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Skin Sensitization to Common Allergens in Turkish Wheezy Children less than 3 Years of Age

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SUMMARY Infants and small children with asthma are not commonly skin tested, as allergy is not considered to be a major cause of infantile asthma. The aim of this study was to determine the frequency of skin test positivity to various allergens in wheezy children less than 3 years of age. We evaluated 161 patients with infantile asthma (median age 20 months) and 100 healthy controls (median age 18 months). Infantile asthma was defined as three or more episodes of wheezing in a child less than 3 years of age, whose symptoms improved on treatment with beta-agonist and anti-inflammatory agents. All children were skin tested to house dust mites (HDM), pollens, molds, and cow milk extracts using prick technique. One hundred and eighteen (73.3%) children in the patient group tested positive to HDM, 84 (52.1%) to pollens, 37 (22.9%) to molds, and 16 (10%) to cow milk. Sensitization rates to HDM were significantly higher in the patient group than in the healthy controls. Sensitization rates to pollens were not statistically different between the two groups. There was no association between family history of atopy and frequency of sensitization to allergens in the wheezy and control groups. We concluded that skin sensitization to allergens was common in wheezy infants. The prevalence of sensitization to indoor allergens was higher than to outdoor or food allergens.

The prevalence of allergic disease in childhood has increased considerably in developing as well as developed countries[1,2] over the last 20-30 years, and accordingly the need of allergy testing has increased as well.[3] Early diagnosis of allergy during infancy can help greatly to reduce the cost and difficulty of managing allergic diseases.[4,5] Skin tests are the primary diagnostic tool for allergy even in infants.[6] Performed properly, allergy skin testing is a very sensitive bioassay for antigen-specific IgE. A positive skin test reaction mirrors the pathophysiologic findings seen in the lung.[7] Geographic variations in the prevalence of sensitization to allergens are determined by differences in living conditions rather than by genetic characteristics.[8] This study aimed to investigate the sensitization pattern to a range of allergens in young wheezy Turkish children.

PATIENTS AND METHODS

The study was conducted at the Pediatric Allergy Department of the Istanbul Medical Faculty between January 2000 and February 2001. Children with three or more wheezing episodes and whose symptoms improved upon treatment with beta-agonists and anti-inflammatory agents under 3 years of age were defined as wheezy children or infantile asthma. The patient group consisted of 161 wheezy children diagnosed with infantile asthma. The age of the patients ranged from 3 to 36 months (median age 20 months). None of the wheezy patients had any other chronic respiratory problems such as bronchopulmonary dysplasia, cystic fibrosis, tuberculosis, gastro-esophageal reflux, or congenital abnormalities. One hundred clinically healthy children in the same age group (median age 18 mounts) with no history of al-

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lergy, recurrent infections or immunodeficiency were included in the control group. These healthy children attended the well-child clinic of the same hospital from which the wheezy children were selected, thus they had similar environmental and socioeconomic characteristics. Informed consent was obtained from the patient's family, and the study was approved by the ethical committee of the institution.

Patients and controls were divided into the three age groups; group 1: 3-11 months, group 2: 12-23 months and group 3: 24-36 months. Skin prick tests (SPT) to various allergens were performed in all children with a standard panel (Stallergenes, France). With this panel the following allergens were tested; house dust mites (HDM, *Dermatophagoides pteronyssinus, D. farinae*), pollens (5 grasses, eastern trees, weeds), mixtures of molds (*Alternaria*, *Aspergillus*, and *Cladosporium*), and cow milk. We did not investigate dog and cat allergen sensitization, as most Turkish families do not allow pets in their homes for various reasons (e.g. religion, economy). Antihistamines, corticosteroids, and mast cell membrane stabilizers were stopped for a required period before the skin tests. Histamine (0.1%) in phosphate buffered saline, and physiological saline were used as positive and negative controls, respectively. A wheal after 15 minutes with a diameter of at least 3 mm or greater than the negative control was accepted as positive result. The test was performed on the volar surface of the forearm. We used very thin one millimeter prick lancets (Allergopharma, Germany). The needle was introduced into the skin through a drop of the tested solution at a 45° angle. All SPT's were carried out by trained personnel and under the supervision of a physician who was experienced with the same equipment and technique. All children who were included into the study were tested for all allergens. Children with missing values were excluded from the study group. A careful medical and environmental history (e.g. family history of atopic disease, exposure to tobacco smoke, home dampness, number of people living in the home) was obtained from all cases by questionnaire. Family history of atopy was defined as a doctor–diagnosed allergic disease (atopic eczema, allergic rhinoconjunctivitis and allergic asthma) in family members or first degree relatives. Allergic rhinitis is very difficult to differentiate from recurrent infectious rhinitis in small children. Although some clinical findings such as persistent obstruction or discharge can be of help, the symptoms are usually very similar. Even nasal provocation tests are difficult to interpret and are of limited value in this age group. Therefore, we did not include allergic rhinitis in our evaluation.

Chi- square ($\chi 2$) test was used to compare the results between the groups. P values ≤ 0.05 were considered statistically significant. SPSS/PC 10.0 version for windows (SPSS, Inc., Chicago, IL, USA) was used for statistical analysis.

RESULTS

One hundred and sixty one wheezy children (74 males) with a median age of 20 months (3 months-3 years) and 100 healthy children (47 males) with a median age of 18 months (3 months-3 years) were evaluated. There was no statistically significant difference in the age distribution between the wheezy and

Table 1 Distribution of allergen sensitization by age in wheezy and healthy children

Allergens	Group 1 (3-11 months)		Group 2 (12-23 months)		Group 3 (24-36 months)		Total	
	Wheezy (N = 62)	Healthy (N = 37)	Wheezy (N = 48)	Healthy (N = 37)	Wheezy (N =51)	Healthy (N = 26)	Wheezy (N = 161)	Healthy (N = 100)
	No. (%)	No. (%)	No. (%)	No. (%)	No. (%)	No. (%)	No. (%)	No. (%)
House dust mites	43 (69.4)*	5 (13.5)	34 (70.8)*	5 (13.5)	41 (80.4)*	8 (30.7)	118 (73.3)*	18 (18)
Pollens	35 (56.4)**	18 (62.1)	27 (56.2)**	17 (45.9)	22 (43.1)**	12 (46.1)	84 (52.1)**	47 (47)
Mold mixtures	18 (29)**	9 (24.3)	8 (16.7)**	5 (13.5)	11 (21.6)**	7 (26.9)	37 (22.9)**	21 (21)
Cow milk	8 (12.9)**	3 (8.1)	6 (12.5)**	2 (5.4)	2 (3.9)**	2 (7.7)	16 (9.9)**	7 (7)

*$p < 0.05$
**$p > 0.05$

the control group. Of all wheezy children, 73.3% were sensitized to at least one of the two house dust mites, 52.1% to at least one of the pollens, 22.9% to mold mixtures and 9.9% to cow milk (Table 1). Of all 84 pollen-sensitized children, 22.5% were sensitized to 5 grass mixture, 66.2% to tree pollens and 11.2% to weeds.

The sensitization rate to HDM was significantly higher in the wheezy group than in the controls ($\chi^2 = 72.76$; $p < 0.001$). Sensitization rates to pollens were not statistically different between the two groups ($\chi^2 = 0.034$; $p > 0.05$). The frequency of sensitization to HDM and pollens were similar in the age groups ($\chi^2 = 1.7$; $p > 0.05$), although sensitization to HDM was more frequent than sensitization to pollens. The frequency of sensitization to molds was similar in all groups, and sensitization rates were not statistically different between study and control groups ($\chi^2 = 0.14$; $p > 0.05$, Table 1). The frequency of sensitization to cow milk was similar in the two groups ($\chi^2 = 0.663$; $p > 0.05$). Sensitization of wheezy children to HDM increased with age. On the other hand, cow milk sensitization decreased with age in the same children.

The distribution of sensitization to allergens according to the family history of atopy is summarized in Table 2. There was no significant difference in the prevalence of HDM and molds sensitization between children with and without family history of atopy in the two groups. A statistically significant association was found between the sensitization to pollens and a negative family history of atopy in the wheezy group. Cow milk sensitization was significantly higher among children in the control group who had a positive family history of atopy. The percentage of passive smoking and the distribution of the number of persons per household were similar in the study and control groups (Table 3).

DISCUSSION

Our findings indicate that sensitization to indoor allergens rather than to food allergens are higher in wheezy children than in the controls with or without a family history of atopy. The incidence of specific sensitization to HDM tends to increase by age. In contrast, there was no similar trend for sensitization to pollens, molds or cow milk. Sensitization to HDM was detected in 69.4% of wheezy children under 1 year of age. This value reached nearly 80% above 2 years of age, confirming the allergenic relevance of HDM in our country.[9] On the contrary, cow milk sensitization was irrelevant in children under 1 year old (12.9%) and the percentage of positive results decreased progressively with age (Table 1). However, the proportion of children in the wheezy group with cow milk sensitization was higher than in the controls. Our results also showed that sensitization to outdoor allergens like pollens was not different between wheezy and healthy infants. A possible explanation for this result may be the higher exposure of young children to indoor allergens than to outdoor allergens. McCready[10] showed in his study, that there was no correlation between the aerobiological prevalence of grass, weed pollens, and mold spores and emergency room visits diagnosed as "asthma, asth-

Table 2 Sensitization to various allergens and the family history of atopy in wheezy and healthy children

Allergens	Wheezy children		Healthy controls	
	Atopy+ (N = 86)	Atopy- (N = 75)	Atopy+ (N = 61)	Atopy- (N = 39)
	No. (%)	No. (%)	No. (%)	No. (%)
House dust mite (Der p 1, Der f 1)	62 (72.1)**	56 (74.7)	23 (37.7)**	16 (41.1)
Pollens	34 (39.5)*	50 (66.6)	33 (54.1)**	18 (46.1)
Mold mixtures	21 (24.4)**	16 (21.3)	10 (16.4)**	11 (28.2)
Cow milk	7 (8.1)**	9 (12)	7 (11.5)*	0 (0)

*$p < 0.001$
**$p > 0.05$

Table 3 Some risk factors in wheezy and healthy children

Risk factors	Wheezy children (N = 161) No. (%)	Healthy controls (N = 100) No. (%)
Family size (number of members)		
3	72 (44.7)*	51 (51)*
4	73 (45.3)*	41 (41)*
≥ 5	16 (9.9)*	8 (8)*
Passive smoking		
Yes	72 (46.6)*	45 (45)*
No	86 (53.4)	55 (55)*

*$p > 0.05$

matic bronchitis, asthma exacerbation, wheezy bronchitis and asthma attack". In another study[11] the authors pointed out that, exposure to allergenic pollens in early life does not appear to increase the risk of acquiring symptoms of respiratory allergy.

Many studies have recently investigated the frequency of sensitization to inhalant and food allergens as a potential trigger for the development of allergic diseases. Although food allergens may occasionally be associated with wheezing, inhalant allergens appear to be the most important precipitants of wheezing in infancy.[12-14] Trindade[15] pointed out that, early sensitization to food allergens does not necessarily imply atopic disease, but is usually associated with current, future or previous. Delacourt *et al.*[16] showed that skin test positivity to inhalant allergens was significantly associated with the diagnosis of infantile asthma as early as in the first three years of life.

A number of recent studies demonstrate that atopy and inhalant allergy are major causative factors for childhood asthma.[16,17] However, in our study we did not find a significant association between major indoor allergen (HDM) sensitization and a family history of atopy. Nickel *et al.*[18] showed that there was no association between mite allergen sensitization at 6 and 18 months of age and a family history of atopy in wheezy children.

Allergy testing in infancy is very important for the early identification of infants at increased risk for development of allergic diseases later on and for avoidance measures of specific allergens.[3] Prick tests can be easily done in infants, although the relative hyporeactivitity of the infant skin must be taken into consideration.[19] There is no lower age limit for performing skin prick tests, even though earlier a lower age limit of 3 years has been wrongly recommended. The most useful panel of allergens for skin prick testing depends on the age of the child and the case history and varies between regions.[3]

Great differences exist between indoor and outdoor allergen sensitization all over the world.[8] Even within one country, sensitization levels to indoor allergens from house dust mites or pets may vary over 3 orders of magnitude.[20,21] Geographic differences in the prevalence of sensitization to various allergens are determined by differences in the living conditions rather than by the genes.[7,22] Our findings were similar to Silvestri's[23] results, whose study was carried out in Italy, a Mediterranean country like ours. However, different results have been published in the literature from other geographic regions all over the world. For example, in the USA, and South Asia, the prevalence of sensitization to food allergens is higher than to inhalant allergens in the first 3 years of life.[24,25] On the other hand, the incidences of sensitization to foods and inhalants are equally common in northern European children during the first 2 years of life.[26] These differences have been explained by differences in environmental conditions rather than genetically.

In conclusion, indoor allergens (mainly HDM) may especially be important in Turkish wheezy children. Outdoor allergens and foods should be of consideration later on in life. Skin prick testing may be included in a workup for evaluating the sensitization to allergens in wheezing children even if infants. Indoor and food allergen

sensitization were not affected by a family history of atopy in Turkish infants.

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