation period was 7 days before the start of administration of the trial drug, during which time the physician’s examination, rhinoscopy and blood collection were performed. Following completion of the pre-observation period, patients were assigned at random to receive test drug or placebo and administration was started. A fexofenadine HCl 60 mg tablet (fexofenadine group) or placebo tablet (placebo group) was administered twice a day, once in the morning and once in the evening, for 14 days (Fig. 1).

Patients were asked to record in the patient diary pollinosis symptoms (sneezing, runny nose, nasal congestion, itchy eyes and watery eyes) and compliance with the drug administration schedule.

During the study period, any concurrent use of drugs that could influence the evaluation of efficacy was prohibited. However, when drugs had to be used, as judged by the physician-in-charge, the drugs used were recorded in the survey form.

Evaluation items

The JRQLQ

The JRQLQ, which was used as the primary standard for evaluation, is composed of three parts: nasal and eye symptoms (JRQLQ I), a QOL-related questionnaire (JRQLQ II) and an overall face scale.

The nasal and eye symptoms included the six categories of runny nose, sneezing, nasal congestion, itchy nose, itchy eyes and watery eyes. Each subject evaluated symptoms on a five-point scale, which included 0 for no symptoms, 1 for mild, 2 for moderately severe, 3 for severe and 4 for very severe symptoms. Mean scores for...
these six categories were determined as the mean nasal and eye symptom scores (JRQLQ I).

The QOL-related questionnaire included 17 items concerning: (i) reduced productivity at work/home/school; (ii) poor mental concentration; (iii) reduced thinking power; (iv) impaired reading book/paper; (v) reduced memory loss; (vi) limitation of outdoor life (e.g. sports, picnic); (vii) limitation of going out; (viii) hesitation visiting friend or relatives; (ix) reduced contact with friends or others by telephone or conversation; (x) not an easy person to be around; (xi) impaired sleeping; (xii) tiredness; (xiii) fatigue; (xiv) frustration; (xv) irritability; (xvi) depression; and (xvii) unhappiness. Each item was evaluated on a five-point scale as 0 for no significant problem, 1 for a mild problem, 2 for moderately severe, 3 for severe and 4 for very severe (Fig. 2). Mean scores for these categories were determined as the mean QOL-related questionnaire scores (JRQLQ II). In addition, these categories were divided into six domains, including ‘usual daily activities’ for items i–v, ‘outdoor activities’ for items vi and vii, ‘social functioning’ for items viii to x, ‘sleep problem’ for item xi, ‘general physical problems’ for items xii and xiii, and ‘emotional function’ for items xiv to xvii. The mean score for each domain was calculated for analysis.

Overall face scale, including overall symptoms, condition and feelings, was evaluated on a scale from 0 for ‘happy’ to 4 for ‘crying’ for the past 1–2 weeks.  

The present study evaluated the mean score for each domain in the QOL-related questionnaire as well as JRQLQ I, JRQLQ II and overall face scale.

Allergy diary
In the allergy diary, each item from a list including sneezing (number of attacks in a day), runny nose (number of incidences of nose blowing per day), nasal congestion, itchy eyes and watery eyes was evaluated on
a scale from 0 for the most mild to 4 for the most severe. The total scores for sneezing, runny nose, nasal congestion, itchy eyes and watery eyes were calculated as the TSS for statistical analysis. The severity in the season was compared between the fexofenadine and placebo groups.

Safety
All unfavorable signs and symptoms observed during the period of administration of the test drug were classified as adverse events, regardless of the presence or absence of a causal relationship to the test drug.

The safety items evaluated included analysis of data obtained during the study period (clinical laboratory analysis, physical examination and physician’s examination) and symptoms experienced during the study period (only adverse events reported at the physician’s examinations, but not those described in the allergy diary).

Statistical analysis
Continuous variables and categorical variables were analyzed by the Mann–Whitney U-test and Chi-squared test, respectively, for characteristics related to patients’ background (age, sex, address, occupation and work place).

Changes in JRQLQ scores from baseline were analyzed by analysis of covariance (ANCOVA), with the treatment group as the main effect and the baseline values as the covariate. For TSS, the statistical significance between two groups was examined using the Mann–Whitney U-test.
RESULTS

Patient population

Of a total of 250 subjects screened, 210 were randomized to receive treatment; 104 received fexofenadine HCl 60 mg b.i.d. (fexofenadine group) and 103 received placebo b.i.d. (placebo group). All 207 randomized subjects completed the 2 week study period.

Overall, 207 subjects were enrolled in the Intent-to-Treat (ITT) population (patients who received at least one dose of treatment and completed a baseline and not less than one valid QOL assessment): 104 subjects in the fexofenadine group and 103 in the placebo group. There were no differences between the two treatment groups in terms of demographic characteristics (Table 1). The mean age of subjects in the fexofenadine group was 32.7 years compared with 34.2 years in the placebo group. The majority of patients were male (60% fexofenadine group; 56% placebo group). There were almost equal numbers of students (47% fexofenadine group; 45% placebo group) and non-students (53% fexofenadine group; 55% placebo group).

Baseline JRQLQ scores were comparable between the two treatment groups (Table 2). The mean QOL-related questionnaire score (JRQLQ II) was 1.00 in the fexofenadine group and 0.89 in the placebo group, showing that patients were greatly troubled by pollinosis symptoms. Individual JRQLQ domain scores at baseline indicated that patients were less troubled by their symptoms in relation to their social functioning and were more troubled in their usual daily activities, outdoor activities and by general physical problems.

Table 1  Patient characteristics at baseline (Intent-to-Treat population)

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Fexofenadine HCl 60 mg b.i.d (n = 104)</th>
<th>Placebo (n = 103)</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mean (±SD) age (years)</td>
<td>32.7 ± 9.8</td>
<td>34.2 ± 9.8</td>
<td>0.631*</td>
</tr>
<tr>
<td>Sex</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>No. males (%)</td>
<td>62 (60)</td>
<td>58 (56)</td>
<td>0.674†</td>
</tr>
<tr>
<td>No. females (%)</td>
<td>42 (40)</td>
<td>45 (44)</td>
<td></td>
</tr>
<tr>
<td>Occupation</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>No. students (%)</td>
<td>48 (47)</td>
<td>45 (45)</td>
<td>0.769†</td>
</tr>
<tr>
<td>No. non-students (%)</td>
<td>55 (53)</td>
<td>56 (55)</td>
<td></td>
</tr>
</tbody>
</table>

*Wilcoxon test.
†Chi-squared test.

Table 2  Baseline Japanese Allergic Rhinitis Standard Quality of Life Questionnaire (JRQLQ) scores (Intent-to-Treat population)

<table>
<thead>
<tr>
<th>Scores</th>
<th>Fexofenadine HCl 60 mg b.i.d (n = 104)</th>
<th>Placebo (n = 103)</th>
<th>P (Wilcoxon test)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Nasal and eye symptoms</td>
<td>1.60 ± 0.73</td>
<td>1.60 ± 0.73</td>
<td>0.864</td>
</tr>
<tr>
<td>QOL-related questionnaire</td>
<td>1.00 ± 0.86</td>
<td>0.89 ± 0.73</td>
<td>0.557</td>
</tr>
<tr>
<td>Scores by domain</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Usual daily activities</td>
<td>1.19 ± 1.0</td>
<td>0.96 ± 0.8</td>
<td>0.123</td>
</tr>
<tr>
<td>Outdoor activities</td>
<td>1.03 ± 1.0</td>
<td>1.08 ± 1.0</td>
<td>0.682</td>
</tr>
<tr>
<td>Social functioning</td>
<td>0.66 ± 0.8</td>
<td>0.64 ± 0.7</td>
<td>0.75</td>
</tr>
<tr>
<td>Sleep problem</td>
<td>0.93 ± 0.9</td>
<td>0.83 ± 0.9</td>
<td>0.285</td>
</tr>
<tr>
<td>General physical problems</td>
<td>1.12 ± 1.1</td>
<td>0.96 ± 1.0</td>
<td>0.495</td>
</tr>
<tr>
<td>Emotional function</td>
<td>0.96 ± 1.0</td>
<td>0.87 ± 0.9</td>
<td>0.993</td>
</tr>
<tr>
<td>Condition of past 1 or 2 weeks</td>
<td>2.46 ± 0.9</td>
<td>2.45 ± 0.9</td>
<td>0.961</td>
</tr>
</tbody>
</table>

Data are the mean ±SD.
QOL, quality of life.
Fig. 3  Mean Japanese Allergic Rhinitis Standard Quality of Life Questionnaire (JRQLQ) scores at baseline (□) and at the end of the 2 week administration period (■) for (a) placebo and (b) fexofenadine HCL 120 mg (60 mg b.i.d.).

Fig. 4  Mean changes in scores from baseline (■, nasal and eye symptoms; □, quality of life-related questionnaire; ☐, overall face scale) following 2 week administration of (a) placebo or (b) fexofenadine HCL 120 mg (60 mg b.i.d.). *P < 0.001 compared with placebo.
Outcome

Quality of life

Mean scores in each domain are shown for JRQLQ I and JRQLQ II in Fig. 3. Scores of all domains, except outdoor activities, decreased or worsened in the placebo group, whereas all showed an improvement in the fexofenadine group.

Significant improvements in scores from baseline were clearly seen in the fexofenadine group for JRQLQ I, JRQLQ II and the overall face scale (P < 0.001; Fig. 4). In addition, with regard to each domain of JRQLQ II, a significant improvement in scores was observed for usual daily activities (P < 0.001), social functioning (P = 0.002), general physical problems (P < 0.001) and emotional function (P = 0.002) in the fexofenadine group (Fig. 5). Scores for outdoor activities (P = 0.055) and sleep problems (P = 0.064) tended to improve, albeit not significantly, in the fexofenadine group.

In JRQLQ II by domain in each week, there was a significant improvement in the first week for all the domains in the fexofenadine group. No significant change was seen in the fexofenadine group for outdoor activities (P = 0.055) and sleep problems (P = 0.064) in the second week (end-point), which could have been due to changes in the pollen count (Fig. 6).

Symptom severity

The daily TSS (total score of sneezing, runny nose, nasal congestion, itchy eyes and watery eyes), as calculated from the subject diary, significantly improved in the fexofenadine group from the first day after administration compared with the placebo group. This improvement was sustained at the peak pollen count, showing improvement every day throughout the administration period (Fig. 7).

Safety

No serious adverse events were reported throughout the study period. There was no significant difference in the number of adverse events between the two groups (P = 0.568). A high white blood cell count and headache occurred most frequently.
Fig. 6  Changes in quality of life-related questionnaire domains from baseline to end-point following 2 weeks administration of placebo (○) or fexofenadine HCL 120 mg (60 mg b.i.d.; ●). *P < 0.05, **P < 0.01, ***P < 0.001 compared with placebo. The starting day of administration (baseline), 1 week after the start of administration and 2 weeks after the start of administration (end-point) are indicated on the graphs as 0, 1 and 2 weeks, respectively.
DISCUSSION

Allergic rhinitis has been regarded as a ‘life style disease’ that interferes with daily life rather than as a ‘chronic disease’. This is based on the fact that allergic rhinitis is not a life-threatening disease but, rather, it worsens QOL. The World Health Organization defines QOL as an individual’s perception of their position in life in the context of the culture and value systems in which they live and in relation to their goals, expectations, standards and concerns. To determine whether an improvement or deterioration of QOL has taken place, oral and written questionnaires are administered. Among the questionnaires that are currently used mainstream methods of surveying, some (SF-36 etc.) are not specific to particular diseases and examine general health status, whereas others examine QOL specific to a disease. From a survey using SF-36, Fukuroku et al. reported that among nasal symptoms in perennial allergic rhinitis, nasal congestion was the one that interfered most severely with the QOL. The Juniper questionnaire is the only one specific to allergic rhinitis and is regarded as the standard questionnaire in the US and Europe. The findings of the present study demonstrate that fexofenadine HCl 60 mg b.i.d. significantly improved the overall QOL and total symptom score in Japanese subjects with pollinosis compared with placebo during the 2 week treatment period. This improvement in QOL was associated with significant symptom relief in the fexofenadine treatment group. Furthermore, fexofenadine-treated subjects experienced significant improvement in nasal and eye symptoms, usual daily activities, social functioning, general physical problems and emotional function. These significant improvement scores ranged from 0.19 to 0.35 in the Rhinoconjunctivitis Quality of Life Questionnaire (RQLQ). This improvement rate is not consistent with the Juniper theory of 0.5.

The results presented here are consistent with those published previously, in which fexofenadine significantly
improved QOL in pollinosis and chronic idiopathic urticaria (CIU) patients.\textsuperscript{8–11} Tanner et al. assessed the impact of fexofenadine HCl 60 mg b.i.d. on patients’ QOL in a pooled analysis of two placebo-controlled trials in patients with pollinosis.\textsuperscript{8} A significant ($P = 0.05$) improvement in overall RQLQ score was reported for patients receiving fexofenadine HCl 60 mg b.i.d. compared with placebo.\textsuperscript{8} In a more recent study, van Cauwenberge et al.\textsuperscript{11} assessed the impact of once-daily administration of fexofenadine HCl 120 mg, loratadine 10 mg or placebo on patients’ QOL in the treatment of pollinosis. A total of 509 pollinosis patients aged 12–75 years completed the QOL assessment (RQLQ). For all treatment groups (fexofenadine, loratadine and placebo), there was a significant improvement from baseline in overall QOL ($P < 0.0001$); however, the improvement in the fexofenadine group was significantly greater than that obtained in either the loratadine ($P = 0.03$ for fexofenadine vs loratadine) or placebo ($P = 0.005$ for fexofenadine vs placebo) groups. In addition, fexofenadine was significantly better than either loratadine or placebo in reducing overall mean 24 h reflective symptom scores for itchy, watery or red eyes and nasal congestion from baseline ($P = 0.05$), whereas the effect of loratadine on these two symptom scores did not differ from that of placebo.\textsuperscript{11} Furthermore, in patients with CIU, fexofenadine HCl 60 mg b.i.d. significantly improved overall QOL compared with placebo.\textsuperscript{9} These results corroborate the findings presented here that fexofenadine improved overall QOL in Japanese subjects with pollinosis.

The present clinical study demonstrated the usefulness of the recently validated JRQLQ instruments in assessing QOL in a Japanese patient population with pollinosis during the peak cedar pollinosis season. The JRQLQ, as a measure of QOL, will soon be adopted as an outcome measure for clinical trials in the Japanese population.\textsuperscript{12} The results presented here support the use of the JRQLQ questionnaire for assessing the impact of pollinosis symptoms on QOL.

**Conclusions**

In conclusion, the present clinical study showed that fexofenadine HCl 60 mg b.i.d. significantly improves QOL in Japanese patients with pollinosis during the peak cedar pollinosis season, using a recently validated Japanese instrument.

**References**