Atopy in young children with asthma

Li Xiang, Qi Zhang, Kun-Ling Shen

Beijing, China

Background: **A close relationship between outcome in patients with early-onset asthma and atopy has been reported. Allergic sensitization in early life seems to be an important risk factor for subsequent persistent asthma during childhood and adulthood. It might be valuable to evaluate atopy in patients with early-onset asthma in order to predict prognosis and take early intervention.**

Methods: **Clinical data of 62 asthmatic children under 4 years of age were collected. The atopy status of each patient was determined by both personal allergic history (eczema and/or allergic rhinitis) and specific diagnosis of allergens (screening tests of fx5E, mx2 and Phadiatop conducted by fluoroenzyme-immunometric assay using the UniCAP100 system). The total serum IgE level was also measured. Logistic regression was used to analyze the effect of clinical characteristics on allergic sensitization.**

Results: **There were 74.2% children who reported personal history of atopy and 33.9% reported parents' history of atopy based on the clinical data. The positive rates of fx5E, mx2, and Phadiatop were 40.3%, 14.5%, and 14.5% respectively. The total rate of allergic sensitization was 46.8% and the rate of sensitization to inhalant allergens was 24.2%. The allergic history of parent(s), the sensitization to food allergen, the age of first wheezing attack, and the total serum IgE level were main factors influencing sensitization to inhalant allergens.**

Conclusion: **The asthmatic history of parent(s), the sensitization to food allergens, the age of first wheezing attack above 2 years and the significantly higher total serum IgE level may increase the possibility of sensitization to inhalant allergens in asthmatic children under 4 years of age.**

World J Pediatr 2007;3(4):282-285

Key words: **asthma;**
atopy;
children

Author Affiliations: Center of Asthma, Beijing Children's Hospital Affiliated to Capital University of Medical Sciences, Beijing 100045, China (Xiang L, Zhang Q, Shen KL)

Corresponding Author: Kun-Ling Shen, MD, Center of Asthma, Beijing Children's Hospital Affiliated to Capital University of Medical Sciences, Beijing 100045, China (Tel: 86-10-68028401 ext 2894; Fax: 86-10-68011503; Email: kunling_shen@hotmail.com)

Introduction

A close relationship between outcome in patients with early-onset asthma and atopy has been reported in several population studies.[1-3] Allergic sensitization in early life seems to be an important risk factor for subsequent persistent asthma during childhood and adulthood.[4] It might be valuable to evaluate atopy in patients with early-onset asthma in order to predict prognosis and take early intervention. In this study we investigated the relationship between results of allergens screening tests, total IgE level and clinical data from 62 asthmatic children under 4 years of age, attempting to investigate what clinical characteristics may be associated with atopy in asthmatic children of this age group.

Methods

Patients

Sixty-two infants and young children, aged 8 months to 3 years and 11 months (mean age: 2 years and 5 months), 46 boys and 16 girls, who attended the Asthma Clinic in Beijing Children's Hospital between October 2005 and March 2006 were diagnosed as having asthma and enrolled in the study. The diagnostic criteria for asthma were based on the national guidelines for asthma.[5] Clinical data of these children included age, sex, the age of first wheezing onset, the total times of wheezing attack, the history of wheezing, the personal history of atopic disease (clinical diagnosis of atopic dermatitis and allergic rhinitis), and the history of atopic disease in parents (asthma and allergic rhinitis diagnosed clinically).

Screening test on allergens and measurement of serum total IgE

Screening tests of allergens were conducted by fluoroenzyme-immunometric assay using the UniCAP100 system[6] including fx5E (screening test

for sensitization to mixed food allergens including egg white, milk, wheat, peanut, soybean, cod), mx2 (screening test for sensitization to mould allergens), and Phadiatop (screening test for sensitization to mixed inhalant allergens). The level of serum total IgE was also measured by the system. The results of the screening tests on allergens were defined positive when the actual levels were above a cutoff level of predetermined control sample. Patients with sensitization to inhalant allergens were determined by positive result(s) of Phadiatop and/or mx2 test.

Statistical analysis

Statistical analysis was carried out using the SPSS software (version 11.5). Logistic regression was used to analyze the effect of clinical factors on sensitization to inhalant or food allergens. Univariate analysis of independent effect of each clinical factor on sensitization to inhalant or food allergens was performed initially. For analyzing the factors on sensitization to inhalant allergens, Student's *t* test was performed to analyze the age of first wheezing onset, the total times of wheezing attack, and the duration of wheezing history; the chi-square test was performed to analyze sex, sensitization to food allergens, personal history of atopy, and parents' history of atopy; Wilcoxon's rank-sum test was performed to analyze age and serum level of total IgE. For analyzing the factors on sensitization to food allergens, Student's *t* test was performed to analyze age, and the statistical methods used in the other clinical factors were the same as mentioned above. Further logistic regression was used to analyze the clinical significant factors screened by univarite analysis.

Results

Atopy spectrum determined by allergen screening test

The positive rates of fx5E, mx2, and Phadiatop were 40.3%, 14.5%, and 14.5% respectively, and the rate of total allergic sensitization was 46.8%. The sensitization to inhalant allergens was 24.2%. The distribution of atopy spectrum is shown in Table 1.

Table 1. Distribution of results from allergens screening tests

Distribution	Cases	Percent (%)
fx5E, Phadiatop and mx2 negative	33	53.2
fx5E positive	14	22.6
fx5E and mx2 positive	5	8.1
fx5E and Phadiatop positive	3	4.8
fx5E, mx2 and Phadiatop positive	3	4.8
Phadiatop positive	3	4.8
mx2 positive	1	1.6

Effect of clinical factors on sensitization to inhalant allergens

Clinical factors showing independent statistical significance for sensitization to inhalant allergens at univariate analysis are shown in Table 2. They included age, age of first wheezing onset, sensitization to food allergens, serum total IgE level, and parents' history of asthma. Further logistic regression analysis excluded the effect of age on sensitization to inhalant allergens. According to the Exp(B) value (Table 3), parents' history of asthma and sensitization to food allergens were of greater statistical significance.

Effect of clinical factors on sensitization to food allergens

Only such two clinical factors as sensitization to inhalant allergens and serum total IgE were of

Table 2. Univariate analysis of effect of clinical factors on sensitization to inhalant allergens

Clinical factors	Phadiatop and/or mx2 positive	Phadiatop and mx2 negative
Age (y)	3.1 (1.5-3.9)*	2.3 (0.7-3.8)
Sex (male/female)	11/4	35/12
Age of first wheezing onset (y)	2.2±0.9†	1.1±0.8
Duration of wheezing history (mon)	9.7±7.2	13.4±8.4
Total times of wheezing attack	6.7±5.7	7.5±5.5
Total serum IgE (kU/L)	439 (49.2-4175)‡	47.8 (2.0-754)
Sensitization to food allergens (positive/negative)	11/4§	14/33
Personal history of atopy		
No	1	15
Eczema	6	15
AR	4	8
Eczema and AR	4	9
Parents' history of atopy		
No	8‖	33
Father AR	4	6
Father asthma	0	2
Mother AR	0	6
Mother asthma	3	0

Data of age, total IgE expressed as median (min-max). *: u=17.9, w=1213.5, P<0.05; †: t=4.412, P<0.01; ‡: u=85.5, w=1307.5, P<0.01; §: χ^2=8.961, P<0.01; ‖: χ^2=13.805, P<0.01. AR: allergic rhinitis.

Table 3. Logistic regression analysis of effect of clinical factors on sensitization to inhalant allergens

Clinical factors	B	Wald	P	Exp(B)
Parents history of asthma	3.514	4.479	0.034	33.598
Sensitization to food allergens	2.586	5.343	0.021	13.277
Age of first wheezing onset	1.406	6.893	0.009	4.080
Serum total IgE	0.004	4.004	0.045	1.004
Constant	-6.135	15.181	0.000	0.002

B: coefficient of partial regression.

Table 4. Univariate analysis of effect of clinical factors on sensitization to food allergens

Clinical factors	fx5E positive	fx5E negative
Age (y)	2.4±1.0	2.4±0.9
Sex (male/female)	20/5	26/11
Age of first wheezing onset (y)	1.4±1.0	1.4±0.9
Duration of wheezing history (mon)	12.2±9.6	12.7±7.3
Total times of wheezing attack	7.4±5.5	7.2±5.6
Total serum IgE (kU/L)	152 (9.1-4175)*	38.2 (2-805)
Sensitization to inhalant allergens (positive/negative)	11/14†	4/33
Personal history of atopy		
No	4	12
Eczema	9	12
AR	6	6
Eczema and AR	6	7
Parents' history of atopy		
No	17	24
Father AR	4	6
Father asthma	0	2
Mother AR	2	4
Mother asthma	2	1

Data of total IgE expressed as median (min-max). *: u=203, w=906, P<0.01; †: χ^2=8.961, P<0.01. AR: allergic rhinitis.

Table 5. Logistic regression analysis of effect of clinical factors on sensitization to food allergens

Clinical factors	B	Wald	P	Exp(B)
Total serum IgE	0.001	0.883	0.347	1.001
Sensitization to inhalant allergens	1.432	3.655	0.056	4.187
Constant	-0.983	7.933	0.005	0.374

B: coefficient of partial regression.

independent statistical significance for sensitization to food allergens as shown by univariate analysis (Table 4), but logistic analysis did not show any statistical significance of these two clinical factors on sensitization to food allergens (Table 5).

Discussion

The majority of infants and young children with asthma presented with clinical subgroups of early transient wheezing. Sheriff et al[7] reported that over 70% of children who wheezed in the first 6 months no longer wheezed 3 years later based on a birth cohort study of 7224 samples. Another longitudinal study from birth to 10 years of age in a whole-population birth cohort (1456 subjects) confirmed that asthmatic heredity, predisposition to early life atopy, plus early passive smoke exposure and recurrent chest infection were important factors for the occurrence of wheezing and asthma at 10 years of age.[2] Ponsonby et al[8] studied the results of the skin-prick test (10 common aeroallergens) in 758 school children aged 8 to 10 years and a hospital-based sample of 78 children attending the hospital for asthma. Regression analysis indicated increased rate of aeroallergen sensitization in moderate and severe asthmatic children. A recent study reported the presence of airway hyperresponsiveness and concomitant atopic manifestations in childhood increased the risk of developing asthma in adulthood.[3] It has been accepted that allergic sensitization is an important risk factor for persistent asthma. The results from a birth cohort study in Tucson suggested that patterns of wheezing prevalence were established by the age of 6 years.[9] Furthermore, Stein and Martinez[4] concluded that identifying those children who were or would be affected by persistent asthma before 6 years of age might enable physicians to treat them at the critical time. While in the present study we aimed to understand atopy spectrum in younger asthmatic children.

The concept of atopy generally refers to the genetic predisposition for sensitization to allergens.[2] In addition to personal history of atopic disease, the subject is defined as being atopic when a positive result of the skin prick test is investigated or specific IgE above cutoff level is measured in serum. Allergens screening test seems to be more convenient in clinical practice for young children with asthma.

Phadiatop test is regarded as a regular screening test to determine sensitization to common inhalant allergens. The subjects in the present study were subjected to tests of Phadiatop and mx2 in the meantime. Six of 53 children (11.3%) with negative results of the Phadiatop test presented positive in mx2 test, meanwhile 6 of 9 children (66.7%) with positive mx2 test results presented negative Phadiatop test result. These results suggested that mould sensitization is not uncommon in young children with asthma, and that Phadiatop test should not be selected as a sensitive screening test to determine sensitization to mould. Therefore, in the present study, sensitization to inhalant allergens was defined as a positive result of Phadiatop and/or mx2 test. Although 74.2% of children reported personal history of atopy and 33.9% reported parents' history of atopy in this study, only 46.8% of children were testified as having allergic sensitization by allergens screening tests. It was shown that there was difference in atopy distribution between the results from allergen screening tests and clinical manifestations.

In this study, parents' history of asthma had the most significant effect on sensitization to inhalant allergens. In 5 children whose parents had asthma, 3 with maternal asthma presented with sensitization to inhalant allergens and the other 2 with paternal asthma showed negative results of inhalant allergens by screening tests. Because of the small sample size in the

present study, we could not conclude whether the factor of maternal asthma plays a key role in sensitization to inhalant allergens in young children with asthma.

Sensitization to food allergens is another factor for sensitization to inhalant allergens. In this study, the mean age of children with sensitization to food allergens was younger than that of children with sensitization to inhalant allergens. Did the children with early sensitization to food allergens have potential risk for subsequent atoptic sensitization to inhalant allergens? One study found that early allergic reaction to food, especially egg, increased the risk for later reaction to aeroallergens. It seems necessary to follow up the atopy status in young asthmatic children with sensitization to food allergens in order to find sensitization to inhalant allergens early.

Age of first wheezing onset and serum total IgE level are not powerful factors influencing sensitization to inhalant allergens. The present study revealed children with late-onset wheezing (above the median age of 2.2 years) and those with a higher level of serum total IgE (median 439 kU/L) were more likely to present sensitization to inhalant allergens. Rusconi et al[10] assessed the relationship between total serum IgE at 0.5-3 and 3-6 years and the risk of allergic sensitization and persistent wheezing up to 8 years of age, but no relationship was found between total serum IgE in early life (0.5-3 years) and the recurrence of wheezing or allergic sensitization up to 8 years of age. The fact that IgE levels at 3-6 years of life were higher in sensitized children was clinically irrelevant because sensitization did not seem to be an important risk factor for wheezing. They concluded that in infants with frequent wheezing, measurement of total IgE will not help to predict the subjects who are either at risk for recurrent or persistent wheezing symptoms or atopic sensitization by school age.

The result that we did not find independent clinical factors affecting sensitization to food allergens in this study might be due to inclusion criteria for cases and small sample size.

In conclusion, almost a quarter of asthmatic children under 4 years of age in this study presented sensitization to inhalant allergens as shown by allergens screening tests. The asthmatic history of parent(s), the sensitization to food allergens, the age of first wheezing onset above 2 years, and the significantly higher total serum IgE level may increase the possibility of sensitization to inhalant allergens in asthmatic children under 4 years of age.

Funding: None.
Ethical approval: This study was approved by the Institutional Review Board of Capital University of Medical Sciences, China.
Competing interest: None declared.
Contributors: XL wrote the first draft of this paper. All authors contributed to the intellectual content and approved the final version.

References

1 Illi S, von Mutius E, Lau S, Niggemann B, Grüber C, Wahn U. Perennial allergen sensitisation early in life and chronic asthma in children: a birth cohort study. Lancet 2006;368:763-770.
2 Kurukulaaratchy RJ, Matthews S, Arshad SH. Relationship between childhood atopy and wheeze: what mediates wheezing in atopic phenotypes? Ann Allergy Asthma Immunol 2006;97:84-91.
3 Porsbjerg C, von Linstow ML, Ulrik CS, Nepper-Christensen S, Bacher V. Risk factors for onset of asthma, a 12-year prospective follow-up study. Chest 2006;129:309-316.
4 Stein RT, Martinez FD. Asthma phenotypes in childhood: lessons from an epidemiological approach. Paediatr Respir Rev 2004;5:155-161.
5 Respiratory Section of Chinese Pediatric Association. Guideline for prevention and treatment of child asthma (trial). Chin J Pediatr 2004;42:100-106.
6 Sander I, Kespohl S, Merget R, Goldscheid N, Degens PO, Brüning T, et al. A new method to bind allergens for the measurement of specific IgE antibodies. Int Arch Allergy Immunol 2005;136:39-44.
7 Sherriff A, Peters T, Henderson J, Strachan D. Risk factor associations with wheezing patterns in children followed longitudinally from birth to 3(1/2) years. Int J Epidemiol 2001;30:1473-1483.
8 Ponsonby AL, Gatenby P, Glasgow N, Mullins R, McDonald T, Hurwitz M. Which clinical subgroups within the spectrum of child asthma are attributable to atopy? Chest 2002;121:135-142.
9 Morgan WJ, Stern DA, Sherrill DL, Guerra S, Holberg CJ, Guilbert TW, et al. Outcomes of asthma and wheezing in the first 6 years of life: follow-up through adolescence. Am J Respir Crit Care Med 2005;172:1253-1258.
10 Rusconi F, Patria MF, Cislaghi GU, Sideri S, Gagliardi L. Total serum IgE and outcome in infants with recurrent wheezing. Arch Dis Child 2001;85:23-25.

Received March 30, 2007
Accepted after revision June 27, 2007