

## Poor perception of dyspnea following methacholine challenge test in patients with asthma\*

Baixo grau de percepção da dispneia após teste de broncoprovocação induzida por metacolina em pacientes com asma

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### Abstract

**Objective:** To determine the proportion of asthma patients with a poor perception of dyspnea, correlating the level of that perception with the severity of acute bronchoconstriction, bronchial hyperresponsiveness, use of maintenance medication, and asthma control. **Methods:** Uncontrolled clinical trial involving asthma patients treated at the Pulmonology Outpatient Clinic of the São Lucas Hospital, in Porto Alegre, Brazil. Methacholine challenge testing was performed using a five-breath dosimeter protocol. The perception of dyspnea after each breath was determined using the Borg scale. Data concerning asthma control, medication in use, and use of rescue short-acting bronchodilators were recorded. **Results:** Of the 65 patients included in the study, 53 completed the evaluation. Of those, 32 (60.5%) showed adequate perception of dyspnea after the methacholine challenge test, whereas 21 (39.5%) did not perceive any changes in the degree of dyspnea even after a 20% fall in FEV<sub>1</sub>. There were no significant differences between the two groups regarding baseline FEV<sub>1</sub>, percentage fall in FEV<sub>1</sub>, and the dose of methacholine causing a 20% fall in FEV<sub>1</sub>. The perception of dyspnea was not significantly associated with age ( $p = 0.247$ ); gender ( $p = 0.329$ ); use of maintenance medication ( $p = 0.152$ ); asthma control ( $p = 0.562$ ), bronchial hyperresponsiveness ( $p = 0.082$ ); or severity of acute bronchoconstriction ( $p = 0.749$ ). **Conclusions:** A significant proportion of asthma patients have a poor perception of dyspnea. The factors related to the inability of these patients to identify changes in pulmonary function have not yet been well defined. In order to reduce asthma-related morbidity and mortality, it is essential that this group of patients be identified and counseled.

**Keywords:** Asthma; Dyspnea; Airway obstruction.

### Resumo

**Objetivo:** Determinar o percentual de asmáticos com má percepção da dispneia, correlacionando-a com gravidade da broncoconstrição aguda, hiper-responsividade brônquica, uso de medicação de manutenção e controle da asma. **Métodos:** Ensaio clínico não controlado com pacientes asmáticos do Ambulatório de Pneumologia do Hospital São Lucas em Porto Alegre (RS). Foram realizados testes de broncoprovocação com metacolina com protocolo dosimetrado em cinco doses, e foi avaliada a percepção da dispneia após cada dose administrada, utilizando a escala de Borg. Dados sobre controle da asma, medicação em uso e uso de broncodilatador de curta ação de resgate foram coletados. **Resultados:** Dos 65 pacientes incluídos, 53 completaram a avaliação. Desses, 32 (60,5%) apresentaram percepção adequada da dispneia após o teste de broncoprovocação com metacolina, ao passo que 21 (39,5%) não perceberam nenhuma alteração no grau de dispneia mesmo após uma queda de 20% em VEF<sub>1</sub>. Não houve diferenças significativas entre os dois grupos em relação a VEF<sub>1</sub> basal, percentagem de queda do VEF<sub>1</sub> e dose de metacolina causadora de queda de 20% do VEF<sub>1</sub>. Não houve correlação significativa entre percepção da dispneia e idade ( $p = 0,247$ ), sexo ( $p = 0,329$ ), uso de medicação de manutenção ( $p = 0,152$ ), controle da asma ( $p = 0,562$ ), hiper-responsividade brônquica ( $p = 0,082$ ) e gravidade da broncoconstrição aguda ( $p = 0,749$ ). **Conclusões:** Uma percentagem significativa dos asmáticos apresenta baixo grau de percepção da dispneia. Os fatores relacionados com a incapacidade de identificação da modificação da função pulmonar não estão bem definidos. A identificação e a orientação desse grupo de pacientes são fundamentais para a redução de morbidade e mortalidade por asma.

**Descritores:** Asma; Dispneia; Obstrução das vias respiratórias.

\* Study carried out at the *Pontifícia Universidade Católica do Rio Grande do Sul* – PUCRS, Pontifical Catholic University of Rio Grande do Sul – São Lucas Hospital, Porto Alegre, Brazil.

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## Introduction

Many asthma patients have a poor perception of airway obstruction. Studies have found that the proportion of such patients ranges from 15% to 60%.<sup>(1-3)</sup> A study conducted in the state of Bahia, Brazil, found that 51% of the patients with moderate to severe asthma had a poor perception of dyspnea.<sup>(4)</sup>

Limited patient ability to identify the degree of airway obstruction is a risk factor for asthma-related mortality. A previous study found that, in addition to the risk of death, poor perception of bronchoconstriction increases the risk of emergency room visits, hospitalizations, and near-fatal attacks.<sup>(5)</sup>

Although not yet fully defined, the pathophysiological mechanisms of bronchial obstruction and the factors influencing its perception have been correlated with airway inflammation, gender, age, and use of maintenance medication, especially inhaled corticosteroids. However, the results obtained to date are conflicting, precluding definitive conclusions.

Treatment adherence and asthma control can be influenced by failure to recognize bronchoconstriction.<sup>(6,7)</sup> Therefore, poor patient perception of dyspnea has significant implications for asthma-related morbidity and mortality. In order to reduce the risk of death and other complications from asthma, it is essential that patients with a poor perception of dyspnea be identified.

The objective of this study was to assess perception of dyspnea in asthma patients and to determine whether the perception of dyspnea correlates with the severity of acute bronchoconstriction, bronchial hyperresponsiveness, use of maintenance medication, and asthma control.

## Methods

This was an uncontrolled clinical trial involving asthma patients treated between January and December of 2007 at the Pulmonology Outpatient Clinic of the São Lucas Hospital of the *Pontifícia Universidade Católica do Rio Grande do Sul* (PUCRS, Pontifical Catholic University of Rio Grande do Sul), located in the city of Porto Alegre, Brazil. The study was

approved by Research Ethics Committee of the PUCRS São Lucas Hospital.

Asthma severity and asthma control were classified in accordance with the IV Brazilian Consensus on Asthma Management.<sup>(8)</sup> Gender, age, and body mass index were recorded, and all patients were asked whether they used maintenance medication to treat asthma and whether they needed to use short-acting bronchodilators as rescue medication. Patients who had had a stroke or an acute myocardial infarction in the last three months were excluded, as were those with aortic aneurysm, those with systolic blood pressure > 200 mmHg or diastolic blood pressure > 100 mmHg, those who were unable to perform the maneuvers involved in the spirometric measurements, and those who were using cholinesterase inhibitors, as well as pregnant women and women in the puerperium. None of the patients had a history of smoking.

All patients gave written informed consent, after which they were asked to report to the pulmonary function laboratory, where methacholine challenge testing was performed. A Koko spirometer (PDS Instrumentation Inc., Louisville, CO, USA) was used in order to carry out a five-breath dosimeter protocol, in accordance with the recommendations of the American Thoracic Society and the Brazilian Thoracic Association.<sup>(9,10)</sup> The Borg scale was applied in order to determine patient perception of the symptom of dyspnea. If baseline FEV<sub>1</sub> was < 60% of predicted, the challenge test was not performed. After each dose of methacholine and immediately after pulmonary function measurement, the Borg scale was again applied. After methacholine challenge, inhaled albuterol (400 µg) was administered. The patients were allowed to leave only when FEV<sub>1</sub> had returned to the baseline value.

Using the correlations between the Borg scale scores and the fall in FEV<sub>1</sub>, we divided the patients into two groups: adequate perception and poor perception. We attempted to determine whether the perception of dyspnea correlated with the severity of acute bronchoconstriction, the severity of bronchial hyperresponsiveness, use of maintenance medication, and asthma control.

Descriptive analysis was performed for all data. The unpaired chi-square test was used for categorical variables, and the unpaired Student's

t-test was used for continuous variables. Spearman's correlation coefficient was used to determine the correlation between dyspnea perception (Borg scale) and percentage fall in FEV<sub>1</sub> after methacholine challenge.

### Results

The initial sample comprised 65 asthma patients treated at the pulmonology outpatient clinic (Figure 1). Of those, 12 were excluded: 8 for having a baseline FEV<sub>1</sub> < 60% of predicted and 4 for declining to participate in the subsequent assessment.

The population analyzed comprised patients with predominantly mild asthma and normal baseline pulmonary function. There were no statistical differences between the two groups in terms of demographic or clinical characteristics (Table 1).

As shown in Table 1, the perception of dyspnea did not correlate significantly with age (p = 0.247); gender (p = 0.329); use of

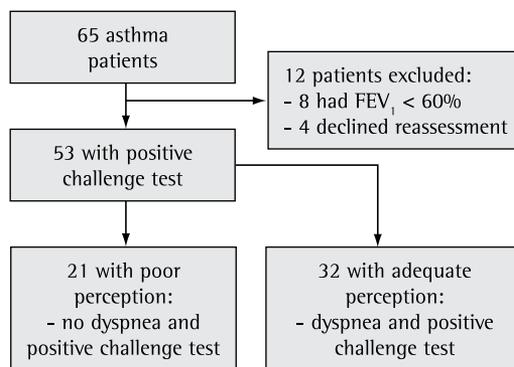


Figure 1 - Study algorithm.

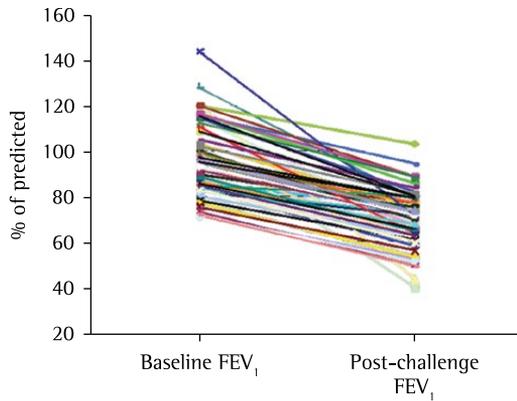
maintenance medication (p = 0.152); asthma control (p = 0.562); severity of bronchial hyperresponsiveness (p = 0.082); or severity of acute bronchoconstriction (p = 0.749).

All 53 patients who remained in the study tested positive on the methacholine challenge test (Figure 2). Of those 53 patients, 32 (60.5%) reported dyspnea after methacholine challenge.

Table 1 - Demographic and clinical characteristics of the group of patients with adequate perception of dyspnea and the group of patients with poor perception of dyspnea.<sup>a</sup>

Characteristic	Perception of dyspnea		p
	Adequate (n = 32)	Poor (n = 21)	
Age, years	40.9 ± 13.5	37.0 ± 14.1	0.247
Male/female gender, n/n	11/21	9/12	0.329
BMI, kg/m <sup>2</sup>	28.7 ± 7	26.1 ± 4.6	0.451
Type of asthma, n (%)			0.681
Mild intermittent	20 (62.5)	11 (52.4)	
Mild persistent	6 (18.8)	6 (28.5)	
Moderate persistent	5 (15.6)	4 (19.1)	
Severe persistent	1 (3.1)	0 (0.0)	
Medication in use, n (%)			0.152
β <sub>2</sub> agonist alone	24 (75.0)	13 (61.9)	
Inhaled corticosteroid	4 (12.5)	7 (33.3)	
Inhaled corticosteroid + long-acting β <sub>2</sub> agonist	4 (12.5)	1 (4.8)	
Asthma control, n (%)			0.562
Good	26 (81.2)	13 (61.9)	
Partial	3 (9.4)	8 (38.1)	
None (uncontrolled)	3 (9.4)	0 (0.0)	
Baseline FEV <sub>1</sub> , mL	2.86 ± 0.88	3.14 ± 0.88	0.680
Baseline FEV <sub>1</sub> , % of predicted	96.7 ± 15.7	96.3 ± 17.1	0.887
Post-challenge FEV <sub>1</sub> , mL	2.14 ± 0.83	2.38 ± 0.73	0.427
Post-challenge FEV <sub>1</sub> , % of predicted	70.2 ± 14.4	70.6 ± 9.7	0.173
Post-bronchodilator FEV <sub>1</sub> , mL	2.86 ± 0.87	3.07 ± 0.82	0.476
Post-bronchodilator FEV <sub>1</sub> , % of predicted	96.8 ± 12.7	91.6 ± 10.3	0.615
Dose of methacholine causing a ≥ 20% fall in FEV <sub>1</sub>	3.63 ± 4.7	4.32 ± 4.86	0.082
Percentage fall in FEV <sub>1</sub>	25.5 ± 10.2	24.1 ± 5.8	0.749

BMI: body mass index. <sup>a</sup>Results expressed as mean ± SD, except where otherwise indicated.

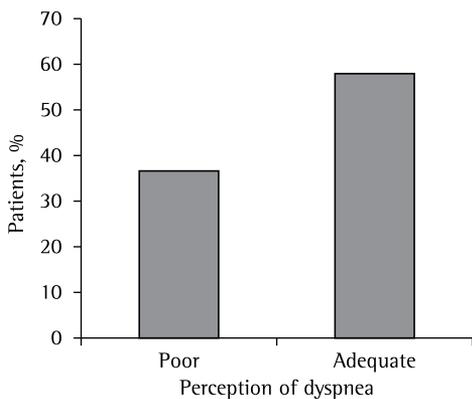


**Figure 2** - Baseline FEV<sub>1</sub> (% of predicted) and FEV<sub>1</sub> after methacholine challenge (% of predicted) for all of the patients evaluated.

However, 21 (39.5%) did not perceive any changes in the degree of dyspnea even after a 20% fall in FEV<sub>1</sub> (Figure 3).

In the group of patients with poor perception, the percentage reduction in FEV<sub>1</sub> had no impact on the perceived degree of dyspnea, as determined by the Borg scale. However, in the group of patients with adequate perception, the percentage fall in FEV<sub>1</sub> was accompanied by an increase in the perception of dyspnea on the Borg scale (Figure 4).

The mean baseline FEV<sub>1</sub> in the group of patients with adequate perception and in the group of patients with poor perception was 2.86 ± 0.88 L (96.7 ± 15.7%) and 3.14 ± 0.88 L (96.3 ± 17.1%), respectively. The mean fall in FEV<sub>1</sub> after methacholine challenge in those two groups, respectively, was 25.5 ± 10.2% and 24.1 ± 5.8%, whereas the dose of methacholine



**Figure 3** - Proportion of asthma patients with poor or adequate perception of dyspnea.

causing a 20% fall in FEV<sub>1</sub>, respectively, was 3.63 ± 4.70 mg/mL and 4.32 ± 4.86 mg/mL.

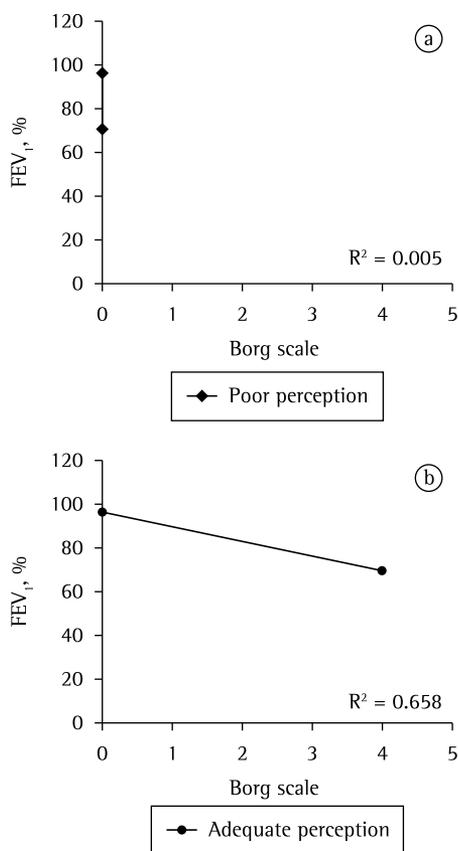
## Discussion

Asthma patients often have difficulty in recognizing their own degree of airway obstruction. In our study, 39% of the patients did not notice the fall in FEV<sub>1</sub> after the methacholine challenge test. This finding supports data in the literature, revealing the importance of this assessment for the detection of groups that are more susceptible to severe asthma-related complications. The proportion of patients with poor perception varies from study to study. However, in all studies, the number is high. One group of authors,<sup>(4)</sup> analyzing patients with moderate to severe asthma, correlated dyspnea with FEV<sub>1</sub>, with the use of a visual analog scale, and found that 51% of the patients had poor perception.

The two groups assessed were similar regarding mean baseline FEV<sub>1</sub>, the severity of acute bronchoconstriction, and the provocative dose of methacholine. Therefore, the inability to recognize changes in pulmonary function does not depend on the baseline FEV<sub>1</sub> value or its percentage fall. This phenomenon involves other factors that might explain the poor perception of bronchoconstriction. However, those factors have yet to be fully defined. Although many studies have attempted to describe these associations, further investigations are needed in order to clarify them. In order to monitor patients with an inadequate perception of dyspnea more objectively, it is essential that the causes of poor perception be identified. That will have a positive impact on the early diagnosis of severe airway obstruction and its complications, including death from asthma.

Chief among the factors that have been studied in attempts to explain this phenomenon are gender, hyperresponsiveness, use of maintenance medication, asthma control, and treatment adherence.

We found no significant correlation between gender and the perception of dyspnea. Data in the literature are conflicting. Some authors have found that women have a higher perception of dyspnea and more often use short-acting bronchodilators than do men.<sup>(11-13)</sup> Others, however, have found no such association.<sup>(3)</sup>



**Figure 4** - Correlation between mean FEV<sub>1</sub> (in %), prior to and after the challenge test, and mean Borg scale scores in the group of patients with adequate perception of dyspnea (a) and in the group of patients with poor perception of dyspnea (b).

In this study, we found no association between perception of bronchoconstriction and the severity of bronchial hyperresponsiveness. It has been demonstrated that a poor perception of bronchoconstriction is associated with bronchial hyperresponsiveness, suggesting that patients develop a mechanism of tolerance, a theory also supported by another group of authors.<sup>(3,14)</sup>

The use of inhaled corticosteroids as maintenance medication has been related to the perception of bronchoconstriction. Our study found no such association, possibly due to the fact that only a small number of patients used inhaled corticosteroids, alone or in combination with a long-acting bronchodilator. In a recent review of the influence of inhaled corticosteroids on the perception of dyspnea in asthma patients, the results were controversial, that is, some studies found that the use of medication changes the perception of the symptom, whereas others

found no such association. Therefore, to date, there is no definitive conclusion.<sup>(15)</sup>

Treatment adherence and asthma control can be influenced by poor perception of bronchoconstriction. Patient ability to identify asthma control has a direct impact on the management of the disease by the physician, who makes decisions regarding treatment primarily on the basis of the symptoms reported. A study conducted under the auspices of the Bahia State Asthma and Allergic Rhinitis Control Program found that the degree of concordance between physicians and patients regarding the perception of asthma control is low. In that study, 23% of the patients had an inadequate perception of asthma control. Of those, most were elderly, had a low family income, and had less severe asthma.<sup>(7)</sup> Our data revealed no correlation between asthma control and the perception of dyspnea. There was, however, a tendency toward a lower proportion of patients with controlled asthma in the group of patients with poor perception, suggesting that poor perception of airway obstruction influences asthma control. Nevertheless, it is unknown whether this is a consequence or a cause of the poor perception.

In our study, 81% of the patients had mild intermittent or mild persistent asthma, and the mean baseline FEV<sub>1</sub> was, respectively, 96.7% and 96.3% in the group of patients with adequate perception and in the group of patients with poor perception. It is noteworthy that, even in the population analyzed, a significant proportion of individuals had a poor perception of dyspnea. Obviously, our results cannot be extrapolated to the population of asthma patients as a whole. However, findings of previous studies emphasize that poor perception of dyspnea occurs in patients with normal or abnormal baseline pulmonary function.

The authors of one study found that, in a population of patients with mild asthma and normal pulmonary function, 23% had a poor perception of dyspnea.<sup>(16)</sup> Another group of authors, correlating the histamine challenge test results with those obtained on a visual analog scale, found poor perception of dyspnea in asthma patients with normal baseline FEV<sub>1</sub> values (mean, 86% of predicted). However, when the patients were stratified by FEV<sub>1</sub>, the authors observed, by means of multiple regression analysis, that low baseline FEV<sub>1</sub> was associated with poorer perception of dyspnea.<sup>(3)</sup> Another

study showed that asthma patients treated with inhaled corticosteroids for eight weeks showed an improvement in the perception of dyspnea if there was a significant increase in FEV<sub>1</sub>.<sup>(2)</sup> Therefore, regarding patients with mean baseline FEV<sub>1</sub> within the predicted range, our findings are in agreement with previous findings.

In summary, patients with a poor perception of dyspnea can be oligosymptomatic and be unable to assess the severity of bronchial obstruction, reporting symptoms only when their respiratory reserve has been depleted. Therefore, in order to reduce the risk of complications related to poor asthma control, it is essential that these patients be identified. Clinical evaluation alone is insufficient to determine the severity of airway obstruction with precision. Therefore, these patients need an objective measure of pulmonary function and medical advice for an effective monitoring and early intervention strategy aimed at preventing severe complications or death from asthma.

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