

Pulmonary functions in atopic and nonatopic asthmatic children

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SUMMARY

Background: we examined how lung function and certain clinical and laboratory characteristics in asthmatic children were changed according to skin test positivity to aeroallergens.

Methods: a skin prick test was conducted using standardized extracts of 10 different allergens in 56 children with bronchial asthma, aged 5-15 years, in Dicle University Hospital. Lung function was measured by Microplus spirometer.

Results: among the 56 subjects, asthma was classified as mild in 16, moderate in 42 and severe in 3. At least one skin prick test was positive (monosensitized) in 35 subjects (62 %) and positive reactivity to two or more aeroallergens (polysensitized) was found in 17 subjects (30 %). Positive skin test reactions to aeroallergens were associated with a decrease (as percentage of the predicted decrease) in FEV₁, FVC and PEF values. Significant differences were also found between prick test-positive and -negative asthmatics in duration of breastfeeding (8.5 ± 5 months vs 15 ± 7 months, respectively, $p < 0.007$), age at which cow's milk had been started (5.7 ± 1.6 vs 10.5 ± 5.4 , $p = 0.004$); total serum IgE concentration (350 ± 221 IU/ml vs 234 ± 164 IU/ml, $p = 0.02$), age at onset of asthma symptoms (2.5 ± 1.9 years vs 4.1 ± 2.2 years) and number of asthma attacks per year (7.0 ± 3.1 vs 5.2 ± 3.5 , $p = 0.012$). When one-way ANOVA and a post-Hoc test were used, asthma attacks were more frequent and severe and allergic conjunctivitis symptoms were more frequent in the polysensitized group than in the nonsensitized and monosensitized groups ($p = 0.03$).

Conclusions: children with positive skin prick test results, especially those with combined sensitivity

to dust mite, cat and dog, were at increase risk of more severe asthma.

Key words: Asthma. Child. Pulmonary function. Skin test.

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INTRODUCTION

Atopy is often regarded as a risk factor for the development of asthma, particularly in childhood asthma and occupational asthma (1). Despite increasing prevalence of childhood asthma, few studies have quantified the associations between atopy characteristics and pulmonary functions of these patients. These studies would supply knowledge of the atopy characteristics of asthmatic children most at risk.

It was aimed in this study to assess whether atopy, measured as total IgE level and/or skin prick test (SPT) reactivity is related to bronchial asthma severity in children by determining the association of these factors with lung functions. The atopic status in our study population was also determined.

MATERIAL AND METHOD

The result of SPTs performed between 1995 and 1997 on 61 patients with asthma aged between 5-15 years, in Dicle University Hospital were evaluated considering their pulmonary functions. Skin prick test was conducted using standardized extracts of different allergens (house dust mite, cat and dog dander, mixed grass pollens, tree pollens, molds and feathers, ALK laboratories, Denmark) applied to the fore-

Table I
Skin test positivity and some patient characteristics

Characteristics	Nonatopic ^a	Atopic			Significance ^{ab}
		Total ^b	Monosensitized	Polysensitized	
n	26	35	18	17	
FEV ₁ /FVC < %75*	8	22	10	12	0.03
PEF, % predicted < %80*	6	19	9	10	0.03
Total serum IgE (kU/l)	234 ± 164	346 ± 181	321 ± 177	395 ± 195	0.02
Asthma attacks per year	5.2 ± 3.5	7.0 ± 3.1	6.4 ± 3.2	7.7 ± 3.1	0.04
Duration of breastfeeding (months)	14.8 ± 7.0	8.5 ± 5.0	10.5 ± 5.4	8.2 ± 3.8	0.001
Age onset (years)	4.1 ± 2.2	2.5 ± 1.9	1.5 ± 1.7	3.4 ± 3.3	0.004
Introduction with cow's milk (months)	10.5 ± 5.4	5.7 ± 1.6	5.6 ± 1.5	5.1 ± 1.2	< 0.001
Preteral history of atopy (n)*	2	7	3	4	> 0.05

*p: with Chi-square test, others with Student's t-test.

arm. Histamine (10 mg/ml) and saline were used as positive and negative controls. Fifteen minute after application of the allergens, wheal size was recorded as the mean of the long axis and its perpendicular, and was regarded as positive if 3 mm greater than the negative control. If there was no reaction to the positive control or a reaction more than 1 mm to the negative control, the results were excluded from the analyses. Children having at least one positive reaction in the SPTs were defined as being atopic.

Lung functions were measured using Micro Plus spirometer (Micro Medical, England) at symptom free intervals after provocation with exercise. Subjects performing unsatisfactory forced expiratory maneuvers were not included in the data analysis. The largest spirometric results were selected from a minimum of three valid expiratory recordings. Subjects who had taken a beta-agonist earlier than 6 h before the test were asked to make another appointment. Each subject underwent assay for serum total IgE level, measured nephelometrically using a commercial device and kit (Dade Behring, Marburg GmbH, Germany). Statistical analyzes were done by using one-way ANOVA and post Hoc Student-Newman-Keuls, unpaired t test and Chi-square test. P value less than 0.05 was accepted as significant.

RESULTS

Of all 61 children participated in the study group, 16 were classified as having mild asthma, 42 with moderate and 3 with severe. Parenteral history of atopy and asthma was found to be present in 9 (14.7 %) of all patients and 7 (20.0 %) of atopics. Atopy according

to SPT results was found in 35 (57 %) of all children, and positive reactivity to two or more aeroallergens (polysensitized) was found in 17 (29 %) subjects. Of all 35 positive SPT results, 32 (91.4 %) were for *Dermatophagoides pteronyssimus* and *Dermatophagoides farinae*. Positive SPT reactions to aeroallergens were found to be associated with a decrease (as % of predicted) in forced expiratory volume in one second (FEV₁), forced vital capacity (FVC) and peak expiratory flow (PEF) values as shown in the table I.

Significant differences were found between SPT positive and negative asthmatics in number of asthma attacks per year (7.0 ± 3.1 vs 5.2 ± 3.5 , respectively, $p = 0.04$). Duration of breastfeeding (8.5 ± 5.0 months vs 14.8 ± 7.0 respectively, $p < 0.001$), and age at introduction of cow's milk during infancy (5.7 ± 1.6 vs 10.5 ± 5.4 respectively, $p < 0.001$) were statistically different between the SPT positive and negative asthmatics. The frequency of positive parental history of atopy was similar in atopic and non-atopic asthmatic children ($p > 0.05$) (table I).

DISCUSSION

Although the prevalence of asthma has risen significantly during the last decades, it is not clear whether this has occurred primarily in persons with a strong atopy. Much of the increase in asthma prevalence was found to be associated with specific IgE sensitization (2). It has long been known that atopy is the strongest risk factor for the development of asthma, increasing the risk by 10-20 fold compared with those who are non-atopic (3). Studies have shown that majority of

asthmatics have a family history of asthma or atopy and most of the patients were atopic (3-5). It still remains a question whether atopic asthma patients are at greater risk to have more severe and frequent asthma attacks. Several investigators have studied the relationship between atopy and childhood asthma; and it has been claimed that if atopy was a factor in aggravating asthma, severity of asthma would increase with increased allergy defined by symptoms and numbers of positive prick skin tests (6).

There are several studies in due course with our findings, which show that children with large skin wheal reactions to certain allergens appear to have more severe illness. Atopic status and increased bronchial responsiveness were all found to be associated with lower levels of lung function in a recent study (7). In the study of Studnicka et al (8), children with a diagnosis of asthma, those with a positive skin-prick test demonstrated increased airway responsiveness as well as with those reported with exposure to maternal smoking. In 81 atopic subjects out of 118 paediatric symptom-free asthma patients, lung functions were found to be lower than the remaining 37 nonatopic patients (9). Ulrik and Baker (10) have found that subjects with new or persistent atopy to house dust mites had significantly increased bronchial responsiveness compared with nonatopic subjects; and, moreover, prechallenge FEV₁ percent predicted was significantly correlated with bronchial responsiveness. A frequent positive bronchial response to exercise was reported to be closely associated with atopy, defined as skin test positivity to 1 of 7 common aeroallergens (11). In a cross sectional study carried out in China, the odds ratios for having respectively slight, mild or moderate, and severe bronchial hyperresponsiveness were found to be 5.9, 21.0, and 30.4 for atopy (12). According to spirometric lung function and skin prick test results among asthmatic children, atopy, positive skin test reactions to house dust mite and cat and lower level (as % of predicted) in FEV₁ were associated with an increased variation in PEF (13).

Atopic individuals were shown to have significantly more often increased bronchial responsiveness, current asthma, and total asthma than nonatopics, and the odds ratios of increased bronchial responsiveness and asthma were found to be increased with the number of positive skin test reactions (14). In the study of Zimmerman et al (6), there was an increase in the number and size of positive skin tests with increasing severity of asthma. Similarly, there was increased reporting of allergic symptoms, such as sensitivity to animals with increasing severity of asthma.

Under the light of these literatures, the issue is that why those atopic children may have more severe and frequent asthma attacks. Positive skin test indicates

that specific IgE antibody is also present on the mast cells in the tissue of the clinically affected organ whatever the allergic disorder is. The basic immune mediator-induced mucosal injury is similar in both atopic and nonatopic patients. However atopic patients may be associated with more easily identified stimuli of mediator release than nonatopic patients. If there is an allergic-extrinsic component in the patient, chronic nonspecific stimulation of the mast cell allergen-induced late-phase immune reactions may create a prolonged nonspecific airway hyperreactivity, which can produce broncospasm even in the absence of identifiable extrinsic factors. On the other hand, positive skin test does not indicate that the patient will necessarily have clinical symptoms on exposure to the allergen. Some atopic individuals may have no symptoms following natural exposure to allergens (15).

Short duration of time of breastfeeding and early age of month at which cow's milk has been started both seem to increase the prevalence of atopic status in our study population. In one of the few studies investigating the influence of prolongation of breast-feeding and postponement of introduction of solid food during infancy, no preventive effect of the diet consumed during infancy was seen on subsequent skin test results in relation to common allergens (16).

We conclude that the two markers of atopy studied (serum total IgE and SPT) were related to lung functions and severity of bronchial asthma. Our findings support the concept that children with positive skin prick test results may have more frequent and severe asthma attacks. So as not to reduce the pulmonary functions of atopic asthmatic children, it is imperative that we design interventions for the dominant allergens.

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RESUMEN

Antecedentes: examinamos cómo se modificaban las funciones pulmonares y algunas características clínicas y de laboratorio en niños asmáticos en función de su reacción positiva a los aeroalergenos en las pruebas cutáneas.

Métodos: se realizó una prueba de punción cutánea (*prick test*) utilizando extractos estandarizados de 10 alérgenos distintos en 56 niños con asma bronquial, de edades comprendidas entre 5 y 15 años en el hospital de la Universidad de Dicle. Las funciones pulmonares se midieron con un espirómetro Microplus.

Resultados: el asma de 16 de dichos sujetos se clasificó como leve, en 42 de los casos, como moderada, y en 3 de grave. Por lo menos una prueba de punción cutánea fue positiva (monosensibilizados) en 35 sujetos (62 %), y se detectó una reacción positiva a dos o más alérgenos (polisensibilizados) en 17 sujetos (30 %). Reacciones positivas a los aeroalérgenos asociadas con una disminución en los valores de volumen espiratorio forzado en el primer segundo (VEMS/FEV₁), capacidad vital forzada (CVF/FVC) y flujo espiratorio máximo (FEM/PEF). También se detectaron diferencias significativas entre los asmáticos con prueba de punción cutánea positiva y negativa en la duración de la lactancia materna ($8,5 \pm 5$ meses vs 15 ± 7 respectivamente, $p < 0,007$); en los meses de vida a los que se comenzó a tomar leche de vaca ($5,7 \pm 1,6$ vs $10,5 \pm 5,4$, $p = 0,004$); en concentración total en suero de inmunoglobulina E (350 ± 221 IU/ml vs 234 ± 164 IU/ml, $p = 0,02$); en la edad de la aparición de los síntomas asmáticos ($2,5 \pm 1,9$ años vs $4,1 \pm 2,2$ años); y en el número de ataques de asma anuales ($7,0 \pm 3,1$ vs $5,2 \pm 3,5$, $p = 0,012$). Los análisis de varianza unidireccional ANOVA y post-Hoc mostraron que el grupo de polisensibilizados sufría ataques de asma más frecuentes y graves y síntomas frecuentes de conjuntivitis alérgica que los grupos no sensibilizados y monosensibilizados ($p = 0,03$).

Conclusión: los niños con resultados positivos a las pruebas de punción cutánea, especialmente los que muestran sensibilidad combinada a los ácaros del polvo, perros y gatos, presentaban un riesgo mayor de padecer asma más grave.

Palabras clave: Asma. Niños. Función pulmonar. Pruebas cutáneas.

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