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ABSTRACT

Background: This study intended to assess the severity of Japanese cedar pollinosis using the Practical Guideline for the Management of Allergic Rhinitis in Japan (PG-MARJ) and the Allergic Rhinitis and its Impact on Asthma (ARIA) Guideline.

Methods: An Internet questionnaire survey of patients with pollinosis was conducted in mid-May 2011 and responses were obtained from 3382 individuals who had potential symptoms of Japanese cedar pollinosis from February to early May 2011 and who had experienced such symptoms for at least two pollen seasons.

Results: According to PG-MARJ, 23.5% of the respondents had severest rhinitis, 29.4% severe rhinitis, 31.3% moderate rhinitis, 13.8% mild rhinitis and 2.0% asymptomatic rhinitis. According to ARIA, 67.2% of them had moderate/severe persistent rhinitis, 23.8% moderate/severe intermittent rhinitis, 4.4% mild persistent rhinitis and 4.6% mild intermittent rhinitis.

Conclusions: Moderate to severe rhinitis was diagnosed in more than 80% of the respondents according to PG-MARJ, while moderate/severe rhinitis was diagnosed in more than 90% of the respondents according to ARIA. Most of the respondents suffered relatively severe pollinosis. More than 80% of the respondents had all the three major symptoms (i.e., sneezing, rhinorrhea and nasal blockage). Disagreement in the severity assessment between the two guidelines was noted in approximately 20% of the respondents.

KEY WORDS

Allergic Rhinitis and its Impact on Asthma (ARIA), Internet survey, pollinosis, Practical Guideline for the Management of Allergic Rhinitis in Japan (PG-MARJ)

INTRODUCTION

A survey carried out in 20081 revealed that the prevalence of perennial allergic rhinitis and seasonal allergic rhinitis (pollinosis) was 23.4% and 29.8%, respectively, and the prevalence of all types of allergic rhinitis was as high as 39.4% in Japan. Seasonal allergic rhinitis in Japan is caused by allergens including pollen of Japanese cedar and cypress in spring, orchardgrass in early summer and ragweed and wormwood in autumn. Among them, Japanese cedar pollen is the most important allergen: the prevalence of...
Japanese cedar pollinosis is as high as 26.5% and the number of patients is increasing year by year. It is assumed that intensive planting of cedar and cypress trees encouraged by the Japanese forestry policy from the late 1950s to the 1960s have resulted in a yearly increase of cedar and cypress pollens dispersed from the grown artificial forest leading to the recent sharp increase of patients with Japanese cedar pollinosis.

Pollens of cedar and cypress start to fall in February every year and their dispersal is observed until early May. This large-scale Internet questionnaire survey was conducted in mid-May 2011 when dispersal of cedar and cypress pollens had almost ended. The subjects of the survey were individuals who had symptoms of Japanese cedar pollinosis from February to early May 2011 and who had experienced such symptoms for at least two pollen seasons.

In Japan, the Practical Guideline for the Management of Allergic Rhinitis in Japan (PG-MARJ)\(^2\) that describes standard diagnosis and treatment strategies has been widely used and the severity of allergic rhinitis has been classified based on the three major symptoms (i.e., sneezing, rhinorrhea and nasal blockage) into five grades (i.e., severest, severe, moderate, mild and asymptomatic). On the other hand, the Allergic Rhinitis and its Impact on Asthma (ARIA) Guideline\(^3\) that is regarded as the international guideline for allergic rhinitis divides the disease into persistent and intermittent types and classifies the severity as mild or moderate/severe depending on the disease’s impact on the daily life activities of the patients. When the disease type and the severity are combined, allergic rhinitis can be classified into four categories: moderate/severe persistent, moderate/severe intermittent, mild persistent and mild intermittent.

This survey included questions about the severity of symptoms and the impact on daily life activities; moreover, it intended to assess the severity of Japanese cedar pollinosis according to PG-MARJ and ARIA and examine differences in their assessment.

**METHODS**

**SURVEY PERIOD**

The survey was conducted in the 8-day period from May 11 to May 18, 2011 when the pollen dispersal had almost ended.

**CONTRACTED RESEARCH COMPANY**

ANTERIO Inc. (Tokyo, Japan) was contracted to conduct the survey via INTAGE Inc. (Tokyo, Japan), a net monitor (Cue Monitor/Yahoo! Research Monitor).

**SUBJECTS**

Net monitors of INTAGE Inc. have been registered after strict proof of identity by sending a registration form to their home address. A broad range of attributes of monitors including their profile were collected at recruitment.

All monitors in the country, except those in Hokkaido and Okinawa where there are very few patients with Japanese cedar pollinosis, were screened to select those who met the following criteria:

1. Individuals who had potential symptoms of Japanese cedar pollinosis (e.g., sneezing, nasal discharge, nasal obstruction, itchy eyes and teary eyes) in the pollen season from February to May 2011.
2. Individuals who had experienced those symptoms for at least two pollen seasons.
3. Individuals who were not healthcare professionals or worked at a publicity agent or market research company, or had any family member, friend or acquaintance who was a healthcare professional or worked at a publicity agent or market research company.

**QUESTIONS**

The questionnaire consisted of questions that were prepared based on classifications in PG-MARJ and ARIA. Responses were used to assess the severity of the condition in each respondent according to PG-MARJ and ARIA separately. Generally speaking, Internet survey may be less reliable because the monitors themselves judge the degree of their illness. To deal with that problem, we made sure that the questions should be clear so that the monitors wouldn’t mistake the meaning.

Q1 When did you notice symptoms that could indicate pollinosis (e.g., sneezing, nasal discharge, nasal obstruction, itchy eyes and teary eyes)? Please mark all that apply.

   a) February 2011, b) March 2011, c) April 2011, d) May 2011
Q2 When did you visit a medical institution (e.g., hospital, clinic) for symptoms of pollinosis or for the treatment/prevention of pollinosis? Please mark all that apply.

Q3 Did you use any over-the-counter (OTC) drug (sold at a pharmacy or drug store) from February to May 2011 for symptoms of pollinosis?
a) Yes, b) No

Q4 How often did you experience each of the following symptoms in the period with the severest symptoms? Please select only one for each question.
(1) Sneezing (average number of episodes per day)
a) 21 or more, b) 11 to 20, c) 6 to 10, d) 1 to 5, e) None
(2) Nasal discharge (average number of blowing per day)
a) 21 or more, b) 11 to 20, c) 6 to 10, d) 1 to 5, e) None
(3) Nasal obstruction
a) Complete obstruction all day long
b) Very severe nasal obstruction with mouth breathing most of the time
c) Severe nasal obstruction with mouth breathing several times per day
d) Nasal obstruction without mouth breathing
e) No nasal obstruction

Q5 What was the average number of days per week with any symptoms of pollinosis?
a) 4 or more days per week on average, b) Less than 4 days per week on average

Q6 How long did the symptoms of pollinosis persist?
a) 4 consecutive weeks or longer, b) Less than 4 consecutive weeks

Q7 Did you have the following during the period with the severest symptoms?
(1) Sleep disorder
a) Yes, b) No
(2) Disturbance during daily life, leisure and/or sport activities
a) Yes, b) No
(3) Disturbance during school work or work
a) Yes, b) No
(4) Any bothersome symptom
a) Yes, b) No

RESULTS
DEMOGRAPHIC AND OTHER CHARACTERISTICS OF THE RESPONDENTS
In the Internet questionnaire survey conducted between May 11 and May 18, 2011, responses were obtained from 3382 monitors who had symptoms of pollinosis from February to May 2011 (e.g., sneezing, nasal discharge, nasal obstruction, itchy eyes and teary eyes) and who had experienced the symptoms for at least two pollen seasons. The mean age of the overall population was 38.2 years (range: 2 to 81 years). They comprised 1708 males (mean age: 39.3 years) and 1674 females (mean age: 37.1 years). Table 1 shows the distribution of the respondent population by age.

As for symptoms of pollinosis, 1655 respondents (48.9%) had presented the symptoms in February, 2804 (82.9%) in March, 2822 (83.4%) in April, and 1790 (52.9%) in May 2011 (respondents could have presented the symptoms in more than one period). A total of 1417 respondents (41.9%) visited a medical institution for symptoms of pollinosis or for the treatment/prevention of pollinosis between January and May 2011, while 1133 respondents (33.5%) did not visit any medical institution in that period but had visited one before and 832 respondents (24.6%) had never visited any medical institution. In addition, 1080 respondents (31.9%) used OTC drugs for symptoms of pollinosis.

SEVERITY ACCORDING TO PG-MARJ
Figure 1 shows the severity in the period with the severest symptoms in 3382 respondents: (1) sneezing (average number of episodes per day), (2) nasal discharge (average number of blowing per day) and (3) nasal obstruction (degree). Based on the severity of these three symptoms, the severity of rhinitis in each respondent was assessed using the five-grade classification of PG-MARJ. As a result, 795 respondents (23.5%) had severest rhinitis, 995 (29.4%) severe rhinitis, 1057 (31.3%) moderate rhinitis, 468 (13.8%) mild rhinitis and 67 (2.0%) asymptomatic rhinitis. In addition, the disease type was determined based on the combination of severity of sneezing, rhinorrhea and nasal blockage. The distribution of disease type in the 3382 respondents is shown in Table 2.
82.0% of the overall population had all three major symptoms (i.e., sneezing, rhinorrhea and nasal blockage). The severity by age group is shown in Figure 2.

**SEVERITY ACCORDING TO ARIA**

1) Disease type

   In the ARIA Guideline, the term “persistent” denotes presence of symptoms for ≥4 days per week and for ≥4 weeks, while the term “intermittent” denotes presence of symptoms for <4 days per week or for <4 weeks. The average number of days with the symptoms of pollinosis per week was ≥4 days in 2750 respondents (81.3%) and <4 days in 632 respondents (18.7%). The duration of the symptoms was ≥4 weeks in 2675 respondents (79.1%) and <4 weeks in 707 respondents (20.9%).

   Based on the above results, 2423 patients (71.6%) had persistent rhinitis (with symptoms for ≥4 days per week and for ≥4 weeks) and 959 patients (28.4%) had intermittent rhinitis.

2) Severity

   Figure 3 summarizes the presence of (1) sleep disorder, (2) disturbance during daily life, leisure and/or sport activities, (3) disturbance during school work or work and (4) any bothersome symptom during the period with the severest symptoms of pollinosis. According to ARIA, presence of any of these four conditions [ (1) to (4) ] is regarded as moderate/severe rhinitis, and absence of all of them as mild rhinitis. Based on the replies to these questions, 3079 respondents (91.0%) had moderate/severe rhinitis and 303 respondents (9.0%) had mild rhinitis.

3) When ARIA was applied to the above replies from 3382 respondents, 2274 respondents (67.2%) had moderate/severe persistent rhinitis, 805 (23.8%) moderate/severe intermittent rhinitis, 149 (4.4%) mild persistent rhinitis and 154 (4.6%) mild intermittent rhinitis. The distribution of the overall population by severity and age group is shown in Figure 4.

**PROPORTION OF RESPONDENTS VISITING A MEDICAL INSTITUTION**

The proportion of respondents visiting a medical institution was calculated for each degree of severity determined separately according to PG-MARJ and ARIA. In the overall population, 41.9% of the respondents visited a medical institution for symptoms of suspected pollinosis between January and May 2011, while 33.5% did not during that period but had visited a medical institution before. Thus, 75.4% had visited a medical institution regardless of the time and 24.6% had never visited one. As shown in Figure 5, respondents were more likely to have visited a medical institution as the severity level according to PG-MARJ increased. However, approximately 20% of the respondents with severest or severe rhinitis had never visited a medical institution for pollinosis. On the other hand, respondents considered to have persistent rhinitis according to ARIA were more likely to have visited a medical institution than those considered to have intermittent rhinitis, as shown in Figure 6. In the overall population, 31.9% used OTC drugs between February and May 2011. Of the 1417 respondents who visited a medical institution between January and May 2011, 17.3% used OTC drugs in contrast to 48.2% of the 1133 respondents who did not visit any medical institution during the same period but who had visited a medical institution before and 34.7% of the 832 respondents who had never visited any medical institution.

**CORRELATION OF SEVERITY ASSESSMENT BETWEEN PG-MARJ AND ARIA**

Figure 7 shows the severity classification according to ARIA for subgroups of respondents defined according to PG-MARJ (i.e., severest, severe, moderate, mild and asymptomatic). As a result, 79.7% of 468 respondents considered to have mild rhinitis and 67.2% of 67 respondents considered to have asymptomatic rhinitis according to PG-MARJ had moderate/severe
Severity Assessment by PG-MARJ & ARIA

AGREEMENT OF SEVERITY ASSESSMENT BETWEEN ARIA AND PG-MARJ

Respondents were grouped by severity according to PG-MARJ and ARIA into the following four categories: ARIA mild rhinitis and PG-MARJ severest/severe/moderate rhinitis, ARIA severe/moderate rhinitis and PG-MARJ mild/asymptomatic rhinitis, ARIA mild rhinitis and PG-MARJ mild/asymptomatic rhinitis, and ARIA severe/moderate rhinitis and PG-MARJ severest/severe/moderate rhinitis.

Thus, 117 respondents (3.5%) had mild/asymptomatic rhinitis according to both guidelines and 2661 respondents (78.7%) had moderate or more severe rhinitis. On the other hand, 418 respondents (12.4%) who had moderate/severe rhinitis according to ARIA had mild/asymptomatic rhinitis according to PG-MARJ, while 186 respondents (5.5%) who had mild rhinitis according to ARIA had moderate or more severe rhinitis according to PG-MARJ. This means that severity assessment by the two guidelines did not agree in 17.9% of the respondents. The distribution of the four categories by age group is shown in Figure 8. The disagreement rate was higher in the age group of <10 years (25.3%) and that of ≥60 years (22.0%).

DISCUSSION

In order to determine the severity of symptoms in patients with springtime pollinosis, an Internet questionnaire survey was conducted between May 11 and May 18, 2011 when the cedar and cypress pollen dispersal season (from February to early May) had already ended, in individuals who had symptoms of pollinosis in the current pollinosis season and who had experienced those symptoms for at least two pollen seasons.

In Japan, the Practical Guideline for the Management of Allergic Rhinitis in Japan (PG-MARJ) was first established in 1993 to improve treatment for al-
Allergic rhinitis and now the 2009 revised version (Version 6) is being widely used.\textsuperscript{2,4,5} The classification of severity in this guideline was used to assess the symptoms in the current season in each of the survey respondents. As a result, more than half of the respondents were considered to have severest or severe rhinitis and more than 80% to have moderate or more severe rhinitis. Severest or severe rhinitis was most prevalent in the respondents in their 20s and 30s (approximately 60%). In addition, more than 80% of all respondents had the three major symptoms (i.e., sneezing, rhinorrhea and nasal blockage). Approximately 2% of the respondents were considered to have asymptomatic rhinitis. Probably because the PG-MARJ classification of severity depends on the three major symptoms and does not take into account eye symptoms (itchy eyes and teary eyes), respondents who had eye symptoms alone may have been deemed to have asymptomatic rhinitis.

According to ARIA, due to symptoms of pollinosis, approximately one third of the respondents complained of sleep disorder, about half complained of disturbance during daily life, leisure and/or sport activities or school/work, and more than 80% complained of bothersome symptoms. According to ARIA, approximately 90% of the respondents had moderate/severe rhinitis and approximately 10% had mild rhinitis. Based on the duration of symptoms, ap-
approximately 70% of the respondents had persistent rhinitis and approximately 30% had intermittent rhinitis. Based on the combination of disease type and severity, 2274 respondents (67.2%) had moderate/severe persistent rhinitis, 805 (23.8%) moderate/severe intermittent rhinitis, 149 (4.4%) mild persistent rhinitis and 154 (4.6%) mild intermittent rhinitis. The analysis by age group indicated that younger respondents were less likely to have persistent rhinitis but more likely to have intermittent rhinitis.

It was naturally expected that the distribution of severity would vary among different causal antigens and among different geographical regions. A survey conducted in Europe where ARIA has been widely used reported that the proportion of mild intermittent, mild persistent, moderate/severe intermittent and moderate/severe persistent rhinitis was 10%, 14%, 17% and 59%, respectively. This result showed less imbalance in different severity classes compared to the result of the present survey of Japanese cedar pollinosis. However, it has been reported that 90% of the patients seen at medical institutions had moderate/severe rhinitis as is the case in the present survey. This means that the results may vary depending not only on antigens and geographical regions but also on the type of medical institutions where patients are seen. In the present survey, 41.9% of the 3382 respondents visited a medical institution between January and May 2011 and 17.3% used OTC drugs, while 42.5% did not visit any medical institution in the current pollen season and more than 40% of them used OTC drugs. Moreover, approximately 40% of the re-
Respondents who used OTC drugs experienced drowsiness as a side effect (data not shown). The mainstream OTC oral drugs for the relief of pollinosis symptoms include first- and second-generation antihistaminics, which may cause drowsiness. The first-generation antihistaminics, which may cause severe drowsiness and dizziness and have a strong anticholinergic effect, are contraindicated in patients with glaucoma, benign prostatic hypertrophy and asthma. Concomitant use of other medications for the treatment of concurrent diseases or use of such OTC drugs without the supervision of a physician by patients who are engaged in driving or potentially hazardous activities is extremely dangerous and may cause decreased operating efficiency even during non-hazardous work or decreased academic performance. The results of the present survey indicate that it is necessary to improve awareness concerning allergic rhinitis (especially pollinosis) in the general public.

Severity assessment according to PG-MARJ and ARIA revealed higher prevalence of ARIA-defined persistent rhinitis and moderate/severe rhinitis in individuals with severer disease according to PG-MARJ. This result indicates a positive correlation between the two guidelines. However, as high as approximately 80% and 70% of the respondents considered to have mild and asymptomatic rhinitis, respec-
tively, according to PG-MARG were deemed to have moderate/severe rhinitis according to ARIA. The disagreement rate of the severity assessment was approximately 18% in the overall population. The analysis by age group revealed higher disagreement rates of approximately 25% and 22% in the age group of <10 years and in that of ≥60 years, respectively. Probably because the severity classification in ARIA depends mainly on the impact on the quality of life (QOL) of patients, patients who had only mild symptoms but felt a large impact on daily life activities were likely to be classified as having moderate or more severe rhinitis. The classification in ARIA, which uses “presence or absence of bothersome symptoms” alone to assess the severity of nasal symptoms, may not accurately reflect the degree of nasal symptoms themselves.

The results of the present survey indicated that the majority of patients with Japanese cedar pollinosis had severe disease: more than 80% of the individuals who had symptoms of pollinosis during the current pollinosis season had moderate or more severe rhinitis according to PG-MARJ and more than 90% moderate/severe rhinitis according to ARIA. The classification system of ARIA may provide an incorrect diagnosis of severity since it may classify patients with severe nasal symptoms as having mild rhinitis. On the contrary, PG-MARG, which has been prepared based on the real conditions of allergic rhinitis in Japan, is considered to be a useful guideline in clinical practice.

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REFERENCES