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Is the bronchodilator test an useful tool to measure asthma control?

Marta Ferrer Galván*, Francisco Javier Alvarez Gutiérrez, Auxiliadora Romero Falcón, Beatriz Romero Romero, Antonia Sáez, Juan Francisco Medina Gallardo

Asthma Unit, Medical-Surgical Unit for Respiratory Diseases, Virgen Del Rocio University Hospital, Seville, Spain

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ABSTRACT

Introduction: Asthma control includes the control of symptoms and future risk. We sought to evaluate the usefulness of the degree of spirometric reversibility of the forced expiratory volume in one second (FEV_1) as the target parameter of control.

Methodology: Patients with bronchial asthma were followed up for one year. The clinical, functional, inflammatory and control parameters of the asthma were collected. The area under the curve (AUC) was estimated to establish the cutoff point of the post-bronchodilator FEV_1 reversibility in relation to non-control asthma. In the univariate analysis, the differences between groups were studied based on the degree of estimated reversibility. Factors with a significance <0.1 were included in the multivariate analysis by binary logistic regression.

Results: A total of 407 patients with a mean age of 38.1 ± 16.7 years were included. When the patients were grouped into controlled and non-controlled groups, compared with post-bronchodilator FEV_1 reversibility, the cutoff point obtained for the non-controlled group was ≥10% (sensitivity: 65.8%, specificity: 48.4%, positive predictive value: 69.5%, and AUC: 0.619 [0.533–0.700], $p < 0.01$). In the year-long follow-up of this group (post-bronchodilator FEV_1 ≥10), an increased use of relief medication was observed, along with a significantly progressive drop in post-bronchodilator FEV_1 and post-bronchodilator FEV_1/FVC (forced expiratory volume in one second/forced vital capacity).

Conclusions: Spirometric reversibility can be useful in assessing control in asthmatic patients and can predict future risk parameters. The cutoff point related to the non-control of asthma found in our work was ≥10%.

Summary at a Glance

Until now, Guides include clinical and numerical self-administered questionnaire to determinate asthma control. We think an objective functional parameter should help us to guide the control an therefore to adjust treatment. This is the first document to establish the post-bronchodilator reversibility cutoff point.

1. Introduction

The principal objective in the management of asthma is achieving and maintaining disease control. The two domains of asthma control include symptom control (formerly called “current clinical control”) and future risk [1].

Guides include clinical and functional criteria that the doctor considers to establish the degree of symptom control of the patient [1–3]. In addition, numerical self-administered questionnaires that are simple and easy to complete by the patient are used. Of these, the Asthma Control Test (ACT) have been validated. Therefore, most of these traditional instruments of control that guide the changes in treatment may not always correspond with changes in endobronchial inflammation, bronchial hyper-responsiveness or airway obstruction. In addition, according to the performance of the self-administered test, the control estimated by the physician and indicated by the patient differs in most studies. It therefore seems necessary to pursue other more objective instruments, such as pulmonary function tests, to complete the evaluation of the degree of control of current asthma symptoms.

Pulmonary function, especially the forced expiratory volume in one second (FEV_1), which is expressed as a percentage of the expected value, is an important part of the evaluation of future risk. Currently, we know that a low FEV_1 value in the percentage of the

* Corresponding author. C/ Hnos. Segura Covarsí, Portal 2, 5º D., 06011, Badajoz, Spain.
E-mail address: Martina11@hotmail.com (M. Ferrer Galván).

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predicted value 1) identifies patients at risk of asthmatic exacerbations, independent of the symptoms, especially if the FEV_1 is <60% [4–7], and 2) is a risk factor for the reduction of the pulmonary function, independent of the levels of symptoms [8]. However, in asthma control the usefulness of reversibility after treatment with a bronchodilator has not been well established.

Our objective was to evaluate the relationship of the degree of FEV_1 reversibility with control according to the scoring of ACT, establishing a cutoff point of reversibility related to the non-control of asthma. Additionally, the relationship of this cutoff point with future risk parameters was studied. In a previous work, we established the ACT cutoff points for control by correlating them with the levels of control according to the 2006 Global Initiative for Asthma (GINA) report [9]. We have not yet found published works that have established this cutoff point, although reversibility with a bronchodilator may be a parameter to consider in habitual practice to establish the clinical state of the condition.

2. Patients and methods

2.1. Study design

A prospective study was performed in a outpatient asthma clinic between March 2007 and March 2009. The study follow-up period was one year, with visits every four months, comprising a total of four visits. This work was part of the Pulmonary Function/Nitric Oxide Symptoms study (**Fu**nción pulmonar, **si**ntomas **ó**xido **n**ítrico-FUSION), whose principal objective is the development of a multidimensional index of control that includes three variables: the Asthma Control Test (ACT) test, FeNO levels (nitric oxide fraction exhaled) and FEV_1 reversibility.

2.2. Patients

Inclusion criteria were: Patients over 12 years of age, diagnosis of asthma from mild to severe based on clinical and functional criteria established in the 2006 GINA review [9], patients not treated with oral steroids in the month prior to their inclusion, history of current or past smoking, but with a cumulative consumption less than 10 packs per year. Exclusion criteria: Patients with very severe asthma, multiple exacerbations or frequent use of oral steroids, or history of other respiratory diseases (COPD, bronchiectasis, interstitial or tumor pathologies) were excluded.

2.3. Methods

Initially, all of the epidemiological and clinical variables of the patients included in the study were collected. Functional tests (FeNO, forced spirometry with bronchodilation) were performed and the ACT was completed, both at the initial visit and at the follow-ups. In cases with continuing treatment, suspending the latest dose prior to performing the functional tests was indicated. The measurement of FeNO was performed using an electrochemical technique (NIOX MINO® Aerocrine, Solna, Sweden) [10]. Forced spirometry was performed with a MasterScope-PC spirometer (Viasys™ Healthcare), JLAB software and LabManager v5.3.0 following the American Thoracic Society/European Respiratory Society (ATS/ERS) recommendations [11]. A baseline test was carried out, followed by another after the administration of 200 mcg (two inhalations) of salbutamol or 160 mcg (four inhalations) of ipratropium bromide. The subsequent measurement was performed 15 min after the β_2-agonist and after 30 min in the case of ipratropium bromide treatment. The FEV_1 is expressed in absolute values and % of the predicted value, as well as the FEV_1/FVC, both baseline and post-bronchodilator. The spirometries performed fulfilled the quality criteria in their implementation, acceptability and reproducibility [12]. The ACT questionnaire, was administered [13]. The allergic sensitization test for common allergens in our environment was performed by the prick technique [14].

Patients were classified at different levels of control (according to GINA 2006 controlled, partially controlled, non-controlled). The appropriate changes in the treatment of the patient were determined during each of the clinical visits. The equivalent dose of beclomethasone in each of the visits as well as the rest of the prescribed medication were also collected.

Severe exacerbation was defined according to International ERS/ATS guideline [15]. (Worsening moderate exacerbation) was defined as an increase in the habitual symptomatology of the patient that provokes an increase of the controlling medication. Based on this definition, the variations of symptoms that only required the use of β2 on demand for their control were excluded, provided that such use was no more than two days, in which case an increase in the controller medication was indicated and was considered moderate exacerbation. The use of rescue β2 was recorded throughout the follow-up period.

Days without total control were defined as those days during which the patient had any symptomatology of asthma and had to use rescue medication or increased controller medication.

The recorded medical visits were those that were not previously scheduled and were requested by the patient because of presenting symptoms that could not be controlled by the patient alone. On the first visit, a blood count was performed to collect the levels of eosinophils. A symptom journal was given to the patient to record all of the clinical events during the follow-up, and it was further revised at four, eight, and 12 months. During these visits, the patient was evaluated clinically (degrees of control according to GINA, ACT) and spirometry with a bronchodilator test was performed, along with the measurement of FeNO. On the last visit, a new blood count was also performed to collect levels of eosinophils.

The inhalation technique and the degree of compliance were also examined in each of the visits by the same technician Compliance was defined as good if = 75% of the total prescribed dose was realized, moderate if the dose taken was 50–75% of the total and poor if it did not reach 50% of the total dose prescribed.

Written informed consent for the inclusion of clinical data in the database was requested. The study was approved by the Subcommittee on Health Research of Virgen del Rocio's Hospital.

3. Statistical analysis

The data were analyzed using IBM® SPSS® Statistics version 20 software. In the univariate analysis, the differences between the quantitative variables were studied using Student's *t*-test for independent samples and the differences between the variables among the reviews were tested using the *t*-test for related samples. Previously, the homogeneity of variance (Levene's test) was compared between the groups. For the comparison of ordinal independent variables or variables that did not meet the criteria of normality and randomness, the Mann–Whitney U test or the Wilcoxon test for paired samples was used. The chi-square test was used to evaluate differences between qualitative variables. Those variables with a significance <0.1 in the univariate analysis were included in the multivariate binary logistic regression model, with the odds ratios consigned to a 95% confidence interval. Differences with a $p < 0.05$ were considered significant. The sensitivity, specificity and positive and negative predictive values were established, and the analysis (receiver operating characteristic, ROC) was performed, estimating the area under the curve for each cutoff point of the reversibility of the post-bronchodilator FEV_1 in relation to asthma control or non-control, as they are the two extreme groups