

A Survey of the Prescription Patterns of Allergen Immunotherapy in Korea

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Purpose: Allergen immunotherapy (AIT) has been used as a curative and specific treatment of allergic diseases. However, no data on the prescription patterns of AIT in Korea is available. Therefore, we surveyed the prescription patterns of AIT by allergy specialists in Korea. **Methods:** We emailed a questionnaire on AIT prescription patterns to the 690 members of the Korean Academy of Asthma, Allergy and Clinical Immunology (KAAACI) with clinical practice experience. All returned answers were evaluated. **Results:** The response rate was 21.0%. Only 69.0% of the respondents performed AIT in practice. Hindrance factors for performing AIT in the practice included a lack of facilities (21%), lack of practical experience during their subspecialty or postgraduate educational training programs (15.8%), no need for AIT because of sufficient pharmacotherapy (14.5%), insufficient economic profits (14.5%), and risks for adverse reactions (13.2%). Ninety-two allergy specialists (82%) performed AIT subcutaneously subcutaneous immunotherapy (SCIT) and 20 allergy specialists (18%) performed it sublingually sublingual immunotherapy (SLIT). Only 8 specialists performed both SCIT and SLIT. The allergens used for SCIT were house dust mites (98.9%), pollens (72.8%), and animal dander (23.9%). SLIT was prescribed only for house dust mites. Twenty-eight physicians (30.4%) observed anaphylactic reactions during SCIT. Eight physicians (40.0%) who prescribed SLIT observed adverse reactions, including local reactions, but none of them observed anaphylactic reactions. **Conclusions:** In this survey, 69.0% of the respondents performed AIT in clinical practice. SCIT prescription is more popular than SLIT. The Lack of facilities and clinical education is a critical barrier to performing AIT. Therefore, proper clinical education of AIT is necessary for Korean allergists.

Key Words: Allergen immunotherapy; allergic rhinitis; asthma; survey

INTRODUCTION

Allergen immunotherapy (AIT) with allergens has been used as the only specific treatment of allergic diseases, such as allergic mild asthma, allergic rhinitis, and bee venom anaphylaxis.^{1,2} There have been several reports of the positive effects of AIT in atopic dermatitis, suggesting that AIT may also have a therapeutic value in the treatment of atopic dermatitis.^{3,4} AIT may change the natural course of the disease and has several disease-modifying effects. Randomized clinical trials have shown that AIT can decrease symptom-medication scores by 30%-40%.^{5,6} In addition, the effects of AIT can be maintained long after the discontinuation of AIT, particularly when it is performed for 3 years or longer.^{7,8} Furthermore, AIT can prevent the development of allergic asthma in allergic rhinitis patients⁹⁻¹¹ and new

sensitization in children with house dust mite mono-sensitized asthma.^{12,13}

In Korea, prescription of AIT is not popular compared to that in Western countries, and data on the current prescription pattern of AIT in Korea are not available. Therefore, we conducted a survey of the prescription pattern of Korean allergy specialists and analyzed underlying causes of the low AIT prescription rate in Korea.

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MATERIALS AND METHODS

We emailed a questionnaire on AIT prescription patterns to the 690 members of the Korean Academy of Asthma, Allergy and Clinical Immunology (KAAACI) with clinical practice experience. We obtained responses to the questionnaire by August 2009. The questionnaire was again circulated to the same Academy members at 1-month intervals in order to increase the response rate. The questionnaire consisted of 24 questions regarding practice patterns. The questionnaire included demographics, insight into AIT for the treatment of allergic disease, practice patterns of AIT, and adverse reactions during AIT. The detailed questionnaire is shown in Figure. All returned answers were evaluated and analyzed using descriptive statistics.

RESULTS

Characteristics of the respondents

Table 1 shows the characteristics of the respondents. We obtained responses from 145 (21.0%) of the 690 members members. Of these who respondents, 67 (42.8%) were in their 30s, 47 (32.4%) were in their 40s, and 20 (13.8%) were in their 50s. Five

respondents (3.4%) were at the age of over 60 years. The majority (75.2%) of the respondents were in their 30s and 40s. Of these respondents, 62 (42.8%) were physicians, 47 (32.4%) were pediatricians, 30 (20.7%) were otolaryngologists, and 2 (1.4%) were dermatologists. Approximately half of the respondents (49.0%) worked at university hospitals, 46 (31.7%) worked at general hospitals, and the remaining (19.3%) worked at private clinics. The institutes of more than half (62.1%) of the respondents were located in Seoul and its metropolitan area.

Insights into AIT

Most respondents agreed on the necessity of AIT to treat allergic diseases (143/145, 98.6%). However, only 100 (69.0%) were currently using AIT in their practice. Although the remaining 45 (31.0%) were not yet using AIT, 30 (20.7%) respondents desired to use it in the future practice. Table 2 shows the obstacles to starting AIT in their own practice based on responses from the members without AIT experience. The most frequent reason was lack of facilities, including lack of trained health professionals (35.5%), and lack of practical AIT experience during the training course of their subspecialty (26.7%). Some respondents answered that they did not trust therapeutic effects of AIT

<p>1. What is your age group? ① 21–30 ② 31–40 ③ 41–50 ④ 51–60 ⑤ >61</p> <p>2. What is your specialty? ① Internal medicine ② Pediatrics ③ Otorhinolaryngology ④ Dermatology ⑤ Others _____</p> <p>3. Which is your practice type? ① University hospital ② General hospital ③ Private clinic</p> <p>4. Where is your practice located? ① Seoul ② Busan ③ Daegu ④ Incheon ⑤ Gwangju ⑥ Daejeon ⑦ Ulsan ⑧ Gyeonggi ⑨ Kangwon ⑩ Chongcheong ⑪ Jeolla ⑫ Gyeongsang ⑬ Jeju</p> <p>5. Do you feel SIT is necessary? ① surely necessary ② a little necessary ③ not necessary</p> <p>6. Do you prescribe SIT in your practice? ① Yes ② No ③ Not yet, but I will prescribe it in future (If you answered ① to number 8) (If you answered ② and ③ to number 7)</p> <p>7. What are the reasons not to prescribe SIT in your practice? (select all that apply) ① lack of facilities or trained health professionals ② lack of experience ③ distrust of its therapeutic effect ④ unnecessary for management of allergic disease ⑤ risk of adverse reactions ⑥ little economic profit to doctors ⑦ Others _____</p> <p>8. Which are the indicated diseases to SIT? (select all that apply) ① asthma ② allergic rhinoconjunctivitis ③ atopic dermatitis ④ bee venom anaphylaxis ⑤ food allergy</p> <p>9. Which do you use to detect allergen-specific IgE Ab for SIT? (select all that apply) ① skin prick test ② RAST ③ UniCAP ④ MAST (including RIDA and AdvanSure) ⑤ Immunelite ⑥ Others _____</p> <p>10. Which SIT do you use in your practice? (select all that apply) ① SCIT ② SLIT (If you are using SCIT to number 11)</p>	<p>(If you are using SLIT alone, to number 22)</p> <p>11. Approximately how many patients are you putting on SCIT? ① 1–10 ② 11–20 ③ 21–30 ④ 31–40 ⑤ over 41</p> <p>12. For which type of allergens are you using SCIT? (select all that apply) ① House dust mite ② Mold ③ Pollens ④ Cockroach ⑤ Animal dander ⑥ Foods ⑦ Bee venom ⑧ Others _____</p> <p>13. What is the manufacturing company used in SCIT? (select all that apply) ① Allergopharma ② Allergy Therapeutics ③ Hollister-Stier ④ Others _____</p> <p>14. How many allergen extracts do you mix in SCIT? ① None ② 2 ③ 3 ④ 4 ⑤ 5 ⑥ >6</p> <p>15. Do you mix allergen extracts yourself? ① Yes ② No</p> <p>16. Who determines the maintenance dose for SCIT? ① Physician ② as manufacturing instruction</p> <p>17. Which build-up methods are you using in SCIT? (select all that apply) ① conventional ② cluster ③ rush (including ultrarush)</p> <p>18. How frequently do you put on SCIT during maintenance? _____ days</p> <p>19. Who administers the SCIT dose for your patient? ① physician ② nurse ③ technician ④ Others _____</p> <p>20. Have you ever observed anaphylaxis in SCIT? ① Yes ② No</p> <p>21. How is SCIT reimbursed? (select all that apply) ① take doctor bill in every visit ② take injection fee in every visit ③ Others _____</p> <p>22. What is the manufacturing company using in SLIT? (select all that apply) ① ALK-Abello ② Stallergenes</p> <p>23. Approximately how many patients are you putting on SLIT? ① <10 ② 11–20 ③ 21–30 ④ 31–40 ⑤ >41</p> <p>24. Have you ever observed adverse reactions in SLIT? ① No ② Yes (describe in detail: _____)</p>
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Figure. Questionnaire regarding allergen immunotherapy (AIT) sent to the Korean Academy of Asthma, Allergy and Clinical Immunology (KAAACI) members. SCIT, subcutaneous immunotherapy; SLIT, sublingual immunotherapy.

Table 1. Characteristics of the survey respondents

	n (%)
Number of respondents	145 (21.0)
Age (years)	
31-40	67 (42.8)
41-50	47 (32.4)
51-60	20 (13.8)
≥ 61	5 (3.4)
Specialty	
Internal medicine	62 (42.8)
Pediatrics	47 (32.4)
Otolaryngology	30 (20.7)
Dermatology	2 (1.4)
Others	4 (2.8)
Location of work	
University hospital	71 (49.0)
General hospital	46 (31.7)
Private clinic	28 (19.3)
Province of work	
Seoul	52 (35.9)
Gyeonggi	38 (26.2)
Busan	8 (5.5)
Gwangju	9 (6.2)
Daegu	7 (4.8)
Daejeon	2 (1.4)
Ulsan	3 (2.1)
Others	26 (17.9)

(17.8%); they thought AIT was unnecessary because pharmacotherapy alone was sufficient for the management of allergic diseases (24.4%). These respondents also reported that AIT did not provide enough economic profits (24.4%) considering the risks of serious adverse events (22.2%).

AIT in practice

Table 3 shows target diseases for which the respondents used AIT. Allergic rhinoconjunctivitis (92.0%), allergic asthma (76.0%), atopic dermatitis (20.0%), and bee sting anaphylaxis (10.0%) were ranked as the major indications. We asked the methods used to detect causative allergens and found that skin prick tests and serologic tests, including ImmunoCAP, RAST, and MAST, were all popular for the diagnosis of causative agents (94.0% vs. 100.0%). Approximately 94.0% of the respondents used both skin prick tests and serologic tests for the identification of culprit allergens. 92 of all allergy specialists, (82.0%) performed subcutaneous immunotherapy (SCIT) and 20 (18.0%) performed sublingual immunotherapy (SLIT). Only 8 allergy specialists performed both SCIT and SLIT. The respondents who performed SCIT were asked as to which allergens they used for SCIT. House dust mite (98.9%) was the most common

Table 2. Reasons for not performing allergen immunotherapy

	n (%)
Lack of facilities	16 (35.5)
Lack of experience	12 (26.7)
Distrust of therapeutic effect	8 (17.8)
Unnecessary for management of allergic diseases	11 (24.4)
Risk of adverse reactions	10 (22.2)
Little profit to doctor	11 (24.4)
Other	8 (17.8)
All respondents	45 (100.0)

Numbers are not mutually exclusive.

Table 3. Diseases indicated for allergen immunotherapy

	n (%)
Bronchial asthma	76 (76.0)
Allergic rhinoconjunctivitis	92 (92.0)
Atopic dermatitis	20 (20.0)
Bee venom allergy	10 (10.0)
Food allergy	1 (1.0)
All respondents	100 (100.0)

Numbers are not mutually exclusive.

Table 4. Culprit allergens for subcutaneous immunotherapy

	n (%)
House dust mite	91 (98.9)
Pollens (<i>e.g.</i> , tree, weed, <i>etc.</i>)	67 (72.8)
Animal dander	22 (23.9)
Molds	19 (20.7)
Bee venom	10 (10.9)
Cockroach	5 (5.4)
Other	0 (0.0)
All respondents	92 (100.0)

Numbers are not mutually exclusive.

allergen for SCIT, followed by pollen allergens (72.8%), animal dander (23.9%), and fungal species (20.7%) (Table 4). In addition, 13.2% of the respondents did not prescribe poly allergens for SCIT, whereas the remaining respondents prescribed combined up to poly allergens containing 5 different allergen extracts. Only 10.9% of the respondents mixed and prepared the allergen extract from bulk extracts at their clinics. The remaining respondents used a tailor-made extract set provided by pharmaceutical companies. For the build-up phase, 72.3% of the respondents used a conventional schedule of increasing doses of allergen immunotherapy extract administered 1-2 times per week, whereas 16.0% used a rush protocol and 11.8% used a cluster schedule protocol. Only house dust mites were prescribed for SLIT in Korea.

Adverse reactions during AIT

Twenty-eight (30.4%) of the 92 SCIT respondents reported anaphylaxis during the SCIT. Of the 20 SLIT respondents, none reported anaphylaxis, but 8 (40.0%) reported adverse local reactions, including oral swelling and itching sensations of the throat or tongue.

DISCUSSION

Numerous similar surveys of AIT prescription patterns have been conducted in Mexico,¹⁴ Italy,¹⁵ and the United States.^{16,17} In addition, a worldwide survey of AIT practice patterns which focused on AIT doses and durations has been published recently.¹⁸ In this study, 69.0% of the allergy specialists in Korea used AIT. This figure may be higher than that of all Korean allergy practitioners. Most respondents to our survey were physicians, pediatricians, and otolaryngologists. They were generally young (between ages of 30 and 40) and worked at general hospitals located in Seoul and Gyeonggi-do Province, the metropolitan area of Korea. Young allergists are willing to accept recent information and to update their medical skills. People living in Seoul and its vicinity show higher prevalences of atopic diseases, including allergic rhinitis, asthma, and atopic dermatitis. They had higher socioeconomic statuses and were more interested in AIT than people living in other regions in Korea. Most respondents practiced at university hospitals and only a few worked at private clinics. This reflects the composition of KAAACI members. Most Korean allergy specialists are working at university hospitals, which is quite different from Western allergy specialists.

Regarding the need for AIT, most Korean allergists (98.6%) agreed to its role in the treatment of allergic diseases. However, some were reluctant to recognize this role because 17.8% of the respondents did not believe the efficacy of AIT in managing allergic diseases. One-third of the respondents did not prescribe AIT in clinical practice. Lack of facilities, including lack of trained health professionals, and lack of instruction on how to perform AIT through training or postgraduate programs were the most common reasons for not prescribing it.

Diseases indicated for SCIT include allergic rhinoconjunctivitis (92.0%), asthma (76.0%), atopic dermatitis (20.0%), and bee sting anaphylaxis (10.0%) in this study. It suggests that allergic asthma and rhinoconjunctivitis are the main diseases treated with AIT in Korea. The role of AIT for the management of allergic rhinoconjunctivitis and bee sting anaphylaxis is apparent,^{19,20} but it is controversial for asthma management.²⁰⁻²² AIT is prescribed more frequently for allergic asthma in Korea than in other countries. This may be because the majority of KAAACI members are physicians trained in the Department of Internal Medicine and they more focus on the treatment of allergic asthma than on allergic rhinoconjunctivitis. Another reason is that Korean allergy specialists are in favor of AIT for the management

of atopic dermatitis. Recently, favorable data from randomized and nonrandomized clinical trials of AIT in atopic dermatitis have been reported.^{4,23-25}

Both skin prick and serologic tests are popularly used to determine offending allergens. Skin tests are performed for screening in most allergy clinics (94%) and serologic tests, including ImmunoCAP, RAST, and MAST, are used to confirm the presence of specific IgE.

House dust mites are the most common culprit allergen, followed by pollen allergens, animal dander, and fungal species, which are consistent with the prevalences of offending allergens in Korea.²⁶ Korean allergists are prudent in the identification of offending allergens. They use skin prick tests for screening and confirm the presence of specific IgE by serologic tests. In Korea, poly allergen immunotherapy is more popular than mono-allergen immunotherapy. Only 13.2% of the respondents used a single allergen extract, such as house dust mite alone, whereas most respondents prescribed mixed allergen extracts in multiple-sensitized patients. The cross-reactivity of allergens, dose optimization of each constituent, and enzymatic degradation of allergens must be considered when allergen extracts are mixed.²⁷ KAAACI recommended a mixture of up to 5 different allergens.²⁸ For the immunotherapy schedule, only 25% of the respondents performed rush or cluster AIT in the build-up phase. AIT was administered by physicians (37%) or nurses (63%).

Only 13.8% of the respondents prescribed SLIT in clinical practice; most were otolaryngologists. Because SLIT was introduced in Korea 2 years prior to our study, a relatively low prescription rate was expected compared to SCIT. More clinical experiences are needed for SLIT to be prescribed widely by physicians and pediatricians.

The frequency of adverse systemic reactions during SCIT has been reported to be 2.1%-2.9% of all patients.²⁹ In this survey, ~30% of the respondents observed severe systemic reactions after SCIT. SLIT is known to be safer than SCIT because few cases of severe systemic reactions have been reported during SLIT.³⁰ In this study, no respondents observed severe systemic reactions to SLIT, but 40% had local adverse reactions, including oral swelling and itching.

In conclusion, 69.0% of the respondents performed AIT in clinical practice. The prescription of SCIT is more popular than SLIT; however, SLIT is increasingly prescribed, particularly among otorhinolaryngologists. Lack of facilities, including trained health professionals, and lack of clinical experience and instruction on AIT are the critical barriers to the prescription of AIT by Korean allergy specialists. Therefore, proper clinical instruction that introduces and updates information on AIT is necessary to encourage AIT in Korea.

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