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Investigation of Allergic Sensitization Pattern in 4,203 Children in Northern China

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Abstract
Objective: The objective of this study is to investigate the allergen sensitization pattern among 4,203 children in the Shanxi region of China and to provide guidance for diagnosis and prevention of allergic diseases. ***Methods:*** A retrospective analysis was conducted on the allergen-specific immunoglobulin E (sIgE) results of 4,203 children aged 0–12 years from January to December in 2019. SIgE antibodies to 19 allergens in the serum sample were detected by enzyme ALLERGO-SORBENT testing. ***Results:*** In total, 49.70% (2,089/4,203) of children with allergic diseases were positive for sIgE, and the top 5 allergens were egg white 18.63% (783/4,203), artemisia 14.47% (608/4,203), milk 13.04% (548/4,203), ragweed 8.66% (364/4,203), and poplar/willow/elm 8.52% (358/4,203). Significant differences in the positive rate of food allergens and aeroallergens in different ages were found ($p < 0.05$). 50.98% (1,065/2,089) patients were sensitive to 2 or more allergens. The high sensitization rate in the >3-year group was significantly higher than the ≤3-year group ($p < 0.05$). ***Conclusion:*** Egg white and artemisia are the most common allergens in children in northern China. This study provides allergic sensitization pattern of children and clinical epidemiological data in the region.

Introduction

Allergic diseases are a relatively common pediatric disease, including bronchial asthma, allergic rhinitis, eczema, urticaria, food allergy, and so on, which seriously affect the patients' quality of life and increase the economic burden on society and family. Allergic diseases have been on the rise yearly and become the most important noninfectious diseases affecting children's health [1]. At present, the focus of clinical medicine on allergic diseases has shifted from secondary and tertiary prevention to primary prevention. Avoiding allergens can effectively prevent the emergence and development of diseases, which rely on the identification of causation allergens [2].

However, the allergen sensitization pattern is diverse in different regions due to the geography, temperature, cli-

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mate, lifestyle, and dietary habits [3, 4]. Located in the North China, Shanxi Province is an arid region with less forest vegetation. There have been limited studies on the allergic sensitization pattern in the region. The aim of this study was to investigate the characterization of allergens in children in the region. Allergens are subdivided into aeroallergens and food allergens. Serum allergen-specific immunoglobulin E (sIgE) test is the main method to detect the allergens in vitro. Therefore, in our study, peripheral blood of children with clinically suspected and confirmed allergic diseases was collected, and sIgE antibodies in serum were detected by enzyme ALLERGO-SORBENT testing. The results can identify the common allergens and their distribution characteristics in this region and provide guidance for clinical prevention and treatment of allergic diseases.

Materials and Methods

Study Population

A total of 4,203 children with allergic symptoms were enrolled in this study. They were all from Children's hospital of Shanxi province from January 1 to December 31, 2019. The following symptoms were suspected to be a cause of allergy by the pediatricians: sneezing, runny nose, stuffy nose, itchy nose, dyspnea, rashes, urticaria, diarrhea, indigestion, and itchy eye. Children with immune diseases and no clinical data were excluded.

Detection Methods

Two-milliliter venous blood samples were collected from children. Serum was separated and stored at − 80°C before being tested. The samples were determined semi- quantitatively via enzyme ALLERGO-SORBENT test, using EUROLINE Atopy China (IgE) test kit (EUROIMMUN, Germany). The kit contains test strips coated with parallel lines of 19 different allergen extracts. All strips were incubated in an automatic immunoassay system using EUROBlotMaster (EUROIMMUN) according to the directions of the manufacturer. After incubated with 400 μL serum, the bound sIgE antibodies were detected using an enzyme-linked antihuman IgE catalyzing a color reaction. Then strips were scanned and analyzed by EUROLineScan software automatically. CCD positive patients had been excluded from this study. The coated allergens on the strips include poplar/willow/elm, ragweed, artemisia, dust mite, house dust, cat dander, dog dander, cockroaches, combination of mold (mold spore aspergillus/branches/smoke mildew), humulus, milk, egg white, peanut, soybean, beef and mutton, cod/lobster/scallops, shrimp, and crab.

The results were presented as the color depth of the strips. Seven grades were classified as follows: grade 0 (<0.35 kU/L), grade 1 (0.35–0.7 kU/L), grade 2 (0.70–3.5 kU/L), grade 3 (3.50–17.5 kU/L), grade 4 (17.5–50 kU/L), grade 5 (50.0–100 kU/L), and grade 6 (>100.00 kU/L); Positive result was defined as greater than or equal to 0.35 kU/L. Grade 5 or higher was considered as high sensitization. At least 1 positive sIgE was counted as the number of positive cases. This study was approved by the Ethics Committee of Children's Hospital of Shanxi Province (No. 2017-16).

Statistical Analysis

IBM SPSS 22.0 for Windows software was used for all the data analyses. Quality values such as positive rate were presented using percentage or frequency. χ^2 was used for the intergroup difference. $p < 0.05$ was considered as statistically significant.

Results

Patients

The total 4,203 patients consisted of 2,475 (58.89%) males and 1,728 (41.11%) females, with an age ranging from 6 months to 12-year old. There were 1,628 patients, who were ≤3 years, including 963 males and 665 females. Among 2,575 patients who were >3 years, 1,512 cases were male and 1,063 cases were female. There was no significant difference in gender between the 2 groups.

Rates of Positive Detection

Among the 4,203 children with allergic symptoms in this study, 2,089 of them had positive results for at least 1 allergen, with a positive rate of 49.70%. Among the aeroallergens, artemisia was the most common allergen (14.47%), followed by ragweed (8.66%), poplar/willow/elm (8.52%), cat dander (7.83%), and dust mite (5.33%). The most common food allergens were egg white (18.63%), milk (13.04%), soybean (7.59%), and peanut (4.26%). All results are displayed in Table 1. There was no significant difference in positive rate between the 2 different age-groups (46.0% vs. 52.06%; $p > 0.05$). However, for the positive rates of food allergens and aeroallergens, there were highly significant in the 2 groups (Table 2).

Patients with Multi-Sensitization

Among the 2,089 cases of positive sIgE, 1,226 (58.69%) patients were sensitive to 2 or more allergens. SIgE tests for seasonal allergens including poplar/willow/elm, ragweed, artemisia, and humulus were performed. 15.22% (318/2,089) patients showed co-sensitive to poplar/willow/elm, ragweed, and artemisia. 17.42% (364/2,089) patients were sensitive to ragweed. Among them, all patients had also sensitization to artemisia, while 68.96% (251/364) to poplar/willow/elm. No patients were mono-sensitive to ragweed or humulus.

The Degree of Allergic Sensitization

The sIgE antibody levels in 464 patients were equal to or greater than grade 5. There were 94 cases in ≤3-year group and 370 cases in >3-year group. The high allergic sensitization rate was 27.61% in the >3-year group, which was significantly higher than 12.55% in the ≤3-year-old group ($\chi^2 = 63.08$, $p = 0.000$).

Table 1. The positive rate of aeroallergens and food allergens in 4,203 patients

Aeroallergens	*N*	%	Food allergens	*N*	%
Poplar/willow/elm	358	8.52	Egg white	783	18.63
Ragweed	364	8.66	Milk	548	13.04
Artemisia	608	14.47	Peanut	179	4.26
Dust mite	224	5.33	Soybean	319	7.59
House dust	65	1.55	Cod/lobster/scallops	70	1.66
cat dander	329	7.83	Shrimp	10	0.24
Dog dander	100	2.38	Crab	75	1.78
Cockroach	169	4.02	Beef	80	1.90
Combination of mold	194	4.61	Mutton	102	2.42
Humulus	120	2.85			

Discussion

Avoidance is still the most economical and effective treatment of allergic diseases. Therefore, research on allergen sensitization patterns can benefit the prevention of diseases. 4,203 children with allergic symptoms ranging from 6 months to 12 years were included in this study. In order to reduce bias, the enrolled patients were not only based on nasal symptoms but also other symptoms related to food allergies, such as rashes, urticaria, diarrhea, indigestion, and itchy eye. Boys are more often affected than girls. The positive rate of allergen sIgE was 49.7%, which was lower than the 62.1% reported by Han et al. [5] and the 78.7% reported by Chen et al. [6]. This may be due to different disease distribution of included patients in different studies.

The most common aeroallergen detected in our study was artemisia (14.47%), which is not consistent with the highest dust mite reported in other Chinese regions [5–9]. Moreover, the positive rate of artemisia was mounting up from spring to autumn and reached its maximum (29.09%) in August, which is the growing season of Artemisia. Shanxi Province is an arid region of northern China. In order to solve the problems of soil erosion and sand storms, artemisia has been sown extensively in and around the region in recent years. Other common aeroallergens included ragweed and poplar/willow/elm, which are all seasonal allergens. Gao et al. [10] also conducted a research involving 240 patients with allergic asthma and demonstrated that the frequency of sensitization to artemisia in patients from northern China was significantly higher than in those from southwestern China, which is consistent with our results. These results suggest that children in the region should wear masks to avoid exposure to these seasonal allergens. Some studies also showed indoor air purifiers used could improve nasal congestion, sneezing, runny nose, itchy eyes, tearing, and other allergy symptoms [8]. The following aeroallergen was cat dander. This is in agreement with other domestic reports [6], indicating that with the improvement of economic conditions, more and more families are raising pets. However, children with such positive allergens should avoid contacting with animals. It is well accepted that egg white and milk are the most common food allergens worldwide [11], which have also been proved in our study. Other common food allergens were peanut and soybean, which are plant-derived high-protein food. Fewer food allergens were shrimp and crab. The result is in contrast to the survey in southern China, which showed shrimp and crab were the most common food allergens [9]. That is, due to that most cities of southern China are coastal areas, where more seafood is consumed.

Table 2. Comparison of positive rates between ingested and inhaled allergen in different age-groups (*n* (%))

Age-group	Food allergens	Aeroallergens	χ^2	*p* value
≤3 years	629 (38.64)	225 (13.82)	259.07	<0.001
>3 years	538 (20.90)	1,072 (41.65)	257.61	<0.001

In this study, the children were divided into 2 groups according to their age. The positive rate of food allergens in the ≤3-year-old group was significantly higher than that in the aeroallergens, and the positive rate of aeroallergens was significantly higher in the >3 years group. Food allergens decrease with age, while aeroallergens increases, which are in accordance with other reports in China [12], indicating that this feature has nothing to do

with regions. The trend is mainly because the digestive system function of infants is not fully developed, and the barrier function of allergenic antigens is not perfect, resulting in allergy. With the increase of age, the immune system and digestive tract are gradually developed. Meanwhile, outdoor activities increase in children, and the positive rate of aeroallergens increases.

We also found that 58.69% patients were sensitive to 2 or more allergens. Multi-sensitization has mainly been found in seasonal allergens. 15.22% patients had co-sensitive to poplar/willow/elm, ragweed, and artemisia. The phenomenon indicates that crossing reactivity may exist in seasonal allergens. In terms of the degree of allergic sensitization, significant difference has been found between the 2 age-groups. Older children are more likely to develop high-sensitization allergy. This may be due to the fact that the immune systems have been developed with age. Therefore, older children should be alert to allergic diseases and need treatment as soon as possible.

This study is a first comprehensive investigation, providing unique data for the prevalence of allergens in Shanxi population. The results of this study are contributing to a better understanding of the disease, serving as a basis for the development of strategies for preventing and treating allergies. In seasons of allergic disease's flood tide, artemisia plays an important position in child patients in northern China. The government should take effective measures to reduce artemisia growing and improve patients' quality of life. However, the limitation of this study is that the enrolled patients are only based on symptoms, and we do not discuss the correlation between allergic sensitization and different clinical symptoms. The next research direction is to analyze the allergen characteristics in different diseases.

Statement of Ethics

This study was approved by the Ethics Committee of Children's Hospital of Shanxi Province (No. 2017-16).

Conflict of Interest Statement

The authors have no conflicts of interest to declare.

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Author Contributions

W.W. and X.Z. contributed to the literature search, conception and design, statistical analysis, and the initial draft of the manuscript; L.Z. contributed original material and data collection. Y.L. revised the article critically.

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