Aeroallergen Sensitization in Wheezing Children From Rosario, Argentina

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Background: Wheezing is a highly frequent symptom in infants and children. Its major causes are respiratory infections and bronchial asthma. In this context, allergen sensitization plays an important role, and it can be detected by a skin prick test, a safe and effective technique that can be easily performed on any age-group. To assess the prevalence of aeroallergen sensitization in a pediatric population with recurrent episodes of wheezing.

Materials and Methods: Cross-sectional study that evaluated 100 patients, 50 (50%) girls and 50 (50%) boys, from 6 months to 10 years. These children had consulted frequently at the Allergy and Immunology Division of the Eva Perón School Hospital due to recurrent episodes of wheezing. Skin prick test were performed on all of them and also on 20 healthy children.

Results: Overall, 58% of the patients presented sensitization to dust mite, 13% to pollen, 9% to epithelium, 8% to fungi, 6% to cockroach, and 1% to soybean hull. Overall, 60% of the patients were positive to at least one of the extracts, and we observed a significant and gradual increase in the frequency of sensitization in older age-groups ($P < 0.005$). This increase persisted when analyzing separately the dust mite group and the pollen group. None of the cases presented any adverse local or systemic reaction during the procedure or the following 24 hours after the procedure. The 20 individuals in the control group turned out negative when tested.

Conclusions: This study found high aeroallergen sensitization prevalence in a pediatric population with recurrent episodes of wheezing examined in the Allergy and Immunology Division of the Eva Perón School Hospital, which is in the southern area of the province of Santa Fe in Argentina.

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Wheezing is a highly frequent symptom in pediatric populations. Its main causes are viral infection and asthma. Etiologic diagnostic is complex and becomes more difficult with younger children.[1] Given that asthma is the most frequent chronic disease and the first cause of admission in pediatrics, an accurate diagnosis is mandatory to lead to an early and correct treatment.[2]

During the past decade, the International Study of Asthma and Allergy Childhood has been determining worldwide high rates of wheezing, on average between 15% and 19%, in children aged 13 to 14 years and 6 to 7 years, respectively.[3] Viral infections, size and structure of airways, and allergen sensitization are quite important risk factors to develop wheezing.[4] For asthma, allergen exposure plays a fundamental role in sensitization, and subsequent acute and chronic symptoms.[5] Skin prick test (SPT) allows detection of sensitization in a safe and efficient way in all age-groups.[6]

The objective of the study is to assess the prevalence of sensitization to aeroallergens in a pediatric population with recurrent wheezing episodes using SPT.

MATERIALS AND METHODS

Design

Cross-sectional observational study to assess the type of allergic sensitivity in a pediatric population of Rosario, Argentina.

Sample

We recruited 100 patients (50% boys) aged between 6 months and 10 years (mean = 4.5 ± 2.6), who consulted in the Allergy and Immunology Division at the Eva Perón School Hospital because of recurrent episodes of wheezing (Table 1).

This hospital is in the industrial belt of Rosario, Argentina. The period studied was between April 2007 and April 2008. At the end of the study, SPT was conducted in 20 nonallergic children (negative controls) of the same age range, who were randomly selected among children who attended the Pediatric Division for a health check.

Assessment tools

In this study, we included children who had recurrent episodes of wheezing as defined by the Asthma Consensus of the Argentina Society of Pediatrics.[7]

For the purpose of assessing skin sensitivity against aeroallergens, SPT was performed according to the Pepys technique, in which drops of allergen extracts and control solutions (histamine and saline serum) were placed on the

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TABLE 1. Sample Demographic Profile (n = 100)

Variable	Value
Sex, n (%)	
Female	50 (50.0)
Male	50 (50.0)
Age, yr	
Medium	4.5
SD	2.6

forearm skin. A lancet was passed through the drop into the epidermis. After 20 minutes, reading was performed, considering positive those wheals with a diameter over 3 mm and 10 mm of erythema. The positive data of previous ingestion of antihistamines or dermographism were considered exclusion criteria for the test.

A battery of allergen extracts (Diater Laboratory, Buenos Aires, Argentina), as detailed below, was used: mites (Dermatophagoides *pteronyssinus*, *Dermatophagoides farinae*, *Blomia tropicalis*), anemophilous fungi (*Alternaria alternata*, *Cladosporium herbarum*, *Aspergillus fumigatus*), epithelia of dog (*Canis familiaris*) and cat (*Felis domesticus*), cockroach (*Periplaneta americana*), anemophilous pollens (Grass mix, Chenopodiaceae mix, *Fraxinus excelsior*, Platanus mexicana, *Ligustrum lucidum*, *Ambrosia elatior*), and soybean hull (*Glycine max*). All extracts were measured in protein nitrogen units. Patients were divided into 4 groups according to age: from 6 months to 2 years old (group 1), from 2 to 5 years old (group 2), from 5 to 7 years old (group 3), and from 7 to 10 years old (group 4). Informed consent was signed by at least 1 parent. Institutional review board approval was obtained to conduct this study.

Statistical Analysis

The statistical analysis of the information was conducted using EPI-INFO (Epi Info 6.04d; Centers for Disease Control and Prevention, Atlanta, GA). To analyze the significance of the associations between qualitative variables χ^2 and P value with Yates correction were used.

RESULTS

Sensitiveness was found for any of the aeroallergens in 60% of children. In addition, there was a significant increase in the frequency of sensitization in older ages ($\times 2 = 15$; $P < 0.005$) (see Figure 1).

Significant changes making a point cut at 5 years were found (Table 2). Of the 60 patients with positive SPT, only 10 were sensitive to only 1 allergen extract (16.7%), 40 were positive to 2 extracts (66.7%), and 10 cases to 3 extracts simultaneously (16.6%).

The sensitivity of patients to different groups of aeroallergens is shown in Figure 2. The frequency of each positive allergen, sorted from highest to lowest, is shown in Figure 3.

There were significant differences among all groups of different ages and sensitivity to mites ($P < 0.005$) and pollens ($P < 0.005$). It was not so with the rest of allergens (see Figs. 4, 5).

There was no evidence of sensitization to *Aspergillus fumigatus*, *Fraxinus excelsior*, *Ambrosia elatior*, or Chenopodiaceae mix in this study. Soybean hull, *Canis familiaris*, and *Ambrosia elatior* counted up 1% each of total sensitivities. In none of the cases, local or systemic adverse reactions during and after 24 hours of the procedure were detected. SPT performed in the 20 control individuals yielded negative results.

DISCUSSION

The increased prevalence of allergic diseases worldwide in the past decades is well known. In Europe, allergic diseases affect 1 in 4 individuals.[8] The increase of these disorders is particularly important in children because they are now being considered as the most common cause of chronic symptoms in childhood.[9]

In this context, 60% of children with recurrent wheezing, who were examined for the Eva Peron School Hospital, showed specific IgE for at least 1 aeroallergen studied by SPT. Sensitivity to aeroallergens increased significantly with age. For example, the frequency of sensitization was 32% among children aged 6 months to 2 years and 80% in those older than 7 years old. The main group of aeroallergens involved in the sensitivity proved to be the house dust mite, with a frequency 4 or more times higher than any other group. Local[10] or international[11] studies showed that house dust mite concentrations at home increase the frequency and severity of asthma in children.

Surprisingly, in our survey, *Blomia tropicalis* shows higher levels of positivity than *Dermatophagoides*

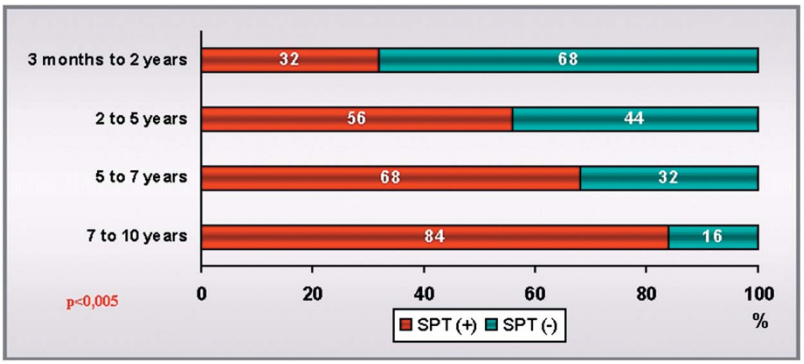

FIGURE 1. Age-group and sensitization to any aeroallergen.

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TABLE 2. Increased Frequency of Sensitization in Children Aged 5 or Older

Age	Frequency of SPT (+)	Odds Ratio	CI 95%	P
3 months to 5 years	44%	4.03	1.58 <odds ratio< 10.44	0.001
5 to 10 years	76%			

CI, confidence interval.

pteronyssinus and *Dermatophagoides farinae*. However, local studies exhibit an increase in the importance of *Blomia tropicalis* as a relevant aeroallergen in provinces like Santa Fe, Corrientes, and Posadas.[12,13]

Allergy to pollens presents only in children older than 5 years (8%) and 7 years (44%). It is likely that a greater number of pollinic seasons are required to sensitize to young children. Overall, only 13 patients (13%) have positive pricks test to any pollen extract. *Ligustrum lucidum* account for 61.5% of total positivities (8 of 13). Grass mix and *Platanus americana* appears with 2 positivities each, and 1 for *Ambrosia elatior*. These results contrast with other studies in areas such as Virginia and the United States, where authors found high levels of sensitivity to pollen in young children. It shows positive prick test in 29% children aged 1 to 2 years, and it increases to 50% in those in the range of 3 to 4 years.[14]

Ligustrum lucidum (privet tree) was the most allergenic pollen in our study. It is abundant in Argentina, mainly planted in streets. Privet tree release heavy grains of pollen in December (late spring). In a previous research, we also found that privet tree was the most sensitizing pollen in 281 allergic children aged 1 to 10 years. In this research, 29 (10.3%) had positive skin tests to any extracts of pollen studied. Overall, 36 SPT was positive. *Ligustrum lucidum* was positive in 10 opportunities (27.7%) followed by *Cynodon dactylon* in 7 (19.4%), *Poa annua* in 3 (8.3%), *Sorghum vulgare* in 3 (8.3%), *Platanus acerifolia* in 3 (8.3%), *Fraxinus excelsior* in 3 (8.3%), *Morus alba* in 3 (8.3%), *Ambrosia elatior* in 3 (8.3%), and *Zea mays* in 1 (2.7%).[15] Privet tree is a huge problem in New Zealand and the east coast of Australia. It is banned from sale or cultivation in New Zealand due to the effects of its pollen on asthma patients. Privet pollen is known to cause asthma and eczema in people who live close to them. Besides, the leaves and berries are poisonous to people and animals.[16] In Argentina, many people feel that privet tree is the source of sudden asthma attacks during his pollination. Lig v 1 and Lig v 2 are the 2 allergen molecules of privet responsible to linking IgE and promoting symptoms.[17]

Soybean hull was included in the panel because it is an important aeroallergen in our geographic area. It has been linked to several worldwide outbreaks of asthma-related deaths.[18] Argentina exports this oilseed in many harbors around Rosario. Soybean transport and storage in silos promote the dispersion of fine pellets particles. In the same way, at the time of discharge grains into the ships, dust were delivered in sizeable proportions to the air. There is substantial

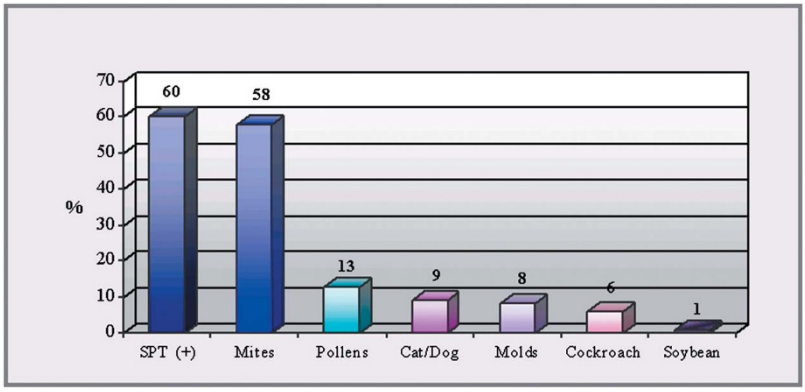

FIGURE 2. Frequency of overall sensitivity to different groups of aeroallergens.

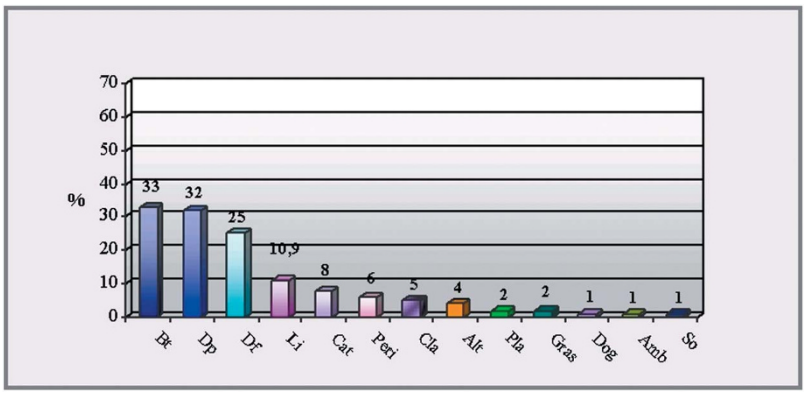

FIGURE 3. Percent of positive skin test to all allergens.

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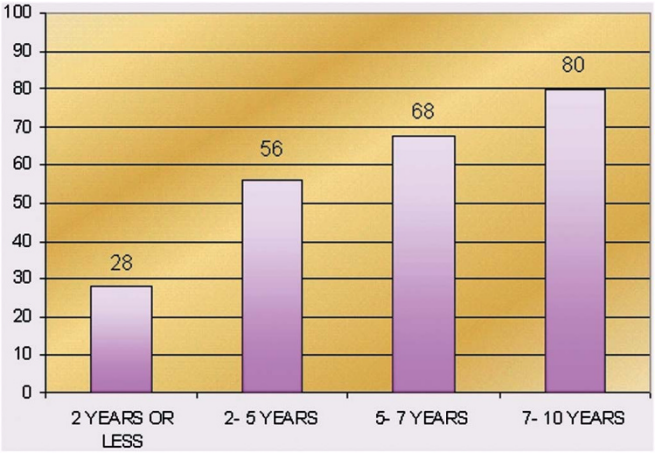

FIGURE 4. Sensitivity to mites.

evidence of the direct relation between respiratory exposure and sensitivity to soybean pellets as aeroallergens that cause asthma and rhinitis. Moreover, an association between sensitivity to soybean hull, severity of asthma, and level of patient exposure has been proposed.[19]

Soybeans allergens are located in the skin of the grain. They produce strong sensitizations in some susceptible individuals causing IgE-mediated severe bronchial asthma. Asthma attacks are typically sudden and life threatening. Other research in adults with asthma and allergic rhinitis, living in urban areas like our study, showed 8.4% of sensitization to aeroallergens.[19] In our study, only 1 patient (1%) showed positive prick test against soybean hull extract. Probably, as an outdoor allergen, the soybean hull needs several seasons to sensitize. Gly m 1 and Gly m TI (soybean trypsin inhibitor) are the most important soybean hull allergens.[20,21]

Asymptomatic sensitization was well demonstrated in healthy people as an important risk factor to develop allergies.[22] House dust mite is the most involved allergens. Because of that, we expect some positive prick test in control group. However, in this healthy population, all test resulted negative. We believe that the small size of control group could explain this situation.

Much controversy has caused the lower age limit to practice skin tests. Group 1 included wheezing patients from 6

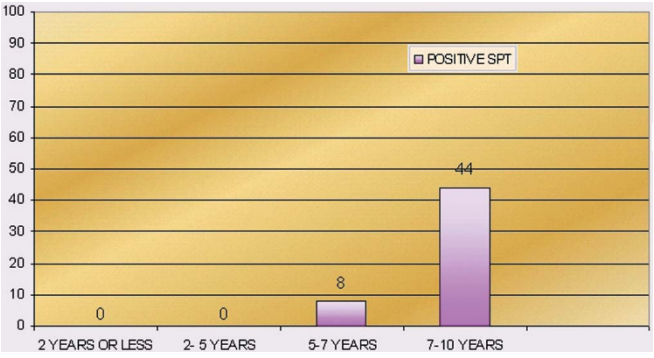

FIGURE 5. Sensitivity to pollens.

months to 2 years of age. It is well known that skin reactivity to allergen extracts is low in this population and that this age is not the best to evaluate sensitization to aeroallergens. However, it has been observed that a significant wheal was detectable after 3 months of age in most infants tested with histamine, codeine phosphate, or allergen extracts. According to Demoly et al,[23] it is therefore possible to perform skin tests to diagnose allergic disorders in infancy, but the size of the wheal is often reduced, and criteria of positivity should always compare the size of the wheal induced by allergen extracts with that elicited by positive control solutions. However, we detect 32% of positivities to any extract in group 1.

CONCLUSIONS

This study found a high tendency of sensitization to aeroallergens in a children population with recurrent wheezing who were examined at the Eva Perón School Hospital in the province of Santa Fe. House dust mites are found to be the more common allergens. Pollen allergy seems to be gaining importance in children older than 7 years. *Ligustrum lucidum* was more sensitizing pollen. Soybean hull shows 1% of sensitivities.

There were no published studies related to allergic sensitivity in children younger than 5 years in our region in the past decade. Given the high level of evidence regarding the risk involved in exposure to aeroallergens is of interest to continue with studies in other parts of the country to setup a map of allergens involved in the etiology of wheezing in our pediatric patients. The absence of side effects during SPT suggests their safety at an early age. Because the small number on patients registered in this work compared with total population of Grand Rosario (close to 2 million of people), large studies are required to confirm this findings.

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