ORIGINAL ARTICLE

Influence of Atopy on Asthma Severity in Adult Female Patients

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Abstract

Background: Although allergy is known to play an important role in the development of asthma, its influence on the severity of the disease remains under discussion.
Objective: The aim of our study was to examine the relationship between asthma severity and intensity of atopy in adult female asthmatic patients.
Methods: One hundred two consecutive female patients (mean [SD] age, 51.7 [13.4] years) defined as asthmatics according to criteria of the Global Initiative for Asthma (GINA) were prospectively included in the study and their atopic status was investigated by skin prick tests and immunoglobulin (Ig) E levels in serum.
Results: Fifty-six patients were determined to be atopic. The 2 most common allergens were mites (37.2%) and pollens (36.3%). According to GINA classification, 16.7% of the patients had mild intermittent asthma, 27.2% had mild persisten asthma, 33.4% moderate persisten asthma, and 22.5% severe persistent asthma. The mean IgE level was 190.3 (293.8) IU/mL. No differences between atopic and nonatopic asthmatic women were found with regard to severity of asthma, lung functions, age, smoking status, or duration of the disease. Although we found that mean serum total IgE levels tended to increase progressively with asthma severity, the differences were not statistically significant.
Conclusion: Intensity of allergy as measured by number of positive skin prick tests, size of wheal in positive tests, level of total IgE in serum did not influence asthma severity in adult female asthmatics.

Key words: Asthma severity. Allergy. Immunoglobulin E. Skin prick test. Women.

Resumen

Antecedentes: A pesar de que se conoce que la alergia desempeña un papel importante en el desarrollo del asma, su influencia en la gravedad de la enfermedad aun está en debate.
Objetivo: Este estudio pretende estudiar la relación existente entre la gravedad del asma y la intensidad de la atopia en mujeres asmáticas.
Métodos: En el estudio participaron 102 mujeres consecutivas (media [DE] edad, 51,7 [13,4] años) clasificadas como asmáticas según las directrices del *Global Initiative for Asthma* y se examinó su estado atópico mediante la prueba cutánea y las concentraciones séricas de inmunoglobulina (Ig) E.
Resultados: Se determinó que 56 mujeres presentaban atopia. Los dos alérgenos más habituales fueron los ácaros (37.2%) y los pólenes (36.3%). Según la clasificación GINA, el 16,7% de las pacientes padecía asma intermitente leve, el 27,2% tenía asma leve, el 33,4% asma moderada y el 22,5% asma persistente grave. El nivel medio de IgE fue de 190,3 (293,8) IU/mL. No se observaron diferencias entre las mujeres con asma que presentaban atopia y las que no, en relación con la gravedad del asma, las funciones respiratorias, la edad, si eran fumadoras o no, o la duración de la enfermedad. No obstante, se observó que la media de concentraciones séricas totales de IgE tendía a aumentar progresivamente con la gravedad del asma, aunque estas diferencias no fueron estadísticamente significativas.
Conclusión: La intensidad de la alergia cuantificada por el número de pruebas cutáneas positivas, la dimensión de las ronchas en las pruebas positivas y la concentración sérica total de IgE, no ejerce ninguna influencia en la gravedad del asma en mujeres adultas asmáticas.

Palabras clave: Gravedad del asma. Alergia. Inmunoglobulina E. Prueba cutánea. Mujeres.

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Introduction

Bronchial asthma is a common chronic condition that affects up to 10% of adults and 35% of children worldwide and it is an increasing public health problem [1]. Asthma may develop at least in part as a result of genetic or host susceptibility to allergy or atopy and bronchial hyperresponsiveness, and many studies show a clear relationship between asthma and specific allergens, with sensitization to aeroallergens identified as a dominant risk factor for asthma in population based studies [2,3]. Atopic disposition is caused by the interaction between genetic and environmental factors (allergens), as well as by the various clinical manifestations that favor a mainly T helper type 2 (T_H2) response, with interleukins that lead to the formation of immunoglobulin (Ig) E, pro-inflammatory cytokines, and bronchial hyperreactivity [3]. T cells, derived cytokines, IgE, and mast cells initiate an early asthmatic reaction, and recruitment and activation of eosinophils seem to play roles in the persistent asthma phenotype with chronic airflow obstruction. IgE molecules have been found to play a crucial role in allergic respiratory diseases and possibly cause chronic airway inflammation in asthma through activation of effector cells via high-affinity (Fc RI) or low-affinity (Fc RII) IgE receptors [4,5].

Asthma is a disease of variable severity and in spite of efficient new therapy to control it, a substantial percentage of patients suffer serious shortness of breath affecting quality of life. For better asthma control, it is important to determine the risk factors for asthma severity. The relationship between asthma severity and atopy is complex and the importance of the intensity of allergic sensitization to asthma severity is not well understood. In most studies, this relationship has been investigated in children and the answers have remained debatable. Our aim was to investigate the influence of atopy and intensity of allergic sensitization to asthma severity in adult female asthmatic patients.

Material and Methods

Subjects

A total of 102 adult female patients with asthma defined according to the criteria of the Global Initiative for Asthma (GINA) [6] were enrolled. Respiratory and allergy symptoms were assessed in detail for every subject and pulmonary function tests were performed in a standard fashion using an electronic spirometer (MIR, Medical International Research, Rome, Italy). The patient had to complete at least 3 forced vital capacity maneuvers, and the best one was chosen according to the recommendation of the European Respiratory Society [7]. According to the results of spirometry, asthma symptoms and usage of medication (especially doses of inhaled corticosteroids), asthma patients were classified into 4 groups reflecting severity according to GINA criteria.

Exclusion criteria for the study were treatment with antihistamines or oral corticosteroids, presence of skin diseases that may affect the results of skin prick tests (such as chronic urticaria with dermographism), smoking history of more than 10 pack-years, presence of parasitic infection, and pregnancy or breastfeeding.

Tests of Atopy

A battery of 7 aeroantigens (*Dermatophagoides pteronyssinus*; *Dermatophagoides farinae*; and specific grass, tree, mold, weed and animal dander mixes) (Stallergens SA, Paris, France) were used in skin prick tests (SPT), which were performed in each subject on the volar side of the forearm according to the guidelines of the subcommittee on skin tests of the European Academy of Allergology and Clinical Immunology [8]. Histamine hydrochloride (1 mg/mL) and normal saline solutions were used as positive and negative controls, respectively. The SPTs were read after 15 minutes and, a wheal at least 3 mm greater than the negative control was considered positive. The transverse and vertical diameters of the wheal were measured and scored as 1 for 3 mm to 4 mm, 2 for 5 mm to 7 mm, 3 for 8 mm to 10 mm, and 4 for wheals larger than 10 mm.

Total IgE levels (IU/mL) were measured in serum by the nephelometric method (Dade Behring Marburg GmbH, Eschborn, Germany). All determinations were performed in a single laboratory. The working range for the assay of total IgE determinations was 0 to 2000 IU/mL. For this analysis, IgE levels up to 120 IU/mL were considered within normal range. Atopy was considered to be present with at least 1 positive SPT response. The intensity of the allergic sensitization was assessed by the number of positive SPTs, skin wheal scores, and mean IgE levels.

Statistics

All results were expressed as means (SD) values. The significance of differences between groups was assessed by unpaired *t*-tests or Mann-Whitney *U* tests for continuous variables. The ^{2} test or Fischer's exact test was used for testing the significance of differences in prevalence between groups. The statistical analysis was performed using SPSS version 11 and *P* values less than .05 were considered significant.

Results

The 102 female asthmatic patients had a mean (SD) age of 51.7 (13.4) years. The average duration of asthma was 7.8 (7.7) years. Forty-one patients with asthma also had allergic rhinitis. Fifty-six patients were identified as atopic and the 2 most common allergens were mites (37.2%) and pollens (36.3%). GINA classification of severity showed that 16.7% of these patients had mild intermittent asthma, 27.2% had mild asthma, 33.4% had moderate asthma, and 22.5% had severe persistent asthma. The mean IgE level was 190.3 (293.8) IU/mL. The mean forced expiratory volume in 1 second (FEV_1) was 2017.2 (618.1) mL; the mean FEV_1 expressed as a percentage of predicted was 83.1% (17.8%).

Prevalence of skin test positivity was 33.6% for *D pteronyssinus*, 37.2% for *D farinae*, 36.3% for specific grass mix, 16.8% for tree mix, 11.7% for mold mix, 16% for weed mix, and 18.6% for animal dander mix. Thirty-nine patients were allergic to more than 1 aeroallergen and 34 patients had a wheal score of 3 or more.

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Table 1. Characteristics of Atopic and Nonatopic Adult Female Asthma Patients

	Atopic Asthmatics (n=56)	Nonatopic Asthmatics (n=46)
Age, y	50.9 (13.8)	52.7 (12.3)
Asthma duration, y	7.9 (7.6)	7.8 (7.9)
Total IgE, IU/mL	215.2 (287.1)	62.1 (88.7)[a]
Lung Function		
FVC, mL	2671.5 (751.2)	2556.7 (630.3)
FEV_1, mL	2038.2 (671.3)	1995.5 (567.8)
FEV_1, % predicted	82.6 (19.3)	83.5 (16.7)
Asthma severity		
Mild intermittent	7	10
Mild persistent	17	11
Moderate persistent	17	17
Severe persistent	15	8

Abbreviations: IgE, immunoglobulin E; FVC, forced vital capacity; FEV_1, forced expiratory volume in 1 second.
[a] $P < .05$.

Table 2. Relationship Between Intensity of Allergy and Asthma Severity in Sensitized Adult Female Patients[a]

Severity of Asthma	Intensity of Allergy					
	Total IgE ≥500 IU/mL	More Than 2 Positive SPT	Wheal Score ≥3			
			Mite	Pollen	Animal Dander	Mold
Mild intermittent	2	7	5	6	0	1
Mild persistent	11	12	8	9	3	3
Moderate persistent	9	10	12	8	5	2
Severe persistent	8	10	8	9	4	3

Abbreviation: SPT, skin prick test.
[a] All data indicate number of patients. All differences are nonsignificant ($P > .05$).

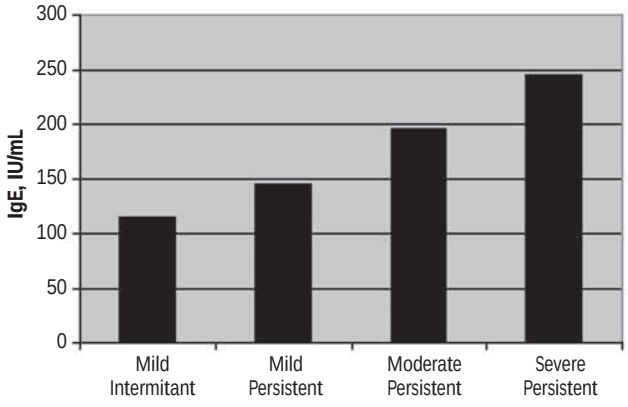

Figure. Mean level of total immunoglobulin (Ig) E, by asthma severity classification.

Twenty-one patients had a history of smoking less than 10 pack-years and 6 of them continued to smoke. When we compared atopic and nonatopic asthmatic women, we found no differences in asthma severity classifications, lung function, age, smoking status, or duration of disease (Table 1).

Although we found that mean total serum IgE levels tended to increase progressively with asthma severity (mild, moderate, and severe), the differences were not statistically significant (figure). We could not find any relationship between severity of asthma and number of positive skin prick tests, size of wheal in positive tests, or level of total IgE (Table 2). We reanalyzed these parameters combining mild intermittent and persistent asthmatics together, but the results did not change. We concluded that neither atopy nor intensity of allergic sensitization affect asthma severity in adult female patients.

Discussion

Since the 1950s asthma has been classified in 2 general categories: extrinsic (allergic) asthma and intrinsic (nonallergic) asthma, depending upon the stimuli that trigger attacks [9]. Generally, intrinsic asthma occurs at later ages and mainly in females [9]. These classifications can be useful for us in

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suggesting a treatment approach. In our study, 54.9% of our patients had allergic asthma and characteristics of these patients were similar to those of the nonallergic asthmatic group. This can be explained by the lack of evidence of pathophysiologic distinction for allergic and nonallergic asthma groups, as eosinophilic bronchitis and desquamation of the bronchial mucosa are salient features of disease in both groups [10,11]. Additionally, smooth muscle cells and parasympathetic nerve fibers are affected similarly in both.

Serum total IgE levels are age related, with peak levels occurring during childhood [12]. Although differences by sex are not well established in younger populations, in adults serum IgE levels are higher in men than in women [13]. We only studied adult female asthmatics to eliminate the effect of gender. Serum IgE levels may also vary by race and smoking history. In the TENOR study, Borish and coworkers [14] found that males, children, smokers, and nonwhite racial groups had higher total IgE levels and that those levels were associated with asthma severity among younger patients. Sears and coworkers [15] showed that the presence and the degree of airway hyperresponsiveness were related to total IgE in children. Juji and colleagues [16] suggested a role for IgE in asthma severity classification based on frequency of attacks and treatment. In contrast, in the EGEA study [17], an association between IgE and the clinical severity score and FEV_1 was not found. In our study, we found a progressive tendency for mean total IgE levels to increase with asthma severity but the differences were not statistically significant. This might be because most of our patients were over the age of 40 years. Our results seem to confirm that an association between IgE and asthma severity is more obvious in children than in adults.

Especially in childhood, aeroallergen allergy is strongly associated with asthma prevalence. In a large population-based study, Jaakkola and coworkers [18] found, that specific IgE antibody titers to mites and some molds, especially *Aspergillus fumigatus*, are significantly related to increased risk of adult-onset asthma. But the role of the intensity of allergic sensitization to asthma severity remains uncertain. Peat and colleagues [19] found linear relationships between dust mite wheal sizes and asthma severity. Sarpong and colleagues [20] found a positive association between number of positive SPTs and asthma severity evaluated by FEV_1 and medication usage. On the other hand, both Siroux et al [17] and Inouye et al [21] showed that asthma severity was mostly independent of the presence of an allergic sensitization, even with a tendency towards less atopy in more severe asthma. Moreover, Chetta and colleagues [22] showed that subepithelial layer thickness as an index of airways remodeling was positively related to the clinical and functional severity of asthma, but not to atopy. Similarly, we could not find any relationship between severity of asthma and number of positive SPTs or size of wheal in positive tests. The reason for these discrepancies may be the absence of a universally accepted and validated measure of asthma severity [23,24]. There are several dimensions to asthma severity, related to lung function tests, peak flow variability, asthma symptoms, medication use (especially dose of inhaled corticosteroids), attack frequency, hospitalization, and emergency visits. Another reason for disagreement may be the examination of different populations, namely children, adolescents, or adults with mostly mild and moderate asthma. We assessed asthma severity based on the GINA guidelines and this allowed us to approach severity more objectively. Another factor which strengthens our study was that we had a sufficient number of patients from all severity groups.

Although atopy was very common for adult female asthmatics in our study, there was no statistically significant positive relationships between asthma severity, total IgE levels and the presence or intensity of allergic sensitization to common aeroallergens We conclude that atopy does not influence asthma severity in adult female patients so risk factors related to the occurrence of a disease are not always necessarily the same as for the severity of that disease.

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