Biomedical Research 2017; 28 (20): 9070-9074

ISSN 0970-938X
www.biomedres.info

Allergic sensitization feature under high pollen exposure in grassland of China.

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Abstract

Objective: To investigate the profiles of inhaled allergens of Allergic Rhinitis (AR) patients and to study its correlation with local airborne pollen distribution under the environment of grassland in northern China.

Method: 353 AR patients were recruited in this study. 131 were male and 221 were female. All subjects received Skin Prick Test (SPT) for 16 allergens. Meanwhile, Durham sampler was applied to acquire the pollen distribution data from local site in 2015.

Result: 317 of 353 patients (89.8%) were positive to at least one allergen. The most common allergens were: *Artemisia* (75.0%), *Humulus* (61.9%), *Chenopodium* (58.5%), *Ragweed* (56.3%), *Ulmus* (47.2%). *Artemisia* tended to be the severest allergens tested with a rate of severe sensitization of 59.1%. The positive rate of grass/weed pollen was significant higher than tree pollen (83.3% *vs.* 62.9%, P<0.001). The allergic sensitization rate decreased along with age increasing (P=0.005). 9.4% of AR patients was mono-sensitized, 3.97% was double-sensitized, 7.7% was triple-sensitized while 68.8% was poly-sensitized (χ^2=584.80, P<0.001). The peak pollen season was July to August in Xilingol grassland. The pollen monitoring showed the main airborne pollen in local region were *Artemisia* and *Chenopodiaceae*, with a portion of 54.2% and 30.7% of the total pollen grains in 2015, respectively.

Conclusion: *Artemisia* was the predominant allergens for AR patients in grassland region both in allergic sensitization and air distribution indicating environmental impact on AR. Grass/weed pollen had a higher sensitization rate than tree pollen and poly-sensitization was the main sensitization type evoked the challenge of precise immunotherapy for those AR patients.

Keywords: Airborne pollen, Skin prick test, Peak season, Poly-sensitization, *Artemisia*.

Accepted on November 17, 2017

Introduction

In recent years, prevalence of Allergic Rhinitis (AR) has increased dramatically, affecting 10%-40% of total population [1]. Patients' performance of daily activities, sleep patterns, cognitive function, work and school productivity, and quality of life are impaired [2]. Both the genetics and environment factors could affect the developing of AR. AR becomes a major public health issues Exploring provoking allergens may help to improve disease management thus relieve the public health burden.

A large scale of allergens could contribute to the pathogenesis of AR. Identifying the allergens is crucial to manage the disease. In daily clinical consultations, the main measurements include sIgE and Skin Prick Test (SPT). SPT is a standardized test widely applied in the diagnosis of suspected IgE mediated allergy [3]. Sensitization allergen profiles evaluated by SPT varied considerably depending on the geographic location of the study population [4-7]. Though in most regions, House Dust Mite (HDM) was the epidemic allergen, pollen is still one of the most important allergens, especially in tree and grass flourishing regions.

Grasslands are the dominant landscape in northern China and account for 40% of the national land area. Geographically, about 78% or some 313 million ha of the grasslands in China occur in the northern temperate zone, constituting an integral part of the Eurasian grassland ecosystem to the east of the continent [8]. Xilingol grasslands, which located in the north of China, cover an area of 180,000 km^2. The grassland is covered with plenty kinds of plants which produce countless airborne pollens during grassland pollen season. Whether ambient pollens locally could induce allergic sensitization directly remains unknown.

Although there were data about common allergens in southern and central China where HDM was epidemic [3,9], there was less information related the main allergens under grassland environment. In present study, we investigated the main allergens and the allergic sensitization type of grassland in Xilingol of Inner Mongolia, China. Meanwhile, we studied the correlation between pollen and SPT sensitization.

Materials and Methods

Study subjects

We recruited 353 AR patients who visited allergy department of Xilingol Mongolian medicine hospital during March to April of 2015. All disease profiles were inquired and recorded. The diagnosis of AR was based on ARIA guideline [1].

Approval to conduct this study was granted by the institutional review boards of Beijing Shijitan Hospital, the affiliated hospital of the Beijing Capital Medical University.

Inclusion criteria

1) Patients had typical symptomatic disorder of the nose induced rhinorrhoea, nasal obstruction, nasal itching and sneezing;

2) Patients had AR history for at least 2 y;

3) Patients recruited from local area who were exposed to the high concentration of pollen for at least one year;

Exclusion criteria

1) Patients had tumor or severe immune system diseases;

2) Patient at pregnancy or lactation period;

3) Patients who lived from other places or who lived in local place temporarily;

4) Patients who were unwilling to receive SPT test.

Allergic sensitization from SPT

SPTs were performed using a standard panel of commercial extracts from Macro-Union Pharmaceutical Company, Beijing, China Oral antihistamines and related other medications were discontinued for at least 3 d prior to the SPT. Histamine 0.1 mg/ml and glycerol solution were used as positive and negative controls, respectively. Morrow-Brown needles were used to prick the skin, and the wheal reactions were read after 15-20 min. A wheal ≥ 3 mm after subtraction of the negative control was regarded as positive. In addition, a positive score based on the wheal size was recorded: class 1: a wheal diameter between 3 and 5 mm; class 2: a wheal diameter between 5 and 10 mm; class 3: a wheal diameter between 1 and 2 cm; class 4: a wheal diameter ≥ 2 cm and present with pseudopods.

Airborne allergens including 16 allergens were tested. The allergens were classified and listed below:

1) Tree pollen: *Populus, Salix, Ulmus*;

2) Weed/grass pollen: *Artemisia, Chenopodiaceae, Humulus scandens, Ragweed*;

3) HDM: *Dermatophagoides farinae* (DF), *Dermatophagoides pteronyssinus* (DP), house dust, cockroach;

4) Animal danders: cat dander, dog dander;

5) Molds: *Mucor racemosus, Aniger, Alternaria*.

In order to analyse the sensitization status of patients, we applied definitions below in this study.

1) Mono-sensitized: the patient was allergic to only one allergen tested;

2) Double-sensitized: the patient was allergic to two allergens tested;

3) Triple-sensitized: the patient was allergic to three allergens tested;

4) Poly-sensitized: the patient was allergic to at least four allergens tested;

5) Overall positive rate: the patient was allergic to at least one allergen tested.

Pollen data

The Durham sampler has been traditionally used to quantify airborne pollens with gravitational settling as a particle collection mechanism [10]. In present study, we also performed Durham sampling to collect pollen and classify the pollen species. Each slide was placed and collected within 24 h and counted by two trained examiners in a blinded manner. The result was reported as the daily total pollen grain per 1000 mm^2. In this study, a mean monthly pollen count was presented during January to December of 2015 in Xilingol. The geographic location of pollen collection was N43º55’2.66”, E116º02’41.48”.

Statistical analysis

All data were entered twice into the database by two independent investigators and then validated. Data were summarized as numbers (n) and frequencies (%) if data were categorical and as mean and Standard Deviation (SD) if data were quantitative. For comparisons of proportions, the χ^2 test and t-test was used when appropriate. For pollen count difference, a Kruskal-Wallis H test was performed. A P-value<0.05 was considered statistically significant. SPSS 23.0 Software was applied (SPSS Inc., Chicago, IL, USA).

Results

Demographic characteristics

Among 353 patients recruited, 131 were male and 222 were female. The age ranged from 3 y-73 y, the average age was 36.76 ± 15.23 y. The patients were classified to three age groups. Child (1-18 y): n=60; Adult (19-59 y): n=278; elder (≥ 60 y): n=15.

Allergic sensitization of AR patients

Among 353 individuals, 317 (89.8%) showed a positive SPT to at least one allergen. The highest positive rate was 75.0% for *Artemisia*, followed by 61.9% for *Humulus scandens*, 58.5% for *Chenopodium*, 56.3% for *Ragweed*. The lowest positive rate was 6.5% for dog dander. All of the most four common allergens tested were grass/weed pollen.

We defined classes 3 and 4 of SPT result as severe sensitization. The positive rate for severe allergic sensitization was 59.1 % for *Artemisia*, 14.8% for *Ulmus* and *Populus*, 13.6% for *Chenopodiaceae*, 12.8% for *Humulus*. There was no severe sensitization of *Mucor racemosus, Aniger* and dog dander. In the SPT result of patients, *Artemisia* tended to be the severest allergens tested.

As regarding to the sensitization pattern of SPT, the positive rate was 62.9% for tree pollen, 83.3% for weed/grass pollen which was significantly higher than tree pollen (P<0.001) (Table 1). The sensitization rate for any pollen was 85.6%, while 24.6% for any mold and 14.4% for any dander (P=0.02, P=0.002, respectively) (Tables 1 and 2).

***Table 1.** The allergic sensitization of different allergen type in 353 patients, expressed as n (%).*

Allergens	Gender n (%)		P value	Age group# n (%)			P value	Total
	Male	Female	Child	Adult	Elder			
	N=132	N=221	N=60	N=278	N=15			
Any tree pollen	94 (71.2)	128 (57.9)	0.012	50 (83.3)	168 (60.4)	4 (26.7)	<0.001	222 (62.9)
Any grass/weed pollen	119 (90.2)	175 (79.2)	0.008	56 (93.3)	230 (82.70	8 (53.3)	0.001	294 (83.3)
Any pollen	122 (92.4)	180 (81.4)	0.005	56 (93.3)	238 (85.6)	8 (53.3)	<0.001	302 (85.6)
Any HDM*	74 (56.1)	111 (50.2)	0.288	32 (53.3)	147 (52.9)	6 (40.0)	0.615	185 (52.4)
Any mold	35 (26.5)	52 (23.5)	0.529	20 (33.3)	66 (23.7)	15 (100.0)	0.075	87 (24.6)
Any dander	20 (15.2)	31 (14.0)	0.771	21 (35.0)	29 (10.4)	1 (6.7)	<0.001	51 (14.4)
Total	126 (95.5)	191 (86.4)	0.007	57 (95.0)	250 (89.9)	10 (66.7)	0.005	317 (89.8)

*HDM: House Dust Mite. #age group: child 0-18 y; adult 19-59 y; elder>60 y; Chi-squared test was performed in this table.

***Table 2.** The comparison of sensitization rate among different allergens expressed as P value.*

Allergen type	Any grass/ weed pollen	Any pollen	Any HDM	Any mold	Any dander
Any tree pollen	<0.001	<0.001	<0.001	0.002	0.001
Any grass/ weed pollen		<0.001	<0.001	0.03	0.002
Any pollen			<0.001	0.02	0.002
Any HDM				<0.001	0.005
Any mold					<0.001

Chi-squared test and Bonferroni test were performed in this table.

The sensitization rate was 95.5% in male which was higher than in female (86.4%, χ^2=7.36, P=0.007). There were significantly difference between male and female in the sensitization rate of tree pollen, grass/weed pollen, any pollen (P=0.012, P=0.008, P=0.005, respectively). No difference was found with genders in perennial allergens (P>0.05) (Table 1). We analysed the sensitization rate among different age groups. The allergic sensitization rate was 95.0% in child group, 89.9% in adult group and 66.7% in elder group. The sensitization rate decreased along with age increasing (χ^2=10.54, P=0.005). The decrease trend was similar in the sensitization rate of tree pollen, grass/weed pollen and any pollen like gender difference (P<0.001, P=0.001, P<0.001, respectively) (Table 1). Surprisingly, the sensitization to dander also decreased with age (P=0.005).

In present study, 9.4% of AR patients was mono-sensitized, 3.97% was double-sensitized, 7.7% was triple-sensitized while 68.8% was poly-sensitized (χ^2=584.80, P<0.001). The main sensitization type was poly-sensitization. The phenomenon was similar in grass/weed pollen while poly-sensitized type (43.63%) undertook advantage of sensitization rate (χ^2=159.13, P<0.001) (Table 2).

Pollen data and association with allergic sensitization

The total local pollen concentration was 30381 grains/1000 mm^2. The peak season of pollen exposure was in August, accounting for 63.7% of total pollen; followed by July (16.1%). The least pollen was seen in December (0.3%). The seasonality of pollen exposure in Xilingol was obvious in Spring (May) and Autumn (July and August). The Autumn peak season was accounting for 2/3 total pollen in 2015 which was significantly higher than Spring peak season ($P<0.001$).

The predominant airborne pollen in Xilingol grassland was monitored throughout the whole year. The most common was *Artemisia* (54.2%) which was presented mostly in July to August. Followed by *Chenopodiaceae* (30.7%). Those two pollens consisted 84.9% of total pollen count all year long. In the peak pollen season of August, the pollen rate was 67.3% for *Artemisia*, 27.8% for *Chenopodiaceae*. Those two pollens consisted of 95.1% of the total pollen. Other common pollen was *Poaceae* and *Humus*. The most common airborne pollens were *Artemisia*, *Chenopodiaceae* in both ambient air and SPT test.

Discussion

Our main findings of this study was as follows: 1) *Artemisia* was the predominant allergens for AR patients in grassland region both in allergic sensitization and air distribution indicating environmental impact on AR. 2) grass/weed pollen had a higher sensitization rate than tree pollen. 3) poly-sensitization was the main sensitization type.

Xilingol grassland, locating in north China, has a vast territory and is one of the fourth China great grasslands, featured by rich vegetation [8]. Thus, study on its airborne pollen and its relationship with allergic diseases such as AR is important. In present study, our findings demonstrated that *Artemisia* was the key pollen in grassland which was different from other areas of China where HDM was the predominant allergen [3,9]. We presumed the reason: 1) Distinct from the humidity of southern and central China, the northern grassland had a dry climate which was against the development of HDM and molds. 2) The scale of city in Inner Mongolia was small compared with other large cities in China. Thus, the local cities were covered by grassland and the allergen sensitization showed a local feature. We also found that the *Artemisia* had a severer allergic sensitization compared with other allergens indicating a stronger allergenicity.

In our study, we also could reveal that the allergic sensitization decreased with age with the lowest prevalence in >60 age group. This finding was in consistent with Katja et al. [4]. and Salo et al. [11]. We found this phenomenon was apparently in pollen sensitization group but not in HDM and mold group. The animal dander was inconsistent with other perennial allergens which child group had a higher sensitized status. The more opportunities exposing to animals could contribute to this difference. It is worth to mention that in child group, the allergic sensitization rate was higher than adult which was inverse to population based study [12]. This could be the bias of our study due to the child patients tend to seek more medical services in the city.

Since the weed/grass pollens were the main allergic pollen in local AR patients, we dig into the reason why this phenomenon occurred. We monitored the pollen distribution in 2015. In our pollen data, *Artemisia*, *Chenopodiaceae* and *Poaceae* were the most common pollens. *Artemisia*, accounting for 2/3 of the total pollen count, was the crucial pollen locally. Pollen kinds and mounts could variate among different geographical regions or even in the same region. In US, tree pollen was account for 91.2% of total pollen; in Europe, birch was the predominant pollen; in Japan, cedar was epidemic [10,13]. In present study, *Artemisia*, *Chenopodiaceae* and *Poaceae*, representative pollens of grass/weed pollens in northern grassland of China, showed predominance both in SPT sensitization and ambient air distribution. This main finding revealed the strong positive relationship of allergen sensitization and pollen exposure which was similar to previous studies [14-17]. But in our study, we also found a high sensitization rate of ragweed in AR patients without ragweed pollens exposure in local air. This inconformity could be the consequence of cross-reactivity which was common in grass/weed pollens. But this could also evoke dispute on the kinds of SIT which would perform to the AR patients. Whether ragweed should add to SIT still be controversial.

There is a large body of evidence to show that poly-sensitization is common worldwide with a rate of 50%-80% [18]. The exact prevalence depends on the population and the region. Patients tend to gain sensitization over time. The poly-sensitization pattern was apparently high in this study which was more than 2/3 of the overall sensitization group and higher than previous studies. This draws the attention of cross-sensitivity in the direct exposure of high concentration pollens surrounding by pollen environment. This poly-sensitization phenomenon may be explained by the sensitization to profilin or other highly cross-reactive allergen components. The multiple sensitization status, especially in grass/weed pollens, may have a consequence on the propensity to prescribe Specific Immunotherapy (SIT) of pollen to patients [19]. Which allergens should be chosen for SIT or whether main allergen SIT could be effective in this grassland region would be a challenge for allergist. In Europe, the poly-sensitized patient is normally treated with the single allergen (or no more than three allergens). In US, allergists tend to prescribe SIT comprising allergens that correspond to all key allergies identified in SPTs containing an average of eight components. Whether single or multiple allergens should be included in SIT is still undergoing debate. Sastre et al. [20]. applied ISAC®, the molecular diagnosis to poly-sensitized patients, and found 54% of patients would change the allergen prescription in SIT. Thus, the molecular diagnosis, also known as Component Resolved Diagnosis (CRD) could be the solution of poly-sensitization in the future. A key remaining issue in the detection of sensitization is when to rely on SPTs alone and when to investigate further with sIgE assays and CRD. The latter could be the solution of poly-sensitization and the dilemma of allergens chosen in SIT.

This study had several limitations. First, this is a retrospective study of single clinical center, the population sample is small and not representative of the general population. Second, the severity and quality of life impairment from AR symptoms were not evaluated, therefore the association with SPT classification could not be determined. Third, we are aware of the limitations of the Durham Sampler technique where the volume of air sampled is unknown, so the catch of pollen cannot be converted to a volumetric measure of concentration.

Conclusions

In general, sensitization prevalence seems to be highly dependent on the pollen exposure pattern in grassland. It is becoming more and more evident that *Artemisia* allergic and poly-sensitization may become an increasing problem for societies in grassland. In our opinion, this emerging health problem will require increasing attention and research.

Declaration of Interest

The authors declare no conflicts of interest. The authors alone are responsible for the content and writing of the paper.

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