



ORIGINAL ARTICLE

Alternative functional criteria to assess airflow-limitation reversibility in asthma



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Abstract

Introduction: International guidelines define significant bronchodilator response as absolute and percentage change from baseline in forced expiratory volume (FEV₁) in the first second and/or forced vital capacity (FVC) $\geq 12\%$ and 200 mL. However, bronchodilator effects on other lung function parameters have also been correlated to some degree of reversible airflow limitation.

Objectives: To determine whether changes in other lung function parameters apart from FEV₁ and FVC detect functional responses to bronchodilator in asthmatic patients.

Materials and methods: Spirometry and body plethysmography were performed at baseline conditions and after administration of 400 μg of salbutamol by metered-dose inhaler through a space chamber device in asthmatic patients. Paired *t*-tests were used to compare lung function parameters between those with and without criteria for reversibility of airway obstruction according to ATS/ERS criteria. Cut-off values were obtained from the corresponding ROC curves. Measurements evaluated were FEV₁, FVC, maximum mid-forced expiratory flow (FEF_{25–75%}), residual volume (RV), inspiratory capacity (IC), airway resistance (Raw) and specific airway conductance (sGaw).

Results: From a total of 100 consecutive asthmatic patients (46% of them men; average age 58.7 ± 14.1 years; 76% with mild to moderate obstruction), 50 patients had a significant bronchodilator response. All of these had noteworthy variations ($p < 0.004$) in PEF, FEF_{25–75%}, RV, Raw and sGaw. The most accurate in predicting a significant bronchodilator response were the absolute and percentage improvements in PEF (≥ 0.4 L/s and 8%), FEF_{25–75%} (≥ 0.087 L/s and 27%) and the percentage of sGaw compared with that at baseline ($\geq 25\%$). Based on these cut-off values, a sizeable number of the patients defined as non-responders had important changes in airway caliber. 17 patients had significant increments in the percentage of PEF and 10 had changes in absolute volume; 6 patients had increments in percentage and 16 in absolute change of FEF_{25–75%}; 22 patients had increments in the percentage change of sGaw.

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Conclusions: Changes of FEV₁ and/or FVC may underestimate significant functional response to bronchodilators in asthmatic patients with airway obstruction when considering the change in other lung function parameters.

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Introduction

Airway obstruction reversibility, evaluated by the bronchodilator response, is routinely assessed to assist and support the diagnosis of asthma.^{1,2} The most recent guidelines published by the American Thoracic Society and the European Respiratory Society (ATS/ERS) in 2005 on reversibility testing define significant bronchodilator response as a 12% per cent increase from baseline and a 200 mL absolute increase in forced expiratory volume in 1 s (FEV₁) and/or forced vital capacity (FVC).³

However, there is considerable variation within the guidelines as to the degree of reversibility considered significant. The British Thoracic Society,⁴ for example, recommends at least 15% increase of baseline FEV₁ while the Global Initiative for Asthma (GINA)² recommends at least 12% of baseline FEV₁ for the bronchodilator response to be considered positive.

Airway obstruction reversibility is still a controversial topic also because there is still a lack of consensus on which variables should be used to express bronchodilator response. In fact, despite the general use of FEV₁ or FVC criteria, some studies have concluded that changes in these measurements can frequently underestimate significant responses to bronchodilator in both adults and children.^{5–12}

On the other hand, when reversibility is expressed by the percentage increase in FEV₁, it shows bronchodilator responses more frequently in the most severely obstructed patients.^{13,14}

Also, when changes in FEV₁ are not meaningful, alternative criteria such as decrease in lung hyperinflation, can establish a substantial response.^{3,5,7} In the same way, absolute changes in peak expiratory flow (PEF) have proved to be a good substitute to establish airway obstruction reversibility in asthma.¹⁵

Difficulties in performing a forced expiratory maneuver may further limit use of FEV₁ or FVC, particularly in children and older patients. In these cases, criteria such as airway resistance (Raw) or specific airway conductance (sGaw) may be useful.^{16,17}

Assuming that the significant changes in other ventilatory parameters can explain the bronchodilator improvement of dyspnea even without significant changes in FEV₁ and/or FVC, we performed the present study to investigate alternative criteria of positivity in a population of asthmatic patients with documented airway obstruction. Baseline and post-bronchodilator spirometry and body plethysmography were performed on all patients. Unusual pulmonary function variables – PEF, maximum mid-forced expiratory flow (FEF_{25–75%}), total lung capacity (TLC), residual volume (RV), inspiratory capacity (IC), Raw and sGaw – which could

possibly assess bronchodilator response were retrospectively collected and analyzed.

Methods

Subjects

One hundred never-smoker asthmatic patients referred to our Pulmonary Physiology Laboratory by their immunology or pulmonology physician were included in the present study. This population included two matched groups of 50 consecutive patients with and without a significant bronchodilator response defined according to the 2005 ATS/ERS guidelines. Patients under 20 years old, smokers, with severe asthma, recent asthma acute exacerbations or cardiovascular disease, were excluded.

Lung function measurements

Spirometric measurements were made using a pneumotachograph (MasterScreen PTF Jaeger®). Plethysmography measurements were obtained through a body plethysmograph (MasterScreen Body Jaeger®). All spirometric and plethysmographic tests were performed according to accepted standards as recommended by the ATS.^{18,19}

Reversibility testing

All medication likely to interfere with bronchomotricity was previously suspended.¹⁸ Short- and long-acting β -agonists bronchodilators were suspended 4 h and 12 h prior to the test, respectively, while oral theophyllines were stopped 12–24 h before. Patients were instructed not to smoke and avoid food containing caffeine (coffee, tea, cola) or theobromine (chocolate) for at least 1 h before the test.

All patients underwent spirometric and lung volumes evaluation at baseline conditions. An obstructive ventilatory defect was defined by a FEV₁/FVC ratio less than 0.70. Only those with verified airflow obstruction and three satisfactory records of FEV₁, FVC and PEF were submitted to further challenge with bronchodilator. Airway-obstruction reversibility was tested 10 min after administration of four equal and separate doses of 100 μ g (total dose 400 μ g) of salbutamol given by a metered-dose inhaler connected to a space chamber device.^{20,21}

Statistical analysis

Data analysis was performed by IBM SPSS® for Windows version 20.0. All patient demographic and clinical features were

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