

Original article

Coincidence of atopy profile in terms of monosensitization and polysensitization in children and their parents

Background: Results from epidemiologic studies have shown that childhood atopy is probably a hereditary disorder, because the offspring of affected parents have a higher risk of developing atopy. Among the atopic population, some subjects are sensitized to only one class of allergens (monosensitized), while other subjects are sensitized to more than one class of allergens (polysensitized). The aim of this study was to investigate whether atopy profile (monosensitization/polysensitization) in children is linked to the same conditions in their parents.

Methods: We evaluated sensitization to five classes of aeroallergens (house dust mites, animal danders, pollens, molds, and cockroach) by skin prick testing in a group of 494 children with suspicious allergic symptoms and in their parents.

Results: The frequency of parental atopy was highest (51.6%) in polysensitized children ($n = 189$), intermediate (37.1%) in monosensitized children ($n = 178$), and was lowest (22.4%) in nonsensitized children ($n = 127$). The proportion of polysensitized subjects among atopic parents was significantly higher for polysensitized children (45.6%) than for monosensitized children (31.1%). Polysensitized children were found to more frequently have one or both parents polysensitized (32.3%, 7.4%) than monosensitized children (18.5%, 2.2%) with odds ratios of 2.09 (95% CI: 1.29–3.40) and 3.48 (1.12–10.78), respectively, whereas the likelihood of having one or two monosensitized parents was not increased for polysensitized children.

Conclusion: Our data suggest a familial coincidence of atopy profile in terms of monosensitization and polysensitization, although the relative importance of genetic or environmental influence should be studied further.

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Key words: atopy; familial coincidence; house dust mite; monosensitization; polysensitization.

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Accepted for publication 1 December 2004

In childhood, sensitization to common aeroallergens, i.e., atopy, is a major cause of respiratory diseases such as hay fever and bronchial asthma (1, 2). Our knowledge of the risk factors for atopy is limited, although a number of genetic and environmental factors have been implicated (3). Results from epidemiologic studies have shown that childhood atopy is probably a hereditary disorder, because monozygotic twins are more frequently affected than dizygotic twins (4), and the offspring of affected parents have a higher risk for atopy (5).

It is well-recognized that among the atopic population, some subjects are sensitized only to one class of allergens (monosensitized), whereas other subjects are sensitized to more than one class of allergens (polysensitized) (6, 7). However, the majority of studies that have evaluated familial associations of atopy did not take monosensitization or polysensitization into account (5, 8–10). Only one study, as far as we know, addressed this issue, but this study explored only the influence of parental atopy profile (monosensitization/polysensitization) on the development

of atopy in offspring (11). Therefore, it is still not clear whether atopy profile in children is linked to the same conditions in their parents.

In order to investigate this relationship, we analyzed skin prick test (SPT) data from a group of children with suspicious allergic symptoms and from their parents. Our study population was chosen based on the assumption that atopy tends to 'run in families', so as to allow this relationship to be investigated expeditiously.

Methods

We investigated atopy profile in a group of children with symptoms suspicious of allergic diseases and in their parents. The children were recruited from patients who were referred to the allergy clinic of Seoul National University Children's Hospital from January, 2001 to December, 2002, by their primary care physicians. Children were chosen from 7 to 10 year age group, had lived in the Seoul Metropolitan area since birth, and had natural parents. The evaluation of these children included case history, physical examination,

measurements of serum total immunoglobulin E (IgE) and blood eosinophil count, methacholine inhalation test, and SPT. Children with a negative histamine skin test, previous immunotherapy, immunosuppression, or any other serious disease, were excluded.

Both parents of the children were asked if they would participate in the study. After obtaining consent, the parents underwent SPT. If any parent refused to participate, the family was excluded. Testing was performed by a single investigator who had no knowledge of the children's test results.

Sensitization to 13 aeroallergens was evaluated by SPT in children and parents. The allergens tested included: (i) house dust mites (*Dermatophagoides pteronyssinus*, *D. farinae*), (ii) animal danders (cat epithelium, dog epithelium), (iii) pollens (mugwort, ryegrass, ragweed, hazel, alder, oak), (iv) molds (*Aspergillus fumigatus*, *Alternaria alternata*), and (v) cockroach (*Blattella germanica*). These allergens were supplied by Allergopharma (Reinbek, Germany). Histamine and isotonic saline were used as positive and negative controls. A mean wheal diameter 3 mm larger than a negative control was considered to indicate a positive reaction (12).

In terms of defining monosensitization and polysensitization, it was considered that atopic subjects are frequently sensitized to more than one allergen belonging to clusters of allergen classes (13, 14). Thus, subjects sensitized to only one class of allergens were defined as monosensitized, and those sensitized to two or more classes of allergens were defined as polysensitized.

Statistical analysis

Results are expressed as mean $\pm$ SD, unless otherwise stated. Differences in continuous data between the three children study groups were compared using one-way ANOVA and the *post hoc* Tukey honestly significant difference test for multiple comparisons. Linear-by-linear association was used to evaluate potential relationships between the atopy profile in children and the frequency of parental atopy. Proportional differences between two groups were analyzed by the chi-square test. Odds ratios (ORs) and their 95% confidence intervals (CIs) for polysensitized children to have various parental atopy conditions, relative to monosensitized children, were computed. All data analyses were performed using SPSS version 10.0 (SPSS Inc., Chicago, IL, USA). In each case, statistical significance was accepted when two-sided *P*-values were < 0.05 .

Results

Among the 494 children enrolled, 367 (74.3%) were found to have at least one positive skin test to the allergens (Table 1). Among the 367 atopic children, 178 (48.5%) were reactive to only one class of allergen (monosensitized), and 189 (51.5%) to two or more classes of allergens (polysensitized). As expected from the sensitization rate of house dust mites, most monosensitized subjects (161 of 178, 90.4%) were reactive to house dust mites, and most polysensitized subjects (177 of 189, 93.7%) were reactive to house dust mites plus at least another allergen class. Sensitization to at least one of the allergens tested was found in 208 fathers (42.1%) and in 176 mothers (35.6%). The allergen class-specific sensitization rates among the atopic subjects were not significantly different between fathers and mothers. Polysensitization was less frequent among the atopic

Table 1. Sensitization rates to each allergen or class of allergen in atopic subjects

	Children (n = 367)	Fathers (n = 208)	Mothers (n = 176)
House dust mites	338 (92.1)	168 (80.8)	129 (73.3)
<i>Dermatophagoides pteronyssinus</i>	332 (90.5)	154 (74.0)	124 (70.5)
<i>Dermatophagoides farinae</i>	332 (90.5)	157 (75.5)	111 (63.1)
Animal danders	118 (32.2)	42 (20.2)	40 (22.7)
Dog epithelium	89 (24.3)	20 (9.6)	22 (12.5)
Cat epithelium	60 (16.3)	30 (14.4)	28 (15.9)
Cockroach (<i>Blattella germanica</i>)	83 (22.6)	57 (27.4)	42 (23.9)
Molds	66 (18.0)	16 (7.4)	10 (5.7)
<i>Alternaria alternata</i>	61 (16.6)	13 (6.3)	8 (4.5)
<i>Aspergillus fumigatus</i>	26 (7.1)	7 (3.4)	6 (3.4)
Pollens	54 (14.7)	61 (29.3)	60 (34.1)
Mugwort	26 (7.1)	37 (17.8)	39 (22.1)
Oak	24 (6.5)	23 (11.1)	19 (10.8)
Alder	20 (5.4)	20 (9.6)	19 (10.8)
Hazel	20 (5.4)	16 (7.7)	17 (9.7)
Ragweed	19 (5.2)	21 (10.1)	22 (12.5)
Ryegrass	7 (1.9)	11 (5.3)	7 (4.0)

The values expressed are n (%).

subjects in fathers (40.4%) or mothers (38.6%) than in children (51.5%).

The clinical characteristics of nonsensitized, monosensitized, and polysensitized children are shown in Table 2. Blood eosinophil counts, serum IgE levels, and the frequency of methacholine hyperreactivity were significantly higher in monosensitized or polysensitized children than in nonsensitized children. Serum IgE levels were significantly higher in polysensitized than monosensitized children, but the other parameters were not significantly different between these two groups.

The frequencies of atopy, monosensitization, and polysensitization in parents were compared among the three children groups (Table 3). The frequency of atopy was highest in fathers (57.7%) and mothers (45.5%) of polysensitized children, intermediate in those (39.9%,

Table 2. Clinical characteristics of the three children groups

	Nonsensitized children (n = 127)	Monosensitized children (n = 178)	Polysensitized children (n = 189)
Age (year)	8.4 $\pm$ 0.6	8.5 $\pm$ 0.7	8.6 $\pm$ 0.7
Sex (M/F)	76/51	102/76	116/73
Blood eosinophils (/mm ³)	237 $\pm$ 178	383 $\pm$ 204*	391 $\pm$ 183*
Total IgE (IU/ml)†	74 (23–234)	282 (89–891)*	407 (135–1230)*, **
FEV ₁ (% predicted)	96.2 $\pm$ 10.5	94.7 $\pm$ 10.1	93.4 $\pm$ 9.8
Bronchial hyperreactivity‡ (n)	32/97 (33.0%)	95/149 (63.8%)*	108/156 (69.2%)*

P* < 0.05, compared with nonsensitized children; *P* < 0.05, compared with monosensitized children.

†Geometric mean (range of 1 SD).

‡Methacholine PC₂₀ < 16 mg/ml.

IgE, immunoglobulin E; FEV₁, forced expiratory volume in 1 s.

Table 3. The frequencies of atopy, monosensitization, and polysensitization among the parents of the three children groups

	Nonsensitized children (<i>n</i> = 127)	Monosensitized children (<i>n</i> = 178)	Polysensitized children (<i>n</i> = 189)
Atopy			
Parents	57 (22.4)	132 (37.1)*	195 (51.6)*, **
Fathers	28 (22.0)	71 (39.9)*	109 (57.7)*, **
Mothers	29 (22.8)	61 (34.3)*	86 (45.5)*, **
Monosensitization			
Parents	35 (13.8)	91 (25.6)*	106 (28.0)*
Fathers	16 (12.6)	45 (25.3)*	63 (33.3)*
Mothers	19 (15.0)	46 (25.8)*	43 (22.8)
Polysensitization			
Parents	22 (8.7)	41 (11.5)	89 (23.5)*, **
Fathers	12 (9.4)	26 (14.6)	46 (24.3)*, **
Mothers	10 (7.9)	15 (8.4)	43 (22.8)*, **

P* < 0.05, compared with those of nonsensitized children; *P* < 0.05, compared with those of monosensitized children.

The values expressed are *n* (%).

34.3%) of monosensitized children, and lowest in those (22.0%, 22.8%) of nonatopic children (both, *P*-value for linear trend < 0.001). The frequency of polysensitization was higher in the parents (23.5%) of polysensitized children than in the parents (11.5%) of monosensitized children or in the parents (8.7%) of nonsensitized children, whereas the frequency of monosensitization was higher in the parents (28.0%) of polysensitized children and in the parents (25.6%) of monosensitized children than in the parents (13.8%) of nonsensitized children. Among atopic parents, more parents of polysensitized children were polysensitized (89 of 195, 45.6%) than parents of monosensitized children (41 of 132, 31.1%).

To examine the influence of parental atopy profile on the atopy profiles of children, the proportions of the various combinations of parental atopy profile were analyzed in the three children groups (Fig. 1). The frequency of unilateral or bilateral parental atopy was highest in polysensitized children, intermediate in monosensitized children, and lowest in nonsensitized children (51.3% vs 40.4% vs 27.6%; 25.9% vs 16.9% vs 8.7%; both, *P*-value for linear trend < 0.001). Polysensitized children were found to have at least one polysensitized parent (39.7%) more frequently than monosensitized (20.8%) or nonsensitized children (16.5%). The same figures were observed, when the frequencies of having one polysensitized parent (32.3%, 18.5%, 15.7%) or both polysensitized parents (7.4%, 2.2%, 0.8%) were examined separately. No significant differences were observed in these frequencies between monosensitized and nonsensitized children. In contrast, the frequencies of families with one or two monosensitized parents were significantly higher in polysensitized (34.9%, 10.6%) and monosensitized children (30.9%, 10.1%) than in nonsensitized children (19.7%, 3.9%). No significant differences were found in these frequencies between polysensitized and monosensitized children.

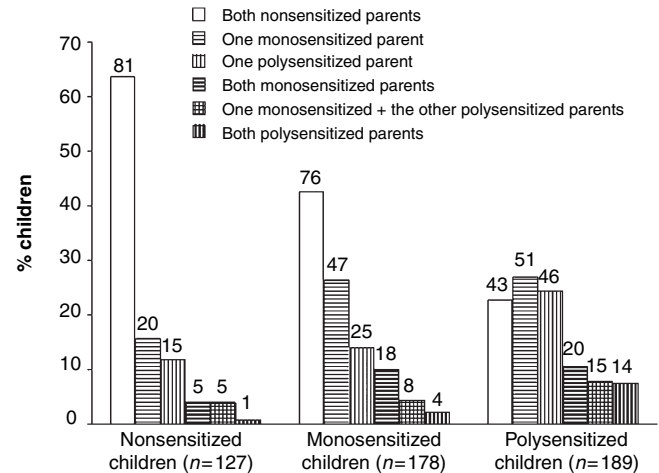


Figure 1. The proportions of the various parental atopy profiles in the three children groups. Number of subjects are shown on the top of each column.

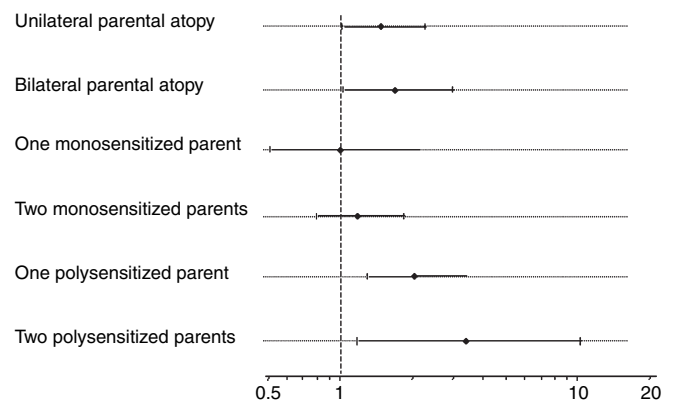


Figure 2. Odds ratios and 95% confidence intervals of polysensitized children having various parental atopy conditions, compared with monosensitized children.

The ORs of polysensitized children having various parental atopy conditions, compared with monosensitized children, are shown in Fig. 2. Polysensitized children had significantly higher chances of having unilateral or bilateral atopic parents with ORs of 1.55 (95% CI: 1.03–2.35) and 1.73 (1.04–2.88). The risks of polysensitized children having one or two monosensitized parents were not increased [1.05 (0.54–2.06), 1.17 (0.76–1.81)]. In contrast, the risks of having one or two polysensitized parents were increased for polysensitized children [2.09 (1.29–3.40), 3.48 (1.12–10.78)].

Discussion

This study confirms that atopic children are more frequently born to atopic parents than nonatopic children. It also shows – for the first time, to our knowledge –

that atopic profiles in terms of monosensitization and polysensitization tend to coincide in children and their parents.

Evaluations of familial associations of atopy based on epidemiologic studies are hampered by the relatively low prevalences of atopy in the population at large (15). Our study population comprised a group of 494 families of children who attended our allergy clinic. We found higher prevalences of atopy in both children and their parents than would occur in the general population (16). This is not a surprising finding, because the group of children evaluated reflects those who required medical assistance for suspicious allergic symptoms, and because atopy is known to 'run in families' – whether through genetic or environmental factors. Consequently, our study design benefited from the recruitment of many cases of atopy in both children and parents, although the study group is not representative of the general population.

Parental atopic history has been used as an important predictor of childhood atopy. Several studies reported proportional increases in the development of allergy in children with increases in the number of sensitized parents (8, 17, 18). The present study also shows that atopic children are more frequently born to atopic parents than nonatopic children. In our analysis of the role that parental atopy has on the development of patterns of sensitization in offspring, we found that the frequencies of unilateral or bilateral parental atopy were highest in polysensitized children, intermediate in monosensitized children, and lowest in nonsensitized children. This observation is novel and suggests that the presence of atopy in parents is important not only for the development of atopy but also for determining the atopy profile in the offspring.

No previous study has examined whether atopy profiles in children are linked to the same conditions in parents. One previous study explored the influence of parental atopy profile on the incidence of atopy in offspring (11). However, this study did not incorporate an analysis of the atopy profiles of children and thus could not provide information on the familial coincidence of atopy profile. Another study observed associations between allergen-specific sensitizations in children and parents, but did not address the familial coincidence of atopy profile in terms of monosensitization and polysensitization (8). In the present study, we found a significantly higher frequency

of polysensitized subjects among the parents of polysensitized children than among the parents of monosensitized children. This might have been caused by a higher frequency of atopy in the former group. However, among atopic parents, the proportion polysensitized was significantly higher in the former group than in the latter group. Polysensitized children were found to have one or two polysensitized parents more frequently than monosensitized children. The risk of polysensitized children having one or two polysensitized parents was significantly increased, compared to monosensitized children, with ORs of 2.09 and 3.48, respectively, whereas the risk of having one or two monosensitized parents was not increased.

The coincidence of atopy profile in terms of monosensitization and polysensitization in children and parents may underline the primary role of genetic predisposition, as all families studied had lived within the same macroenvironment. However, we cannot rule out the possibility that a difference in microenvironment may have contributed to our findings. One previous study suggested that the frequencies of mono- and polysensitization might not primarily reflect allergen exposure, by showing different prevalences among the study samples under identical geographical and climatic conditions for years (13). Unless environmental factors are strictly controlled, epidemiologic studies like the present study cannot adequately answer the question as to whether an accumulation of a specific atopy profile within families is more a consequence of genetic similarities or of an effect of equal allergen exposure resulting from living under the same environmental conditions (19). Further investigations such as twin studies, which would offer a more rigorous genetic interpretation, will be needed to more accurately solve this issue.

In conclusion, our data suggest a familial coincidence of atopy profile in terms of monosensitization and polysensitization, although the relative importances of genetic and environmental influences require further study.

Acknowledgments

This study was supported by a grant (no. 04-2002-050-0) from the Seoul National University Hospital Research Fund and by the BK 21 Project for Medicine, Dentistry and Pharmacy.

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