Patterns of Drug Prescription for Japanese Cedar Pollinosis Using a Clinical Vignette Questionnaire

Goro Takahashi1, Zensei Matsuzaki1, Takeo Nakayama2 and Keisuke Masuyama1

ABSTRACT

Background: Although prescribed drugs directly affect patient outcome, the variation in physicians’ attitudes towards drug therapy for cedar pollinosis has not been quantitatively assessed. This research investigated the prescription patterns of drugs for cedar pollinosis by ear, nose, and throat specialists (ENTs), general physicians (GPs) and internal medicine doctors (IMs) in Yamanashi Prefecture, Japan.

Methods: A cross-sectional study was conducted by mailing questionnaires to 532 physicians in autumn 2006. The main part of the questionnaire constituted clinical vignettes of pollinosis cases with nasal and ocular symptoms ranging from mild to severe. We requested that the physicians fill out prescription medications they considered appropriate for each vignette.

Results: Responses from 172 physicians (32%) for six clinical vignettes were analyzed. The number of drugs prescribed by ENTs was significantly higher than that by GPs and IMs for vignettes representing moderate to severe cases ($p < 0.004$). The percentage of physicians who said they would prescribe nasal corticosteroid and eye drops was higher in the ENT group compared to the other two groups in these vignettes. In terms of second-generation antihistamines, no differences were observed between the three groups for all vignettes.

Conclusions: Our investigation suggested that, compared to ENTs, GPs and IMs have a lower tendency to concomitantly prescribe drugs for localized treatment such as nasal corticosteroids and eye drops with oral medication. There may be differences in prescription patterns of drugs for pollinosis between ENTs and non-specialist physicians.

KEY WORDS

allergic rhinitis, guideline, Japan, physician’s practice patterns, questionnaires

INTRODUCTION

Allergic rhinitis is not a life-threatening illness, nevertheless patients suffer from highly uncomfortable symptoms that disrupt the quality of everyday life and productivity of academic or professional work.1 Symptoms of cedar pollinosis begin to appear around February to March every year, and it is the most common type of seasonal allergic rhinoconjunctivitis in Japan. According to a nationwide epidemiological study, the prevalence of Japanese cedar pollinosis is estimated to be 13%. However, recent studies based on statistical analyses predict potential annual increases in this figure.2,3 Such high figures demonstrate that Japanese cedar pollinosis is indeed a large problem in society.

In recent years, variation in the medical practice of physicians has been the subject of research across many clinical fields, from the perspective of the quality of healthcare.4-7 When considering the huge impact cedar pollinosis has on society, it is important to research the variations in medical practice for this particular illness, especially with regard to the patterns of drug prescription.

Currently, nasal corticosteroid drops are considered to be the first-line drug for patients with moderate to severe allergic rhinitis.1 However, a cross-sectional study has suggested that, in actuality, the
prescription of nasal corticosteroids by general physicians may be limited.8 According to Demoly et al. whose research involved patients and general physicians, oral antihistamines were prescribed for 92% of the patients, whereas only 45% were prescribed nasal steroids.8 Similarly, a patient survey conducted in Japan by Okuda et al. revealed a higher tendency of general physicians to singly prescribe oral medication compared to otolaryngologists.30 Furthermore, Van Hoecke et al. have shown with reference to the Allergic Rhinitis and its Impact on Asthma (ARIA) guideline that 30% of medicines prescribed by general physicians for moderate or severe persistent allergic rhinitis patients were considered as undertreatment.10 This is a problem concerning compliance with the guidelines for drug therapy. However, additional research conducted in, these previous studies on clinically prescribed medication that are often influenced by many factors such as the patients’ clinical conditions, personal values, healthcare environments, medical resources and annual variance in antigen levels suggest that it is not appropriate to interpret the results simply as patterns of decision-making processes or patterns of drug prescription by individual physicians.

To date, the prescription patterns of drugs for cedar pollinosis have not been investigated. In this study, we have investigated such prescription patterns by Japanese physicians under the hypothesis that general physicians depend less on nasal steroids than otolaryngologists.

Traditionally, this type of research has been conducted using methods such as assessments involving simulated patients, or by reviewing medical records. Recently, the validity and advantages of using clinical vignettes for such research have been shown, and this is now becoming a method of interest.12,13

The aim of this research is to compare the prescription patterns of drugs for cedar pollinosis by ear, nose, and throat specialists (ENTs), general physicians (GPs) and internal medicine doctors (IMs) in Yamanashi Prefecture, Japan.

METHODS

RESEARCH DESIGN, SETTINGS AND SUBJECTS

This research was designed as a cross-sectional study carried out using mailed questionnaires. Subjects were ENTs, GPs and IMs working in Yamanashi Prefecture. The exact number of subjects was unknown at the time of this study, although there were 59 ENTs and 491 physicians (total number of GPs and IMs) in 2004 according to a report by the Ministry of Health, Labour and Welfare.14

QUESTIONNAIRE DESIGN

The questionnaire was constructed by three ENTs. It consisted of questions regarding 1) occupational background of the subjects, 2) medical consultation for allergic rhinitis, and 3) clinical vignettes for cedar pollinosis. In principle, questionnaires were answered anonymously and were self-completed. For each vignette, the most effective prescribed medication was decided by the subjects and noted together with any co-administered drugs or required medication.

RESEARCH METHODS

The names and addresses of 53 ENTs, 214 GPs and 265 IMs were found individually by searching through phone books and the Internet. Questionnaires were mailed to them on October 10, 2006. Reminders were sent twice thereafter and the questionnaires were collected by November 10, 2006. This research was conducted upon the approval of the Ethics Review Board of the University of Yamanashi Hospital.

STATISTICAL ANALYSIS

Background factors of the subjects were presented descriptively. Responses for six clinical vignettes were analyzed (Appendix). The names of prescribed medication given for each vignette were categorized and sorted into second-generation antihistamines, oral steroids, antileukotrienes, other oral medication (first-generation antihistamines, Chinese herbal medicines, chemical mediator release inhibitors etc.), nasal corticosteroid drops, non-steroidal anti-allergy nasal drops (antihistamines, chromones etc.), nasal vasoconstrictive agents and eye drops (steroids, anti-histamines, chromones etc.). Fexofenadine hydrochlorides and loratadins that were not accompanied with a product leaflet containing information on precautions for vehicular driving were categorized as non-sedative antihistamines, and analysis was carried out accordingly.

The Kruskal-Wallis test was used to compare the number of prescribed medications between the 3 groups of prescribers for each vignette. The significance level was used according to the method by Bonferroni at $\alpha = 0.008$ (two-tailed). This test was carried out for the null hypothesis: there was no difference in the number of prescribed medications between the 3 groups. For vignettes where the null hypothesis was rejected, analysis was repeated using a Mann-Whitney test between the 2 groups using a two-tailed significance level of $\alpha = 0.004$, again using the Bonferroni method.

Furthermore, for each type of drug and for each vignette, both the percentage of physicians who prescribed the drug and its 95% confidence intervals (or one-sided 97.5% confidence interval) were used to compare the 3 groups.

All statistical analyses were performed in Stata version 9.2 (StataCorp, College Station, Tx, USA).
Prescribing Pattern for Cedar Pollinosis

Table 1  Characteristics of physicians included in the survey

<table>
<thead>
<tr>
<th></th>
<th>ENT</th>
<th>GP</th>
<th>IM</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>n = 45</td>
<td>n = 72</td>
<td>n = 55</td>
</tr>
<tr>
<td>Male, no. (%)</td>
<td>39 (87)</td>
<td>68 (94)</td>
<td>48 (87)</td>
</tr>
<tr>
<td>Years since graduation from medical school, median (IQR)</td>
<td>20 (14–27)</td>
<td>25 (20–33)</td>
<td>13 (8–20)</td>
</tr>
<tr>
<td>Physicians with a solo practice, no. (%)</td>
<td>24 (53)</td>
<td>56 (78)</td>
<td>3 (5)</td>
</tr>
<tr>
<td>Greatest number of pollinosis patients per day examined in the Japanese cedar pollinosis season of 2006, no. (%)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>1–10</td>
<td>7 (16)</td>
<td>0 (0)</td>
<td>42 (76)</td>
</tr>
<tr>
<td>11–30</td>
<td>16 (36)</td>
<td>45 (63)</td>
<td>10 (18)</td>
</tr>
<tr>
<td>31–50</td>
<td>3 (7)</td>
<td>25 (35)</td>
<td>2 (4)</td>
</tr>
<tr>
<td>51–</td>
<td>19 (42)</td>
<td>1 (1)</td>
<td>1 (2)</td>
</tr>
<tr>
<td>Unknown</td>
<td>0 (0)</td>
<td>1 (1)</td>
<td>0 (0)</td>
</tr>
<tr>
<td>Usefulness of Japanese practical guideline for AR in the Japanese cedar pollinosis season of 2006, no. (%)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Very useful</td>
<td>12 (27)</td>
<td>11 (15)</td>
<td>11 (20)</td>
</tr>
<tr>
<td>Useful</td>
<td>27 (60)</td>
<td>51 (71)</td>
<td>27 (49)</td>
</tr>
<tr>
<td>Neutral</td>
<td>5 (11)</td>
<td>2 (3)</td>
<td>4 (7)</td>
</tr>
<tr>
<td>Not useful</td>
<td>0 (0)</td>
<td>0 (0)</td>
<td>0 (0)</td>
</tr>
<tr>
<td>Not useful at all</td>
<td>0 (0)</td>
<td>0 (0)</td>
<td>0 (0)</td>
</tr>
<tr>
<td>No experience of use</td>
<td>1 (2)</td>
<td>7 (10)</td>
<td>13 (24)</td>
</tr>
<tr>
<td>Unknown</td>
<td>0 (0)</td>
<td>1 (1)</td>
<td>0 (0)</td>
</tr>
</tbody>
</table>

ENT, ear, nose, and throat specialists group; GP, general physicians group; IM, internal medicine doctors group; IQR, interquartile range.

RESULTS

Questionnaires were collected from 186 physicians (response rate 36%). Fourteen questionnaires in total were excluded from the analysis; this included 1 ENT, 2 GPs and 5 IMs who left the clinical vignettes blank and 6 IMs who did not examine pollinosis patients during the 2006 cedar pollen season. Overall, responses were received from 172 (32%) physicians consisting of 45 ENTs, 72 GPs and 55 IMs, and were included in the statistical analysis.

BACKGROUND OF SUBJECTS

The ENT and GP groups compared with the IM group demonstrated a trend in seeing a larger number of cedar pollinosis patients each day. Furthermore, approximately 70% of subjects in all groups approved of the validity of the Practical Guideline for the Management of Allergic Rhinitis in Japan (PGMARJ) (Table 1).15

REPORTED NUMBER OF PRESCRIBED DRUGS FOR EACH VIGNETTE

The number of drugs reported by physicians that they would prescribe was compared among the 3 groups for each vignette. The drugs that were included in the count were oral drugs, nasal drops, eye drops, co-administered drugs and other required medication. For vignettes 3 to 6, the numbers given by ENTs were significantly higher than for GPs and IMs (p<0.004) (Fig. 1).

TRENDS IN DRUG PRESCRIPTION FOR EACH TYPE OF DRUG

When comparing the percentage of physicians who reported prescribing second-generation antihistamines using the 95% confidence interval, no differences could be observed among the 3 groups for all vignettes (Fig. 2A).

The percentage of physicians who reported prescribing non-sedative antihistamines was as high as 66% (95% CI: 51%–80%) in the ENT group and 64% (95% CI: 52%–75%) in the GP group, compared with 40% (95% CI: 27%–54%) in the IM group for vignette 2 (data not shown). For all other vignettes, the percentage for non-sedative antihistamines was approximately 25% for all groups.

When the percentage of physicians who reported prescribing nasal corticosteroid drops were compared using a 95% confidence interval, an increasing trend in percentages was found with increasing severity of symptoms in all 3 groups (Fig. 2B). In vignettes 4 to 6, this percentage was clearly higher in the ENT group compared to the other 2 groups.

Comparison of the percentage of physicians who prescribed eye drops using 95% confidence intervals for vignettes 3 to 5 revealed that the percentage in the ENT group was clearly much higher than in the
Fig. 1 Box and whisker plots of the number of prescription drugs by ear, nose, and throat specialists (ENTs), general physicians (GPs), and internal medicine doctors (IMs) for each vignette. The vertical bars indicate the range from lower to upper adjacent values. The horizontal boundaries of the boxes represent the first and third quartiles. The thick bars in the boxes indicate medians. NS means, -not statistically significant. *,  \( p < 0.004 \).

For vignette 6, oral steroids were prescribed by 56% (95% CI: 40%−70%) of the ENT group and 45% (95% CI: 33%−57%) of the GP group, but was lower at 21% in the IM group (95% CI: 11%−34%). For all other vignettes, the percentage for oral steroids prescribed was below 20% in all 3 groups.

As for the percentage of physicians prescribing antileukotrienes and vasoconstrictive agents, there were no significant differences among the 3 groups for all vignettes.

POSSIBLE UNDERTREATMENT BY COMPARISON WITH GUIDELINES

In addition, we analyzed the possibility of some prescription patterns to be considered as undertreatment, by referring to the ARIA or PG-MARJ medical practice guidelines.\(^1\)\(^,\)\(^15\) The criteria for classifying rhinitis and assessment of severity differs extensively between the 2 guidelines. The cedar pollen season in Japan lasts for approximately 2 months, and according to the ARIA, most cedar pollinosis patients will be classified as patients with persistent allergic rhinitis. According to the PG-MARJ, however, the severity of pollinosis is classified into 4 types: mild, moderate, severe, or most severe, on the basis of a patient’s nasal symptoms and QOL grading. In the 2 guidelines, it is recommended to use nasal steroids as the first-choice either singularly or concomitantly for persistent moderate/severe allergic rhinitis or moderate/severe/most severe pollinosis. With reference to the above, we analyzed the answers given for vignettes 4 to 6 which represent severe cases and identified those that could potentially be considered as undertreatment.

For vignette 4 which includes severe rhinorrhea and sneezing symptoms, the prescription decided by 33% of physicians in the ENT group, 64% in the GP and 65% in the IM groups could be considered as undertreatment. For vignette 5 which includes severe nasal congestion, possible undertreatment could be identified in 13% of the ENT group, 37% of the GP group and 57% of the IM group. For vignette 6 which involves a case of severe overall symptoms, possible undertreatment could be identified for 4% of the ENT group, 25% of the GP group and 43% of the IM group (Table 2).
DISCUSSION

In this study we analyzed and compared for the first time the prescription patterns of drugs for cedar pollinosis between physicians classified as ENTs, who are specialists, and GPs and IMs through the use of clinical vignettes. The research purpose for using clinical vignettes was not to test the knowledge of physicians, but to analyze how the physicians would prescribe medication if they encountered such patients in real life as described by the vignettes. Because responses are likely to be biased in many ways, it is important to analyze the responses given by a strictly defined group of physicians rather than that of individuals. Recent studies have confirmed the validity of clinical vignettes by comparing them with simulated patient studies. Clinical vignettes are advantageous in that they are more cost effective and practical compared to simulated patients, and most of all, the problem of case-mix that occurs during medical record reviews can be regulated.

In Japan, many cedar pollinosis patients consult otolaryngologists and general physicians. According to past research conducted on the trend of medical consultation for cedar pollinosis patients, 40% consulted otolaryngologists and 30% consulted general physicians, and when questioned about the type of medical institutions visited, 90% of patients consulted clinics. Our questionnaire has confirmed that larger numbers of cedar pollinosis patients consult ENTs and GPs compared to IMs.

Our results suggest that the most obvious differences in the prescription patterns for cedar pollinosis between ENTs, GPs and IMs are those of nasal corticosteroid drops and eye drops. In actuality, many factors including the patients themselves, features of the medical institution and the amount of airborne pollen present in a given season will affect the decision on drug prescription. Therefore, information obtained from our clinical vignettes is insufficient for use by our respondents. It may be that our results here do not represent the trends occurring in the prescription of drugs in actual clinical settings. However, our research does not focus on how well our results reflect true clinical settings, but on discovering any differences in the prescription patterns of ENTs, GPs and IMs for the same given clinical cases. What is important here is the fact that the differences discovered in the prescription patterns among the 3 groups are clearly reflected by the differences in the percentage of physicians prescribing nasal corticosteroid drops and eye drops. In order to improve the quality of cedar pollinosis treatment, it will be extremely necessary to identify the reasons why GPs tend to be reluctant in prescribing nasal corticosteroid drops and eye drops to patients with moderate/severe symptoms. This is intriguing since these GPs in particular examine a stable fraction of patients and understand the effectiveness of the guidelines. The reasons for reluctance may be that they are afraid of systemic side-effects triggered by steroids, or because patients who consult GPs often have complications and are already taking medication. Nevertheless, the clinical vignettes used here were designed so that complica-

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**Fig. 2** Percentage of physicians prescribing each type of drug for each vignette in the 3 groups by ear, nose, and throat specialists (ENTs), general physicians (GPs), and internal medicine doctors (IMs). The black circles indicate the simple percentages. The two-tailed bars represent the 95% confidence intervals of the percentages. The one-sided bars represent the 97.5% confidence intervals of the percentages. A: Second-generation antihistamines. B: Intra-nasal corticosteroids. C: Antiallergic eye drops.
Table 2  Potential undertreatment of Japanese cedar pollinosis according to the Allergic Rhinitis and its Impact on Asthma guideline or the Practical Guideline for the Management of Allergic Rhinitis in Japan recommendations

<table>
<thead>
<tr>
<th>Vignette 4</th>
<th>Vignette 5</th>
<th>Vignette 6</th>
</tr>
</thead>
<tbody>
<tr>
<td>ENT</td>
<td>GP</td>
<td>IM</td>
</tr>
<tr>
<td>n=45</td>
<td>n=69</td>
<td>n=52</td>
</tr>
<tr>
<td>AH</td>
<td>12 (27)</td>
<td>29 (42)</td>
</tr>
<tr>
<td>AL</td>
<td>0 (0)</td>
<td>0 (0)</td>
</tr>
<tr>
<td>OOt</td>
<td>0 (0)</td>
<td>6 (9)</td>
</tr>
<tr>
<td>NsANS</td>
<td>0 (0)</td>
<td>0 (0)</td>
</tr>
<tr>
<td>ND</td>
<td>0 (0)</td>
<td>0 (0)</td>
</tr>
<tr>
<td>AH + AL</td>
<td>0 (0)</td>
<td>0 (0)</td>
</tr>
<tr>
<td>AH + OOt</td>
<td>1 (2)</td>
<td>6 (9)</td>
</tr>
<tr>
<td>AH + NsANS</td>
<td>2 (4)</td>
<td>2 (3)</td>
</tr>
<tr>
<td>AH + ND</td>
<td>0 (0)</td>
<td>1 (1)</td>
</tr>
<tr>
<td>AL + ND</td>
<td>0 (0)</td>
<td>0 (0)</td>
</tr>
</tbody>
</table>

Number of physicians, (%); ENT, ear, nose, and throat specialists group; GP, general physicians group; IM, internal medicine doctors group; AH, second-generation antihistamines; AL, antileukotriens; OOt, other oral medications (e.g. first-generation antihistamines, herbal medications, etc); NsANS, nonsteroid antiallergic nasal spray; ND, nasal decongestants.

Our study has several limitations. The first is that our research was not conducted during the cedar pollen season. Decisions made by physicians and its patterns may have been elicited more accurately by our vignettes if the research was conducted immediately after the end of the pollen season. Secondly, because our research was based locally in Yamanashi Prefecture, it is somewhat difficult to extend the implications of our results to a nationwide scale. Thirdly, this research was limited by the low response rate of GPs and IMs, who are non-specialist physicians. The motivation of respondents directly influences the quality of responses when using the clinical vignette method. From this standpoint, although the response rate of the GPs and IMs were 33% and 21%, respectively, it can be suggested that those who kindly responded to this complicated vignette method possessed sufficient motivation. Thus, reliability of the results from these physicians can be considered as high. Furthermore, it may be possible to speculate that GPs/IMs who did not respond, compared to those who did, are consulting the guidelines insufficiently, are prescribing simple medication such as oral medicine and have a higher potential for the undertreatment of patients. If these non-respondent physicians could be included in the statistical analysis, the difference between the prescription patterns found between ENTs and the other 2 groups might become clearer.

To conclude, our investigation of the drug prescription patterns for cedar pollinosis in Yamanashi Prefecture has shown that compared to ENTs, GPs and IMs have a lower tendency to concomitantly prescribe drugs for topical treatment such as nasal corticosteroids and eye drops with oral medication.

ACKNOWLEDGEMENTS

We gratefully acknowledge the assistance of Dr. Toshio Inoue and Dr. Kazuya Shimada. This research was funded by the University of Yamanashi Start-up Project (2006).
APPENDIX

For the clinical vignettes shown below, please fill out the names of medications that you feel are most appropriate to prescribe.

A: Vignette 1 & 2

The amount of airborne cedar pollen is expected to be normal this season. The patient is a 34-year-old man who has visited with a major complaint of nasal symptoms which started 5 days previously. The visit was made 7 days after the beginning of cedar pollen dispersal. He mentions that he did not experience similar nasal symptoms at this time the previous year. Following medical tests and examinations, he was given a diagnosis of new-onset cedar pollinosis. He has no history of other allergies.

Vignette 1

The occupation of this patient is a clerical worker. The symptoms of rhinorrhea, sneezing and nasal congestion are all mild, and no symptoms involve the eyes.

Vignette 2

The occupation of this patient is a taxi driver. The symptoms of rhinorrhea, sneezing and nasal congestion are all mild, and no symptoms involve the eyes.

B: Vignettes 3-6

The amount of airborne cedar pollen is expected to be normal this season. The patient is a 34-year-old man who has visited with a major complaint of nasal symptoms which started 7 days previously. The visit was made 10 days after the beginning of cedar pollen dispersal. The level of airborne cedar pollen is estimated to reach its peak 1 week after his visit. He had been experiencing similar nasal symptoms around this time for the past several years, and apparently had medication prescribed by other clinics, although details are unknown. Following medical tests and examinations, he was given a diagnosis of cedar pollinosis. He has no history of other allergies.

Vignette 3

The occupation of this patient is a clerical worker. The symptoms of rhinorrhea, sneezing and nasal congestion are moderate, and symptoms involving the eyes are mild.

Vignette 4

The occupation of this patient is a clerical worker. The symptoms of rhinorrhea, sneezing are severe, but nasal congestion is mild. Symptoms involving the eyes are mild.

Vignette 5

The occupation of this patient is a clerical worker. The symptoms of rhinorrhea and sneezing are mild, but nasal congestion is severe. Symptoms involving the eyes are mild.

Vignette 6

The occupation of this patient is a clerical worker. The symptoms of rhinorrhea, sneezing and nasal congestion are all severe. Symptoms involving the eyes are also severe.

REFERENCES