

Association Between Sensitization to Outdoor Spider Mites and Clinical Manifestations of Asthma and Rhinitis in the General Population of Adults

It has been demonstrated that spider mites such as the two-spotted spider mite (*Tetranychus urticae*) are important allergens for fruit farmers. A total of 2,467 adults (795 metropolitan urban, 788 non-metropolitan urban, and 884 rural subjects) were enrolled. They responded to the questionnaire, and underwent methacholine bronchial provocation tests as well as skin prick tests to locally common aeroallergens including the two-spotted spider mite. The prevalences of asthma and rhinitis as reported on the questionnaire were 7.8% and 16.4% of adults aged 20-35, 9.4% and 24.7% of those 36-50, and 17.7% and 21.7% of those older than 50, respectively. Among the older group, the two-spotted spider mite was the most common sensitizing allergen, although it was second of that of house dust mites among the other two age groups. Sensitization to the two-spotted spider mite was significantly associated with the prevalence of asthma and rhinitis among the younger age group, and associated with the prevalence of rhinitis among the older age group. The two-spotted spider mite might be a common sensitizing allergen in the general population of adults, and sensitization to this mite may play a role in the manifestation of asthma and rhinitis symptoms during adulthood.

Key Words : *Tetranychidae*; Spider Mites; Asthma; Rhinitis

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INTRODUCTION

Asthma is a worldwide problem considered to be more common in developed countries than in developing countries. Although asthma is a common cause of morbidity in adults, the perception remains that it is a childhood disease. Asthma incidence is higher in children than in adults, and remissions are unlikely after the age of 30 yr (1, 2). In children, there is an association between the presence of atopy and the prevalence of asthma and rhinitis during childhood (3). However, there have been relatively few population studies of asthma prevalence and association between atopy and asthma during adulthood.

Asthma and allergic rhinitis due to indoor house dust are major health problem worldwide, and house dust mites *Dermatophagoides farinae* and *D. pteronyssinus* are the most impor-

tant indoor allergens in Korean children (4). Meanwhile, it is the spider mites (family *Tetranychidae*), forming the family of phytophagous mites, which have the heaviest economic burden on agriculture. All spider mites are outdoor phytophagous mites causing significant damage to fruit leaves throughout the world, and belong to the suborder Prostigmata of the order Acari, while house dust mites belong to the suborder Astigmata of the same order. Although predaceous mites do indeed attack spider mites, the predator complex currently in place does not usually control spider mites, particularly when organic phosphates or sulfur spray programs upset natural control (5). Although spider mites were negligible pests in fruit-cultivation before World War II, their number has increased in the fruit-cultivation industry since pesticides were introduced to eliminate fruit moths 40 yr ago. Surveys have demonstrated that the two-spotted spider

mite (*Tetranychus urticae*, TSM) is one of the most common pests in herbaceous plants and fruit leaves. Our previous cross-sectional studies demonstrated that spider mites are important allergens in the development of work-related asthma and rhinitis in fruit farmers (6, 7). The aim of our present study was to evaluate the association between sensitization to TSM and clinical manifestations of asthma and rhinitis in the general population of adults living in urban and rural areas.

MATERIALS AND METHODS

Populations

A total of 2,467 adults over 20 yr, 795 of whom were living in metropolitan city (Seoul), 788 in non-metropolitan cities (Cheonan and Icheon), and 884 in rural area (Khoisan), were randomly enrolled in this study. The male female ratio was the same in all three groups. The questionnaire response rate was 2,432 subjects, with 2,401 undergoing skin prick tests to locally common aeroallergens including the TSM and 1,858 methacholine bronchial provocation tests. All the subjects gave informed written consent and the study protocol was approved by the Ethics Committee of Seoul National University Hospital.

Methods

A modified questionnaire developed by the International Study of Asthma and Allergic diseases in Children (ISAAC) (8) was translated into Korean, of which validity was already studied (9, 10), with demographic data, asthma and rhinitis symptoms, and various risk factors, such as family history of asthma and allergic rhinitis and active cigarette smoking being included. The symptoms of asthma were wheezing, breathlessness, and recurrent nocturnal cough during the previous 12 months, and asthma was regarded as having been positively tested if a subject had experienced two or more of these asthma symptoms. Rhinitis symptoms were sneezing, and runny or blocked nose with itchy eyes during the previous 12 months when a subject did not have a cold or the 'flu'.

Skin prick tests were performed using a panel of 12 common Korean aeroallergens. None of the subjects had received antihistamines orally for five days preceding the tests. The panel consisted of house dust mites (*Dermatophagoides pteromyssinus*, *D. farinae*), cat fur, molds (*Aspergillus fumigatus*, *Alternaria tenuis*), various pollens (tree pollen mixture 1 [alder, hazel, poplar, elm, and willow tree] & 2 [birch, beech, oak, and plane tree], grass pollen mixture [velvet grass, orchard grass, rye grass, timothy grass, Kentucky blue grass, and meadow grass], mugwort, and ragweed), German cockroach (*Blattella germanica*), and TSM (0.1 mg/mL). TSM was obtained from

both the Apple Research Institute, Kyungbuk, Korea, and were extracted as previously described (7). A positive control of histamine (1 mg/mL) along with a negative diluent control was included in all tests. Fifteen minutes after the prick, the mean diameter of the wheal formed by the allergen was compared with that formed by histamine. If the former was greater or equal to the latter (allergen/histamine ratio ≥ 1.0), the reaction was defined as positive. Atopy was defined if a subject exhibited positive skin-test responses to any one or more of the 12 aeroallergens.

Forced expiratory volume in 1 sec (FEV₁) and forced vital capacity (FVC) were measured with a portable spirometer (Micro Spirometer, Micro Medical, Rochester, Kent, U.K.), with the largest values of triplicate FEV₁ and FVC measurements being adopted. Methacholine challenge was carried out to determine bronchial responsiveness using the method described by Chai et al. (11). Subjects with respiratory tract infections during the two weeks immediately prior were excluded to avoid false positive result, and those with baseline FEV₁ lower than either 1,200 mL or 50% of the predictive value were also excluded to avoid the recording of severe bronchoconstrictive reaction. None of the subjects had received any bronchodilators or anti-histamines for five days preceding the challenge. Concentrations of 2.5, 6.25, 12.5, and 25 mg/mL of methacholine were prepared by dilution with buffered saline. A Rosenthal-French dosimeter (Laboratory for Applied Immunology, Baltimore, MD., U.S.A.) was used to deliver the aerosol generated by a nebulizer (DeVilbiss, Somerset, PA, U.S.A.). Subjects inhaled five inspiratory capacity breaths of increasing methacholine concentration until either FEV₁ fell to less than 80% of its baseline value or until the highest concentration was reached. The largest value of triplicate FEV₁ measurements at 90 or 180 sec after each inhalation was adopted for analysis. If the concentration of methacholine which caused a 20% fall in FEV₁ (PC20) was less than 25 mg/mL, the subject was considered to have airway hyperresponsiveness (AHR) to methacholine.

Statistical analysis

Statistical significances of association between the clinical symptoms of asthma and rhinitis and risk factors, including sensitization to TSM were assessed using the χ^2 and χ^2 -trend test. A *p* value of 0.05 or less was regarded as significant.

RESULTS

Table 1 shows demographic and clinical characteristics of the general population according to age. The frequency of active cigarette smoking did not vary with age, but was markedly higher among men than among women. Whereas the prevalences of atopy (positive skin test responses to one or more common allergens) and of rhinitis on the question-

Table 1. Demographic and clinical characteristics of study populations according to age group

	Age (yr)			<i>p</i> *
	≤35 (n=709)	36-50 (n=934)	≥51 (n=824)	
Sex, female (%)	346 (48.8)	442 (47.3)	432 (48.7)	NS
Geographic areas				
Metropolitan area	288	317	190	<0.001
Non-metropolitan area	257	339	192	
Rural area	164	278	442	
Smoking (n=2,394)	276 (39.3)	375 (41.4)	347 (44.1)	NS
Women (n=1,140)	17 (5.0)	12 (2.9)	25 (9.2)	0.01
Men (n=1,254)	259 (71.9)	363 (74.7)	312 (76.5)	NS
Family history [†] (n=2,323)	162 (24.0)	237 (26.7)	135 (17.7)	0.003
Atopy [‡] (n=2,467)	251 (35.4)	262 (28.1)	212 (25.7)	<0.001
<i>D. pteronyssinus</i>	107 (15.5)	93 (10.2)	56 (7.0)	<0.001
<i>D. farinae</i>	101 (14.7)	102 (11.1)	18 (7.3)	<0.001
<i>T. urticae</i>	62 (9.0)	87 (9.5)	95 (11.9)	0.05
<i>T. putrescentiae</i>	49 (7.1)	77 (8.4)	46 (5.8)	NS
German cockroach	41 (6.0)	44 (4.8)	44 (5.5)	NS
AHR [§] (n=1,858)	26 (5.7)	39 (5.4)	98 (14.6)	<0.001
Asthma (n=2,452)	55 (7.8)	87 (9.4)	145 (17.7)	<0.001
Rhinitis (n=2,451)	115 (16.4)	223 (24.7)	175 (21.7)	0.02

*Chi-square trend test. [†]Asthma or allergic rhinitis within family. [‡]Skin-test responses to one or more aeroallergens. [§]PC20-methacholine <25 mg/mL.

naire declined with advancing age, the prevalence of AHR to methacholine and asthma increased inclining with advancing age. On the allergen skin prick tests, five aeroallergens, such as *D. pteronyssinus*, *D. farinae*, TSM, *Tyrophagus putrescentiae*, and cockroach in decreasing order, were common sensitizing allergens with sensitization rates higher than 5% of subjects. The sensitization rate to TSM showed an increasing tendency with advancing age, although to house dust mites *D. pteronyssinus* and *D. farinae* it showed a decreasing tendency.

Table 2 shows relationship between risk factors and asthma as reported on the questionnaire according to age. Among adults younger than 35 yr, sex, a family history of allergic diseases, and active smoking were all found to be not significantly associated with the prevalence of asthma. However, the prevalence of asthma was significantly higher in atopics (11.6% vs. 5.7%), those with sensitization to *D. pteronyssinus* (15.0% vs. 6.4%), and those with sensitization to TSM (19.4% vs. 6.6%). Among adults aged 36-50 yr, sex, a family history of allergic diseases, atopy, and sensitization to *D. pteronyssinus* and TSM were all not significantly associated with the prevalence of asthma. Among adults older than 50 yr, sex, atopy and sensitization to *D. pteronyssinus* and TSM were all not significantly associated with the prevalence of asthma. However, the prevalence of asthma was higher in smokers (21.7% vs. 14.8%), and those with a family history of allergic diseases (26.9% vs. 16.2%).

Table 3 shows relationship between risk factors and non-

Table 2. Relationship between the prevalence of clinical asthma by questionnaire and risk factors according to age

Age (yr) groups		Clinical asthma		<i>p</i> *	
		Negative, No.	Positive, No. (%)		
≤35	Sex				
	Women	318	27 (7.8)	NS	
	Men	333	28 (7.8)		
	Family history [†]	-	475	37 (7.2)	NS
	+	147	15 (9.3)		
	Smoking	-	397	28 (6.6)	NS
	+	249	27 (9.8)		
	Atopy [‡]	-	430	26 (5.7)	0.008
	+	221	29 (11.6)		
	<i>D. pteronyssinus</i>	-	542	37 (6.4)	0.005
+	91	16 (15.0)			
<i>T. urticae</i>	-	583	41 (6.6)	0.001	
+	50	12 (19.4)			
36-50	Sex				
	Women	393	43 (9.9)	NS	
	Men	445	44 (9.0)		
	Family history [†]	-	586	60 (9.3)	NS
	+	214	21 (8.9)		
	Smoking	-	476	50 (9.5)	NS
	+	339	34 (9.1)		
	Atopy [‡]	-	606	55 (7.8)	NS
	+	232	28 (10.8)		
	<i>D. pteronyssinus</i>	-	739	76 (9.3)	NS
+	86	7 (7.5)			
<i>T. urticae</i>	-	749	72 (8.8)	NS	
+	76	11 (12.6)			
≥51	Sex				
	Women	323	77 (19.3)	NS	
	Men	353	68 (16.2)		
	Family history [†]	-	524	101 (16.2)	0.006
	+	98	36 (26.9)		
	Smoking	-	375	65 (14.8)	0.01
	+	270	75 (21.7)		
	Atopy [‡]	-	494	115 (18.9)	NS
	+	182	30 (14.2)		
	<i>D. pteronyssinus</i>	-	608	130 (17.6)	NS
+	47	9 (16.1)			
<i>T. urticae</i>	-	572	127 (18.2)	NS	
+	83	12 (12.6)			

*Chi-square trend test. [†]Asthma or allergic rhinitis within family. [‡]Skin-test responses to one or more of 12 common aeroallergens.

infectious chronic rhinitis as reported on the questionnaire according to age. Among adults younger than 35 yr, neither sex nor active smoking were significantly associated with the prevalence of asthma. However, the prevalence of rhinitis was significantly higher in subjects with a family history of allergic diseases (25.5% vs. 12.8%), atopics (22.6% vs. 13.8%), those with sensitization to *D. pteronyssinus* (24.5% vs. 15.0%), and those with sensitization to TSM (30.6% vs. 15.0%). Among adults aged 36-50 yr, the prevalence of rhinitis was significantly higher in women (28.3% vs. 21.4%), those with family history of allergic diseases (36.2% vs. 19.0%),

Table 3. Relationship between the prevalence of chronic rhinitis by questionnaire and risk factors according to age

Age (yr) groups		Clinical asthma		<i>p</i> *
		Negative, No.	Positive, No. (%)	
≤35				
Sex	Women	282	61 (17.8)	NS
	Men	303	54 (15.1)	
Family history [†]	-	442	65 (12.8)	<0.001
	+	120	41 (25.5)	
Smoking	-	348	73 (17.3)	NS
	+	233	41 (15.0)	
Atopy [‡]	-	393	59 (13.1)	0.001
	+	192	56 (22.6)	
<i>D. pteronyssinus</i>	-	488	86 (15.0)	0.02
	+	80	26 (24.5)	
<i>T. urticae</i>	-	525	93 (15.0)	0.003
	+	43	19 (30.6)	
36-50				
Sex	Women	307	121 (28.3)	0.02
	Men	374	102 (21.4)	
Family history [†]	-	510	120 (19.0)	<0.001
	+	148	84 (36.2)	
Smoking	-	378	139 (26.9)	0.01
	+	293	70 (19.3)	
Atopy [‡]	-	504	146 (22.5)	0.02
	+	177	77 (30.3)	
<i>D. pteronyssinus</i>	-	606	190 (23.9)	NS
	+	63	28 (30.8)	
<i>T. urticae</i>	-	611	193 (24.0)	NS
	+	58	25 (30.1)	
≥51				
Sex	Women	307	89 (22.5)	NS
	Men	326	86 (20.9)	
Family history [†]	-	500	119 (19.2)	0.002
	+	89	42 (32.1)	
Smoking	-	347	89 (20.4)	NS
	+	267	72 (21.2)	
Atopy [‡]	-	481	118 (19.7)	0.03
	+	152	57 (27.3)	
<i>D. pteronyssinus</i>	-	573	153 (21.1)	NS
	+	41	14 (25.5)	
<i>T. urticae</i>	-	552	137 (19.9)	0.007
	+	62	30 (32.6)	

*Chi-square trend test. [†]Asthma or allergic rhinitis within family. [‡]Skin-test responses to one or more of 12 common aeroallergens.

and non-smokers (26.9% vs. 19.3%). The rhinitis prevalence was also higher in atopics, although it did not differ significantly according to sensitization to *D. pteronyssinus* and TSM. Sex and smoking were not significantly associated with the prevalence of rhinitis in adults older than 50 yr. However, rhinitis prevalence was higher in those with a family history of allergic diseases (32.1% vs. 19.2%), and atopics (27.3% vs. 19.7%). Moreover, the prevalence of rhinitis was higher in those with sensitization to TSM (32.6% vs. 19.9%), although this prevalence was not associated with sensitization to *D. pteronyssinus*.

DISCUSSION

Spider mites were negligible pests in fruit-cultivation before World War II, but their deleterious effects on the fruit-cultivation industry have increased since pesticides were introduced to eliminate fruit moths 40 yr ago, an introduction which led to the development of spider mite allergies. In fact, our own previous epidemiological studies have demonstrated that spider mites are common sensitizing allergens among fruit farmers, and that there is an association between sensitization to spider mites and the prevalence of asthma and rhinitis symptoms among non-farmers living nearby fruit farms as well as the fruit farmers themselves (6, 7, 12). The present study demonstrated the possibility that TSM, which is the most important mite infesting herbaceous plants and fruit leaves over a worldwide distribution, is also a common sensitizing allergen among adults living in rural and urban areas, suggesting that the spider mite allergy may be a common public health problem even in adults working other than fruit cultivation.

Whereas the risk factors determining the development and the persistence of asthma symptoms during childhood were relatively well researched, very few studies have examined the prevalence and risk factors for the development of asthma during adulthood. The incidence and period prevalence of asthma is higher in children than adults (1, 13). Prevalence determined from cross sectional data depends on both the incidence and the duration of the disease from its onset. In this instance, duration reflects both the degree to which asthma tends to persist, or remit, and the mortality associated with the disease. Remission from asthma may occur, but is unlikely after the age of 30 yr, and the number of people who die of asthma is relatively small (2). The present study also demonstrated that the prevalence of asthma and AHR to methacholine increased with advancing age.

The association between the prevalence of asthma and skin-test responses to common aeroallergens during adulthood remains controversial, although this association has been reported during childhood (3, 14). Our previous cross-sectional survey to evaluate the sensitization to spider mites and its relationship with bronchial responsiveness among non-asthmatic children living nearby fruit farms has shown that AHR to methacholine is significantly associated with sensitization to spider mites (15). The present study demonstrated that the prevalence of asthma symptoms among adults under 35 yr of age was significantly related with sensitization to both TSM and indoor house dust mites, suggesting the possibility that sensitization to spider mites might be one of the risk factors for the manifestation of asthma symptoms during young adulthood, although TSM contains common shared allergens with the domestic mites in addition to genus and/or species-specific allergens (16). ISAAC questionnaires for symptoms already has been proved valid in the diagnosis of asthma (17).

There is little evidence that adult smokers experience any substantially increased risk of developing asthma, although active cigarette smoking causes serious, adverse effects on the respiratory tract (18). The present study also showed an association between active smoking and asthma prevalence in adults older than 50 yr, but not in adults under 50 yr of age, which was consistent with our previous study (19), suggesting that active smoking rather than sensitization to TSM may be a risk factor for the manifestation of asthma symptoms during old age.

Until recently, relatively little was known about the prevalence of perennial and non-allergic forms of rhinitis and the risk factors for these conditions, and furthermore most of the available epidemiological data relate to seasonal allergic rhinitis or hay fever. Much of our understanding of the epidemiology of rhinitis derives from studies of self-reported disease. In order to distinguish between infective and non-infective rhinitis, the present study used the ISAAC questionnaire, of which as been evaluated (20), asking whether a subject has had a problem with sneezing, or a runny or validity blocked nose in the absence of a cold or the flu. The present study showed that the prevalence of all forms of non-infectious rhinitis ranged from 15% to 25%, a result similar to that produced by a study on 5,349 adults aged 16-65 yr in south London (21).

The prevalence of hay fever appears to be lowest in children under 5 yr of age, rising rapidly to reach a peak in adolescence or early adulthood, and thereafter declining gradually with advancing age (22). The male to female affected ratio has been reported to vary with age, being highest among adolescents and diminishing with advancing age (23). However, very little is known about the age and sex distribution of perennial rhinitis. A retrospective survey of 1,271 clinical trials with perennial rhinitis suggested that, in patients under 20 yr of age, males outnumbered females, whereas in older patients, females outnumbered males, although the overall sex ratio among affected individuals was equal (24). The present study also demonstrated that the prevalence of all-forms of rhinitis was higher in women than men in the middle age group, although this gender prevalence was similar in the younger and older age groups. Interestingly, the present study showed that the prevalence of all-forms of rhinitis and the sensitization to TSM increased with advancing age, although the sensitization rate to indoor house dust mites declined with advancing age. Moreover, the prevalence of rhinitis in the older group was higher in those with sensitization to TSM, although it was not associated with sensitization to indoor house dust mites. In addition, our previous study published on Korean domestic journal recently revealed that there was no definite difference in sensitization rate of TSM according to area including urban area (25). These findings suggest the possibility that sensitization to spider mites newly develops during middle age, followed by the development of rhinitis symptoms during old age after a latent period interval. In

summary, spider mites might be common sensitizing allergens even among non-farming adults, and sensitization to these mites may play a role in the manifestation of asthma and rhinitis symptoms during adulthood.

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