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ORIGINAL ARTICLE

Bronchial hyperresponsiveness and asthma in the paediatric population

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Abstract
Objective: To determine whether the intensity of bronchial hyperresponsiveness (BHR) is correlated to other clinical data such as patient age at the onset of asthma, the serum IgE levels and familial genetic susceptibility, with the purpose of establishing a prognosis or phenotype.
Material and methods: BHR was evaluated using the methacholine provocation test, with the patients divided into six groups according to the amount of methacholine needed to obtain PD20. A total of 138 children and adolescents up to age 18 years (94 males and 44 females) were included. Most had a clinical diagnosis of asthma, while tracheobronchitis or rhinitis was diagnosed among the least reactive subjects. The patients were divided into subjects with a family history of atopic disease (84 cases) and those without such a history (54 cases). In this latter case we discuss possible causes of BHR or dyspnoea triggering factors.
Results: There were no significant differences in patient age at onset or in serum IgE among the patients with different intensities of BHR, or between those with a family history of atopic disease and those without.
Conclusions: No differences were found among the groups. It is therefore concluded that the intensity of BHR is not a valid parameter for establishing a prognosis or phenotype, although it can be used to assess the severity of asthma.

Asthma is a heterogeneous disease with a variety of underlying causes in which bronchial hyperresponsiveness (BHR) is a constant and essential pathogenic element, although the mechanism triggering HBR can differ in each case, as in asthma induced by exercise or by aspirin.[1] However, allergy is the most frequent cause of asthma and initially manifesting in childhood, genetics is known to play a key role – particularly in relation to the existence of BHR and atopic predisposition or susceptibility.[2] Nevertheless, in early childhood, BHR may develop as a consequence of repeated viral infections. In other cases, including children and adolescents, BHR can appear later in life, as also occurs in professional asthma, as a consequence of exposure

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Table 1 Patient characteristics.

Methacholine PD20 (μg)	Patients with atopic relatives			Patients without atopic relatives		
	No. patients	Age at onset (yr) Mean (range)	Mean IgE (KU/l)	No. patients	Age at onset (yr) Mean (range)	Mean IgE (KU/l)
<500	12	4.7 (<1–13)	439	13	3.2 (<1–6)	512
501–1000	16	4.5 (<1–14)	512	14	4.9 (<1–12)	471
1001–1500	10	4.4 (<1–9)	373	7	5.4 (2–10)	559
1501–2000	10	7.7 (3–18)	299	1	3 (3–3)	512
>2000 Asthma	16	4.7 (<1–14)	745	14	4.9 (<1–14)	237
>2000 Tracheobronchitis/ rhinitis	20	5.4 (<1–10)	293	5	9(4–15)	280
Total	84	5.2	443	54	5.0	428

to certain environmental factors (tobacco smoke, different irritants, allergens) which initially produce bronchial inflammation and subsequently BHR secondary to vagal stimulation.

Based on the review of a group of patients with established BHR, most of whom were diagnosed with asthma, while others were diagnosed with tracheobronchitis or rhinitis, the present study was carried out with the main purpose of examining the different factors that participate in the onset of asthma in paediatric patients (including adolescents), taking into account both genetic susceptibility and possible exogenous elements, in an attempt to determine whether the intensity of BHR has prognostic or phenotyping applications.

Materials and methods

Patients

In a total of 138 patients (94 males and 44 females, aged between 8 and 18 years) visiting the clinic with respiratory symptoms, in most cases with suspected asthma (cough, acute dyspnoeic episodes, wheezing and/or frequent or sporadic mild dyspnoea, predominantly at night, and signs of rhinitis), methacholine provocation testing was performed to evaluate the presence of bronchial hyperresponsiveness (BHR). In addition, in all cases we demonstrated allergic sensitisation based on skin tests and total and specific serum IgE.

In order to determine whether the intensity of BHR may be of use in establishing a prognosis or phenotype, the patients were divided into six groups according to the amount of methacholine needed to obtain PD20. Those requiring over 2000 g, without reaching PD20 in most cases, were divided into two groups: one in which the clinical diagnosis was asthma, and another in which the dominant symptoms were cough and sometimes wheezing or noisy breathing, but without dyspnoeic episodes. These latter patients were finally generically classified as presenting tracheobronchitis, without discarding the possibility of eosinophilic bronchitis in some of them.[3,4] Symptoms of rhinitis were dominant in some of these patients. In turn, two groups (patients with and without a family history of atopy) were established in order to evaluate the influence of familial susceptibility to atopic disease. In those patients without familial susceptibility, we evaluated the possible existence of exogenous symptom-triggering factors. Likewise, in all groups we recorded patient age at the onset of the process and the total serum IgE values. Table 1 presents all these data.

Methacholine provocation test

Methacholine testing was carried out using an abbreviated method in which the aerosol is inhaled during inspiration, allowing quantification of the administered methacholine dose from a single concentration of the drug.[5,6] The patients were asymptomatic at the time of provocation with methacholine, without taking bronchodilator or anti-inflammatory medication for at least two days before the test, and with respiratory function in the normal range (with FEV1% >70). The 1/100 dilution of methacholine (Provocholine®, Roche) was prepared with physiological saline solution, yielding a concentration of 10 mg/ml. Spirometry was carried out with the Vicatest Spimco (Mijnhardt, The Netherlands) before testing and two minutes after each of the inhalations (Mediprom FDC 88 dosimeter, Paris, France). After fitting to the nebuliser (De Vilbiss 5610 D) by means of a mouthpiece, the patient was instructed to breathe normally, followed by maximum inspiration (1–2 s) after forced expiration. This was followed by three seconds of apnoea and then gentle expiration.[1,4] The decrease in FEV1 was estimated from the FEV1 value recorded after inhalation of the saline solution with which the test was started. In the first inhalation we administered 100 μg (0.5 μmol) of methacholine, followed by the repeated administration of 200 μg (cumulative dose: 300 μg, 500 μg, 700 μg, 900 μg, etc.). The test ended when FEV1 dropped approximately 20% (PD20) – the value being calculated posteriorly from the dose–response curve. Administration was suspended if the mentioned decrease was not reached with the maximum cumulative dose of 2100 μg.

Results

Methacholine test. BHR was corroborated in all patients (whether with or without a family history of atopic