Perception of dyspnoea during acute changes in lung function in patients with either asthma or COPD

A. Noseda*, J. Schmerber*, T. Prigogine*, V. de Maertelaer† and J-C. Yernault‡

*Pulmonary Division, Department of Internal Medicine, Hôpital Brugmann, †Medical Statistical Unit, IRIBHN, and ‡Chest Department, Hôpital Erasme, Université Libre de Bruxelles, Brussels, Belgium

The aim of the study was to evaluate the relationship between several lung function indices and perceived dyspnoea during bronchoconstriction. Acute changes in lung function were induced by inhaled histamine followed by terbutaline, in 12 asthmatics and 12 subjects with chronic obstructive pulmonary disease (COPD). A bipolar visual analogue scale (VAS), allowing subjects to report either improvement or worsening when moving off from a 'no change' midpoint, was used to rate shortness of breath. Large swings in ratings were seen in all asthmatics and in seven out of 12 COPD subjects (high perceivers). Using linear regression of VAS rating against parallel change in lung function, on a within-subject basis, the highest degree of correlation between dyspnoea and objective response was found to involve the change in specific inspiratory resistance (sRin) in the asthmatics. In the five low perceivers, the ability to discriminate an increase in airway obstruction, estimated as the VAS/change in lung function slope, was very poor. Using a stepwise multiple regression analysis, the sensation of dyspnoea was found to be significantly related to the FEV₁ and the sRin in the asthmatics, to the inspiratory vital capacity and the maximal inspiratory flow at 50% FVC (MIF₅₀) in the COPD subjects with high perception, and to the MIF₅₀ in the COPD subjects with low perception.

Introduction

Since the initial report, by Rubinfeld and Pain in 1976 (1), that some subjects with asthma are unable to perceive marked bronchoconstriction, there have been relatively few studies to investigate this further. The group of Killian using a Borg scale, has quantitated the sensation of dyspnoea during histamine challenge in the lung function laboratory, and reported a linear relationship between the subjective response and the fall in FEV₁ in two studies involving large numbers of asthmatics (2,3). In two studies also performed in the lung function laboratory, Turcotte et al. have emphasized that dyspnoea perception during the early response to either histamine, antigen exposure or exercise does not differ appreciably (4), but that it is reduced during the late asthmatic response, because of temporal adaptation to slowly progressive bronchoconstriction (5). The perception of airway obstruction by asthmatics in everyday life, with its spontaneous within-day and between-day variability, has been studied by Peiffer et al. (6); these authors assessed perception as the strength of the correlation between dyspnoea and peak expiratory flow (PEF) recorded at home and confirmed the early suggestion by Rubinfeld and Pain that some asthmatics are 'poor perceivers'. A common feature of all these studies involving asthmatics is that only forced expiratory indices were analysed.

In the present study, large variations in airway obstruction were induced in two groups of patients having asthma or chronic obstructive pulmonary disease (COPD) using inhaled histamine followed by terbutaline. Shortness of breath was rated on a bipolar visual analogue scale (VAS) validated previously (7), and lung function measurements included forced expiration and inspiration manoeuvres preceded by assessment of the specific airway resistance during tidal breathing. Previous studies performed in a setting of bronchodilation have suggested that inspiratory indices, as they are free from any collapse artefact, may be more relevant (8) and more closely related to dyspnoea (7,9,10) than are the conventionally used FEV₁ and PEF. This study attempted to assess the contribution of several lung function indices to the sensation of perceived dyspnoea during histamine-induced bronchoconstriction.
PATIENTS

Twenty-four outpatients attending the Chest Clinic agreed to participate in a study of respiratory sensations at rest. Conditions for entry into the study were: (1) physician-diagnosed asthma or COPD; (2) airway obstruction (FEV₁ < 85% predicted and a FEV₁/IVC ratio < 65%); (3) baseline FEV₁ > 50% predicted, and (4) no past history of respiratory failure. Lung function testing, including a bronchodilation test with 200 µg salbutamol delivered by a metered dose inhaler, had been performed in all subjects at least three times (at least 1-week interval) over a time span of at least 3 months. Subjects were classified as having either asthma or COPD using the criteria described previously (7).

Briefly, asthmatics were never smokers, had a history of episodic breathlessness and wheeze and had shown an increase in FEV₁ exceeding 15% predicted (11) at least once following 200 µg salbutamol. COPD subjects were smokers or ex-smokers, had a history of chronic cough, sputum production and dyspnoea on exertion and had shown no increase in FEV₁ exceeding 10% predicted. Twelve subjects (eight males, four females) were considered as having asthma, 12 (all men) as having COPD. Mean (±SEM) age, height and weight were 60 (± 4) years, 170 (± 2) cm, 76.5 (± 3.1) kg in the asthma group, and 66 (± 3) years, 169 (± 2) cm, 69.2 (± 4.5) kg in the COPD group, respectively. COPD patients were predominantly ex-smokers (10 out of 12). In the asthma group, 10 out of 12 subjects were on maintenance drug therapy including inhaled steroids (n=10), inhaled sympathomimetics (n=8), oral theophylline (n=5), inhaled anti-cholinergics (n=2), and oral steroids (n=1). In the COPD group, six subjects had no regular therapy while six subjects were on either inhaled sympathomimetics (n=3), inhaled anti-cholinergics (n=3) or oral theophylline (n=2).

STUDY DESIGN

All the subjects gave informed consent and the study protocol was approved by the Ethics Committee of the Hôpital Universitaire Brugmann, Belgium. The study consisted of consecutive inhalations of histamine with assessment of subjective perception and of lung function, and was single blind, with the supervisor knowing which agent was inhaled while the subject did not. All the subjects were naïve to sensory evaluation. The protocol included 1–5 inhalations of histamine, depending on the degree of bronchial reactivity (see below) followed by two inhalations of terbutaline. All subjects were asked to abstain from inhaled bronchodilators after 7 am, with the sessions starting at 3 pm. Oral theophylline preparations were withheld 48 h before testing. Oral and inhaled steroids were not withheld. After arrival in the lung function laboratory, each subject rested comfortably on a chair for 10 min and a full explanation of the method used to evaluate dyspnoea perception was given. Baseline lung function was subsequently measured. The patient was then given the first inhalation and thereafter rested in the sitting position. After a 2-min interval, the subject was invited to rate the change in shortness of breath and lung function was measured again. The subsequent inhalations were given and the procedure of subjective response rating and lung function measurement was repeated at each step. Due to the potential severity of bronchoconstriction induced, a physician with resuscitation equipment was present at all times.

DOSAGE OF INHALED AGENTS

A Mefar MB3 dosimeter (Medicali, Brescia, Italy) activated by the subject's inspiratory manoeuvre was used (12). The method of inhalation was the same as that used in previous studies and is fully described elsewhere (7). Different histamine concentrations were used in asthmatics and in COPD subjects, as shown in Table 1. Histamine doses so obtained were in agreement with usual recommendations, including a first dose of 10 µg or less in subjects with asthma (13) and a dose range up to about 1000 µg in COPD subjects (14,15). The diluent of histamine solutions was phosphate buffered saline. In all subjects, the histamine challenge was stopped when either FEV₁ had fallen below 60% of its baseline value or the specific inspiratory resistance (sRin) had increased above 250% of its baseline value (or above 25 cm H₂O s in subjects having a baseline value ≤ 10). All subjects were subsequently given two inhalations of the commercially available 10 mg ml⁻¹ terbutaline solution (cumulated terbutaline doses 400 and 800 µg). The dose of histamine responsible for a fall of 15% in predicted FEV₁ (PD₁_50, FEV₁) was calculated in each subject by linear interpolation.

VISUAL ANALOGUE SCALE

At the beginning of the session, the patient was given a standardized neutral information, fully described in a previous study (7). Dyspnoea perception was measured using a bipolar VAS (7,16) presenting as a 40 cm horizontal line, with a ‘no change’ midpoint and ‘much shorter of breath’ (left end) and ‘much less short of breath’ (right end) descriptors.
Table 1  Concentration and dose of inhaled histamine used in subjects with either asthma or COPD

<table>
<thead>
<tr>
<th>Concentration (mg ml⁻¹)</th>
<th>Dose (µg)</th>
<th>Cumulated dose (µg)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Asthma</td>
<td>COPD</td>
</tr>
<tr>
<td>Step 1</td>
<td>0.125</td>
<td>0.500</td>
</tr>
<tr>
<td>Step 2</td>
<td>0.125</td>
<td>0.500</td>
</tr>
<tr>
<td>Step 3</td>
<td>0.250</td>
<td>1</td>
</tr>
<tr>
<td>Step 4</td>
<td>0.250</td>
<td>4</td>
</tr>
<tr>
<td>Step 5</td>
<td>2</td>
<td>16</td>
</tr>
</tbody>
</table>

This scale allows subjects to report either improvement or worsening when moving off from the no change midpoint. All ratings were reported as % of line length (range -100 to +100%). It was carefully recommended to the subjects that they rate only shortness of breath, and ignore other sensations such as cough, chest tightness, nasal irritation or throat irritation.

LUNG FUNCTION

The methods used for lung function measurement are fully described elsewhere (7). Briefly, plethysmography aimed to measure sRin during tidal breathing and FRC. The inspiratory vital capacity (IVC) was measured during a smooth and slow inspiratory manoeuvre, from RV up to TLC. Finally, expiratory and inspiratory flow-volume curves were obtained. Indices retained for analysis are sRin (cm H₂O s⁻¹), FRC, IVC, FEV₁ (1 or % predicted) (17) and maximal inspiratory flow at 50% FVC (MIF₅₀) (1 s⁻¹). While two or three technically acceptable curves were obtained for the baseline evaluation as well as after the terbutaline inhalations, only one curve was obtained after histamine inhalation, to minimize deep inspiration-induced bronchodilation, as recommended by Scott and Küng (18). Repeat forced manoeuvre was only performed when the first was technically unsatisfactory or affected by a poor subject effort.

STATISTICAL ANALYSIS

Lung function variables were reported as mean (±SEM) values. The relationship of the subjective perception assessed with the VAS (reference point: beginning of the session) to the changes in lung function [ΔsRin (cm H₂O s⁻¹), ΔFRC, ΔIVC, ΔFEV₁ (% predicted)] ΔMIF₅₀ (1 s⁻¹)] was first studied using linear regression analysis on a within-subject basis. The number of points included in the regression analysis ranged between four and seven. For each index, the strength of the correlation was assessed by the Pearson correlation coefficient. The slope (resolution of the scale) and the VAS axis intercept (perception level when no change has occurred in lung function) were calculated for the VAS/ΔFEV₁ and VAS/ΔsRin analyses. These correlation coefficients, slopes and intercepts were reported as median values (with ranges). Secondly, a stepwise multiple regression of VAS ratings was performed within each group of patients, with the parallel changes in lung function as independent variables. The ratings considered for this analysis were those obtained after the first and last histamine inhalation and after the two subsequent terbutaline inhalations. The criteria used in the stepwise regression were 0.05 for the probability of ‘F-to-enter’ and 0.10 for the probability of ‘F-to-remove’.

Results

BASELINE SPIROMETRY AND HISTAMINE REACTIVITY LEVEL

The baseline FEV₁ (mean ± SEM) was similar in asthmatics: 1.87 (± 0.15) 1 or 68.7 (± 2.4) % predicted, and in COPD subjects: 1.75 (± 0.12) 1 or 62.5 (± 1.9) % predicted. Histamine challenge included two inhalations in five asthmatics and four COPD subjects, three inhalations in three asthmatics and two COPD subjects, four inhalations in two asthmatics and two COPD subjects. Six subjects (two with asthma and four with COPD) were given a fifth inhalation. In the asthma group, sRin (all subjects) and/or FEV₁ (three of 12 subjects) threshold for stopping the challenge was reached in all the subjects. In the COPD group, the threshold was reached in nine subjects (sRin alone in four, sRin and FEV₁ in five). One subject was unresponsive to histamine (end provocation values: sRin 9.7 cm H₂O s, FEV₁ 96% of baseline). The test was stopped in one subject as he felt markedly short of breath (VAS - 60%) before
Fig. 1 Perceived change in shortness of breath, rated on the bipolar visual analogue scale (VAS), in 12 patients with asthma (a), seven COPD patients with high perception (b) and five COPD patients with low perception (c). VAS ratings are expressed as % of line length (range -100-+100%). The two white arrows represent respectively the first and the last histamine inhalation, while the two black arrows represent the two terbutaline inhalations.

sRin (202% baseline) and FEV₁ (69.5% baseline) had reached their thresholds and in another subject with low baseline sRin (3.6) when it attained 22.5 cm H₂O s. The median PD₁₅pFEV₁ was 18.8µg (range 5.4-120.0) in the asthma group and 49.0µg (range 17.9-467.7) in the COPD group. Log PD₁₅pFEV₁ and baseline FEV₁ were correlated in the COPD group (r=0.664, P<0.05) but not in the asthmatics (r=0.064).

**PATTERN AND LEVEL OF PERCEPTION**

Individual dyspnoea ratings are shown in Fig. 1. A majority of subjects (17 of 24) rated either no change or an improvement in dyspnoea after the first histamine inhalation. At the end of the provocation, all subjects but two felt shorter of breath than at the beginning of the session. In the asthmatics, AVAS, defined as the difference between the highest and the lowest rating obtained at any time of the study, ranged between 35-102.5% (median 60%). As shown in Fig. 2, a bimodal distribution of AVAS was observed in the COPD group, with seven subjects using a large proportion of the scale (ΔVAS 45-100%, median 80%), like the asthmatics, while the five other subjects had a low level of perception (ΔVAS 5-35%, median 20%). These two subgroups of COPD patients are further designated as 'high perceivers' and 'low perceivers'. Dyspnoea decreased in all subjects following terbutaline, with only a small change in VAS rating in the COPD group.

![Histogram of change in visual analogue scale rating (ΔVAS)](image)

Fig. 2 Histogram of change in visual analogue scale rating (ΔVAS), defined as the difference between the highest and the lowest rating for dyspnoea obtained at any time of the study, expressed as % of line length. The distribution is bimodal in the COPD group.
Table 2 Lung function variables

<table>
<thead>
<tr>
<th>sRin (cm H₂O s⁻¹)</th>
<th>Baseline</th>
<th>Post-histamine</th>
<th>Post-terbutaline</th>
<th>mean (±SEM)</th>
<th>COPE</th>
<th>COPE</th>
<th>COPE</th>
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<tbody>
<tr>
<td>Asthma (n=12)</td>
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<td></td>
<td>10.5 (±0.9)</td>
<td>11.1 (±0.8)</td>
<td>8.7 (±2.3)</td>
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</tr>
<tr>
<td>COPD high perceivers (n=7)</td>
<td>36.5 (±2.6)</td>
<td>28.7 (±1.0)</td>
<td>30.2 (±5.5)</td>
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<tr>
<td>COPD low perceivers (n=5)</td>
<td>9.9 (±1.4)</td>
<td>9.8 (±1.1)</td>
<td>6.7 (±0.7)</td>
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<tr>
<td>FRC (l)</td>
<td>Baseline</td>
<td>Post-histamine</td>
<td>Post-terbutaline</td>
<td>mean (±SEM)</td>
<td>COPD</td>
<td>COPD</td>
<td>COPD</td>
</tr>
<tr>
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<td>COPD low perceivers (n=5)</td>
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<td>9.8 (±1.1)</td>
<td>6.7 (±0.7)</td>
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<td></td>
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</tr>
<tr>
<td>IVC (l)</td>
<td>Baseline</td>
<td>Post-histamine</td>
<td>Post-terbutaline</td>
<td>mean (±SEM)</td>
<td>COPD</td>
<td>COPD</td>
<td>COPD</td>
</tr>
<tr>
<td></td>
<td>10.5 (±0.9)</td>
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<td>6.7 (±0.7)</td>
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</table>

Mean (±SEM) values. sRin, specific inspiratory resistance; MIF₅₀, maximal inspiratory flow at 50% FVC.

low perceivers (Fig. 1). Hence, an alternative definition for low perception could be a terbutaline-induced increase in VAS rating (VAS after 800 μg terbutaline minus VAS after last histamine inhalation) less than 25%. The latter definition, which was successfully used in two previous studies dealing with perception of a 800 μg terbutaline dose (7,10), would lead to the same discrimination between seven high perceivers and five low perceivers within the COPD group, and would classify all asthmatics as high perceivers. Within the COPD group, there was no significant difference between high and low perceivers in either age, proportion of regular users of inhaled bronchodilators or bronchial reactivity level.

SIZE OF CHANGE IN LUNG FUNCTION
Lung function variables are reported in Table 2 at baseline, after maximal bronchoconstriction and after subsequent bronchodilation. There was little difference between asthmatics, COPD high perceivers and COPD low perceivers in either baseline, post-histamine or post-terbutaline values.

RELATIONSHIP OF VAS RATING TO OBJECTIVE RESPONSE: WITHIN-SUBJECT ANALYSIS
The analysis of within-subject correlations between VAS rating and change in lung function is summarized in Table 3. The closest correlations were observed in the asthma group, and the highest median r value corresponded with the relationship between VAS and ΔsRin (r=0.953). To evaluate whether stronger correlations between subjective and objective response were encouraged or not by larger variations in lung function, the correlation between r values (reflecting the strength of the VAS/change in lung function relationship) and size of the corresponding change in lung function in the whole group of 24 subjects was studied, and no significant relationship was found.

Individual examples of linear regression analyses are shown in Fig. 3. From the latter figure, it appears that a relatively high r value in the COPD low perceivers is of limited significance, as all VAS ratings were close to zero, and, as a consequence, the slope of the regression line close to zero, too. Table 4 shows the perceptual characteristics of the three groups of patients, the most striking point again being the very poor resolution of the scale in the COPD low perceivers. Table 4 also shows that median VAS axis intercepts were around +20% in the two groups of subjects with high perception.

RELATIONSHIP OF VAS RATING TO OBJECTIVE RESPONSE: MULTIPLE REGRESSION ANALYSIS
In the asthmatics, the sensation of dyspnoea was significantly related to the change in FEV₁ (P=0.002) and in sRin (P=0.022). No other independent variable entered the equation after ΔFEV₁ and ΔsRin were introduced. In the COPD high perceivers, the significant predictors of the variation in shortness of
Table 3  Relationship between VAS rating and parallel change in lung function (within-subject analysis)

<table>
<thead>
<tr>
<th></th>
<th>Asthma (n=12)</th>
<th>COPD high perceivers (n=7)</th>
<th>COPD low perceivers (n=5)</th>
</tr>
</thead>
<tbody>
<tr>
<td>sRin</td>
<td>0.953 (0.670-0.993)</td>
<td>0.704 (0.359-0.995)</td>
<td>0.797 (0.084-0.968)</td>
</tr>
<tr>
<td>FRC</td>
<td>0.890 (0.055-0.976)</td>
<td>0.518 (0.236-0.974)</td>
<td>0.531 (0.077-0.940)</td>
</tr>
<tr>
<td>IVC</td>
<td>0.946 (0.528-0.995)</td>
<td>0.810 (0.224-0.989)</td>
<td>0.533 (0.077-0.940)</td>
</tr>
<tr>
<td>FEV₁</td>
<td>0.934 (0.276-0.980)</td>
<td>0.693 (0.359-0.956)</td>
<td>0.745 (0.032-0.920)</td>
</tr>
<tr>
<td>MIF₅₀</td>
<td>0.869 (0.276-0.980)</td>
<td>0.805 (0.395-0.970)</td>
<td>0.532 (0.118-0.887)</td>
</tr>
</tbody>
</table>

Data in the table are median Pearson correlation coefficients (range) between VAS rating and parallel change in lung function. VAS, bipolar visual analogue scale; sRin, specific inspiratory resistance; MIF₅₀, maximal inspiratory flow at 50% FVC.

Fig. 3  Individual examples of linear regression of visual analogue scale (VAS) rating against the change in specific inspiratory resistance (sRin): subjects with the best (top) and the worst (bottom) r values from each group; (a) asthma; (b) COPD high perceivers; (c) COPD low perceivers. Numbers refer to the order of the successive inhalations.

Breath were the change in IVC (P=0.010) and in MIF₅₀ (P=0.012); while in the COPD low perceivers, only the change in MIF₅₀ (P=0.003) entered the equation.

The regression equations are:

Asthmatics VAS = 15.1 + 1.19 ΔFEV₁ - 0.83 ΔsRin r=0.811

COPD, high perceivers VAS = 17.2 + 1.36 ΔIVC + 19.18 ΔMIF₅₀ r=0.800

COPD, low perceivers VAS = 3.4 + 28.94 ΔMIF₅₀ r=0.630

(VAS % of line length, ΔFEV₁, ΔIVC% predicted, ΔsRin cm H₂O s, ΔMIF₅₀ l s⁻¹, r multiple coefficient of correlation)
Table 4 Characteristics of the perception of acute changes in lung function

<table>
<thead>
<tr>
<th></th>
<th>Asthma (n=12)</th>
<th>COPD high perceivers (n=7)</th>
<th>COPD low perceivers (n=5)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>FEV&lt;sub&gt;1&lt;/sub&gt;</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Slope</td>
<td>+2.1 (+1.0--3.1)</td>
<td>+3.5 (+1.5--4.0)</td>
<td>+0.6 (0--1.5)</td>
</tr>
<tr>
<td>VAS axis intercept</td>
<td>+19 (--14--45)</td>
<td>+22 (--9--56)</td>
<td>+1 (--1--16)</td>
</tr>
<tr>
<td><strong>sR&lt;sub&gt;in&lt;/sub&gt;</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Slope</td>
<td>-2.4 (--0.9--2.9)</td>
<td>-2.6 (--1.9--3.2)</td>
<td>-0.4 (+0.2--2.6)</td>
</tr>
<tr>
<td>VAS axis intercept</td>
<td>+20 (--28--48)</td>
<td>+16 (--26--30)</td>
<td>+1 (--2--15)</td>
</tr>
</tbody>
</table>

Values are expressed as median (range). Slopes are expressed as % of VAS line length per % predicted of change in FEV<sub>1</sub> (or per cm H<sub>2</sub>O s of change in sR<sub>in</sub>), intercepts as % of VAS line length. VAS, bipolar visual analogue scale; sR<sub>in</sub>, specific inspiratory resistance.

Discussion

In the present study, large variations in airway obstruction, using histamine, and subsequently terbutaline, were induced in 24 subjects with impaired baseline lung function and a diagnosis of either asthma or COPD, and the subjective response was measured as a change in dyspnoea on a bipolar VAS. The swings in VAS ratings were small in five COPD subjects, defined as low perceivers on the basis of a post-800 µg terbutaline increase in VAS <25% of line length. The strongest individual correlation between VAS rating and lung function involved the change in sR<sub>in</sub> in the asthmatics. As judged from a stepwise multiple regression analysis, the significant contributors to the sensation of dyspnoea were FEV<sub>1</sub> and sR<sub>in</sub> in the asthmatics, and IVC and MIF<sub>50</sub> (MIF<sub>50</sub> alone in the low perceivers) in the COPD subjects.

In previous studies dealing with the perceived dyspnoea during bronchoconstriction, only FEV<sub>1</sub> was considered. On a study of 45 asthmatics, Burdon et al. (2) reported a linear relationship between histamine-induced dyspnoea and the fall in FEV<sub>1</sub>, with, however, a large between-subject variability in subjective response for a given decrease in FEV<sub>1</sub>. In a more recent study including 120 asthmatics, the same group confirmed that dyspnoea intensifies significantly, although variably, as FEV<sub>1</sub> decreases (3). In a population study involving 412 subjects with bronchial hyperreactivity, Brand et al. (19) found larger decreases in FEV<sub>1</sub> in those subjects with higher increases in Borg ratings; however, in a multiple regression analysis the relation of the histamine-induced change in FEV<sub>1</sub> to that in dyspnoea was no longer significant after adjustment for such variables as age, sex, skin test reactivity, bronchial reactivity level and smoking habits. The present study was designed to evaluate the correlation between dyspnoea and a large set of lung function indices, including plethysmographic specific resistance, static lung volumes (FRC, IVC) and forced expiratory (FEV<sub>1</sub>) or inspiratory (MIF<sub>50</sub>) indices. In the asthmatics, a variable degree of individual relationship between dyspnoea and change in lung function variables was found, with sR<sub>in</sub> showing the closest correlation (median r=0.953, lowest individual r 0.670). Similar findings were observed when studying the perception of progressive, terbutaline-induced, bronchodilation in a similar group of asthmatics (10), and the strong relationship between dyspnoea and sR<sub>in</sub> was ascribed to the fact that the latter variable better reflects bronchodilation than e.g. forced expiratory indices, which are influenced by changes in large airways collapsibility (20) or in lung elastic recoil (21). In the present study, an additional factor could be the stretch receptors-mediated decrease in bronchial tone induced by deep inspiration in some subjects with pharmacologically-induced bronchoconstriction (22). Every effort was made to minimize the latter phenomenon by asking the subjects to slowly inspire to TLC before the forced expiratory manoeuvre (23), and by recording a single flow–volume curve after each histamine inhalation (18). However, despite this careful design, deep inspiration-induced bronchodilation did occur in some individuals and in those subjects, the indices measured on the forced respiratory manoeuvres underestimated the degree of obstruction present at the time the patient had rated dyspnoea on the scale.

This study included subjects with COPD as well as asthmatics. We are not aware of data in the literature about the perception of bronchoconstriction by COPD subjects. Some COPD patients were found to perceive acute changes in lung function poorly. That some subjects perceive dyspnoea at a low level, and with poor relation to the objective response, has been
a constant finding in previous studies dealing with the perception of bronchodilation in similar groups of COPD outpatients, selected on basis of clinical history and limited reversibility in airway obstruction (7,10). Perception of added resistive loads has been shown to be impaired in COPD subjects, but not in asthmatics (24), and this impairment has been ascribed to a defect in the central nervous system processing of sensory information (25). In the present study, it was not possible to definitely identify any factor associated with high or low perception within the COPD group. It may be hypothesized that the muscular breathing pattern—which was not evaluated in this study—was possibly different, although voluntary use of either the diaphragm or the intercostal muscles by healthy subjects submitted to a resistive load has been found to produce similar intensities of dyspnoea (26). An alternative hypothesis could be that high and low perception reflect different levels of awareness to sensory stimuli, associated with distinct psychologic profiles (27). In a stepwise multiple regression analysis of dyspnoea against lung function, the change in IVC and MIF were found to be significant contributors to the variation in shortness of breath in the COPD group with high perception. This result compares well with previous reports by Bellamy and Hutchinson (9) and by our group (7,10) that the ability of COPD subjects to perceive an acute bronchodilation as a decrease in dyspnoea is linked to some improvement in inspiratory function.

In the present study, the VAS/objective response relationship was found to have a positive intercept in most subjects. The median VAS axis intercept, reflecting the subjective rating for no change in FEV₁, amounted to +19% in the asthma group, and +22% in the COPD subjects with high perception. These results show that a given threshold of bronchoconstriction has to be reached before being perceived as an increase in shortness of breath. Further studies are needed to evaluate the relevance of this finding in a setting of spontaneous bronchoconstriction. Kikuchi et al. studied 11 asthmatics with a history of near fatal asthma and reported in these subjects an increased threshold for dyspnoea when breathing through inspiratory resistances, in comparison with a control group of 11 asthmatics without history of near fatal asthma (28). If we admit that over-tolerance to dyspnoea may lead to failure to appreciate life-threatening asthma, educational interventions aimed to improve awareness of bronchoconstriction are desirable in those subjects with poor perception. Preliminary data suggest that perception of airway obstruction can be trained (29) and that regular recording of PEF at home could be a useful intervention (30).

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References