

Does New Sensitization Correlate with Nasal Symptoms in Children with Allergic Rhinitis?

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Objectives: To evaluate the correlation between the increased number of sensitized allergens and nasal symptoms in patients with allergic rhinitis who were sensitized to house dust mites (HDMs).

Methods: Among the patients who were enrolled in the Allergic Rhinitis Cohort Study for Kids, 174 children with rhinitis symptoms who were sensitized to HDMs were included in the analysis. Skin prick tests, serum total immunoglobulin E, eosinophil count, and bronchial provocation tests were carried out during the initial and 3-year follow-up visits. The patients were divided into two groups depending on the change in the number of sensitized allergens: increased number of sensitized allergens (group I) and maintained or reduced number of sensitized allergens (group II).

Results: In the analysis of allergen sensitization from baseline to the 3-year follow-up, no significant correlation was observed between the changes in the number of allergens and the total nasal visual analog scale score ($R^2 < 0.001$, $P = .813$). Furthermore, the comparison of demographic data and immunological factors between groups I and II did not show any significant differences. The changes in bronchial hyper-responsiveness were not significantly different between the two groups ($P = 1.000$).

Conclusion: New sensitization may not be correlated with nasal symptoms in patients in Asian countries where HDMs play a major role as a dominant allergen. Although further investigation must be conducted, the importance of new sensitization as an indicator of treatment outcome should be reconsidered in individuals in Asia.

Key Words: Allergens, child, rhinitis, allergic.

Level of Evidence: 2b

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INTRODUCTION

Allergic rhinitis is the most common form of non-infectious rhinitis, and its prevalence among children and adolescents has gradually increased over the past few decades. The increased number of sensitized allergens may be a typical natural course in patients with allergies.¹ In contrast, some patients with allergies remain mono-sensitized over several years. According to one study, children with allergic rhinitis who remained mono-sensitized had higher interleukin 10 (IL-10) and interferon-gamma (IFN- γ) levels than did those who became poly-sensitized.² IL-10 is known to have potential anti-allergic effects including suppression of

eosinophils and mast cells.³ In addition, IFN- γ plays a major role in the Th1-mediated immune response, and down regulation of IFN- γ may be associated with the severe symptoms of allergic rhinitis.⁴ These studies may indicate that new sensitization is related to worsening of allergic symptoms in patients with allergic rhinitis. Moreover, the increased number of sensitized allergens makes patients with allergies more likely to react to various allergens, which may cause more discomfort for patients with allergic rhinitis. Supporting this idea, poly-sensitization was found to be a negative factor for quality of life among patients with allergic rhinitis in a previous study.¹ Therefore, the prevention of new sensitization plays a key role in immunotherapy, and is considered a positive outcome.⁵⁻⁷

However, due to the role of the dominant allergen, there is uncertainty regarding whether the increased number of sensitized allergens significantly contributes to the worsening of individual allergic symptoms. House dust mites (HDMs) have been identified as a major allergen in Asian countries.⁸⁻¹⁰ Previous studies conducted in Asian countries reported that immunotherapy with HDMs has comparable effects in patients who are poly-sensitized and mono-sensitized, and these results highlight the significance of controlling the dominant allergen in poly-sensitized patients.^{11,12} However, to the best of our knowledge, only a few studies have evaluated the direct correlation between new sensitization and allergic symptoms. Thus, the present study aimed to assess the

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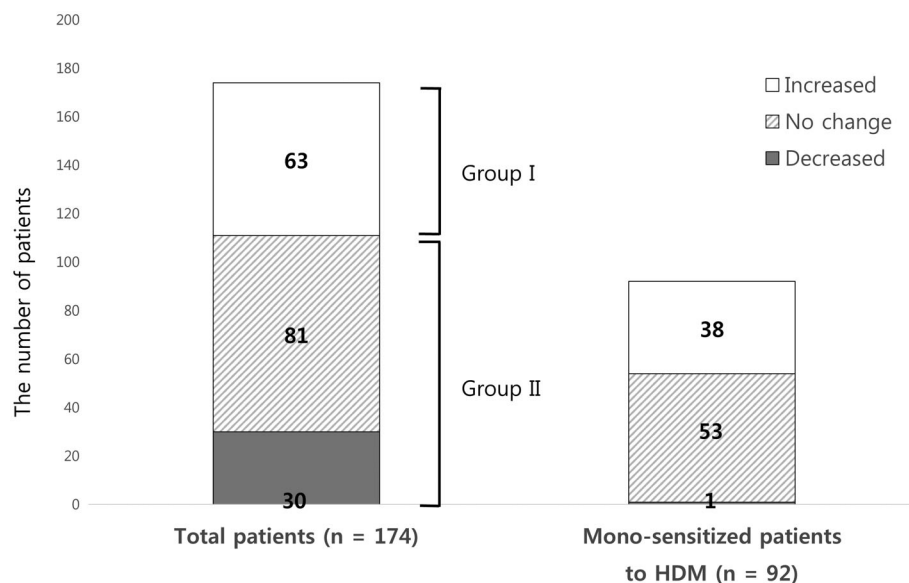


Fig. 1. Changes in the number of allergens after 3 years (n = 174). Patients were categorized by the changes in the number of allergens after 3 years. The number of sensitized allergens increased in 63 out of 174 patients, and these patients were categorized as group I. The number of sensitized allergens did not change in 81 patients and decreased in 30 patients, respectively. These 111 patients were categorized as group II. In patients who were mono-sensitized to HDMs, the number of sensitized allergens increased in 38 patients and remained unchanged in 53 patients. Only one patient experienced desensitization to HDMs. HDM = house dust mite.

correlation between the increased number of sensitized allergens and nasal symptoms in patients with allergic rhinitis who were sensitized to HDMs.

MATERIALS AND METHODS

Study Design and Participants

This study used the data of pediatric patients who were prospectively enrolled in the Allergic Rhinitis Cohort Study for Kids that has been conducted since 2009. A total of 574 pediatric patients who visited two tertiary hospitals between January 2009 and December 2011, with at least two rhinitis symptoms (nasal obstruction, rhinorrhea, sneezing, and itching sensation in the nose) and who were sensitized to HDMs during their first visit were initially enrolled in this study. Routine ear, nose, and throat endoscopic examinations, skin prick tests (SPTs), serum total immunoglobulin E (IgE) levels, eosinophil counts, and methacholine bronchial provocation tests (MBPTs) were carried out during the initial and 3-year follow-up visits. After 3 years of

follow-up, 351 patients remained, and 174 eligible patients who completed the SPT and questionnaires on their nasal symptoms at the 3-year follow-up were selected. All participants were treated with pharmacotherapy and/or sublingual immunotherapy (SLIT). Standardized HDM extracts (SLITone; 50% *Dermatophagoides pteronyssinus* [Dp]/50% *Dermatophagoides farinae* [Df], ALK-Abello, Madrid, Spain) were used for immunotherapy. A single-dose container is comprised of 0.2 mL of extractable volume, which equates to 5 drops of 1000 STU/mL solution. Regardless of age, prepared single dose was taken daily, and the patients were told to keep drops of allergen under their tongue for 2–3 minutes. Written informed consent was obtained from all patients or their parents. This study was approved by the institutional review board of Seoul National University Hospital (IRB no.: 1810-118-982).

Immunological Tests

All participants underwent SPTs with a total of 13 common standardized allergen extracts (Allergo-Pharma, Reinbek, Germany) on the medial sides of both forearms. In this study,

TABLE I.
Distribution of Allergen Sensitization.

	HDM	Animal dander	Cockroach	Molds	Tree	Grass	Weed
Overall patients (n = 174)							
Initial SPT	174 (100%)	48 (27.6%)	9 (5.2%)	16 (9.2%)	32 (18.4%)	10 (5.7%)	18 (10.3%)
3-year f/u SPT	171 (98.3%)	62 (35.6%)	7 (4.0%)	22 (12.6%)	51 (29.3%)	25 (14.4%)	34 (19.5%)
Group I (n = 63)							
Initial SPT	63 (100%)	12 (19.0%)	2 (3.2%)	6 (9.5%)	13 (20.6%)	5 (7.9%)	3 (4.8%)
3-year f/u SPT	63 (100%)	41 (65.1%)	3 (4.8%)	15 (23.8%)	28 (44.4%)	36 (57.1%)	22 (34.9%)
Group II (n = 111)							
Initial SPT	111 (100%)	36 (32.4%)	7 (6.3%)	10 (9.0%)	19 (17.1%)	5 (4.5%)	15 (13.5%)
3-year f/u SPT	108 (97.3%)	21 (18.9%)	4 (3.6%)	7 (6.3%)	15 (13.5%)	3 (2.7%)	6 (5.4%)

HDM = house dust mite; SPT = skin prick test.

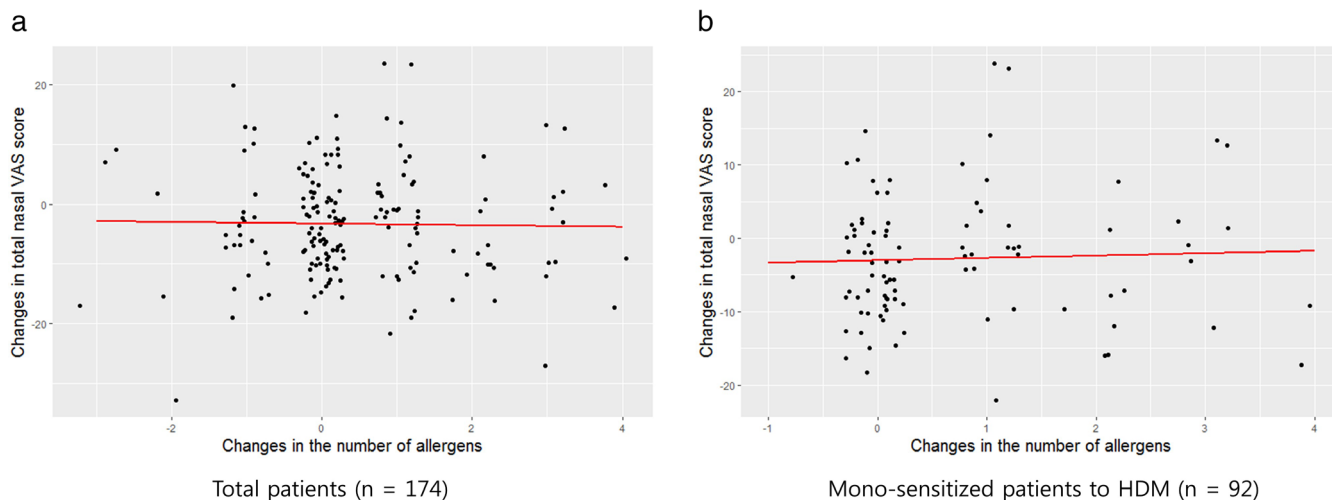


Fig. 2. Correlation between the changes in the number of allergens and the total nasal VAS score. (a) All patients. (b) Patients mono-sensitized to HDMs. HDM = house dust mite; VAS = visual analog scale. [Color figure can be viewed in the online issue, which is available at www.laryngoscope.com.]

the allergens were categorized into seven groups: HDMs (Dp and Df), molds (*Alternaria alternata* and *Aspergillus fumigatus*), animal dander (cat and dog), cockroach (German cockroach), trees (mixture 1: alder, elm, hazel, poplar, and willow trees and mixture 2: beech, birch, oak, and plane trees), grasses (mixture: velvet, orchard, rye, timothy, Kentucky blue, and meadow), and weeds (mugwort and ragweed). Histamine (1% of histamine phosphate) and 0.9% saline were used as positive and negative controls, respectively. A wheal diameter of at least 3 mm was considered positive. The number of sensitized allergens was calculated by summing the positive results in these categorized allergens, not those in individual allergens. The patients were divided into two groups depending on the change in the number of sensitized allergens. Group I was defined as patients whose number of sensitized allergens increased during the 3-year follow-up, and group II was defined as patients whose number of sensitized allergens was

maintained or reduced during the 3-year follow-up. In addition, patients who were mono-sensitized to HDMs were analyzed to evaluate the correlation between nasal symptoms and the development of poly-sensitization. The serum level of total IgE (U/mL) and eosinophil counts (μ L) of each participant were measured. All participants were required to discontinue oral medications at least 7 days before the test. The MBPTs were performed in children aged 6 years or older. Bronchial hyper-responsiveness was defined as the provocative concentration <16 mg/mL that caused a 20% decrease in FEV1 (PC 20).

Assessment of Nasal Symptoms

The parents of all children were asked to complete the questionnaires regarding their children's nasal symptoms during the initial and 3-year follow-up visits. The questionnaire consisted of a visual analog scale (VAS) score of 0–10 (0: no

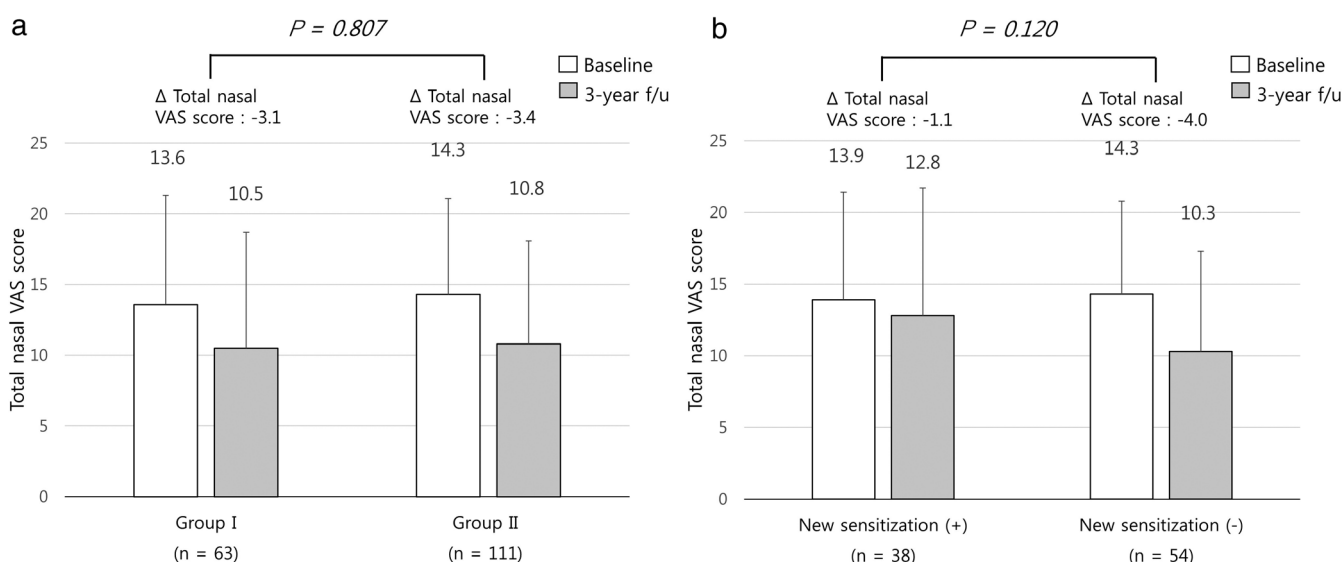


Fig. 3. Comparison of the total nasal VAS score between groups I and II. (a) The changes in the total nasal VAS score did not differ between groups I and II. (b) There was no significant difference in the changes in the total nasal VAS score between groups I and II among the patients mono-sensitized to HDMs. HDM = house dust mite; VAS = visual analog scale.

complaints, and 10: worst complaints) about nasal obstruction, rhinorrhea, sneezing, and itchy nose. The total nasal VAS score was calculated as the sum of all symptom scores.

Statistical Analysis

Continuous variables, such as demographic information, laboratory data, and total nasal VAS scores, are presented as the mean $\pm$ SD; these variables were analyzed using two-sample *t*-tests. Chi-squared tests were carried out to evaluate categorical variables. A simple linear regression analysis was performed to evaluate the association between changes in the number of allergens and those in the total nasal VAS score. To evaluate the changes in continuous variables, changes from baseline were calculated (post-pre). All statistical analyses were conducted using R for Windows version 3.4.2 (R Foundation for Statistical Computing, Vienna, Austria). A *P* value $<.05$ was set as the threshold for statistical significance.

RESULTS

General Characteristics and Distribution of Allergen Sensitization

The 174 enrolled children ranged in age from 4 to 13 years. The number of sensitized allergens in all patients increased from 1.8 ± 1.1 at baseline to 2.1 ± 1.3 at the 3-year follow-up. Figure 1 presents categorization of the patients based on changes in the number of sensitized allergens during the 3-year follow-up, and the patients were divided into two groups depending on the changes in the number of sensitized allergens: group I (*n* = 63) and group II (*n* = 111). Table I depicts the distribution of allergen sensitization at baseline and the 3-year follow-up.

Relationship Between Clinical Effects and Sensitization of Allergens

In the analysis of the changes in allergen sensitization from baseline to the 3-year follow-up, no significant correlation was observed between the changes in the number of allergens and the total nasal VAS ($R^2 < 0.001$, *P* = .813) (Fig. 2a). Moreover, the changes in the number of allergens did not correlate with those in the total nasal VAS score in patients who were mono-sensitized to HDMs at baseline ($R^2 = 0.002$, *P* = .711) (Fig. 2b). The changes in the total nasal VAS score were not significantly different between groups I and II (*P* = .807) (Fig. 3a). Furthermore, no significant difference was observed in the changes in the total nasal VAS score among the patients mono-sensitized to HDMs between groups I and II (*P* = .120) (Fig. 3b).

Immunological Factors

Between the two groups, no significant differences were observed in terms of demographic data, including age, sex, and duration of symptoms (Table II). Although the number of sensitized allergens was not significantly different between the two groups at baseline (*P* = .290), a significant difference was observed in the number of sensitized allergens at the 3-year follow-up and post-pre (*P* $<.001$ for both 3-year follow-up and post-pre).

Comparisons of the immunological factors between groups I and II are shown in Table II. The comparison of the wheal diameters of Dp and Df between the two groups did not show any significant differences. Furthermore, no significant differences were noted in terms of eosinophil counts and total IgE levels between the two groups.

Incidence of Bronchial Hyper-Responsiveness

Among the 174 patients, 61 underwent MBPTs at the baseline and 3-year follow-up visits: 27 patients in group I and 34 patients in group II (Fig. 4). In group I, 15 patients were positive and 12 patients were negative at baseline, and six positive and 21 negative at the 3-year follow-up. In group II, 17 patients were positive, and 17 patients were negative at baseline, and seven positive and 27 negative at the 3-year follow-up. The reversion and change of reaction from positive at the baseline test to negative at the 3-year follow-up occurred in nine (60.0%) and 10 (58.8%) patients in groups I and II,

TABLE II.
Comparison of Clinical Features According to Changes in Sensitized Allergens.

	Group I (<i>n</i> = 63)	Group II (<i>n</i> = 111)	<i>P</i>
Age, y	8.0 $\pm$ 2.1	8.0 $\pm$ 2.6	.976
Sex (male: female)	49: 14	73: 38	.136
Duration of symptoms, y	2.6 $\pm$ 2.1	2.9 $\pm$ 2.0	.437
No. of sensitized allergens			
Initial	1.7 $\pm$ 1.0	1.8 $\pm$ 1.1	.290
3-year f/u	3.3 $\pm$ 1.3	1.5 $\pm$ 0.8	<.001
post-pre	1.7 $\pm$ 0.9	-0.4 $\pm$ 0.7	<.001
Total Nasal VAS			
Initial	13.6 $\pm$ 7.3	14.3 $\pm$ 6.8	.557
3-year f/u	10.5 $\pm$ 8.2	10.8 $\pm$ 7.7	.812
post-pre	-3.1 $\pm$ 10.1	-3.4 $\pm$ 8.6	.807
Dp, wheal diameter (mm)			
Initial	9.2 $\pm$ 4.9	9.2 $\pm$ 4.1	.966
3-year f/u	9.0 $\pm$ 3.5	8.1 $\pm$ 3.8	.127
post-pre	-0.2 $\pm$ 4.4	-1.1 $\pm$ 3.9	.181
Df, wheal diameter (mm)			
Initial	8.1 $\pm$ 3.5	8.2 $\pm$ 3.6	.801
3-year f/u	7.7 $\pm$ 2.6	7.4 $\pm$ 3.0	.498
post-pre	-0.4 $\pm$ 4.3	-0.8 $\pm$ 3.5	.453
Total IgE (U/mL)			
Initial	406.5 $\pm$ 339.3	442.4 $\pm$ 403.9	.664
3-year f/u	463.0 $\pm$ 380.5	440.2 $\pm$ 498.8	.819
post-pre	56.5 $\pm$ 236.2	-2.2 $\pm$ 338.0	.472
Eosinophil count (/ μ L)			
Initial	441 $\pm$ 261	438 $\pm$ 250	.951
3-year f/u	320 $\pm$ 194	390 $\pm$ 254	.156
post-pre	-121 $\pm$ 192	-48 $\pm$ 281	.168

The values are demonstrated as mean $\pm$ SD.

Bold text indicates statistical significance (*P* $<.05$).

Dp = Dermatophagoides pteronyssinus; Df = Dermatophagoides farinae; IgE = immunoglobulin E; VAS = visual analog scale.

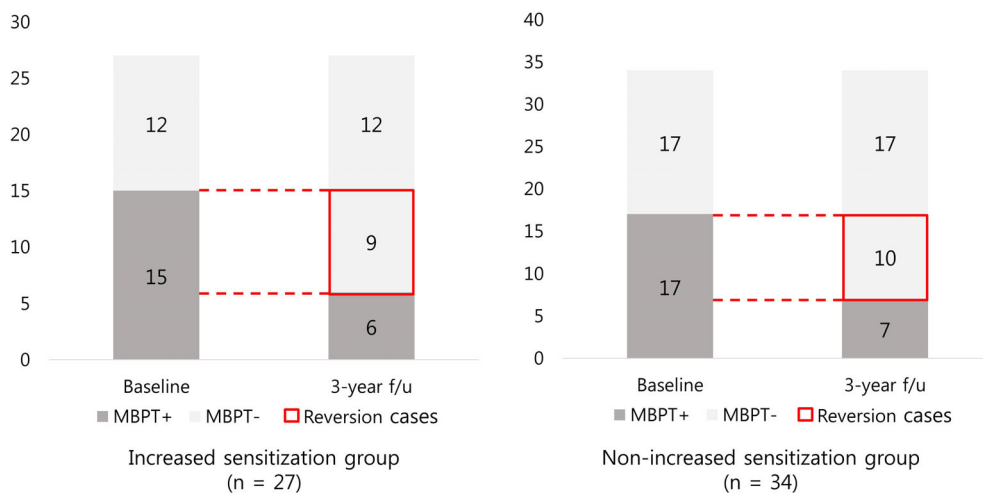


Fig. 4. Changes in the incidence of bronchial hyper-responsiveness after the 3-year follow-up. Reversion refers to the change of reaction from positive at baseline to negative at the 3-year follow-up. The reversion and change of reaction from positive at the baseline test to negative at the 3-year follow-up occurred in nine (60.0%) and 10 (58.8%) patients in groups I and II, respectively. MBPT = methacholine bronchial provocation test. [Color figure can be viewed in the online issue, which is available at www.laryngoscope.com.]

respectively. However, a significant difference was not observed ($P = 1.000$).

Subgroup Analysis Depending on Treatment (SLIT vs. Pharmacotherapy)

Among the 174 patients, 62 were treated with SLIT and 112 were treated without SLIT (pharmacotherapy alone). The mean duration of SLIT in 62 patients was 2.3 ± 0.8 years; the range of SLIT was 1 month to 3 years. The changes in the number of allergens were not significantly different between patients treated with SLIT and those who were not ($P = .595$). In patients treated with SLIT, no significant correlation was observed between the changes in the number of allergens and the total nasal VAS score ($R^2 < 0.001$, $P = .851$) (Fig. 5a).

Moreover, the changes in the number of allergens did not correlate with the changes in the total nasal VAS score in patients who were treated with pharmacotherapy ($R^2 < 0.001$, $P = .810$) (Fig. 5b). Regardless of treatment with SLIT, the total nasal VAS scores were not significantly different between groups I and II at baseline, the 3-year follow-up, and post-pre (Table III). In the additional subgroup analysis of 62 patients treated with SLIT, no significant differences were observed in terms of demographic and immunologic factors except for in the number of sensitized allergens at the 3-year follow-up and post-pre, which was consistent with the data presented in Table II. In the subgroup analysis of 112 patients who were treated with pharmacotherapy, the post-pre wheal diameter of Dp was significantly larger in group I than it was in group II. Otherwise, no significant

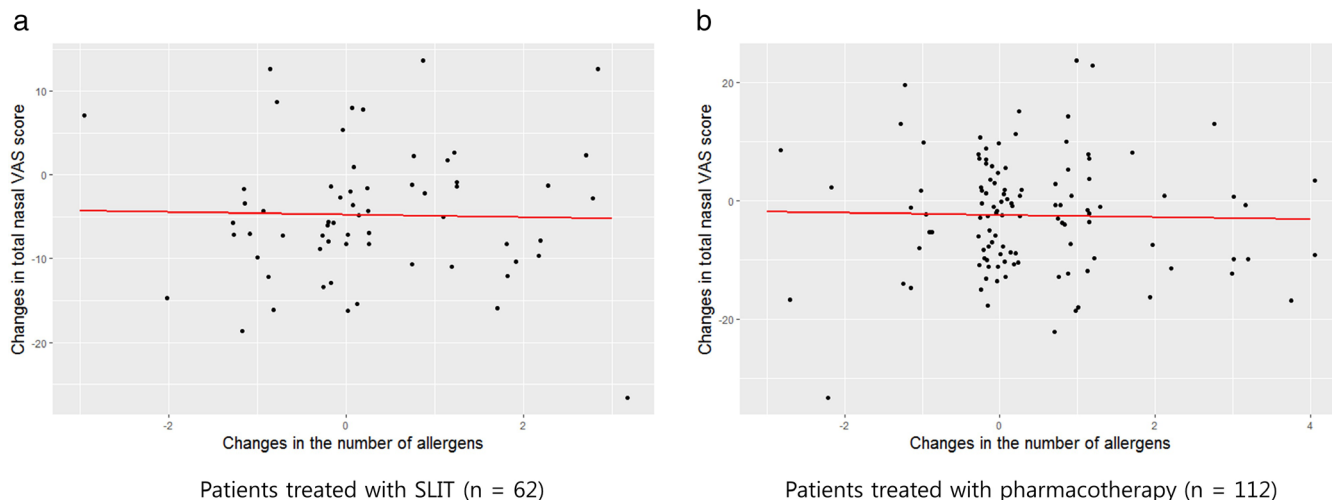


Fig. 5. Correlation between the changes in the number of allergens and the total nasal VAS score. (a) Patients who were treated with SLIT. (b) Patients who were treated with pharmacotherapy. SLIT = sublingual immunotherapy; VAS = visual analog scale. [Color figure can be viewed in the online issue, which is available at www.laryngoscope.com.]

TABLE III.
Comparison of Clinical Features According to Changes in Sensitized Allergens, Subgroup Analysis Depending on Treatment.

	Patients treated with SLIT (n = 62)		P	Patients treated with pharmacotherapy (n = 112)		P
	Group I (n = 22)	Group II (n = 40)		Group I (n = 41)	Group II (n = 71)	
Age, y	8.3 ± 2.1	8.7 ± 2.6	.524	7.8 ± 2.1	7.6 ± 2.6	.701
Sex (male: female)	17: 5	26: 14	.475	32: 9	47: 24	.267
Duration of symptoms, y	3.1 ± 2.1	3.4 ± 2.0	.640	2.3 ± 2.1	2.5 ± 2.0	.520
No. of sensitized allergens, mean ± SD						
Initial	1.6 ± 1.0	1.9 ± 1.1	.342	1.7 ± 1.0	1.8 ± 1.1	.534
3-year f/u	3.3 ± 1.3	1.4 ± 0.8	<.001	3.3 ± 1.3	1.5 ± 0.8	<.001
post-pre	1.7 ± 0.9	-0.5 ± 0.7	<.001	1.6 ± 0.9	-0.3 ± 0.7	<.001
Total Nasal VAS						
Initial	13.5 ± 7.3	13.7 ± 6.8	.924	13.6 ± 7.3	14.5 ± 6.8	.507
3-year f/u	9.4 ± 8.2	8.6 ± 7.7	.656	11.1 ± 8.2	12.1 ± 7.7	.538
post-pre	-4.1 ± 10.1	-5.2 ± 8.6	.627	-2.5 ± 10.1	-2.5 ± 8.6	.974
Dp, wheal diameter (mm)						
Initial	11.8 ± 4.9	10.5 ± 4.1	.277	7.8 ± 4.9	8.4 ± 4.1	.470
3-year f/u	9.5 ± 3.5	8.8 ± 3.8	.443	8.7 ± 3.5	7.7 ± 3.8	.175
post-pre	-2.2 ± 4.4	-1.8 ± 3.9	.705	0.8 ± 4.4	-0.8 ± 3.9	.023
Df, wheal diameter (mm)						
Initial	9.4 ± 3.5	9.8 ± 3.6	.674	7.4 ± 3.5	7.3 ± 3.6	.956
3-year f/u	8.4 ± 2.6	8.6 ± 3.0	.803	7.3 ± 2.6	6.7 ± 3.0	.218
post-pre	-1.1 ± 4.3	-1.2 ± 3.5	.872	-0.0 ± 4.3	-0.6 ± 3.5	.406
Total IgE (U/mL)						
Initial	516.7 ± 421.1	622.9 ± 489.7	.486	319.5 ± 234.5	295.8 ± 238.9	.732
3-year f/u	538.3 ± 399.8	652.8 ± 643.4	.538	403.6 ± 364.2	267.5 ± 234.6	.111
post-pre	21.6 ± 244.8	29.9 ± 471.2	.950	84.1 ± 232.1	-28.3 ± 171.6	.053
Eosinophil count (/uL)						
Initial	424 ± 269	493 ± 284	.420	457 ± 260	391 ± 212	.229
3-year f/u	285 ± 212	422 ± 279	.084	353 ± 173	363 ± 231	.875
post-pre	-139 ± 185	-71 ± 342	.446	-104 ± 203	-29 ± 222	.230

The values are demonstrated as mean ± SD.

Bold text indicates statistical significance ($P < .05$).

Dp = Dermatophagoides pteronyssinus; Df = Dermatophagoides farina; IgE = immunoglobulin E; SLIT = sublingual immunotherapy; VAS = visual analog scale.

differences were observed in terms of demographic and immunologic factors between the two groups.

DISCUSSION

The pathogenic mechanisms underlying allergic sensitization are complicated and still only partially understood. Current concepts of allergen sensitization are characterized by the Th2-deviated immune response and the corresponding deficiency of allergen-specific Th1 cells.^{2,13} However, there are patients with allergies who have persistent mono-sensitization over several years. IL-10 and IFN- γ levels were found to be higher in children with allergic rhinitis who remained mono-sensitized than in those who became polysensitized.² This study implies that new sensitization is related to worse prognosis among patients with allergic rhinitis due to the potential anti-allergic effects of IL-10 and the role of IFN- γ in the Th1-mediated immune response.^{3,4} In addition, the sensitization to allergens is associated with the development of asthma.¹⁴ In one study, the number of patients

who were newly sensitized to mite allergens and developed allergic diseases, such as asthma, eczema, and food allergies, was higher than the number of patients who were not sensitized.¹⁵ Moreover, the prevention of new sensitization was a positive indicator for successful immunotherapy.^{5-7,16,17} However, there is a lack of knowledge about the direct correlation between the newly sensitized allergen and worsening of allergic symptoms. In the present study, the correlation between the increased number of sensitized allergens and nasal symptoms was evaluated in patients with allergic rhinitis who were sensitized to HDMs.

In this study, 174 children were enrolled, and the mean number of sensitized allergens slightly increased from 1.8 at baseline to 2.1 at the 3-year follow-up. In the present study, the simple linear regression analysis revealed no significant correlation between the changes in the number of allergens and the total nasal VAS score in all patients and in patients who were mono-sensitized to HDMs at baseline. The change in the total nasal VAS score was not significantly different between groups I and

II. Moreover, the comparison of demographic and immunological factors between the two groups did not show any significant differences.

Regarding these results, the existence of a dominant allergen may explain the lack of correlation between the increase in sensitized allergens and nasal symptoms in this study. In contrast to previous studies,^{15,18–20} our study evaluated the effects of allergen sensitization in addition to HDMs, which have been identified as the main allergen in Asia. Because HDMs are the dominant allergen in these patients and this allergen plays a major role in the development of nasal symptoms in these patients, the effects of other allergens might not be significant. In previous studies in Asian countries,^{11,12} immunotherapy with HDMs showed comparable effects in patients who were poly-sensitized and mono-sensitized, which indicated the importance of controlling HDMs in poly-sensitized patients in Asia. Considering the significant effects of HDMs on nasal symptoms, the influence of other allergens in this study might have been too small to cause significant differences in patients' allergic rhinitis symptoms.

Another explanation for the lack of correlation between the increase in sensitized allergens and nasal symptoms may be related to the difference between poly-sensitization and poly-allergy. As poly-sensitized patients are not necessarily poly-allergic,²¹ the newly sensitized allergens may not cause a clinical problem. The clinical problems caused by newly sensitized allergens, such as specific seasonal nasal symptoms, were not evaluated in this study. Therefore, the clinical correlation between nasal symptoms and newly sensitized allergens should be assessed in a further investigation.

In relation to treatment, the changes in the number of allergens were not significantly different between patients treated with SLIT and those who were not. In addition, no significant correlation was observed between the changes in the number of allergens and the total nasal VAS score regardless of SLIT. In patients who were not treated with SLIT, the change in the wheal diameter of Dp was greater in group II than it was in group I, and this result is inconsistent with that presented in Table II. To evaluate this result in more detail, an additional simple linear regression analysis was performed. The analysis revealed a significant correlation between the change in the wheal diameter of Dp and that in the number of allergens; however, a low explanatory power was observed ($R^2 = 0.031$, $P = .020$ in all patients, and $R^2 = 0.072$, $P = .004$ in patients who were not treated with SLIT; data not shown). Furthermore, no significant correlation was observed between the change in the wheal diameter of Df and the number of allergens ($R^2 = 0.005$, $P = .347$, data not shown). Interestingly, this analysis indicated that the change in the allergic reaction to Dp may be associated with the change in the number of allergens. To the best of our knowledge, only a few studies have investigated the direct correlation between new sensitization and the increased number of allergens based on skin test reactivity. Therefore, further evaluation with a larger cohort must be conducted to confirm this result. Except for the change in the wheal diameter

of Dp, no other demographic and immunologic factors were significantly different between the two groups in the subgroup analysis according to treatment with SLIT.

Several studies have shown that allergen-specific immunotherapy has a preventive effect for new sensitization in allergic rhinitis and/or asthma patients.^{5–7} In the present study, however, the changes in the number of allergens did not significantly differ between patients treated with SLIT and those who were not. There are some different points from previous studies. First, the age and duration of allergic rhinitis symptoms were different between SLIT and pharmacotherapy groups in the present study ($P = .012$ and $P = .031$, respectively, data not shown). Age and duration of allergic rhinitis symptoms are possible contributing factors that may affect allergen sensitization, and there are some studies that the prevalence of polysensitization was increased with age in children.^{22,23} Moreover, previous studies were conducted in Western countries,^{5–7} while this study was carried out in Korea. Therefore genetic and environmental factors differ from those in previous studies.²⁴ The recent meta-analysis showed no significant difference in new sensitization between allergen-specific immunotherapy and pharmacotherapy.²⁵

The design of our study is distinguishable from those of previous studies in various ways. In previous studies,^{18–20,26} the correlation between the development of allergic diseases and sensitization to allergens at a certain point (instead of the change in sensitization) was commonly evaluated. These studies evaluated the allergic symptoms and risk of asthma depending on the sensitivity of specific allergens in allergic diseases rather than the effects of new sensitization. In prior cohort studies, the relationship between the change in allergic sensitization and allergen exposure was primarily assessed.^{27–30} However, in our study, the direct correlation between the changes in the number of sensitized allergens and nasal symptoms was evaluated by examining skin sensitivity and nasal symptoms at both the baseline and 3-year follow-up visits. Moreover, newly sensitized allergens were assessed in participants who were initially sensitized to HDMs, which was different from the design of previous studies. In contrast to several studies that emphasized new sensitization as an indicator of the progression of allergic disease,^{6,7,16–18} the increased number of sensitized allergens was not correlated with the worsening of nasal symptoms in the present study. This result indicates that clinicians should focus on the allergic symptoms of patients and must not overestimate new sensitization as a negative indicator of successful treatment.

The present study had some limitations. The medication scores of each patient were not recorded, and the duration of SLIT was not controlled among the treated patients. Despite the importance of the treatment period, controlling the duration of SLIT was not the primary focus of the present study because the primary outcome was the correlation between the changes in the number of sensitized allergens and the nasal VAS scores. Therefore, the subgroup analysis we performed that depended on treatment with SLIT was possibly conducted in a heterogeneous patient group.

CONCLUSION

New sensitization may not be correlated with nasal symptoms in patients in Asian countries where HDMs play a major role as a dominant allergen. Therefore, clinicians should advise patients not to be frustrated with their increased number of sensitized allergens. Although further studies are required, the importance of new sensitization as a clinical parameter of immunotherapy should be reconsidered in Asia.

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