CORRELATION OF SERUM SPECIFIC IGE AND SKIN PRICK TESTS IN CHILDREN WITH RESPIRATORY ALLERGY

Orıgınal Artıcle

SOLUNUM YOLU ALLERJİSİ OLAN ÇOCUKLARDA SERUM SPESİFİK IGE VE DERİ PRİCK TESTLERİNİN KORELASYONU

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ABSTRACT

Objectives: The correlation of clinical data with laboratory tests is important in diagnosing atopic diseases. This study was planned to investigate the correlation of environmental allergen specific IgE levels and skin test methods in diagnosing atopic diseases.

Methods: The study comprised 172 patients who had undergone immunotherapy for allergic diseases between November 2005 and July 2008, and had been evaluated with serum specific IgE levels and skin prick tests.

Results: The male/female ratio was 1.6, with a mean age of 12.5±3.6 years (range 5-20 years), and mean age of onset of allergy symptoms at 6.9±3.5 years (range 0-16 years). The sp IgE of 96.3% of the patients was positive. No significant link was found between the age of onset and the existence of atopy in the family (p=0.258), nor the subject gender (p=0.941). Except for molds, all allergens had significant correlations between their serum sp IgE levels and skin test positivities. As the age of onset increases, grass pollens (p=0,000) and cereals pollens (p=0,000) skin test positivities were found to increase, in contrast to the decrease of d1-d2 serum sp IgE levels and skin test positivities. In the patients without any atopy case in the family, serum d1 and d2 sp IgE levels and d1 skin

test positivity were found to be higher ($p<0.05$).

Conclusion: Serum environmental allergen-specific IgE levels, is an important diagnosis method, which correlates with the other laboratory tests and clinical data, for diagnosing atopic disorders in childhood.

Key Words: *Child;skin test, hipersensitivite;cross reactions.*

ÖZET

Atopik hastalıkların tanısında klinik bulgularla laboratuar testlerinin korelasyonu önemlidir. Bu çalışma, allerjik hastalıkların tanısında, çevresel alerjen sp IgE düzeylerinin deri testleri ile korelasyonunu saptamak için planlanmıştır. Ege Üniversitesi Tıp Fakültesi Çocuk Sağlığı ve Hastalıkları AD, Solunum-Alerji BD tarafınca immunoterapi uygulanan ve Kasım 2005-Temmuz 2008 tarihleri arası spesifik IgE ve deri prick testi ile değerlendirilen 172 olgunun test yanıtları ve bu yanıtlara etki eden faktörler araştırılmıştır. Hastaların erkek/kız oranı 1.6, ortalama yaşı 12.5±3.6 yaş (5-20 yaş), ortalama yakınma başlangıç yaşı 6,9±3,5 yaş (0-16 yaş) olarak saptandı. Sp IgE olguların %96.3'ünde pozitif bulundu. Ailede atopi varlığı ($p=0.258$) ve cinsiyet ($p=0.941$) ile yakınmaların başlangıç yaşı arasında anlamlı bir ilişki bulunamadı. Küf mantarları dışında diğer tüm alerjenlerin sp IgE seviyeleri ile aynı alerjenlere karşı oluşan deri pozitiflikleri arasında anlamlı ilişki saptandı. Olguların hastalık başlangıç yaşı arttıkça, ot polenleri ($p=0,000$) ve hububat polenleri ($p=0,000$) deri testi pozitiflikleri artış gösterirken, d1-d2 serum sp IgE düzeylerinde ve deri testi pozitifliklerinde azalma olduğu gözlendi. Ailede atopi olmayan olgularda, serum d1 ve d2 düzeylerinin ve d1 deri testi pozitifliğinin belirgin daha fazla olduğu saptandı ($p<0.05$). Serum alerjen-spesifik IgE düzeyleri, çocukluk çağı atopik hastalıklarında, diğer laboratuar testleri ve klinik bulgularla korelasyon gösteren önemli bir tanı metodudur.

Anahtar Kelimeler : *Çocuk ;deri hastalıkları ;aşırı duyarlılık ; çapraz reaksiyonlar.*

INTRODUCTION

Asthma and other allergic conditions such as allergic rhinitis are major public health problems and the most common chronic diseases of childhood. The incidence of these allergies has been increasing worldwide over recent years (1, 2). Correct diagnosis and identification, and avoidance of the offending allergens where possible are required for the management of these conditions. In assessing children and adults with allergic diseases, a number of tests are now commonly employed (3). Early diagnosis and treatment carries a great importance in order to improve the quality of life and to limit the progression of disease in allergic patients.

Diagnosis of an allergic disease is largely based on medical history, which can be confirmed by means of measurement of antigen-specific IgE levels or skin prick tests. For evaluation of allergic patients and determination of the allergic disease frequency in communities, total serum IgE measuring and skin prick testing are simple and widely available laboratory tools (4-8). Specific IgE-mediated allergic reactivity can easily be tested for by an in vivo skin prick test or by an in vitro enzyme or fluorescence-based immunoassay, commonly called a radioallergosorbent test (9).

Although several epidemiologic studies have demonstrated strong associations among total serum IgE levels, skin test reactivity to different allergens, and allergy prevalence, the details of these associations is still not well-determined (10-16). Allergen-specific IgE determination is widely used in the diagnosis of IgE-mediated atopic diseases,

but the relative merits of in vitro measurement of IgE antibody in comparison to in vivo skin tests are still being debated (17, 18). This study was planned to investigate the correlation of environmental allergen sp IgE levels and skin test methods in diagnosing atopic diseases.

MATERIALS and METHODS

STUDY DESIGN

The study comprised 172 paediatric patients aged between 5 and 20 years who were being followed-up for allergic diseases at the Ege University Faculty of Medicine, Department of Pediatric Pulmonology-Allergy between November 2005 and July 2008. All had been evaluated with serum specific IgE levels and skin prick tests before commencing immunotherapy. Inclusion criteria were a positive history of allergy and a positive skin-prick test or specific immunoglobulin E (IgE) of ≥1.43 kU/l against at least one out of a panel of common aeroallergens. The test responses and the factors contributing to the responses were investigated. A comprehensive history, using a specially prepared protocol, was taken from the patients. This included a history of exposure to the allergen and other irritants, and a previous history of asthma and other chest diseases. All parents gave written consent and received printed information. The study was approved by the Ethics Committee of Ege University Faculty of Medicine.

TOTAL SERUM IGE ANALYSIS

Venous blood samples were taken and total serum IgE levels were measured by enzyme-linked immunosorbent assay (ELISA) method using commercially available kits (Radim, Rome, Italy), with an assay threshold of 0.1 IU/ml.

ALLERGEN-SPECIFIC IGE ANTIBODIES

Venous blood samples were drawn and allergen-specific IgE antibodies to nine common aeroallergens (*Dermatophagoides pteronyssinus* (d1), *Dermatophagoides farinae* (d2), grass pollen, weed pollen, cereal pollen, olive pollen, mold, dog and cat danders) were determined using standard laboratory procedures (RAST-CAP-FEIA, Pharmacia, Uppsala, Sweden). All analyses were done by Pharmacia (Germany, Freiburg) with the same batches of allergen caps. Differences in the numbers of measurements for the single allergens occurred due to an insufficient amount of sera in some cases. The detection limit for RAST reactivity was set at 0.35 kU/l and further cut-off points were selected according to the limits of RAST classes (0.7, 3.5, 17.5, and additionally 1.5 kU/l).

SKIN PRICK TEST

Standard lancet prick tests were performed on the volar aspects of the forearms of the children using the same aeroallergens as for the serological test (Allergopharma, Reinbek, Germany). Histamine and saline were used as controls and results were read after 20 minutes. Tests were considered positive when the wheal diameter reached at least 3 mm. Tests showing wheals >2 mm to saline or <3 mm to histamine were repeated the following day and excluded from further analyses when these findings were confirmed.

STATISTICAL ANALYSIS

Statistical analysis was performed using "SPSS (Statistical Package for Social Sciences) 14.0 for Windows" program. T-test, one-way ANOVA test and chi-square test were used while evaluating the data. The Spearman rank correlation coefficient was estimated to quantify the correlation between skin test diameter size and serum concentration of allergen-specific IgE. A value of $p< 0.05$ was accepted as statistically significant. The skin test sensitivity, specificity and diagnostic

accuracy were calculated using the method advocated by Kirkwood (19).

RESULTS

The male/female ratio was 1.6, with a mean age of 12.5±3.6 years (range 5-20 years), mean age of onset of allergy symptoms at 6.9±3.5 years (range 0-16 years). Seasonal variations in patients experiencing atopic problems were determined as 45.3% (n=78) in spring, 15.1% (n=26) in winter-fall, 11% (n=19) in spring-fall, 6.8% in spring-summer, 2.3% (n=4) continuously. A family history of atopic problems was determined in 49% (n=85) of the patients. Diagnoses for which patients were being monitored were allergic rhinoconjunctivitis in 55.2% (n=95) of patients, asthma in 23.8% (n=41), allergic rhinoconjunctivitis+asthma in 14% (n=24), allergic rhinoconjunctivitis+ urticaria in 2.9% (n=5), allergic rhinoconjunctivitis+atopic dermatitis in 2.3% (n=4), and asthma+atopic dermatitis in 1.7% (n=3) (Figure 1). The sp IgE of 96.3% of the patients was positive. The most frequently sp IgE positive observed allergens were grass pollens (72.2%), and cereals-olive pollens (69%). Likewise, the most frequent skin test positives were grass pollens (65.9%), and cereals pollens (65.8%). No significant link was found between the age of onset, and family history of atopy (p=0.258), nor the subject gender (p=0.941). Based on the seasonal variations and the patient diagnoses, an examination of the serum specific IgE data, determined significant differences in d1, d2 (winter/asthma) and grass pollens (spring/allergic rhinoconjunctivitis) IgE levels. Except for molds, all allergens had significant correlations between their serum sp IgE levels and skin test positivities. Furthermore, significant (p=0.000) relationships (cross-reaction) were found among cereals and grass pollens, and d1 and d2 serum spIgE levels, and skin test results. As the age of onset increases, grass pollen (p=0.000) and cereal pollen (p=0.000) skin test positivities were found to increase, in contrast to the decrease of d1-d2 serum sp IgE levels and skin test positivities (**Figure 1, 2, 3).**

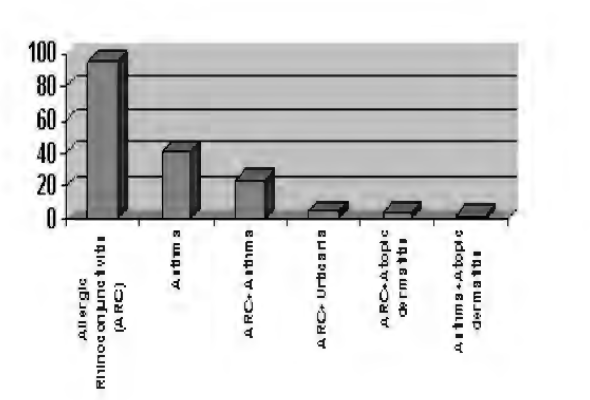

Figure 1. *Diagnosis of the patients.*

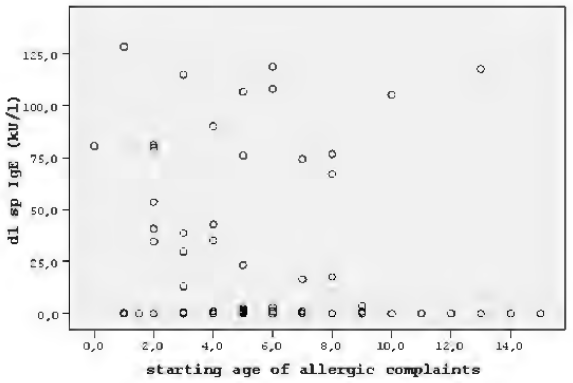

Figure 2. *Relationship between starting age of allergic complaints (years) and d1 specific Ig E (kU/l) levels.*

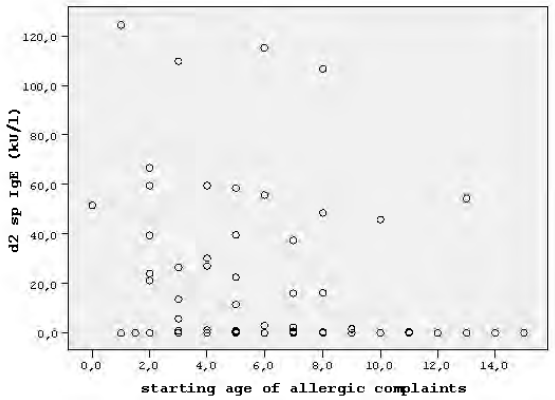

Figure 3. *Relationship between starting age of allergic complaints (years) and d2 specific Ig E (kU/l) levels.*

As the grass pollen serum sp IgE levels increase, the d1-d2 serum sp IgE and skin test positivities were observed to decrease (p=0.000). In patients without a family history of atopy, serum d1 and d2 sp IgE levels and d1 skin test positivity were found to be higher (p<0.05). Of patients who experienced allergic symptoms during spring 84% had a grass pollen specific IgE level higher than 0.41 kU/l and 73% had a olive pollen specific IgE level higher than 0.38 kU/l. In addition, of patients who experienced allergic symptoms during winter, 58% had a d1 specific IgE level higher than 0.37 kU/l and 50% had a d2 specific IgE level higher than 0.39 kU/l.

DISCUSSION

An accurate diagnosis of the allergens responsible for allergic disease introduces therapeutic opportunities for allergen-specific treatment models such as allergen avoidance and immunotherapy (20). Most tests for allergies are actually tests for allergic sensitization, or the presence of allergen-specific IgE. Most patients who experience symptoms upon exposure to an allergen have demonstrable IgE that specifically recognizes that allergen, making these tests essential tools in the diagnosis of allergic disorders (21). Skin testing for IgE-mediated allergy is preferred over in vitro testing for most allergens, because skin testing is more rapidly obtained, less expensive, and more sensitive (22). There are various forms of immunoassays, and they are the most commonly used in vitro tests for IgE-mediated allergy. Allergen-specific IgE in a patient's serum is detected by tests which incubate the serum with the allergen in question, which has been absorbed into a substrate, The bound IgE is then detected with an anti-IgE antibody, which, in turn, has a label attached to permit detection. In vitro testing has certain advantages over skin testing: a) it poses no risk to the patient of an allergic reaction, b) it is not affected by medications the patient may be taking, c) it is not reliant upon skin integrity or affected by skin disease (21).

Serum immunoassays for specific IgE antibodies are occasionally referred to as radioallergosorbent tests, or RASTs, because earlier methods utilized radioactive reagents. However, the methods currently in use are more properly referred to as immunoassays for allergen-specific IgE. These tests generally provide similar information as that obtained from skin tests. According to some studies, immunoassays are less sensitive for the diagnosis of allergy to inhalant allergens than skin testing, because as many as 25% of patients with a positive skin test have a negative immunoassay (23). However, in some other studies, in particular a higher specificity for Pharmacia CAP System in comparison to in vivo skin prick test for grass pollens and a better sensitivity for mites and cat allergens were found (24).

The sensitivity and specificity of immunoassays vary with the system being used and the quality of the allergen. Overall, sensitivity ranges from 60%-95% and specificity from 30%-95% (25, 26). Values of more than 90% sensitivity, specificity, and predictive values have been obtained with pollens of common grasses and trees, dust mites, and cat allergens. More problematic allergens include venoms, foods, weed pollens, latex, drugs, and molds (27, 28). The precise sensitivity and specificity of skin prick testing are dependent on the allergens used as well as the different variables inherent in this bioassay. For skin testing in general, the overall sensitivity is low, and often estimated at approximately 50%. Thus, a positive skin test only suggests the possibility of allergy. However, the negative predictive value of skin prick testing is very high and skin testing can exclude allergy with relative certainty (29). On the other hand, when standardized inhalant extracts with high potency are used, prick/puncture tests generally have high sensitivity and

specificity (>85%) (30, 31). The diagnostic efficacy is generally said to be lower for molds and certain foods (32). In our study, except for molds, all allergens had significant correlations between their serum sp IgE levels and skin test positivities.

Skin testing is useful in diagnosis of many allergic diseases, such as allergic asthma, rhinitis, and conjunctivitis, food allergy, some medication allergies, some venom allergies, and depending on the availability of testing reagents, latex allergy. The performance of skin prick testing for identifying respiratory allergy was studied using 10 pollen allergens, 2 house dust mite allergens, and 1 cat allergen (30). Testing was performed in 50 patients with asthma or allergic rhinitis (group 1), 50 without these conditions but with a positive immediate family history of the disorders (group 2), and 100 subjects without a personal or family history of asthma or allergic rhinitis (group 3). At least one positive test reaction (mean wheal diameter ≥3 mm) was observed in 90%, 46%, and 29% of those in groups 1, 2, and 3, respectively, with accuracy based in part on the allergen. A positive reaction to the cat allergen was associated with a sensitivity, specificity, and diagnostic accuracy of 90%, when compared to the clinical history. In one study of 365 consecutive patients aged 12 years or older, the predictive value of history alone for seasonal allergic rhinitis was found to be 82%-85%, and that of history in combination with prick/puncture skin testing, 97%-99% (29, 33). In this study, based on the seasonal variations and patient diagnoses, an examination of the serum specific IgE data, determined d1 and d2 to be significantly higher in patients with asthma and in children who experienced symptoms during the winter. Also, grass pollens were found to be significantly higher in patients with allergic rhinoconjunctivitis and in children who experienced symptoms during the spring.

In general, cross-reactivities occur when two or more allergens share epitopes and thus bind to the same IgE antibodies. Patients sensitised to one allergen may therefore also react to the other without previous exposure and sensitisation. Patients rarely react to more than one member of a botanical family or animal species (34). Serological cross-reactivity and/or cross-reactivity in the skin are not necessarily associated with clinical disease, which has to be confirmed by challenge [35]. In this study, significant cross-reactivities were found among cereals and grass pollens, and d1 and d2 serum spIgE levels, and skin test results.

Serum environmental allergen-specific IgE levels, is an important diagnosis method, which correlates with other laboratory tests and clinical data, for diagnosing atopic disorders in childhood. In vivo and in vitro tests for allergy, like all forms of allergy testing, must be interpreted in the context of the patient's specific clinical history. A positive test for allergen-specific IgE confirms the presence of the antibody only; actual reactivity must be determined by history or supervised challenge.

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