Unmet Primary Physicians' Needs for Allergic Rhinitis Care in Korea

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Allergic rhinitis (AR) is one of the most common chronic allergic respiratory diseases worldwide. Various practical guidelines for AR have been developed and updated to improve the care of AR patients; however, up to 40% patients remain symptomatic. The unmet need for AR care is one of the greatest public health problems in the world. The gaps between guideline and real-world practice, and differences according to the region, culture, and medical environments may be the causes of unmet needs for AR care. Because there is no evidence-based AR practical guideline reflecting the Korean particularity, various needs are increasing. The purpose of the study was to evaluate whether existing guidelines are sufficient for AR patient management in real practice and whether development of regional guidelines to reflect regional dif-
INTRODUCTION

Allergic rhinitis (AR) is one of the most common chronic allergic respiratory diseases worldwide. Although AR is not a life-threatening disease, it causes a significant healthcare problem through the chronic, and relapsing characteristics, inducing poor quality of life and school/work loss.\(^1\,^2\) The impact of AR on the social, professional, and educational performance has been recognized; furthermore, AR in childhood leads to socioeconomic inequalities.\(^3\) Therefore, early diagnosis and adequate management of AR have been highlighted to achieve healthy aging.

The prevalence of AR has progressively increased over the last 3 decades in developed countries including Korea, and has been estimated approximately 40% in the world population. The nation-wide prevalence of AR in Korea has varied with 28% in 2008 based on the questionnaire alone, and 16.2% in 2010 based on the questionnaire, examination, and test for atopic sensitization.\(^4,^5\) The Korean National Health Insurance Corporation reported an increased trend of medical care-use associated with AR, approximately 4.28 million cases in 2007 (10th ranked prevalent chronic disease) to 6.35 million cases in 2014 (fifth ranked prevalent chronic disease).\(^6\) The direct and indirect costs related with AR have been estimated at $223.68 million and $49.25 million, respectively, in 2007.\(^7\)

Practical guidelines, proposed by Allergic Rhinitis and its Impact on Asthma (AIRA),\(^8\) and Academy of Otolaryngology-Head and Neck Surgery,\(^9\) recommended evidence-based management. However, up to 40% of patients with AR remain symptomatic.\(^10\) Although international practical guidelines are well established, unmet needs for AR care still exist in real-world practice. The existing guidelines were developed on the basis of evidence from randomized controlled trials (RCTs). RCTs would be the best way to assess the effect size under the high-quality design. However, they cannot answer every clinical question in the real-practice.\(^3\) Furthermore, existing guidelines do not reflect the characteristics of Korean patients because these guidelines are based on Western populations. Therefore, unmet needs in the clinical practice of AR should be evaluated.

The purpose of the study was to identify the needs for AR care of primary physicians to manage AR patients in Korea and to evaluate needs on the development of new guidelines reflecting the clinical features of Korean patients.

MATERIALS AND METHODS

A questionnaire-based survey was conducted through e-mail, among a total of 99 clinic based primary physicians consisting of internal medicine (IM), otorhinolaryngology (ORL), and pediatrics (PD) groups (each 33) between June 2 and June 16 of 2014.

Questionnaire development

The questionnaire was developed by the collaborative working group comprising allergists in the departments of IM, ORL, and PD; and the Allergic Rhinitis Work Group (ARWG) in the Korean Academy of Asthma, Allergy and Clinical Immunology (KAAACI). It was based on the free-text questions arising from primary physicians in the clinic-based, real practice. A total of 117 free-text questions were collected and reviewed by the expert panel of ARWG, and consequently developed as 39 questions relating to the respondents’ agreement or disagreement with the existing practical guidelines for the diagnosis, treatment, and prevention of AR. The questionnaire-items were uncategorized and shuffled to minimize the proximity effects. The questionnaire asked “Do you agree that the existing guidelines unclearly answer the following question, and do you need development of a new practical-guideline reflecting real practice?” Each questionnaire item was rated on a 5-point Likert scale from 1 to 5 where 1= strongly disagree, 2= disagree, 3= unsure, 4= agree, and 5= strongly agree.

Statistical analysis

To select items that showed overall high agreement, the responses were presented as mean and standard deviation (SD) and assessed by the average deviation index AD_{med}. The AD_{med} index proposed by Burke and Dunlap\(^11\) provided a clear rationale for defining acceptable levels of interrater agreement on a 5-point Likert scale for values of ≤0.833. We separated the responses into agreement, no opinion, and disagreement. Agreement was the responders choosing 4 (agree) or 5 (strongly agree), and disagreement was considered present if the responders choosing 2 (disagree) or 1 (strongly disagree) for each statement. Therefore, the items were divided into 3 subgroups, including consensus items, polarized items, and neither consensus nor controversy. The criteria of categorized items were follows: (1) consensus items were defined as <25% of respond-
ers indicating neutral opinion and the percentage of agreement was at least 4 times as large as that of disagreement; (2) polarized items were defined as >30% of responders indicating agreement and also disagreement; and (3) neither consensus nor controversy was defined as not included in the consensus or the polarized items. All statistical analyses were performed using R 3.1.3 version (R Foundation for Statistical Computing, Vienna, Austria) and SPSS 14.0 version (SPSS Inc., Chicago, IL, USA).

RESULTS

Of the 39 items, there were 20 "consensus items" (51.3%), 17 "neither consensus nor controversy items" (43.6%), and 2 polarized items (5.1%). Fifteen of the 20 consensus items with $\text{AD}_{\text{med}} \leq 0.833$, showed strong interrater agreement, and the remaining 5 items showed poor agreement ($\text{AD}_{\text{med}} > 0.833$). However, all the proportion of agreement for these items was approximately 70% (Table 1). Table 2 summarizes the proportion of agreement and the value of $\text{AD}_{\text{med}}$ in each specialty-group, respectively, and the specialty-agreement gap. Among 20 consensus items, 15 (Q1-15) showed the overall agreement. However, only 5 items (Q1-5) showed no specialty-specific agreement gaps (each $\text{AD}_{\text{med}} \leq 0.833$), the others did not. The Q1-5 consensus items for AR diagnosis that included the minimum test battery of allergens for AR diagnosis, differential diagnosis with non-AR with eosinophilia syndrome or non-AR, and allergen differences by age, season, and area, showed strong agreement on the lack of guidance in the existing guidelines ($\text{AD}_{\text{med}}$: Q1, 0.53; Q2, 0.48; Q3, 0.59; Q4, 0.55; Q5, 0.54) without specialty-specific agreement gaps. However, Q6-7 for the diagnostic value of allergy test and implications of food sensitization showed weak agreement ($\text{AD}_{\text{med}}$: Q6, 0.83; Q7, 0.74) with a specialty-specific agreement gap. The gap was more prominent in PD group than in the IM and OR (Q6-7 $\text{AD}_{\text{med}}$: PD group, 0.60, 0.55; ORL group, 0.83, 0.97; IM group, 0.95, 0.74).

Only 3 items for the second-generation antihistamines, effectiveness of immunotherapy, and effectiveness of sinus irrigation showed overall poor agreement without specialty-specific agreement gaps ($\text{AD}_{\text{med}}$: Q21, 0.98; Q34, 0.84, Q37, 1.02). Twenty-nine other items showed significant specialty-specific agreement gaps, suggesting respondents’ needs for specialty dependence. The specific-speciality agreement gaps were mainly observed in the PD group. Neither the IM nor the ORL group showed agreement gaps in 20 of 29 items with specialty-specific agreement gaps, while the PD group showed significant opposing responses, resulting in poor agreement on each question. Q16 for the efficacy and safety of oral steroids and Q20 for alternative medicine, showed disagreement ($\text{AD}_{\text{med}}$: 0.84, 0.98) caused by specialty-gaps (PD, ORL, IM groups: Q16, 0.56, 1.09, 0.84; Q20, 0.73, 0.98, 1.26). Q17-19 also showed disagreement and specialty-gap in the PD group.

In PD group, 35 of 39 items showed acceptable interrater agreement and higher proportion of agreement (90.0%) than the other groups. On the contrary, the ORL and IM groups showed less acceptable interrater agreement (28.2% and 30.8%), respectively. Particularly, 4 items showed interrater agreement for the ORL group, but not IM, group 5 items showed agreement to the contrary.

DISCUSSION

This is the first study to identify the needs for AR care in Korea, to evaluate the gap between real-life practice and existing guidelines, and primary physicians’ needs for the development of new guidelines reflecting Korean particularity.

Our results demonstrated various consensus needs for clinical questions, particularly in diagnosis and treatment. There is consensus agreement that existing guidelines are insufficient for AR diagnosis indicating that certain guidance on the minimal selection of allergen tests is needed and should also reflect Korean particularity according to age, area, and season.

However, there are no Korean guides of “How many allergen, and what kind of allergens should be tested to diagnose and exclude AR in Korea?” and “How frequently allergic sensitization should be tested?” An investigation of offending allergens is essential for the diagnosis and treatment of AR. The offending allergens may vary with age, region, and season. Existing guidelines are based on patients outside of Korea; therefore, the minimum test battery of 18 inhalant allergens (Dermatophagoides pteronyssinus and Dermatophagoides farinae, Cat and Dog dander, Artemisia, Blatella, Alternaria, Parietaria, Ambrosia, Aspergillus, Cladosporium, Grass, Cypress-, Olive-, Birch-, Alder-, Plane-pollen, and Hazel) advocated by the Global Allergy and Asthma European Network would not be relevant in Korean patients. In Korea, particular pollens, including Japanese hop (Humulus japonicas) or Japanese Cedar (Cryptomeria japonica) have been reported as the major pollens of AR in south provinces. Furthermore, offending allergens are significantly different according to age, variability of offending allergens from indoor allergens in early childhood to outdoor allergens in late childhood. Indeed, the National Guideline for the Diagnosis and Management of Allergic disease, published by the KAAACI in 1999, recommended 17 allergens in skin prick test. Nevertheless, consensus agreement indicates that respondents still have difficulty in diagnosing AR in the real practice.

Despite existing guidelines, AR primary care seems to be independent of guideline recommendations. Furthermore, specialty-specific knowledge and agreement gaps among allergists, otorhinolaryngologists, and pediatricians are known to exist. Our findings also demonstrated specialty-specific need gaps that may be caused by specialty-knowledge or -interest gaps. We found the specialty-agreement gap even in the consensus items. The gap was prominent in the safety and effectiveness of
First or second-generation antihistamines, what is more effective in treating AR?

What are the decision criteria for the time of a surgical treatment of allergic and non-AR patients?

What are the efficacy of surgical treatment of AR in preschool-age children and school age children, and optimal age?

For how long should immunotherapy for AR be continued?

What is the diagnosis for a patient who exhibit classic symptoms of AR, yet tested negative for the skin prick test or serum specific IgE antibody?

What are the classic symptoms of AR?

Is sinus irrigation effective in treating AR?

What is the efficacy and safety of oral steroids in treating AR?

How can be AR clinically differentiated from non-AR-eosinophilia syndrome?

What is the efficacy and safety of antihistamine and INS treatment in pregnant women with AR?

What are the implications of a positive food allergen test result in AR patients?

What are the allergen selection criteria for AR immunotherapy?

What is the diagnostic value of skin prick test and serum specific IgE antibody test in AR?

What kind of treatment options is available for AR patients with a common cold?

What is the efficacy and safety of high-dose intramuscular corticosteroid in treating severe AR?

What are some objective testing methods used in evaluating the severity of AR and the efficacy of treatment?

Is allergen avoidance therapy effective, in which allergens that cause AR are avoided?

Can INS and corticosteroid eye drop be used concomitantly in AR patients with allergic conjunctivitis?

What are the allergen selection criteria for the skin prick test or serum specific IgE antibody test, their monitoring duration and frequency?

What are the patient selection criteria for the skin prick test or IgE (serum specific IgE antibody) test by season, area, and age?

What is the efficacy and safety of leukotriene receptor antagonist in treating AR?

What is the efficacy and safety of alternative medicine (oriental medicine or home therapy) in treating AR?

What is the efficacy and safety of leukotriene receptor antagonist in treating AR?

What is the diagnostic value of skin prick test and serum specific IgE antibody test in AR?

What are the implications of a positive food allergen test result in AR patients?

What are the allergen selection criteria for AR immunotherapy?

What is the efficacy and safety of oral steroids in treating AR?

What is the efficacy and safety of antihistamine and INS treatment in pregnant women with AR?

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What is the efficacy and safety of oral steroids in treating AR?

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What are the allergen selection criteria for AR immunotherapy?

What is the efficacy and safety of oral steroids in treating AR?

What is the efficacy and safety of alternative medicine (oriental medicine or home therapy) in treating AR?
Table 2. Specialty-agreement gaps for the question “Do you agree that existing guidelines is insufficient to answer the following question, and new guideline to reflect real-practice is needed?”

| Question-items* | PD (n=33) | ORL (n=33) | IM (n=33) |
|-----------------|----------|-----------|-----------|
| Consensus items  | Agree (%) | ADmed † | Agree (%) | ADmed † | Agree (%) | ADmed † |
| Q1              | 96.97    | 0.51     | 87.88    | 0.53     | 72.73    | 0.65     |
| Q2              | 78.79    | 0.48     | 87.88    | 0.35     | 81.82    | 0.78     |
| Q3              | 63.64    | 0.79     | 81.82    | 0.45     | 78.79    | 0.59     |
| Q4              | 93.94    | 0.55     | 84.85    | 0.56     | 66.67    | 0.81     |
| Q5              | 90.91    | 0.50     | 84.85    | 0.54     | 69.70    | 0.82     |
| Q6              | 78.79    | 0.60     | 51.52    | 0.83     | 69.70    | 0.95     |
| Q7              | 81.82    | 0.55     | 45.45    | 0.97     | 78.79    | 0.74     |
| Q8              | 84.85    | 0.57     | 84.85    | 0.74     | 66.67    | 0.83     |
| Q9              | 81.82    | 0.51     | 84.85    | 0.69     | 69.70    | 0.80     |
| Q10             | 60.61    | 0.71     | 81.82    | 0.58     | 48.48    | 0.98     |
| Q11             | 78.79    | 0.52     | 60.61    | 0.90     | 66.67    | 0.73     |
| Q12             | 75.76    | 0.67     | 63.64    | 0.80     | 63.64    | 0.91     |
| Q13             | 78.79    | 0.63     | 78.79    | 0.77     | 66.67    | 0.97     |
| Q14             | 81.82    | 0.48     | 60.61    | 1.04     | 72.73    | 0.83     |
| Q15             | 63.64    | 0.79     | 66.67    | 0.99     | 69.70    | 0.82     |
| Q16             | 75.76    | 0.56     | 57.58    | 1.09     | 72.73    | 0.84     |
| Q17             | 81.82    | 0.47     | 63.64    | 0.87     | 60.61    | 1.19     |
| Q18             | 81.82    | 0.46     | 54.55    | 1.12     | 69.70    | 0.88     |
| Q19             | 78.79    | 0.57     | 66.67    | 1.09     | 63.64    | 1.13     |
| Q20             | 67.88    | 0.73     | 69.70    | 0.98     | 57.58    | 1.26     |
| Polarized items |          |          |          |          |          |          |
| Q21             | 42.42    | 0.87     | 21.21    | 0.98     | 45.45    | 1.06     |
| Q22             | 78.79    | 0.78     | 27.27    | 1.22     | 54.55    | 1.02     |
| Neither consensus nor controversy items |          |          |          |          |          |          |
| Q23             | 72.73    | 0.63     | 60.61    | 0.98     | 66.67    | 0.81     |
| Q24             | 66.67    | 0.73     | 45.45    | 0.90     | 63.64    | 0.97     |
| Q25             | 69.70    | 0.70     | 57.58    | 1.03     | 63.64    | 0.92     |
| Q26             | 60.61    | 0.80     | 60.61    | 0.99     | 54.55    | 1.01     |
| Q27             | 75.76    | 0.52     | 54.55    | 1.17     | 60.61    | 0.93     |
| Q28             | 69.70    | 0.70     | 60.61    | 1.14     | 63.64    | 0.95     |
| Q29             | 72.73    | 0.66     | 33.33    | 0.95     | 69.70    | 0.92     |
| Q30             | 90.91    | 0.53     | 30.30    | 0.87     | 63.64    | 0.97     |
| Q31             | 60.61    | 0.88     | 48.48    | 1.13     | 75.76    | 0.74     |
| Q32             | 75.76    | 0.62     | 51.52    | 1.14     | 69.70    | 0.98     |
| Q33             | 57.58    | 0.80     | 36.36    | 0.84     | 60.61    | 1.15     |
| Q34             | 69.70    | 0.84     | 36.36    | 0.84     | 69.70    | 1.00     |
| Q35             | 72.73    | 0.72     | 54.55    | 1.09     | 60.61    | 1.06     |
| Q36             | 72.73    | 0.77     | 36.36    | 1.10     | 60.61    | 0.94     |
| Q37             | 63.64    | 0.67     | 39.39    | 1.02     | 66.67    | 1.07     |
| Q38             | 66.67    | 0.77     | 33.33    | 1.06     | 72.73    | 0.92     |
| Q39             | 78.79    | 0.72     | 36.36    | 1.17     | 69.70    | 1.00     |

*Criteria of question-items: “Consensus items” if less than 25% of responders indicated neutral opinion and if the percentage of agreement was at least 4 times as large as the percentage of disagreement; “Polarized items” if over 30% of the responders indicated agreement and if over 30% of responders indicated disagreement; “Neither consensus nor controversy” if it was not included in “Consensus items” or “Polarized items.” †Agree: agreement was considered present if the responders choosing 4 (agree) or 5 (strongly agree) for each statement. The overall degree of agreement was ascertained using a 5-point Likert scale with 1 = strongly disagree and 5 = strongly agree; ADmed values less than or equal to 0.833 were interpreted as indicating acceptable interrater agreement.

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treatment. Most guidelines recommend intranasal corticosteroid (INS) as the best monotherapy, while our results showed that 63.6% of respondents still have questioned “How long can INS be safely used?” (Q25). Concerns of INS-safety was stronger in the PD group (69.7% of agreement, ADmed 0.70) than in the ORL group (57.58% of agreement, ADmed 1.03) and IM (63.64% of agreement, ADmed 0.92) groups. The item for the efficacy and safety of oral steroid (Q16) showed specialty-specific agreement gaps between the PD and ORL/IM groups, suggestive of relatively higher concerns of oral steroid use in children than in adults. Therefore, guidance of oral steroid use needs consideration of age specificity. The question on the efficacy and safety of alternative medicine (Q20) also showed conflicting response between the PD and ORL/IM groups. This gap may arise from conflict between guidelines. The ARIA guideline 2010 did not recommend any of acupuncture or herbal medicine in the treatment of AR; however, the American Academy of Otolaryngology-Head and Neck Surgery stated that clinicians may offer acupuncture for patients who are interested in nonpharmacologic therapy. The efficacy and safety of acupuncture or herbal medicine remain controversial. Our results showed high agreement in the PD group, but disagreement in ORL and IM groups. Patients attempt to use alternative or complementary medicine because of several reasons, such as concern of life-long medicine, steroid phobia, and dissatisfaction with the conventional treatments, particularly in children. For this reason, the need for unified guidance is growing.

Most guidelines draw their recommendation not from real-world practice, but from the world of RCTs. Although RCTs are considered the gold standard of treatment intervention efficacy, it occasionally fails to be replicated in the real-life setting because it reflects only 10% of the general population. In real-life practice, patients do not desire life-long use of steroid, have many co-morbidities, tend to suffer from the mixed type of AR and non-AR rather than AR alone. Thus, although RCTs provide highest evidence, guidelines need careful consideration for the acceptance of RCT-driven evidence. Practical guidelines and most of the studies have focused on the management of moderate to severe AR; however, mild intermittent AR is the most prevalent type, comprising approximately >50% of AR at the population level. The grading of recommendation, assessment, development, and evaluation system is accepted as the best tool for grading evidence for developing guidelines. It guarantees the highest evidence from the high-graded study; however, numerous questions derived from real practice cannot be answered. Evidence-based guidelines would be insufficient to answer the real world questions. To resolve these gaps, comparative-effectiveness derived from pragmatic trials or real world observation should be considered. Although there has been no pragmatic AR-guideline up to now, The Global Initiative for Asthma Guideline 2016 began to reflect the evidence from real-world effectiveness studies as well as from efficacy studies in the choice of the preferred asthma-controller.

Taken together, the present survey highlights that existing international guidelines are insufficient for application to real-world practice, and needs of primary physicians for AR care remain unmet; consequently, development of a Korean practical guideline reflecting regional particularity is needed. Furthermore, guideline developers should reflect efficacy from RCTs and effectiveness from the real-world practice, as well the development of regional guidelines.

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