Relationship of airborne pollen count and treatment outcome in Japanese cedar pollinosis patients.

Short Title: Pollen count and treatment outcome in pollinosis

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Abstract

Background

In Japan, information of daily airborne Japanese cedar pollen counts is made public during pollen season. If symptoms severity and treatment outcome are predictable according to these pollen counts, management of seasonal allergic rhinitis may become more precise.

Aims of the study

To evaluate the relationship between airborne pollen counts, symptoms severity and treatment outcome in Japanese cedar pollinosis patients.

Methods

In the randomized study, patients with moderate to most severe Japanese cedar pollinosis were treated with fexofenadine (60 mg BD) or fexofenadine and nasal corticosteroids for 2 weeks. During the same period daily airborne pollen counts were measured.

Results

One hundred and five adult patients were enrolled. No difference of treatment efficacy was seen among groups. Detailed results of efficacy & safety were previously described elsewhere. In univariate analysis, the mean cumulated amount of airborne pollen exposure for 4 days prior to the study tended to affect symptoms severity (p=0.053) and the mean cumulated amount of airborne pollen during the treatment period tended to show difference among five treatment outcome categories (p=0.066).

In multivariate analysis, the mean cumulated amount of airborne pollen exposure for 4 days prior to the study was identified as only significant factor of symptoms severity ($p=0.0327$) and cumulated amount of airborne pollen during the treatment period ($p=0.027$) and allergic history ($p=0.027$) were significant factors of treatment outcomes. No serious adverse effect was reported during the study.

Conclusions

The amount of airborne pollen may be predictive of both symptoms severity and treatment outcome.

Key Words: airborne pollen counts, fexofenadine, Japanese cedar pollinosis, seasonal allergic rhinitis, treatment

Introduction

Japanese cedar pollinosis is a very common disorder in Japan where its prevalence is estimated to be approximately 16% (1). Although a relationship of nasal mucosal sensitivity to allergens is suggested, the reasons for variation of symptom severity and differing response to treatment are poorly understood (2, 3). Difference of individual pollen burden may be responsible for the treatment outcome. In Japan, information on daily airborne Japanese cedar pollen counts is made public by many different government authorities, universities and private institutions in each area. The clinical use of such information is poorly understood. If symptom severity and treatment outcome are predictable according to daily exposure to pollen count, management of seasonal allergic rhinitis may become more precise.

This is a sub-analysis of an efficacy study comparing fexofenadine monotherapy with fexofenadine and nasal corticosteroids to determine the relationship of airborne pollen counts to symptom severity and treatment outcome in Japanese cedar pollinosis patients (4).

Patients and Methods

A prospective, open-label, randomized, observational study in adult patients with Japanese cedar pollinosis was conducted in 3 different areas (Nagasaki, Sasebo and Tagawa area) of Kyushu, Japan. Patient inclusion or exclusion criteria and study design have previously been described (4). Briefly, patients with moderate to most severe disease assessed according to practical guidelines for the management of allergic rhinitis in Japan were enrolled (5). Symptom severity was assessed by number of episode of sneezing and rhinorrhea and state of nasal obstruction. Patients with mild disease were excluded as good response to treatment is expected in these patients. Patients were randomized to treatment with fexofenadine 60 mg BD alone or fexofenadine 60 mg BD and concurrent nasal corticosteroids (there was no restriction on the type or dose). After one week, patients who had poor response to treatment with fexofenadine alone were given additional nasal corticosteroids. At the end of two weeks, response to treatment was assessed by the physician in agreement with the Japanese guideline (5). In each area, a Durham pollen collector was used for measuring the amount of airborne pollen. The study was approved by the ethics committee at each participating hospital and patients gave written informed consent.

Statistical Methods

The correlation between the cumulative amount of airborne pollen during the 4 days prior to the first physician visit and symptom severity was evaluated using Pearson's product moment correlation coefficient. The correlation between the cumulative amount of airborne pollen to which patient was exposed during treatment and the treatment outcome was evaluated using least mean–square estimation with mixed effects models. The trends of daily airborne pollen counts in patients with or without favorable treatment outcome were evaluated by least mean-square estimation. In addition, multivariate analysis was performed regarding symptom severity and treatment outcomes. As no difference was seen in efficacy between treatment groups, all patients were included in the assessment for relationship of pollen count with treatment outcome. Combining all treatment arms is justified due to the small number of each group in this trial.

Results

Between February 16 and March 31 2006, 138 patients were enrolled. One hundred and five patients (85 males and 20 females, mean age: 41.7 years) had data for pollen count assessment. Moderate (34%), severe (52%) and most severe (14%) seasonal allergic rhinitis was diagnosed.

1. Treatment outcome

Forty patients were treated with fexofenadine monotherapy for 2 weeks. Eleven patients were treated with fexofenadine monotherapy for 1 week and nasal corticosteroids were added in the second week. The other 54 patients were treated with combination therapy of fexofenadine and nasal corticosteroid for 2 weeks.

At the end of week one, no significant difference of treatment efficacy was seen between 51 patients who started with fexofenadine monotherapy and 54 patients started to treat with combination therapy. At the end of the study, although additional one-week treatment of nasal corticosteroid was effective in 11 patients who had shown insufficient improvement, no significant difference of treatment efficacy was seen between the two groups (4). Patients with moderate to severe cedar pollinosis benefit from combination therapy with fexofenadine and a nasal corticosteroid as initial treatment. However, using an alternative approach of fexofenadine monotherapy as initial treatment and then followed by nasal corticosteroids as needed resulted in similar efficacy, sparing most patients unnecessary steroid exposure. After 2 weeks of treatment, response was judged by physicians as excellent (12 patients), very good (43 patients), good (35 patients), poor (9 patients) and inefficient (6 patients).

2. The amount of airborne Japanese cedar pollen

The cumulative amount of airborne cedar pollen in the Nagasaki, Sasebo and Tagawa areas during the study was 2,154, 1,747 and 3,553 grains/cm^2, respectively. In each area, exposure to airborne pollen was observed with an approximately 4-day cycle. Mean daily counts are shown in Figure 1. In patients with moderate, severe, or most severe seasonal allergic rhinitis, the mean cumulative amount of airborne pollen 4 days prior to the first physician's visit was 62, 88, 91 grains/cm^2, respectively. Among these three categories of symptom severity, a trend (p=0.053) was observed in terms of pollen count (Figure 2). The sum of airborne Japanese cedar pollen exposure over the 2 week treatment period was compared in each treatment outcome category. As shown in Figure 3, the mean cumulative amount of airborne pollen in patients whose response to treatment was classified as excellent, very good, good, poor and inefficient was 1,025, 1,093, 1,031, 1,544 and 1,380 grains/cm^2, respectively, indicating a tendency among groups (p=0.066). Daily changes in the amount of airborne cedar pollen in patients who improved (classified as excellent and very good) were compared with daily changes in patients who did not improve (classified as poor and inefficient) (Figure 4). The daily changes of airborne cedar pollen in patients who did not improved sustained a significantly higher trend than those in patients who improved (p=0.0004).

In multivariate analysis, only the mean cumulative amount of airborne pollen exposure 4 days prior to the first physician's visit was identified as significant factor of disease severity (p=0.0327). Gender, age, disease type, duration of illness and presence or absence of allergy history were not implicated in symptom severity. The mean cumulative amount of airborne pollen during the treatment period and history of allergy were significant factors for treatment outcome (p=0.027 and 0.027, respectively). Symptom severity was not a significant factor of treatment outcome (p=0.416).

3. Safety

All study medications were well tolerated. No serious adverse effect was reported during the study.

Discussion

This study is the first study to assess the relationship of airborne pollen counts to disease severity and treatment outcome in Japanese sufferers of cedar pollinosis. Our study addressed two questions: 1) does the cumulative amount of airborne pollen just prior to the physician's visit affect disease severity at the diagnosis? 2) Does the total airborne pollen amount during treatment affect treatment response?

Our result shows that airborne pollen burden may affect symptom severity. In multivariate analysis, the mean cumulative amount of airborne pollen 4 days prior to the first physician's visit was the only factor identified as having significant effect on symptom severity for patients with moderate to most severe disease. Baba et al. reported that frequency of patients who complain of symptoms of rhinitis correlates well with the square root of the cumulative amount of daily airborne pollen from the first day of exposure in the pollen season (2, 6).

Is nasal mucosal sensitivity to airborne pollen responsible for symptom severity? Baba et al. also reported that there are two different types of sensitivity to pollen in pollinosis patients (2, 6). In high-sensitivity type patients, their symptoms appear earlier even at low daily amounts of airborne pollen. On the other hand, symptoms appear gradually in low-sensitivity type patients. The mechanism of the difference in sensitivity remains unclear. No correlation was found between overall frequencies of in vivo sensitization to tree pollen allergens in a local population and regional pollen exposure data (7).

In addition, our results show that the mean cumulative amount of airborne pollen during the treatment period and history of allergy were significant factors for positive treatment outcome in multivariate analysis. Our data indicate that patients who were exposed to larger amounts of daily airborne pollen were less responsive to treatment. The amount of airborne pollen plays an important role in treatment response, although nasal mucosal sensitivity may also affect treatment outcome. Expectations for treatment outcome cannot be determined based on the amount of daily airborne pollen at the beginning of the treatment. Although the daily amount of airborne cedar pollen changes, patients with the same cumulative amount have a different daily amount of airborne pollen. Therefore, the daily change rather than cumulative amount to which a patient is exposed may be more responsible for the treatment outcome.

In multivariate analysis, symptom severity was not a significant factor of treatment outcome. Degree of symptom severity of Japanese cedar pollinosis fluctuates according to the exposed amount of airborne cedar pollen, although treatment modality is decided based on symptom severity when seeing a doctor. Therefore, our results suggest that treatment outcome of Japanese cedar pollinosis is more affected on daily degree of exposure to cedar pollen than symptom severity when seeing a doctor.

What can we learn from the daily amount of airborne pollen?

Throughout Japan, there are more than 200 facilities measuring airborne pollen. Our data show that the amount of airborne pollen is predictive of symptom severity, although patients with mild type seasonal allergic rhinitis were not included in this study. Retrospective data suggest a relationship between pollen counts and treatment outcome. Actual and expected information of regional pollen counts may be helpful for the management of seasonal allergic rhinitis in addition to reduction of patients' chance of exposure to pollen antigen.

In conclusion, this is the first study to show that symptom severity and treatment outcome may be partially affected by the daily burden of airborne pollen. Impact of different factors such as individual sensitivity to pollen allergens may have less of an impact on the management of seasonal allergic rhinitis.

Reference

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Figure Legend

Figure 1. Trends of airborne pollen counts in 3 areas.

Figure 2. The relationship between symptom severity and cumulative airborne pollen amounts 4 days prior to the first physician visit. Bar indicates mean ± SD.

Figure 3. The relationship between treatment outcomes and cumulative airborne pollen throughout the 2 week treatment period. Bar indicates mean ± SD. $p=0.066$

Figure 4. Daily trends of airborne pollen from 4 days prior to first physician visit to the end of study.

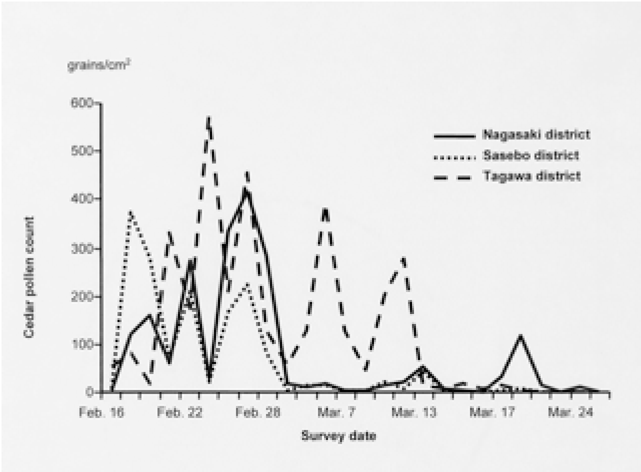
grains/cm2
Cedar pollen count
600
500
400
300
200
100
0
Nagasaki district
Sasebo district
Tagawa district
Feb. 16
Feb. 22
Feb. 28
Mar. 7
Mar. 13
Mar. 17
Mar. 24
Survey date

Fig. 1

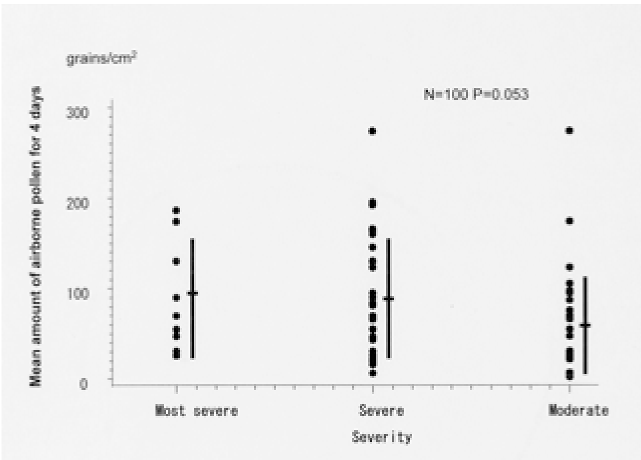
grains/cm2
Mean amount of airborne pollen for 4 days
N=100 P=0.053
300
200
100
0
Most severe
Severe
Moderate
Severity

Fig. 2

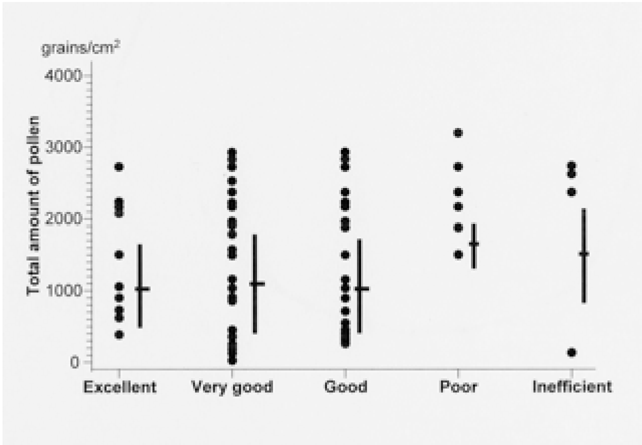
grains/cm2
4000
3000
2000
1000
0
Total amount of pollen
Excellent
Very good
Good
Poor
Inefficient

Fig. 3

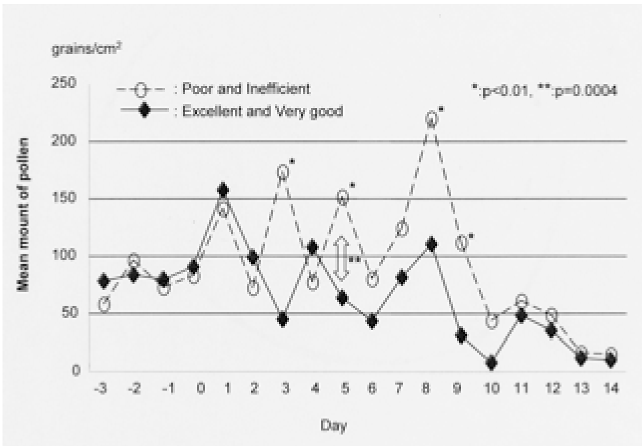
grains/cm2
250
200
150
100
50
0
Mean mount of pollen
: Poor and Inefficient
: Excellent and Very good
*:p<0.01, **:p=0.0004
-3 -2 -1 0 1 2 3 4 5 6 7 8 9 10 11 12 13 14
Day

Fig. 4