Perception Scoring of Induced Bronchoconstriction as an Index of Awareness of Asthma Symptoms

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Perception of asthma symptoms shows a wide interindividual variability. Poor perception of airflow obstruction may lead to undertreatment of asthma. We reviewed the possibility of using a simple test to detect poor perceivers of bronchoconstriction as part of the investigation of asthma. We studied 150 consecutive subjects referred for assessment of airway responsiveness. All had a histamine PC20 within the asthmatic range (<16 mg/ml) and a fall in FEV1 of <20 percent after saline inhalation. On histamine challenge, before each FEV1 measurement, perception of dyspnea was assessed on a modified Borg scale. A perception score of breathlessness at 20 percent fall in FEV1 (PS20) was obtained by interpolation of the two last points on the perception/fall in FEV1 curve. It was concluded that in a hyperreactive population, PS20 (1) showed a normal distribution pattern; (2) was similar in both genders; and (3) increased with age due to high postcontrol saline inhalation scores. Hyperperceivers or hyperperceivers were similar for age, sex, baseline FEV1, and PC20. The PS20 determination may be a useful additional parameter to obtain during provocation tests to assess perception of symptoms associated with bronchoconstriction. Its correlation with clinical outcome remains, however, to be determined. (Chest 1994; 105:1430-33)

Large variations in perception of respiratory symptoms may be observed from one asthmatic subject to another.1 Some report little discomfort with severe bronchoconstriction, while others experience marked discomfort with small increases in airflow obstruction.2 Low perception of bronchoconstriction may result in undertreatment of asthma. If perception is low, even when asthma is stable, this may potentially be a risk factor of worsening severe asthma because of delays in modifying medication according to their action plan or consult.

Assessment of perception of bronchoconstriction has been reported in different studies.3-6 We previously showed that whatever the stimulus, perception of early bronchoconstriction was similar for a given fall in expiratory flows.3 The perception of bronchoconstriction during a provocation test, such as histamine or methacholine challenges, may provide information on how a given subject perceives asthma symptoms. Furthermore, distribution of nociceptive sensations such as breathlessness associated with bronchoconstriction and its determinants, remains to be documented.

The goal of this study was to use a perception score of breathlessness as part of an investigation of asthma during induced bronchoconstriction to detect poor perceivers, to determine the distribution of perception scores for a given fall in expiratory flows in a population of subjects with airway hyperresponsiveness, and to compare the characteristics of high and low perceivers of bronchoconstriction. The distribution of perception was explored in a group of 150 subjects from our tertiary care referral center who were referred for etiologic evaluation of respiratory symptoms or determination of contributing factors to asthma and/or treatment needs. This population of subjects, therefore, reflected a variety of asthma types and severities.

Subjects and Methods

There were 150 consecutive subjects included in the study who were referred to the Laval Hospital pulmonary function laboratory for assessment of airway responsiveness as part of the investigation of respiratory symptoms compatible with asthma. There were 61 male and 89 female subjects, aged 13 to 74 years (mean age: 37.0 ± 1.3) (Table 1). Patients with chronic bronchitis or fixed

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<th>Table 1—Subject Characteristics</th>
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<tr>
<td>Number of subjects</td>
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<td>Age, yr (mean ± SEM)</td>
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<td>(37.0 ± 1.3)</td>
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<tr>
<td>Sex</td>
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<td>Baseline FEV1, % (±SEM)</td>
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<td>Mean Borg score at 20% fall in FEV1 (PS20)</td>
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<td>Mean Borg score after saline inhalation</td>
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<td>Mean Borg score at 20% fall in FEV1 (PS20) in subjects scoring 0 after saline inhalation (number of subjects)</td>
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<td>Age (mean, median)</td>
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<td>Age of subjects (mean, median) scoring &gt;0 following saline inhalation (number of subjects)</td>
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airway obstruction were not strictly excluded although most subjects had a clinical diagnosis of asthma (by their physician). To be included in the analysis, their baseline FEV₁ had to be ≥50 percent of their predicted values, they had to have a provocative dose of histamine inducing a 20 percent fall in forced expiratory volume in one second, the PC2₀ FEV₁ <16 mg/ml, and a fall in FEV₁ of less than 20 percent after inhalation of saline solution.

Histamine inhalation tests were performed according to the method described by Juniper et al. Before the tests, inhaled bronchodilators were withheld for at least 8 h. Dyspnea was estimated immediately before each FEV₁ measurement on a modified Borg scale from 0 (no symptom) to 10 (maximum bearable). Scores between the fixed intervals were permitted (half an interval, 0.5). Subjects were asked to rank the "overall sensation" of respiratory discomfort, defined as breathlessness, associated with the challenge. PS2₀, the perception score on the Borg scale at 20 percent fall in FEV₁ was determined for each subject by interpolation of the two last perception scores, before and after the 20 percent fall in FEV₁.

Analysis

The percentage of fall in FEV₁ is calculated from the post-saline inhalation value; there was a linear relationship, within subjects, between percentage of fall in FEV₁ and Borg score. Results are expressed as mean ± SEM. A distribution curve was obtained from each subject's PS2₀; Shapiro-Wilk's test was used to evaluate the distribution for normality. Low perception of breathlessness (hypoperceivers) was defined as a PS2₀ more than 1 SD under the mean. High perception level was defined as a PS2₀ more than 1 SD over the mean perception score of the group (hyperperceivers). Comparison of subjects' characteristics, such as age, sex, baseline FEV₁, and PC2₀; and baseline perception score between hypoperceivers and hyperperceivers was made using unpaired Student's t test or Mann-Whitney test. Correlations between PS2₀ and subjects' characteristics were made by Spearman's rank correlation test.

RESULTS

Baseline FEV₁ and PC2₀

Mean baseline FEV₁ was 96.2 ± 1.4 percent (range: 52.2 to 139.6 percent), and all subjects had increased airway responsiveness with a geometric mean PC2₀ histamine 3.50 mg/ml (range: 0.05 to 15.9). There was a positive correlation between PC2₀ and baseline FEV₁ (rs=0.459, p<0.001).

Perception Scores of Breathlessness Following Saline Inhalation

Although there was no clinically significant reduction in expiratory flows after control saline inhalation, with a mean fall in FEV₁ of 4.7 ± 0.4 percent (median: 3.5 percent), mean Borg score was 0.92 ± 0.011; 76 subjects scored 0 (50.7 percent); 34, 0.5 or 1 (22.7 percent); 18, 1.5 or 2 (12 percent); 13, 2.5 or 3 (8.7 percent); 6, 3.5 or 4 (4 percent); and 3 scored 5.0 (2 percent). Mean Borg score after saline inhalation was not significantly different between male (0.87 ± 0.17) or female patients (0.96 ± 0.13, p>0.05), but there was a weak age-related correlation, the scores increasing with age (rs=0.222, p=0.006) (Fig 1). The mean age (median, range) of subjects scoring 0 after saline inhalation was significantly different from that of subjects with scores >0 (p=0.038): respectively, 34.3 ± 1.8 (30.5, 13 to 67) years and 39.7 ± 1.8 (40, 14 to 74) years.

Perception of Breathlessness Following Induced Bronchoconstriction

Following histamine inhalation tests, the PS2₀ was positively correlated to the percentage of fall in FEV₁ (rs=0.531 p<0.001, n=150). The distribution curve of the Borg score at a 20 percent fall in FEV₁ showed that the PS2₀ followed a symmetric normal distribution, with a mean PS2₀ of 3.36 ± 1.17 and a median of 3.12 (Fig 2A). This pattern was also observed if only the 76 subjects who scored 0 after saline inhalation were kept to draw the distribution curve, with a mean of 2.50 ± 0.21 and a median 2.26 (Fig 2B).

Mean PS2₀ was not significantly different between male (3.47 ± 0.26) or female patients (3.30 ± 0.21, p>0.05), but it was positively correlated with age (rs=0.226, p=0.005). However, if only the subjects scoring 0 after saline inhalation were kept for analysis, the correlation between the PS2₀ and age was no more significant (rs=0.032, p>0.05). There was no significant correlation between the PS2₀ and baseline FEV₁ (rs=−0.038).
The subjects with a PS20 under (hypoperceivers, n=19) or over (hyperperceivers, n=24) 1 SD (1.02>PS20>5.08) from the mean were compared for age, sex, baseline FEV1, PC20, and perception score after saline inhalation. Their mean PS20 and mean Borg score after saline inhalation were 0.55±0.07 and 0.11±0.06, respectively, for hypoperceivers, and 6.68±0.26 and 2.21±0.34, respectively, for hyperperceivers (both p<0.001). Hypoperceivers included 6 men and 13 women, and the hyperperceivers, 9 men and 15 women. The age of hyperperceivers was not significantly different from that of low perceivers with respective means±SEM of 47.1±2.8 years and 41.9±4.3 years (p>0.05). The PC20 was not significantly different between both groups with a mean of 3.34 mg/ml (−1 SEM: 2.80, +1 SEM: 3.97) for the 19 hypoperceivers and 4.31 mg/ml (−1 SEM: 3.50, +1 SEM:5.27) for the 24 hyperperceivers.

High and low perceivers were compared over a 1-year period for the number of visits to the emergency room or hospitalizations because of asthma exacerbations. In the 24 hyperperceivers, 4 subjects consulted for asthma exacerbations for a total of 9 visits compared to 5 subjects for a total of 6 visits for the 19 hypoperceivers. One of these last was admitted to the hospital and had to be intubated.

**Discussion**

Our results show that perception of bronchoconstriction-induced breathlessness follows a normal distribution pattern in a population of subjects with airway hyperresponsiveness. There is no difference in subjects’ characteristics between high and low perceivers. For the whole group of subjects, perception of bronchoconstriction increased with age. This last observation was, however, due to an increase in perception score after the control saline inhalation, even if there was no significant fall in expiratory flows at that time.

These results are in keeping with previous reports showing that perception of asthma symptoms are quite variable from one subject to another and cannot be predicted from subjects' characteristics. The determinants of this variability are still to be explored. Previous studies have shown that among those factors which can affect perception of dyspnea related to bronchoconstriction are changes in lung volumes, speed of bronchoconstriction, anxiety level, duration of asthma, and age. We previously have shown that perception of acute bronchoconstriction was similar for a given fall in expiratory flows, whatever the type of stimulus, either natural, such as exercise or antigenic, or chemical, such as that induced by histamine/methacholine, but mainly related to the speed of increase in airway obstruction.

We found that perception of bronchoconstriction tends to increase with age but that this reflected the fact that some subjects, mainly older patients, often scored >0 while there was still no significant decrease in expiratory flows. In fact, if these subjects are excluded from the analysis, the perception of bronchoconstriction had no tendency to change with age. This last observation is different from the findings of Connolly et al who showed that compared to 33 young asthmatic or normal subjects, 34 elderly subjects were less aware of bronchoconstriction.

Different factors may explain those discrepancies, such as the fact that they were or were not naive subjects on their first provocation test, duration, severity or stability of asthma, anxiety levels, and other factors such as the type of sensations described (discomfort, chest tightness, breathlessness, or overall sensation), the perception scale, or method of measurement of perception (perception at 20 percent fall
in expiratory flows or at maximal bronchoconstriction).

In many studies, perception of bronchoconstriction-related symptoms is recorded immediately after challenge. We found, however, that at this particular time, there is usually a rapid reduction in perception, possibly from temporal adaptation.\textsuperscript{12} It may explain some discrepancies between these scores and those recorded during the bronchoconstriction phase.

Brand et al\textsuperscript{13} showed that subjects with asymptomatic airway hyperresponsiveness have variable airflow obstruction but are less likely to show an increase in Borg score during histamine challenge than symptomatic individuals. In this last study, an increase in perception score was related to younger age, more severe airflow hyperresponsiveness, atopy, and female sex. The presence of prechallenge dyspnea was associated with increased airway responsiveness and smoking.

It should also be stressed that whatever the age or subject's characteristics, we cannot predict perception of asthma symptoms. Perception scoring during bronchial challenges may then add useful information on how a particular subject will perceive acute asthma symptoms. This may help to detect poor perceivers who may be at risk of severe worsening of asthma, as they may not perceive the loss of control of their asthma early enough to modify their anti-inflammatory therapy according to an action plan. This type of subject may, more than others, require regular measurement of peak expiratory flow rates to detect any significant increase in airflow obstruction which will indicate the need to modify the treatment and/or look for triggering factors in the environment. Determination of PS20 may help to determine if difficulties in asthma control, particularly in those who had severe asthma attacks in the past, could be related to poor perception of fall in expiratory flows. Correlation between day-to-day recording of asthma symptoms and PS20 remains, however, to be further documented.

In conclusion, we found that perception of induced-bronchoconstriction in a population of hyperreactive subjects shows a normal distribution pattern, that response to saline inhalation influences perception scores and explains why perception scores increased with age in our study. We found no differences between hypoperceivers or hyperperceivers of bronchoconstriction for age, sex, and the baseline level of airway obstruction or responsiveness. We propose to add PS20 determination to bronchial challenges to evaluate perception of bronchoconstriction.

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