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Original Article

Prevalence of *Blomia tropicalis* in wheezing children in central Taiwan

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Background and Purpose: In a previous study, we found that wheezing children in rural central Taiwan had a significantly lower average sensitization rate to *Dermatophagoides pteronyssinus* (Der p) than those in Taipei city. We propose that *Blomia tropicalis* (Blo t) might be the major mite allergen in rural central Taiwan.

Methods: Using the preserved sera from our previous study, we retrospectively measured specific immunoglobulin E (IgE) antibody to Blo t and analyzed the correlation between Blo t and Der p in wheezing children in rural central Taiwan. A total of 2206 children with physician-diagnosed asthma and wheezing were enrolled and categorized among five age groups. The sensitization rate and level of specific IgE antibody to Blo t were analyzed.

Results: The age-specific sensitization rates and the level of specific IgE antibody to either Blo t or Der p increased progressively with increasing age, being greatest in the age group 8 to 12 years. A significant positive correlation existed between sensitization rate and age for both Blo t and Der p (p=0.001). Specific IgE antibody to Blo t was undetectable in patients younger than 1.5 years. A significant positive correlation also existed between age and anti-Blo t IgE antibody level (p<0.003). However, the allergen-specific IgE level was lower for Blo t than Der p (p<0.005) in all age groups.

Conclusions: Blo t might be the major mite allergen to associated with early wheeze and atopic asthma in rural central Taiwan.

Key words: Allergens; Child; Hypersensitivity; Immunoglobulin E; Mites; Respiratory sounds

Introduction

The cause of allergy is multifactorial and the development of allergic diseases is likely the result of a complex interaction between genetic and environmental factors [1]. Other than genetic susceptibility to asthma and associated allergic diseases, increasing experimental evidence indicates that exposure followed by sensitization to house dust mite is a primary cause of asthma and allergic diseases in many parts of the world [2]. The distribution of house dust mites in the human living environment is influenced by numerous factors, such as geographical location, climate, lifestyle, building characteristics and the degree of modernization and industrialization [3]. Consequently, mite prevalence varies worldwide.

In our previous study, we found that wheezing children in rural central Taiwan had a significantly lower average sensitization rate to *Dermatophagoides pteronyssinus* (Der p) than children residing in Taipei city. Age and residential areas were significant determinants of allergen-specific immunoglobulin E (IgE) level to Der p. No statistical difference existed between Taipei city and rural central Taiwan for sensitization rates and mean specific IgE levels for cockroach [4]. Therefore, research into the primary allergen in wheezing children in rural central Taiwan is necessary.

The three most common mite species found in human living environments in Taiwan are Der p,

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Dermatophagoides farinae and *Blomia tropicalis* (Blo t) [5,6]. Like *Dermatophagoides*, the storage mite Blo t had been considered as an important aeroallergen in tropical and subtropical regions of Europe, America and Asia, including Taiwan [7].

Allergens produced by Blo t had been identified as an important clinical cause of allergic airway diseases, inducing specific IgE-mediated responses in patients with allergic diseases, such as asthma and allergic rhinitis, in tropical and subtropical regions of Europe, South America, Asia and the United States. The prevalence of sensitization toward Blo t was higher than toward Der p in studies from warm and humid parts of the world, such as Hong Kong, Singapore, Malaysia and Latin America [8-11]. An important description of the potent allergenicity of Blo t and the relevance of specific IgE in asthmatic patients of Taiwan was published by Tsai et al [12]. Blo t is indeed highly prevalent and can be detected in house dust samples in Taiwan (as well as worldwide) in tropical and subtropical regions. However, there are no recent data available regarding the prevalence of Blo t in rural central Taiwan.

We propose that Blo t might be the primary mite allergen in rural central Taiwan. Therefore, using the preserved sera from our previous study [4], we retrospectively measured the specific IgE antibody to Blo t and analyzed the correlation between Blo t and Der p in wheezing children in rural central Taiwan. We believe that this first report might provide valuable information for prevention or sensitization reduction, not only in rural central Taiwan, but also in other tropical areas.

Methods

Patient population

Children enrolled in this analysis were a subset of 2206 patients with recurrent atopic wheezing who visited the Department of Pediatrics, Changhua Christian Hospital, between June 2000 and June 2004. At the first visit, the location of the patients' residence was recorded. Diagnosis of asthma and wheezing were according to the International Study of Asthma and Allergies in Childhood [13]. Recurrent early wheeze was defined as ≥2 reports of wheezing in the first 3 years of life. Frequent early wheeze was defined as ≥2 reports of wheezing per year in the first 3 years of life. At 7 years of age, asthma was defined as physician-diagnosed asthma and wheezing in the previous year.

Exclusion criteria were: wheezing episodes during the first 6 months, recurrent wheezing due to respiratory virus infection with positive respiratory syncytial virus (RSV) or adenovirus antigen test, serum with elevated C-reactive protein level, foreign body aspiration, gastroesophageal reflux and residing outside rural central Taiwan. Wheezing children with RSV infection were mainly determined by the clinical symptoms during a known community outbreak of the disease and positive RSV antigen test and/or polymerase chain reaction test. Otherwise, wheezing children with positive adenovirus antigen test and/or polymerase chain reaction test and/or adenovirus isolated from viral culture were diagnosed as having adenovirus infection.

Serum samples

Venous blood samples were obtained from all children diagnosed with recurrent wheezing when the wheezing was under control. After clotting at room temperature, the samples were centrifuged, and sera were frozen and stored at –20°C before being analyzed. Specific IgE antibodies against Blo t and Der p were examined by a commercial Pharmacia CAP system (Pharmacia Diagnosis AB, Uppsala, Sweden). Analytical results were regarded as positive when values of specific IgE antibody were >0.35 kU/L.

Statistical analysis

Data were expressed as mean ± standard deviation. The prevalence and level of specific IgE antibody to Blo t and Der p were analyzed according to subject age. Differences in sensitization rates to Blo t and Der p between different age groups of children were analyzed by chi-squared test for trend. A univariate general linear model, accounting for subject age and residential area, was performed for level of specific IgE to Blo t. All statistical analyses were conducted using the Statistical Package for the Social Sciences for Windows (Version 11.0; SPSS, Chicago, IL, USA) software package.

Results

A total of 2206 children (1399 males and 807 females) residing in rural central Taiwan were enrolled. Subjects ranged in age from 6 months to 12 years (mean, 5.84 ± 2.87 years) and were categorized among five age groups (Table 1). The number of wheezing children in the age groups 0.5-1.5, 1.5-3, 3-5, 5-8 and

Table 1. Distribution by age and gender of wheezing children in rural central Taiwan

Age (years)	Number of children (%)	Male/female (ratio)
0.5-1.5	64 (2.9)	39/25 (1.6:1)
1.5-3	442 (20.0)	296/146 (2.0:1)
3-5	643 (29.1)	388/255 (1.5:1)
5-8	610 (27.7)	353/257 (1.4:1)
8-12	447 (20.3)	323/124 (2.6:1)
Total	2206 (100.0)	1399/807 (1.7:1)

8-12 years was 64 (39 males, 25 females), 442 (296 males, 146 females), 643 (388 males, 255 females), 610 (353 males, 257 females) and 447 (323 males, 124 females), respectively.

The sensitization rates of children with specific IgE antibodies to Blo t and Der p according to age are shown in Fig. 1. The comparative rates of sensitization to Blo t vs Der p in the age groups 0.5-1.5, 1.5-3, 3-5, 5-8 and 8-12 years were 0% vs 13.9%, 47.7% vs 37.1%, 66.8% vs 44.8%, 76.0% vs 55.2%, and 86.5% vs 64.2%, respectively. Thus, the age-specific sensitization rates to Blo t or Der p increased progressively with increasing age, with the peak in the 8 to 12 years age group. At this age range, the sensitization rate was higher for Blo t than for Der p (86.5% vs 64.2%). A significant positive correlation existed between sensitization rate and age profile for both Blo t and Der p (p=0.001). Furthermore, specific IgE to Blo t in non-atopic individuals was undetectable in this study.

The incidence of age-related allergen-specific IgE antibodies to Blo t and Der p is shown in Fig. 2. The mean (± standard deviation) levels of specific IgE to Blo t vs Der p in the age groups 0.5-1.5, 1.5-3, 3-5, 5-8 and 8-12 years were 0 kU/L vs 1.40 ± 0.14 kU/L,

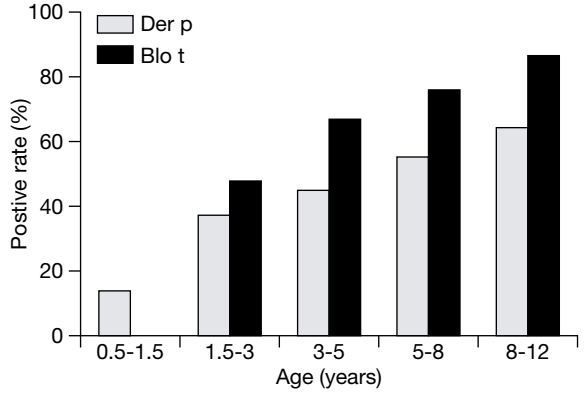

Fig. 1. Prevalence of sensitization to *Dermatophagoides pteronyssinus* (Der p) and *Blomia tropicalis* (Blo t) allergen in wheezing children in rural central Taiwan.

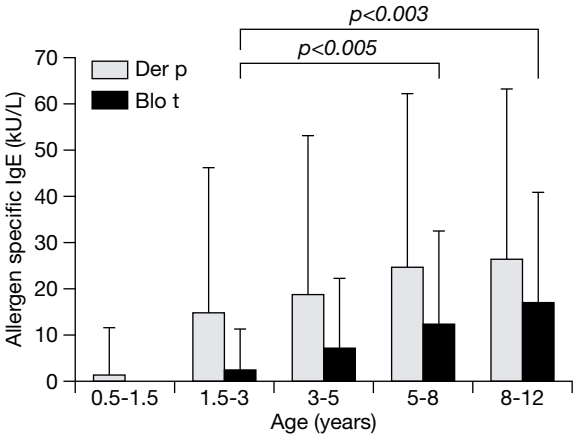

Fig. 2. Age-specific immunoglobulin E (IgE)-specific antibodies to *Dermatophagoides pteronyssinus* (Der p) and *Blomia tropicalis* (Blo t) in wheezing children in rural central Taiwan. Bars indicate standard deviation.

2.66 ± 8.66 kU/L vs 14.93 ± 31.25 kU/L, 2.66 ± 8.66 kU/L vs 14.93 ± 31.25 kU/L, 7.22 ± 15.06 kU/L vs 18.84 ± 34.33 kU/L, 12.43 ± 20.03 kU/L vs 24.70 ± 37.56 kU/L, and 17.15 ± 23.77 kU/L vs 26.53 ± 36.70 kU/L, respectively. Specific IgE antibody to Blo t in subjects younger than 1.5 years was undetectable. Above 1.5 years of age, the level of specific IgE antibody to Blo t increased progressively with increasing age. A significant positive correlation existed between age and anti-Blo t IgE antibody level (p<0.003). At any age group, the allergen-specific IgE level was lower for Blo t than Der p (p<0.005). In order to identify the determinants of specific IgE antibody levels to Blo t, general linear model univariate analysis was performed. Age (p=0.001) and residential area (p=0.001) were significant determinants of specific IgE antibody to Blo t.

Discussion

The development of asthma and allergic disease involves numerous genetic and environmental factors. Increased evidence indicated that complex gene-environmental interactions play a key role in altering the human immune system and developing allergic disease. Although genetics have been identified as contributing to the susceptibility to and development of asthma, environmental factors influence the expression of genes and the clinical phenotype of asthma and allergic disease [14-17].

Blo t frequently coexists with Der p in subtropical and tropical areas, as well as in temperate regions. Dual sensitization to Blo t and Der p was common [9,18],

but Blo t allergens had only low-grade cross-reactivity with *Dermatophagoides* spp. [18,19]. Our previous data showed that wheezing children living in Taipei city had a higher prevalence of sensitization to Der p than those living in rural central Taiwan [4]. Compared with Der p, Blo t showed a biological advantage in inducing mite allergy in the agricultural environment. Therefore, we proposed that Blo t allergens might be more prevalent in rural central Taiwan, and carried out this study in order to clarify our hypothesis.

The present study demonstrated a significant positive correlation between sensitization rate and age profile in both Blo t and Der p (p=0.001). The rate of sensitization to Blo t was zero in children aged younger than 1.5 years, but the age-specific sensitization rates to Blo t increased progressively with age, and were higher than to Der p beyond 1.5 years of age. These findings implied that Blo t allergens were more abundant than Der p allergens in rural central Taiwan. However, it is unlikely that children aged younger than 1.5 years had never encountered Blo t allergens. We suggest that children in this 0.5-1.5 years age group had had contact with Blo t allergens but were not sensitized sufficiently to be detectable by our method. Whether allergen exposure and sensitivity existed in the exposure-response effect requires further study.

Similarly, beyond 1.5 years of age, the level of specific IgE antibody to Blo t increased progressively. A significant positive correlation existed between age and anti-Blo t IgE antibody level (p<0.003). However, the allergen-specific IgE level was lower for Blo t than Der p in all age groups (p<0.005). We propose that differences between Blo t and Der p allergens in affinities of specific IgE-binding epitopes, allergenicity or biologic activity might account for these findings, but further investigation will be needed in order to elucidate these issues.

Repeated exposure to mite allergens is considered to be a risk factor for mite sensitization and development of allergic respiratory diseases in genetically predisposed people. In this study, we showed that wheezing children beyond 1.5 years of age had higher rates of sensitization to Blo t than to Der p (Fig. 1).

We suggest that the biologic traits of Blo t might be the major contributors to the sensitization results observed in this study, with complex environmental factors as climate, lifestyle, building characteristics and individual living habits the minor contributors [3,20].

Studies by Arlian demonstrated that the primary factor affecting mite reproduction and survival was relative humidity (RH), rather than temperature [21, 22]. Large populations of house dust mites were found when indoor air absolute humidity was over 7 g/kg (45% RH at 20°C) [23]. In general, regardless of the indoor or outdoor environment, the optimum conditions for mites are around 25-30°C and 75-80% RH [7].

Blo t was found to be abundant in regions with average annual temperature above 30°C and mean RH above 80% [24], and is adapted to warmer weather to a greater extent than Der p. According to annual statistics of the Taiwan Central Weather Bureau, there are no significant differences in RH and ambient temperature between central Taiwan and Taipei. However, the period of warmer weather is of longer duration in central Taiwan than in Taipei. Thus, favourable RH with higher temperature climate might be a reason for the better growth of Blo t compared with Der p in rural central Taiwan.

There are significant biological differences between Blo t and Der p. The storage mite Blo t feeds on plants and microorganisms, being predominantly found in agricultural environments and more prevalent in tropical and subtropical regions. The house dust mite Der p feeds primarily on compounds in house dusts, including human skin scales, and predominates in temperate regions. The typical habitat of Blo t is barns, grain stores, flour, hay and straw, while Der p was frequently found in beds, clothes, cushions, blankets, upholstered furniture, mattresses and carpeting [7].

Rural central Taiwan is not highly westernized and is economically developing. Most residents live in an agricultural or semi-agricultural situation, having frequent contact with grasslands, farmlands and agricultural products in their daily activities. In addition, residents spend more time in outdoor recreation and have more opportunities for exposure to Blo t allergens than urban dwellers. Thus, our results showing that residents in rural central Taiwan have higher sensitization rates to Blo t than Der p is not unexpected.

Although building characteristics affect indoor humidity, in our study, building characteristics were less important than natural biologic traits of mites in producing of allergen senitization. We also showed that mean age-related allergen-specific IgE antibodies to Blo t were lower than to Der p in any age group (Fig. 2). The specific allergenicity of Blo t was the major reason why wheezing children at any age group did not mount a higher specific IgE response to Blo t than to Der p.

It is known that specific IgE to mites in sera do not exclusively recognize the same IgE epitopes: IgE cross-reactivity in different mites has been demonstrated and unique IgE-binding epitopes do exist [25]. According to the review by Thomas et al [18], house dust mite allergens can be classified into 19 groups by different biochemical functions. They also noted that the glycyphagid mite Blo t is a major source of allergen, which coexists with Der p, especially in subtropical and tropical regions. The group 1 and 2 allergens of *Dermatophagoides* spp. are clearly major allergens, both inducing high titers of IgE and Th2 cytokines in 80% of allergic patients. Blo t 5 is the major allergen of Blo t, and binds IgE in 70% of allergic subjects, with minor cross-reactivity to Der p 5. It has been suggested that the major allergen of Blo t induces lower specific IgE titer than Der p. However, the polymorphisms of allergens in different regions and the adjuvant bioactivities of different allergenic components must also be considered [17,18]. The above deduction may support our result that the specific IgE response to Blo t was lower than to Der p.

Since our study was a retrospective design to measure the anti-Blo t-specific IgE levels in sera from 2206 wheezing children. We have not been able to obtain follow-up data on exposure to house dust mite allergen levels in the wheezing children.

In conclusion, in children with early wheeze and atopic asthma in rural central Taiwan, the age-specific sensitization rate to Blo t increased progressively with age. In those younger than 1.5 years of age, the sensitization rate was absolutely higher for Blo t than Der p. Above 1.5 years of age, the level of specific IgE antibody to Blo t also increased progressively. However, the allergen-specific IgE level to Blo t was lower than to Der p in each age group. Our study has shown a higher prevalence of Blo t than Der p in rural central Taiwan and indicates the importance of Blo t in wheezing children in clinical practice.

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