

Eight Aeroallergen Skin Extracts May Be the Optimal Panel for Allergic Rhinitis Patients in Central China

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Keywords

Aeroallergen · Allergic sensitization · Allergic rhinitis · Mite

Abstract

Background: The prevalence of allergic rhinitis (AR) is increasing rapidly in Central China. The skin prick test (SPT) is the standard tool with which to determine the allergen sensitization status in AR patients. Changes in allergen sensitization patterns have been observed within countries and regions due to geographical and seasonal variations. **Objective:** The aim of this study was to evaluate the profile of SPT reactivity to different aeroallergens in AR patients and to suggest a minimal panel of allergens to detect sensitized patients in Central China. **Methods:** From January 2015 to December 2016, patients who presented to Tongji Hospital with suspected AR were tested with the same panel of 19 aeroallergens. The results of SPT were analyzed to determine the minimum test battery panel necessary to cover 99% of the cases of SPT sensitization in different age subgroups. **Results:** A total of 2,416 patients (male:female ratio 1.2:1) were enrolled in our study with an average age of 22.0 years. The overall rate of sensitization to any allergen was 79.0%, and 64.3% of the subjects were monosensitized. The highest sen-

sitized rate was found in the subgroup aged 14–18 years (92.0%), followed by the subgroups of 6–14 years (86.4%), >18 years (75.6%), and ≤6 years (74.9%). The most common sensitization was to *Dermatophagoides farinae* (71.1%). Testing with 8 allergens (*D. pteronyssinus*, *D. farinae*, *Platanus*, *Artemisia*, *Cryptomeria*, *Blatella germanica*, *Humulus*, and *Alternaria*) was sufficient to identify over 99% of the sensitized patients. **Conclusion:** An SPT panel covering 8 allergen extracts was able to detect almost all sensitized patients suffering from AR symptoms in Central China.

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Introduction

Allergic rhinitis (AR) is the most common allergic disease and affects 10–40% of the population worldwide [1]. In China, self-reported AR in the general adult population significantly increased over a 6-year period [2]. A skin prick test (SPT) is the standard procedure for the diagnosis of AR. Kong et al. [3] reported that the prevalence of AR in 3- to 6-year-old children in Wuhan, China, was 27.1% with the diagnostic criterion of AR symptoms, while it was adjusted to 10.8% with both AR symptoms

Table 1. Characteristics of the study population

	≤6 years (n = 517)	6 to ≤14 years (n = 587)	14 to ≤18 years (n = 137)	>18 years (n = 1,175)	Whole group (n = 2,416)
Age, years					
Mean ± SD	4.2 ± 1.3	9.8 ± 2.1	16.1 ± 1.0	36.7 ± 10.8	22.0 ± 16.4
Median	4.0	10.0	16.0	36.0	17.0
Interquartile range	3.0–5.0	8.0–11.0	15.0–17.0	28.0–44.0	7.0–35.0
Gender, n (%)					
Male	366 (70.8)	402 (68.5)	78 (56.9)	486 (41.4)	1,332 (55.1)
Female	151 (29.2)	185 (31.5)	59 (43.1)	689 (58.7)	1,084 (44.9)
Positive SPT, n (%)	387 (74.9)	507 (86.4)	126 (92.0)	888 (75.6)	1,908 (79.0)

and positive SPT results. Previous studies have indicated that dust mite, cockroach, and pets are the major aeroallergens among respiratory allergic patients in Southern China [4]. However, geographical and seasonal variations in allergen sensitization have been observed within countries and regions, and changes in allergen sensitization patterns have also been observed over time [5]. While a standard allergen test panel for AR patients in Europe has already been proposed [6], there is still not a standard panel in China. Furthermore, the optimal number of allergen extracts to be used during an SPT for the diagnosis of sensitized patients that make it cost-effective and limit the degree of pain for children, both of which are important from scientific and economic aspects, remains to be clarified. The aim of our study was to evaluate the profile of SPT reactivity to different aeroallergens in AR patients in Central China, and to suggest a minimal panel of allergens that should be used to detect sensitized patients.

Methods

Patients

The study was conducted in the allergy department of Tongji Hospital, a tertiary university hospital in Central China. From January 2015 to December 2016, all the patients with recurrent nasal symptoms (sneezing, nose itching, rhinorrhea, nasal obstruction) and a suspected diagnosis of AR were enrolled in our study. They were tested with the same panel of 19 aeroallergens. Oral antihistamines were forbidden for at least 3 days before SPT, and other medications that might have an impact on SPT were also prohibited before the SPT according to the current SPT guidelines [7]. The study was approved by the Independent Ethical Committee of Tongji Hospital and all of the participants or their statutory guardian provided informed signed consent.

Skin Test Procedures

A panel consisting of 19 aeroallergen extracts (Macro-Union Pharmaceutical, Beijing, China) was tested for each patient, in-

cluding dust mite (*Dermatophagoides pteronyssinus* and *D. farinae*), cockroach, mulberry silk, animal dander (cat, dog, sheep, and duck), tree pollens (*Sabina chinensis*, *Platanus*, *Populus*, *Cryptomeria*), weed pollens (*Artemisia*, *Ambrosia*, *Humulus*), and molds (*Alternaria*, *Cladosporium*, *Aspergillus*, *Paecilomyces*). Histamine (10 mg/mL) and diluent were used as positive and negative controls. The SPTs were evaluated 15–20 min after application. A positive skin reaction was defined as a wheal size of ≥3 mm after subtraction of the negative control. The skin index (SI) was calculated by the ratio of wheal diameter of each allergen to the wheal diameter induced by histamine and scaled by the following criteria: 1+, SI <0.5; 2+, 0.5 ≤ SI <1.0; 3+, 1.0 ≤ SI <2.0, and 4+, SI ≥2.0 [8]. Monosensitization was defined as a positive reaction to 1 kind of allergen such as dust mite, *Platanus* pollen, or *Artemisia* pollen. Multisensitization was defined as a positive reaction to 2 or more kinds of allergens.

Statistical Analysis

The prevalence of sensitization to each allergen extract was first determined using frequencies and percentages. A step-by-step conditional approach was used to classify allergens from those causing the highest increase in the prevalence of sensitization to those causing the lowest increase. Beginning with the most frequent allergen and continuing in decreasing order of frequency, the allergen source causing the highest prevalence of sensitization was investigated in the subgroup of subjects not sensitized to the previous allergen [9]. The procedure was repeated until 99% coverage for the presence of SPT sensitization was achieved. In addition, the same procedure was repeated with patients allocated by age subgroup as follows: ≤6 years, 6–14 years, 14–18 years, and >18 years of age. SPSS 16.0 software (Chicago, Ill., USA) was used for the statistical analysis.

Results

A total of 2,416 patients with SPT results were evaluated. Among them, 1,332 were male, the average age was 22.0 years (range 1–81), and 1,908 (79.0%) were found to be sensitized to at least 1 of the 19 aeroallergen extracts (Table 1). The most common aeroallergens were *D. fari-*

Table 2. Distribution of the frequencies of sensitization for each allergen used in the SPTs by age subgroup and in the whole study population

	≤6 years, n (%)	6 to ≤14 years, n (%)	14 to ≤18 years, n (%)	>18 years, n (%)	Whole group, n (%)
House dust mite					
<i>D. farinae</i>	367 (71.0)	482 (82.1)	121 (88.3)	748 (63.7)	1,718 (71.1)
<i>D. pteronyssinus</i>	346 (66.9)	466 (79.4)	118 (86.1)	701 (59.7)	1,631 (67.5)
Weed					
<i>Artemisia</i>	12 (2.3)	24 (4.1)	21 (15.3)	133 (11.3)	190 (7.9)
<i>Humulus</i>	15 (2.9)	32 (5.5)	10 (7.3)	113 (9.6)	170 (7.0)
<i>Ambrosia</i>	7 (1.4)	15 (2.6)	6 (4.4)	90 (7.7)	118 (4.9)
Tree					
<i>Platanus</i>	26 (5.0)	52 (8.9)	9 (6.6)	105 (8.9)	192 (8.0)
<i>Populus</i>	12 (2.3)	21 (3.6)	1 (0.7)	45 (3.8)	79 (3.3)
<i>Cryptomeria</i>	0 (0.0)	10 (1.7)	4 (2.9)	47 (4.0)	61 (2.5)
<i>Sabina</i>	0 (0.0)	12 (2.0)	3 (2.2)	41 (3.5)	56 (2.3)
Mold					
<i>Alternaria</i>	33 (6.4)	46 (7.8)	10 (7.3)	23 (2.0)	112 (4.6)
<i>Cladosporium</i>	1 (0.2)	4 (0.7)	0 (0.0)	9 (0.8)	14 (0.6)
<i>Aspergillus</i>	2 (0.4)	1 (0.2)	1 (0.7)	7 (0.6)	11 (0.5)
<i>Paecilomyces</i>	0 (0.0)	0 (0.0)	0 (0.0)	8 (0.7)	8 (0.3)
Animal dander					
Cat	25 (4.8)	51 (8.7)	18 (13.1)	57 (4.9)	151 (6.3)
Dog	4 (0.8)	10 (1.7)	4 (2.9)	14 (1.2)	32 (1.3)
Sheep	7 (1.4)	4 (0.7)	2 (1.5)	6 (0.5)	19 (0.8)
Duck	0 (0.0)	0 (0.0)	1 (0.7)	3 (0.3)	4 (0.2)
<i>Blatella germanica</i>	6 (1.2)	30 (5.1)	14 (10.2)	161 (13.7)	211 (8.7)
Mulberry silk	3 (0.6)	4 (0.7)	1 (0.7)	27 (2.3)	35 (1.5)

nae (71.1%), *D. pteronyssinus* (67.5%), *Platanus* (8.0%), *Artemisia* (7.9%), and *Humulus* (7.0%; Table 2). A total of 1,227 (64.3%) were monosensitized; in multisensitized patients, 13.8% were cosensitized to dust mite and animal dander, 12.2% were cosensitized to dust mite and tree pollen, and 12.0% were cosensitized to dust mite and weed pollen (Table 3).

The highest positive rate of sensitization was found in the subgroup aged 14–18 years (92.0%), followed by the groups aged 6–14 years (86.4%), >18 years (75.6%), and ≤6 years (74.9%; Table 1). The average number of allergens increased with age: there were 2.24 allergens in the subgroup ≤6 years, 2.49 allergens in group aged 6–14 years, 2.73 allergens in group aged 14–18 years, and 2.63 allergens in subgroup >18 years ($p < 0.05$). SPTs with a panel of 3 allergens (*D. farinae*, *D. pteronyssinus*, *Platanus*) provided a positive sensitization rate >95%, and SPTs with 8 allergens (*D. pteronyssinus*, *D. farinae*, *Platanus*, *Artemisia*, *Cryptomeria*, *Blatella germanica*, *Humulus*, and *Alternaria*) presented a rate of >99% (Table 4).

Discussion

Our study identified the aeroallergen sensitization profile among AR patients from children to adults in Central China, which was rather different from other regions [4, 10–11]. We found that the predominant aeroallergen was dust mite, with a sensitization rate of over 90% in the whole group, while other allergens, such as pollen, mold, and cockroach, affected less than 10%. In Northern China, pollens including weeds (*Artemisia* and *Humulus*) and tree pollen (birch) are the significant allergens that cause seasonal AR symptoms [11]. In contrast, airborne pollens are much less significant and cause very few nasal symptoms in Southern China, where cockroach is a major allergen [12]. Geographical and climate variations lead to a diverse exposure to aeroallergens in general populations and it is impossible to apply a uniform allergen test panel in China. Thus, there is an urgent requirement to determine the most common allergens in Central China.

Our study showed that a panel of 8 allergens were needed to identify 99% of sensitized AR patients in Cen-

Table 3. Mono- and multisensitization profile of AR patients

	<i>n</i>	%
Monosensitization	1,227	64.3
HDM		
<i>D. farina</i>	79	6.4
<i>D. pteronyssinus</i>	29	2.4
<i>D. farina</i> and <i>D. pteronyssinus</i>	1,033	84.2
Weed		
<i>Artemisia</i>	5	0.4
<i>Ambrosia</i>	5	0.4
<i>Humulus</i>	5	0.4
Tree		
<i>Platanus</i>	8	0.7
<i>Cryptomeria</i>	7	0.6
<i>Sabina</i>	2	0.2
Mold		
<i>Alternaria</i>	6	0.5
Animal dander		
Cat	2	0.2
Dog	1	0.1
Sheep	1	0.1
<i>B. germanica</i>	14	1.1
Multisensitization	681	35.7
HDM + weed	82	12.0
HDM + tree	83	12.2
HDM + mold	52	7.6
HDM + animal dander	94	13.8
HDM + <i>B. germanica</i>	112	16.4
Weed + tree	23	3.4
HDM + weed + tree	35	5.1
HDM + weed + mold	13	1.9
HDM + weed + animal dander	16	2.3
HDM + weed + <i>B. germanica</i>	31	4.6
HDM + tree + animal dander	11	1.6
HDM + tree + <i>B. germanica</i>	11	1.6
HDM + weed + tree + mold	10	1.5
HDM + weed + tree + animal dander	14	2.1
Other combinations	94	13.8
HDM, house dust mite.		

tral China, which included *D. farina*, *D. pteronyssinus*, *Platanus*, *Artemisia*, *Cryptomeria*, *B. germanica*, *Humulus*, and *Alternaria*, while only 3 allergens were needed to identify 95% of sensitized patients. Thus, we suggest a panel of *D. farina*, *D. pteronyssinus*, and *Platanus* could be utilized in further epidemiologic studies conducted in the area with limited budgets, and the whole battery of 8 allergens might be sufficient in clinical practice. This result was in line with another AR study conducted in Central China which revealed that 91.1% of AR patients were sensitized to dust mite [13]. However, the minimum battery of test aeroallergens needed to cover over 95% of all

Table 4. The offered test panel for different age groups and the percent of sensitization by given aeroallergen extracts

	<i>n</i>	%	Cumulative %
≤6 years			
<i>D. farina</i>	367	94.8	94.8
<i>D. pteronyssinus</i>	11	2.8	97.6
<i>Alternaria</i>	5	1.3	98.9
Sheep	2	0.5	99.4
Dog	1	0.3	99.7
<i>Populus</i>	1	0.3	100.0
6 to ≤14 years			
<i>D. farina</i>	482	95.1	95.1
<i>D. pteronyssinus</i>	13	2.6	97.6
<i>Alternaria</i>	4	0.8	98.4
<i>Blatella germanica</i>	4	0.8	99.2
<i>Humulus</i>	2	0.4	99.6
<i>Artemisia</i>	1	0.2	99.8
Cat	1	0.2	100.0
14 to ≤18 years			
<i>D. farina</i>	121	96.0	96.0
<i>Alternaria</i>	3	2.4	98.4
<i>Artemisia</i>	1	0.8	99.2
<i>D. pteronyssinus</i>	1	0.8	100.0
>18 years			
<i>D. farina</i>	748	84.2	84.2
<i>Artemisia</i>	44	5.0	89.2
<i>Platanus</i>	27	3.0	92.2
<i>D. pteronyssinus</i>	20	2.3	94.5
<i>Cryptomeria</i>	16	1.8	96.3
<i>Humulus</i>	12	1.4	97.7
<i>Blatella germanica</i>	11	1.2	98.9
<i>Ambrosia</i>	6	0.7	99.6
Cat	2	0.2	99.8
<i>Sabina</i>	2	0.2	100.0
Whole group			
<i>D. farina</i>	1,718	90.0	90.0
<i>D. pteronyssinus</i>	53	2.8	92.8
<i>Platanus</i>	42	2.2	95.0
<i>Artemisia</i>	30	1.6	96.6
<i>Cryptomeria</i>	16	0.8	97.4
<i>Blatella</i>	16	0.8	98.2
<i>Humulus</i>	12	0.6	98.8
<i>Alternaria</i>	7	0.4	99.2
<i>Ambrosia</i>	6	0.3	99.5
Cat	4	0.2	99.7
<i>Sabina</i>	2	0.1	99.8
Dog	1	0.1	99.9
Sheep	1	0.1	100.0

the sensitizations varied in different age subgroups: *D. farina* and *D. pteronyssinus* could identify 95% of sensitized patients aged below 18 years, while 5 allergens were needed in patients above 18 years of age. Also, the average

number of allergens increased with age, with 2.24 allergens in the subgroup ≤ 6 years of age, 2.49 allergens in group aged 6–14 years, and 2.73 allergens in the group aged 14–18 years. This phenomenon might reflect the “allergy march” from infant to adult, as documented in several position papers indicating that individuals can develop from monosensitization to multisensitization with a prolonged duration of disease [14]. However, this was not a cohort study. More studies are needed to elucidate the mechanism of the progressive allergen sensitization pattern in the development of allergic diseases.

In our study, only 35.7% of the AR patients were multisensitized, which is a lower rate than in other areas. This might be due to the very high rate of dust mite sensitization in this area – as Central China is subtropical the climate and indoor environment facilitate the growth and reproduction of dust mites. Zheng et al. [15] reported that the dust mite concentration in house dust was 50-fold higher in family homes in Southern China compared to Northern China. Wang et al. [16] also reported that the content of Der p 1 and Der f 1 was above 10 $\mu\text{g/g}$ in bedding samples from Wuhan, the biggest city in Central China with a population over 10 million, which might explain the dust mite sensitization rate of about 80% in Southern China compared to only 40% in Northern China [17]. Conversely, although more than 40 types of airborne pollens could be captured in Central China [18], only a few, such as *Platanus* and weed pollens (*Artemisia* and *Humulus*) could cause notable clinical symptoms in the population. *Platanus* is highly prevalent as an ornamental tree all over Central China, while *Platanus* represents the predominant spring pollen, accounting for nearly 40% in the whole year, and is always the cause of an epidemic of pollinosis from March to May in Central China. The positive skin test rate to *Platanus* pollen is about 27.0% among pollinosis patients and has a high correlation with serum IgE test results [19], which contrasts with European studies. For weed pollens, previous studies demonstrated that *Artemisia* and *Ambrosia* are predominant allergenic pollens in Central China. Recently, *Humulus* pollen has been shown to be another important allergen in autumn, when it represents 9.69% of airborne pollens in Wuhan, and the positive skin test rate was 7.43% among AR patients [20]. Besides the different allergenicities among pollens, frequent rain in this area also restricts the spread of pollens. In contrast, the dry, windy, and rainless climate in Northern China leads to the epidemic of pollinosis [21]. Similar to other regions, mold sensitization is usually less common than mite and pollen causes [22]. In our study, the sensitization rate to *Alternaria* and *Cladosporium* in AR

patients was only 4.6 and 0.6%, respectively. The allergen extracts might have had an impact on the results as some molds were notoriously difficult to standardize [23].

Since our sample size and study population (patients consulting for AR symptoms) allowed us to observe uncommon sensitizations ($<1\%$), our study included several local allergens, such as mulberry silk and *Cryptomeria*. We found that these allergens presented low sensitizations in our study, which implied a larger panel might be unnecessary for general practitioners in this region. We did not include grass pollens in our study. Although grass pollens are major allergenic pollens in Northern China [24], only a few grass pollens can be captured in Central China [18], which might be due to plants such as *Sorghum* and *Cynodon* being sparsely distributed in this area. However, since 21.0% of our patients with nasal symptoms had negative skin test results, we can surmise that some of them were nonallergic patients, and that the others suffered AR with allergens not included in our test panel. Thus, it is crucial to combine the botany, airborne pollen, and mold survey with allergen skin tests in Central China to achieve the best diagnostic efficiency.

Some limitations may hamper our study. Firstly, although the AR patients we tested were from different cities of Central China, it was a single-center study. Secondly, the patient number and male:female ratio in the different age subgroups were not adjusted according to the general population, which might have led to bias. Thirdly, while the aim of our study was to use a minimal allergen panel to achieve the highest positive rate in the AR population, some clinically relevant allergens, such as cat (6.3% sensitized in our study) and dog dander (1.3% sensitized in our study), might have been missed in the context of polysensitization when this statistical method was applied. It should be acknowledged that cat and dog are relevant indoor allergens to those sensitized. Therefore, cat and dog still represent useful allergens in clinical practice. Finally, given that the number of allergens we tested in our study was limited, some clinically relevant allergens, especially pollens, could have been missed. Our previous studies indicated that Moraceae and Gramineae pollens could be potentially important allergenic pollens in this area; however, due to a lack of commercial skin test extracts, these pollens were not tested in the study.

In conclusion, we found a high sensitization amongst AR patients in Central China. Dust mite is the most common allergen in the majority of the population and a panel with 8 allergens was sufficient to identify over 99% of the sensitized patients. There is a need to identify more allergens in Central China in future.

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Disclosure Statement

The authors have no conflicts of interest to declare.

Author Contributions

Jingru Wang performed SPTs, data collection, statistical analysis, and the writing of the paper. Yuying Wu performed SPTs, data collection, and statistical analysis. Jie Li performed SPTs, statistical analysis, and data collection. Xinyuan Huang performed SPTs and data collection. Rongfei Zhu supervised the SPTs, data collection, and the writing and revision of the paper.

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