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ORIGINAL ARTICLE

Correlation between Asthma Severity and Serum IgE in Asthmatic Children Sensitized to *Dermatophagoides pteronyssinus*

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Background. We undertook this study to test the possible correlation between serum concentration of total and specific IgE antibodies and asthma severity in asthmatic children sensitized to the house dust mite *Dermatophagoides pteronyssinus.*

Methods. The study included 157 asthmatic children aged 5–15 years (8 ± 3 years). Clinical diagnosis was based on personal and family history, physical examination, pulmonary function testing and skin tests. Asthma severity was determined according to GINA guidelines. *In vitro* tests included serum concentration of total and specific IgE.

Results. All asthmatic children had elevated serum concentration of total IgE. The children with elevated serum concentration of total IgE also showed an increased serum concentration of specific IgE. Asthma of higher higher severity was present in patients with total IgE concentration >288.0 kIU/L (AUC = 0.736) and specific IgE to *Dermatophagoides pteronyssinus* >44.1 kIUA/L (AUC = 0.843). Intermittent asthma was present in 76.9% of children with specific IgE concentration <44.1 kIUA/L. The positive predictive value suggested with 79.2% probability that a child with a concentration of specific IgE to *Dermatophagoides pteronyssinus* >44.1 kIUA/L would have a more severe form of asthma.

Conclusions. Asthmatic children with higher asthma severity have a higher serum concentration of both total IgE (>288.0 kIU/L) and specific IgE to *Dermatophagoides pteronyssinus* (>44.1 kIUA/L), respectively.

Key Words: Asthma severity, Child, House dust mite, Total IgE, Specific IgE.

Introduction

The manifestation of asthma can vary according to the severity and frequency of symptom exacerbations. At present, classification of asthma into four grades has been accepted: intermittent asthma, mild permanent asthma, moderate permanent asthma, and severe permanent asthma (1). The clinical picture of asthma, i.e., the disease severity, results from a series of complex pathophysiological processes determined by numerous known and unknown factors, from genetic to environmental. Identification of the disease severity is a precondition for appropriate therapeutic approach in asthma patients. Daily practice has shown that airway obstruction can also be confirmed by spirometry in patients with seemingly normal physical finding of the respiratory system. Thus, measurement of pulmonary function is necessary to evaluate the severity of airway obstruction. According to GINA guidelines (Global Initiative in Asthma), repeated pulmonary function testing is required to determine the severity and frequency of acute asthma attacks.

Recent studies have shown that adult patients with higher asthma severity had a more severe form of the disease in childhood (2). This observation suggests the importance of the earliest possible evaluation of asthma severity in each individual patient to enable an early introduction of appropriate and efficacious therapy and eventually the control of asthma, i.e., minimal chronic symptoms including nocturnal symptoms, minimal number of attacks (rarely) that do

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not require medical intervention, minimal need of β_2-agonists, no limitation of daily activities including exercise, $<20\%$ peak expiratory flow (PEF) variability, nearly normal PEF, and absence of medication side effects (1).

Determination of serum concentrations of total and specific IgE antibodies plays a major role in the diagnosis of childhood asthma. Although IgE are generally circulating intravascularly, they may also be found extravascularly, bound to the high-affinity receptors on mastocytes and basophilic granulocytes (3). Serum concentration of IgE depends on the genetic predisposition to an increased IgE synthesis and exposure to a broad array of environmental allergens (4–6). Elevated serum concentration of IgE can be found in patients with parasitic diseases (7). Both animal studies (8) and human studies in adults (9) have shown that the concentration of IgE antibodies could vary with the degree of immune stimulation, i.e., with the frequency, dose and route of allergen exposure, respectively (8). Very few adult individuals diagnosed with asthma have low concentration of IgE (10). Simpson et al. have also shown that probability of wheeze was less in children with low specific IgE to inhalant allergens (11).

The aim of the present study was to assess the possible correlation between serum concentration of total and specific IgE antibodies and asthma severity in children sensitized to the house dust mite *Dermatophagoides pteronyssinus*.

Patients and Methods

Patients

Study subjects were a cross-sectional cohort of 157 children aged 5 to 15 years (8 ± 3 years), stratified by symptoms, and referred by primary care physicians to the Children's Hospital Srebrnjak in Zagreb between August 2004 and July 2005 for evaluation of lower respiratory tract symptoms of >4-weeks duration. Sensitization to the house dust mite *Dermatophagoides pteronyssinus* was verified after recruiting the children for the study, using *in vivo* (skin prick) and *in vitro* (serum specific IgE) tests. Diagnosis of asthma was made on the basis of a standardized diagnostic work-up, whereas asthma severity was determined according to GINA guidelines (1). Briefly, asthma was classified at the degree to which airflow has been obstructed, frequency and duration of symptoms, and the extent symptoms have interfered with daily activities. The following parameters were evaluated: family history of atopic diseases, symptoms and symptom structure, precipitating and/or aggravating factors, and course of disease. On physical examination, attention was paid to the presence of rhinitis, sinusitis, hyperinflation, eczematous skin lesions, and respiratory sounds on auscultation to identify airway obstruction.

Methods

Respiratory Function Testing

Respiratory function was tested by a portable Jaeger spirometer, determining the parameters of FEV_1 and FEV_1/VC ratio (Tiffeneau's index). The measured values of respiratory function were compared with the expected values, determined at Department of Clinical Laboratory Diagnosis, Children's Hospital Srebrnjak, Zagreb (12,13).

Allergy Skin Testing

Allergy skin testing (14) was performed to 13 inhalation allergens manufactured by the Institute of Immunology, Zagreb. Standard inhalation allergens were used: bacterial vaccine, house dust, *Dermatophagoides pteronyssinus*, feather, mold, *Monilia albicans*, bedding of plant and animal origin, animal hair, tree, grass and weed pollen, and tobacco. Testing for *Dermatophagoides pteronyssinus* was performed by the standard national preparation (15).

Laboratory Methods

Blood samples were obtained after clinical examination at the allergology clinic between 8:00 a.m. and 3:00 p.m. Serum concentrations of total IgE and specific IgE to particular allergens chosen according to the skin test result were determined in each study subject.

Determination of Total IgE Concentration

Serum concentration of total IgE was determined by the fluoroimmunochemistry method (Abbott, Abbott Park, IL) on an IMx autoanalyzer from the same manufacturer. The analysis is based on the sandwich technique and enzyme labeling of the antigen–antibody complex (16). The method sensitivity is 0.048 kIU/L (data from the manufacturer's instructions). The 95^{th} centile reference values were used for result comparison (17).

Determination of Specific IgE Concentration

Serum concentration of specific IgE to *Dermatophagoides pteronyssinus* allergen was determined by the UniCAP method (Pharmacia, Uppsala, Sweden), where high sensitivity is achieved by use of a three-dimensional cellulose carrier (flexible hydrophilic polymer) (18). The World Health Organization secondary standard, WHO 75/502, was applied. The range of confidence was 0.35–100 kIU_A/L.

Statistics

Data storage and preparation for statistical analysis were done by use of the Microsoft Office Excel 2000 software (Microsoft, Redmond, WA). Quantitative variables were expressed as arithmetic mean ($\bar{x}$), standard deviation (SD),