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Evolution of occupational asthma: Does cessation of exposure really improve prognosis?

X. Munoz [a,b,*], M. Viladrich [a], L. Manso [b,c], V. del Pozo [b,d], S. Quirce [b,e], M.J. Cruz [a,b], F. Carmona [f], A. Sánchez-Pla [f], J. Sastre [b,c]

[a] Servicio de Neumología, Hospital Vall d'Hebron, Barcelona, Spain
[b] Ciber Enfermedades Respiratorias (CibeRes), Spain
[c] Servicio de Alergia, Fundación Jiménez Díaz, Madrid, Spain
[d] Servicio de Inmunología, IIS Fundación Jiménez Díaz, Madrid, Spain
[e] Department of Allergy, Hospital La Paz Institute for Health Research (IdiPAZ), Madrid, Spain
[f] Departamento de Estadística, Universidad de Barcelona, Spain

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Summary
Aim: To assess the evolution of occupational asthma (OA) depending on whether the patient avoids or continues with exposure to the offending agent.
Methods: Study in patients diagnosed with OA using a specific inhalation challenge. Patients underwent the following examinations on the same day: clinical interview, physical examination, forced spirometry, methacholine test and determination of total IgE. Clinical improvement, deterioration or no change were defined according to the changes seen on the GINA severity scale at the time of diagnosis.
Results: Of the 73 patients finally included, 55 had totally ended exposure and 18 continued to be exposed at work. Clinical improvement was observed in 47% of those who had terminated exposure and in 22% of those who remained exposed; clinical deterioration was observed in 14% and 17% respectively ($p = 0.805$). Logistical regression analysis, including the type of agent and the persistence or avoidance of exposure among the variables, did not show any predictive factors of clinical evolution. Similarly, the changes in FEV_1 and in bronchial hyperresponsiveness were not associated with the avoidance or continuation of exposure to the causative agent.

* Corresponding author. Servei de Pneumologia, Hospital General Vall d'Hebron, Passeig Vall d'Hebron, 119, 08035 Barcelona, Spain. Tel.: +34 93 274 6157; fax: +34 93 274 6083.
E-mail address: xmunoz@vhebron.net (X.Munoz).

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Conclusions: Avoiding exposure to the causative agent in patients with OA does not seem to improve prognosis in this disease. Despite these findings, there is insufficient evidence to recommend a change in current management guidelines.

Introduction

Occupational asthma (OA) is the most frequent work-related respiratory disease in developed countries [1,2] and it is estimated that roughly 10% cases of bronchial asthma and between 15 and 25% of adult onset asthma may be of occupational origin [3,4].

For workers with OA caused by a respiratory sensitizer, complete and definitive removal from exposure to the sensitizing agent has usually been recommended as the most efficient therapeutic approach [5—9]. However, bearing in mind that cessation of exposure is often not feasible [10], in recent years a number of meta-analyses have been carried out to compare the effects of these two management options [11—14]. The results of these systematic reviews indicate that the available data on the prognosis of OA are insufficient to enable physicians to provide confident, informed advice to patients with the disease.

Probably this conclusion is reached because the majority of the more than 100 papers published so far are heterogeneous single-center studies, with small patient samples and based on a single causative agent; all apply an observational approach and, for ethical reasons, none have randomized patients to avoid or continue exposure to the causative agent [15,16].

The aim of the present study is to assess the evolution of all patients diagnosed with OA in the last ten years at two centers in our country according to the persistence or cessation of exposure to the causative agent and, on the basis of the GINA classification, of asthma severity [17]. The study design also allows an assessment of the influence on the prognosis of OA of variables that have not been widely studied to date, such as the medical treatment received and the type of causative agent.

Material and methods

Patients and design

This cross-sectional study was approved by the Ethics Committee of the two participating centers. Using the databases from each center, all patients who had been diagnosed with immunological OA by specific inhalation challenge (SIC) were selected. All patients included had at least one year of follow-up since diagnosis. Between September 2010 and June 2011, patients were scheduled for a visit at the pulmonary function laboratory after having discontinued treatment with inhaled corticosteroids and long-acting beta2 agonists 24 h previously and the use of short-acting beta2 agonists at least six hours previously. All patients provided written informed consent prior to participation.

First, a careful review of clinical histories at the time of diagnosis was carried out. The GINA classification that patients had at the time of diagnosis was made retrospectively with data from the clinical history and was based primarily on the treatment that patients were receiving at this time. Later, patients were interviewed again, placing special emphasis on whether they had avoided exposure with the causative agent, time between diagnosis and avoidance of exposure and, in the case of persistence of exposure, whether they worked with protection or not. They were also asked about any medication they used. With this information, the classification of asthma severity was established in accordance with the new GINA guidelines [17]. Patients also completed the asthma control questionnaire (ACQ) [18]. Spirometry and a methacholine challenge were then performed. Finally, blood analysis was performed, and eosinophil count and total IgE were recorded.

Patients were considered to present clinical improvement or deterioration when a change in the GINA asthma severity classification in either direction was observed. Improvement or deterioration in bronchial hyperresponsiveness and/or the degree of bronchial obstruction was recorded when changes in the PC20 $>$ 2 folds were observed or in FEV_1 $>$ 10% with respect to the value at the time of diagnosis.

Atopy and smoking status

Patients were considered atopic if they had at least one positive prick test to any common environmental allergen [19]. Non-smokers were patients who had never smoked and ex-smokers were those who had not smoked for at least six months. The number of pack-years was calculated.

Spirometry and methacholine challenge

Spirometry was performed with a Datospir 200 (Sibel, Barcelona) instrument, following the European Respiratory Society (ERS) and American Thoracic Society (ATS) guidelines [20]. The reference values used were those proposed for the Mediterranean population [21]. Bronchial challenge with methacholine was performed with the method described by Chai et al. [22] (Online repository). The methacholine challenge was considered negative if the PC20 FEV_1 was higher than 16 mg/ml, in accordance with ATS guidelines [23].

Statistical analysis

Data are tabulated providing median and range of each variable for quantitative variables and absolute frequencies