

ORIGINAL ARTICLE

Performance of a word labeled visual analog scale in determining the degree of dyspnea during exercise-induced bronchoconstriction in children and adolescents with asthma*, **

Desempenho de uma escala analógica visual legendada na determinação do grau de dispnéia durante teste de broncoespasmo induzido por exercício em crianças e adolescentes asmáticos

Patrícia Bueno Lima, Ilka Lopes Santoro, Lilian Ballini Caetano, Anna Lúcia de Barros Cabral, Ana Luisa Godoy Fernandes

Abstract

Objective: There is an indirect relationship between airway obstruction in asthma and the intensity of breathlessness (dyspnea). A word labeled visual analog dyspnea scale with a 0-3 score has been widely used for the assessment of the degree of bronchoconstriction, although the perception of such obstruction varies considerably. The objective of this study was to determine whether children and adolescents are able to perceive acute exercise-induced bronchoconstriction (EIB), as well as to measure the discriminatory power of a word labeled visual analog dyspnea scale in relation to the intensity of the EIB. **Methods:** A cross-sectional study involving 134 children and adolescents with asthma and submitted to a six-minute steady-state exercise test on a cycle ergometer. The intensity of dyspnea was determined using a word labeled visual analog dyspnea scale prior to each determination of FEV₁. The scale is scored from 0 to 3, with a logical sequence of pictures, ranging from “no symptoms” to “severe dyspnea”. Variables were determined at baseline, as well as at 5, 10, and 20 min after the exercise test. The accuracy of the dyspnea scale in identifying the degree of EIB was determined by means of ROC curves for the post-exercise fall in FEV₁, using cut-off points of 10%, 20%, 30%, and 40%. **Results:** Of the patients selected, 111 finished the study, and 52 (46.8%) presented with EIB. The area under the ROC curve increased in direct proportion to increases in the degree of bronchoconstriction. **Conclusions:** Among children and adolescents with asthma, the accuracy of this dyspnea scale improves as the post-exercise percentage fall in FEV₁ increases. However, the predictive value of the scale is suboptimal when the percentage fall in FEV₁ is lower.

Keywords: Asthma; Asthma, exercise-induced; Dyspnea.

Resumo

Objetivo: Existe uma relação indireta entre a obstrução das vias aéreas em asma e a intensidade de falta de ar (dispnéia). Uma escala visual analógica legendada de dispnéia com escore de 0-3 pontos tem sido amplamente utilizada na avaliação da broncoconstrição, embora a percepção de tal obstrução seja muito variável. O objetivo deste estudo foi determinar se crianças e adolescentes são capazes de perceber a broncoconstrição aguda induzida por exercício (BAIE), bem como medir o poder discriminatório de uma escala visual analógica legendada de dispnéia em relação à intensidade de BAIE. **Métodos:** Estudo transversal com 134 crianças e adolescentes asmáticos que foram submetidos a um teste de broncoespasmo induzido por seis minutos de exercício em um cicloergômetro. A intensidade da dispnéia foi determinada utilizando-se uma escala visual analógica legendada de dispnéia antes de cada determinação de VEF₁. A escala tem um escore de 0-3 pontos, com desenhos em uma sequência lógica variando entre “sem sintomas” e “dispnéia grave”. As variáveis foram determinadas no momento basal, assim como em 5, 10 e 20 minutos após o término do teste de exercício. A acurácia da escala de dispnéia em detectar o grau de BAIE foi determinada através de curvas ROC para a queda de VEF₁ após o exercício, usando pontos de corte de 10%, 20%, 30% e 40%. **Resultados:** Dos pacientes selecionados, 111 completaram o estudo, e 52 (46,8%) apresentaram BAIE. A área sob a curva ROC progressivamente aumentou com o aumento do grau de broncoconstrição. **Conclusões:** Em crianças e adolescentes asmáticos, a acurácia desta escala de dispnéia melhora com o aumento do percentual de queda em VEF₁ após o exercício. Entretanto, o valor preditivo da escala é subótimo quando a porcentagem de queda em VEF₁ é menor.

Descritores: Asma; Asma induzida por exercício; Dispnéia.

* Study carried out in the Department of Internal Medicine, Division of Pulmonology, Federal University of São Paulo, São Paulo, Brazil. Correspondence to: Ana Luisa Godoy Fernandes. Disciplina de Pneumologia, Rua Botucatu, 740, 3º andar, CEP 04023-004, São Paulo, SP, Brasil.

Tel 55 11 5549-1830. Fax: 55 11 5904-2897. E-mail: analuisa@pneumo.epm.br

Financial support: Patrícia Bueno Lima is the recipient of a fellowship from the *Coordenação de Aperfeiçoamento de Pessoal de Nível Superior* (CAPES, Coordination of the Advancement of Higher Education).

Submitted: 7 August 2009. Accepted, after review: 29 April 2010.

** A versão completa em português deste artigo está disponível em www.jornaldepneumologia.com.br

Introduction

Asthma is the most common chronic disease of childhood, with a prevalence of up to 25% among children and adolescents in Latin America.⁽¹⁻³⁾ Patients with asthma show considerable variation in their perception of breathlessness (dyspnea).⁽⁴⁻⁶⁾ When individuals with asthma experience dyspnea, the intensity of the symptoms does not correlate with the degree of airway obstruction observed by spirometry.⁽⁷⁾ Although patients with stable asthma always recognize an increase in the degree of dyspnea due to induced bronchospasm, there is a wide range in the magnitude of dyspnea perception for the same value of FEV₁.^(7,8) It has been suggested that this variability is attributable to certain pathophysiological and psychological factors.⁽⁹⁾

To determine the level of dyspnea perception, various types of scales have been devised, including visual analog scales, verbal category scales, and hybrid scales. Each has specific advantages and limitations. Word labeled visual analog scales have been developed for the study of pain, and they are currently being applied to measure the degree of dyspnea.^(10,11) Meaningful “guide words” help make the use of the scale consistent.⁽¹¹⁾

The objective of this study was to determine whether children and adolescents with asthma are able to perceive acute exercise-induced bronchoconstriction (EIB), as measured by a word labeled visual analog dyspnea scale. An additional objective was to assess the discriminatory power of this scale for the degree of bronchoconstriction. Our hypothesis was that there is an indirect relationship between airway obstruction in asthma and the intensity of dyspnea.

Methods

In this study, we evaluated children and adolescents (7-16 years of age), recruited from among those under regular treatment at the Asthma Outpatient Clinic of the Darcy Vargas Hospital, located in the city of São Paulo, Brazil. The institutional review board of the hospital approved the study, and the parents or legal guardians of all participants gave written informed consent.

Participants were considered to have “diagnosed asthma” if their parents or legal guardians reported that the child or adolescent had physician-diagnosed asthma. In accordance with the recommendations of the Global Initiative for Asthma (GINA),⁽¹²⁾ the patients were classified as having intermittent asthma, mild persistent asthma, moderate persistent asthma, or severe persistent asthma.⁽¹²⁾ The patients were under regular treatment in accordance with the GINA recommendations for each presentation of the disease: a prescribed-as-needed β_2 agonist for patients with intermittent asthma; low doses of an inhaled corticosteroid for those with mild persistent asthma; the combination of a long-acting β_2 agonist and low doses of an inhaled corticosteroid for those with moderate persistent asthma; and the combination of a long-acting β_2 agonist and high doses of an inhaled corticosteroid, with or without a systemic steroid, for those with severe persistent asthma. All of the patients were instructed in how to complete a symptoms diary card and the dyspnea scale described below. Asthma was considered controlled when the patient had daytime symptoms ≤ 2 times a week, no nocturnal symptoms/awakenings, need for relief/rescue medication ≤ 2 times a week, no limitations of activities of daily living, and no exacerbations in the last month.⁽¹²⁾ An EIB test was defined as positive if there was a fall in FEV₁ $\geq 10\%$ in relation to the baseline value.⁽¹³⁾

Forced spirometry was carried out with a Koko spirometer (PDS Instrumentation Inc., Louisville, CO, USA), in accordance with standard procedures.⁽¹⁴⁾

A six-minute steady-state exercise test was carried out with a cycle ergometer at 80% of the maximum HR of the patients, as previously determined during the clinical examination.⁽¹⁵⁾ We measured FEV₁ at baseline, as well as at 5, 10, and 20 min after the end of the test. The change in FEV₁ was expressed as the percentage fall in relation to the baseline value. The test was interrupted if any of the following occurred: inability to maintain the pedaling frequency; leg discomfort; or dyspnea.

The intensity of dyspnea was assessed prior to each measurement of FEV₁ using a word labeled visual analog dyspnea scale with a score of 0, 1, 2, or 3 points. As can be seen in Figure 1, the scale displays a series of pictures, in

a logical sequence, in which the picture of a boy doing exercise, at one end of the scale, means “no symptoms” (0 points), and the picture of the same boy sitting down, at the opposite end of the scale, means “severe dyspnea” (3 points).

After the participants had undergone baseline spirometry, each was submitted to a six-minute exercise test, which was carried out in a temperature- and humidity-controlled laboratory ($22 \pm 2^\circ\text{C}$ and $40 \pm 10\%$, respectively). All tests were conducted in the morning, between 8:00 and 9:00 a.m.

Assuming that 35% of the participants testing negative for EIB would report any degree of dyspnea (a score of 1, 2, or 3), each study arm should include 48 participants in order to provide a statistical power of 80% for the detection of an additional 30% difference in the degree of dyspnea.

Data are expressed as means and standard deviations or as percentages. The Kolmogorov-Smirnov test was used in order to test the normality of the continuous variables. The comparison between patients with and without EIB was performed using the chi-square test for categorical variables and the Student's t-test for continuous variables. The interindividual variability in FEV_1 (absolute and predicted values), the percentage fall in FEV_1 , and the number of participants testing positive for EIB, all of which related to the severity of the disease, were assessed using ANOVA and Tukey's post hoc test. The discriminatory power of the word labeled visual analog scale—absence of dyspnea (0) vs. presence of dyspnea (score of 1, 2, or 3)—in identifying the degree of the obstructive condition—measured by the proportional fall in FEV_1 (cut-off points of 10%, 20%, 30%, and 40%)—was determined with ROC curves. The level of significance was set at $p < 0.05$.

Results

Of the 134 eligible participants, 23 were excluded: 14 because there were missing data; 4 because they were unable to complete the six-minute exercise test; and 5 because they did not meet the technical criteria. Therefore, 111 patients completed the study. Of those, 52 (47%) tested positive for EIB. The mean age of the participants was 10.3 ± 2.2 years, and the majority were male. Most had either moderate persistent asthma or severe persistent asthma

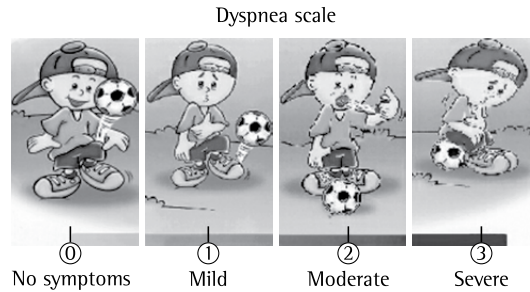


Figure 1 – Word labeled visual analog dyspnea scale, scored from 0 to 3.

(Table 1). None were regularly engaged in physical exercise.

The participants with EIB differed from those without regarding the presentation of asthma and baseline FEV_1 . The Kolmogorov-Smirnov test showed that the numerical variables had a normal distribution, allowing the use of parametric tests (Table 2): for age (Z score = 1.28; $p = 0.07$); for FVC in L (Z score = 0.94; $p = 0.35$); for FEV_1 in L (Z score = 1.25; $p = 0.08$); and for the FEV_1/FVC ratio (Z score = 0.70; $p = 0.71$).

We found a significant, inverse association between the presentation of asthma and the baseline FEV_1 , in L and in percentage of the predicted value. The percentage fall in FEV_1 in relation to the baseline value was significantly greater among the patients with severe persistent asthma or moderate persistent asthma than among those with other presentations ($p < 0.001$; Table 3).

The ROC curves showed the accuracy of the visual analog dyspnea scale in identifying the degree of EIB (fall in FEV_1), using the cut-off

Table 1 – Characteristics of the 111 children and adolescents studied.

Variable	Result ^a
Age, years	10.3 ± 2.2
Male, n (%)	62 (55.9)
Weight, kg	40.4 ± 9.8
Height, cm	146.8 ± 10.3
Body mass index, kg/m^2	18.7 ± 0.4
Presentation of asthma, n (%)	
Intermittent	41 (36.9)
Mild persistent	20 (18.0)
Moderate persistent	26 (23.4)
Severe persistent	24 (21.6)

^aData presented as mean \pm SD, except where otherwise indicated.

Table 2 – Characteristics of the participants by the presence of exercised-induced bronchoconstriction.^a

Variable	EIB+	EIB–	p
	(n = 52)	(n = 59)	
Fall in FEV ₁ , %	26.7 ± 14.9	1.2 ± 7.6	
Age, years	10.6 ± 2,3	10.0 ± 2.0	0.09*
Male gender, n (%)	32 (61.5)	30 (50.0)	0.26**
Presentation of asthma, n (%)			
Intermittent	11 (21.2)	30 (50.8)	< 0.001**
Mild persistent	6 (11.5)	14 (23.7)	
Moderate persistent	20 (38.5)	6 (10.2)	
Severe persistent	15 (28.8)	9 (15.3)	
FVC, L	2.68 ± 0.74	2.46 ± 0.73	0.12*
FEV ₁ , L	1.96 ± 0.57	2.03 ± 0.66	0.51*
FEV ₁ /FVC	0.74 ± 0.11	0.83 ± 0.09	< 0.001*

EIB: exercise-induced bronchoconstriction. ^aData presented as mean ± SD, except where otherwise indicated. *Student's t test. **Chi-square test.

points of 10%, 20%, 30%, and 40%. The area under the curve (AUC) showed a positive association with the degree of EIB (Figure 2). The AUC peaked (at 0.69) only when the 40% fall in FEV₁ cut-off point was applied.

Regardless of the cut-off point applied, the sensitivity and specificity of the dyspnea scale, in relation to the percentage fall in FEV₁, remained constant (55-58% and 52-58%, respectively).

Discussion

Among the children and adolescents with asthma evaluated in the present study, the accuracy of the dyspnea scale increased in direct proportion to the degree of decrease in FEV₁ during exercise. However, the predictive value of the dyspnea scale was suboptimal, especially when it was applied to the participants with lower percentage falls in FEV₁.

Variations in the level of perception of dyspnea, represented by the scores 1, 2, and 3 on the word labeled visual analog dyspnea scale,

might be attributable to differences in the type of airway constriction during exercise. As an initial response, large and small airways both become constricted during exercise,⁽¹⁶⁾ and this early response usually occurs in the morning hours.^(6,17)

Patients with asthma can have a diminished perception of dyspnea during EIB. This phenomenon might be associated with reduced chemosensitivity⁽¹⁸⁾ or with low baseline FEV₁ and high bronchial responsiveness.^(19,20) However, the Dalhousie Dyspnea Scales (pictorial scales for measuring dyspnea) have been described as constituting a useful and accurate tool to measure dyspnea during histamine bronchoconstriction challenge in children.⁽²¹⁾

In obese individuals, dyspnea is a common complaint. In one study,⁽²²⁾ obese individuals showed a pronounced reduction in expiratory reserve volume and an increase in the alveolar-arterial oxygen gradient. The authors concluded that obesity itself plays a role in the genesis of

Table 3 – FEV₁ at baseline and percentage fall in FEV₁ in relation to baseline by the presentation of asthma in the children and adolescents evaluated.

Variable	Presentation of asthma				p
	Intermittent	Mild persistent	Moderate persistent	Severe persistent	
	(n = 41)	(n = 20)	(n = 26)	(n = 24)	
FEV ₁ at baseline, L	2.17 ± 0.69	2.18 ± 0.59	1.93 ± 0.39	1.64 ± 0.59	0.004*
FEV ₁ at baseline, % of predicted	96 ± 14	93 ± 13	79 ± 15	66 ± 15	< 0.001**
Fall in FEV ₁ , %	5.1 ± 8.5	10.1 ± 20.7	19.3 ± 13.1	22.7 ± 22.1	< 0.001***

ANOVA and Tukey's post hoc test. *Severe persistent < intermittent and moderate persistent. **Severe persistent < moderate persistent < intermittent and mild persistent. ***Severe persistent > moderate persistent > intermittent.

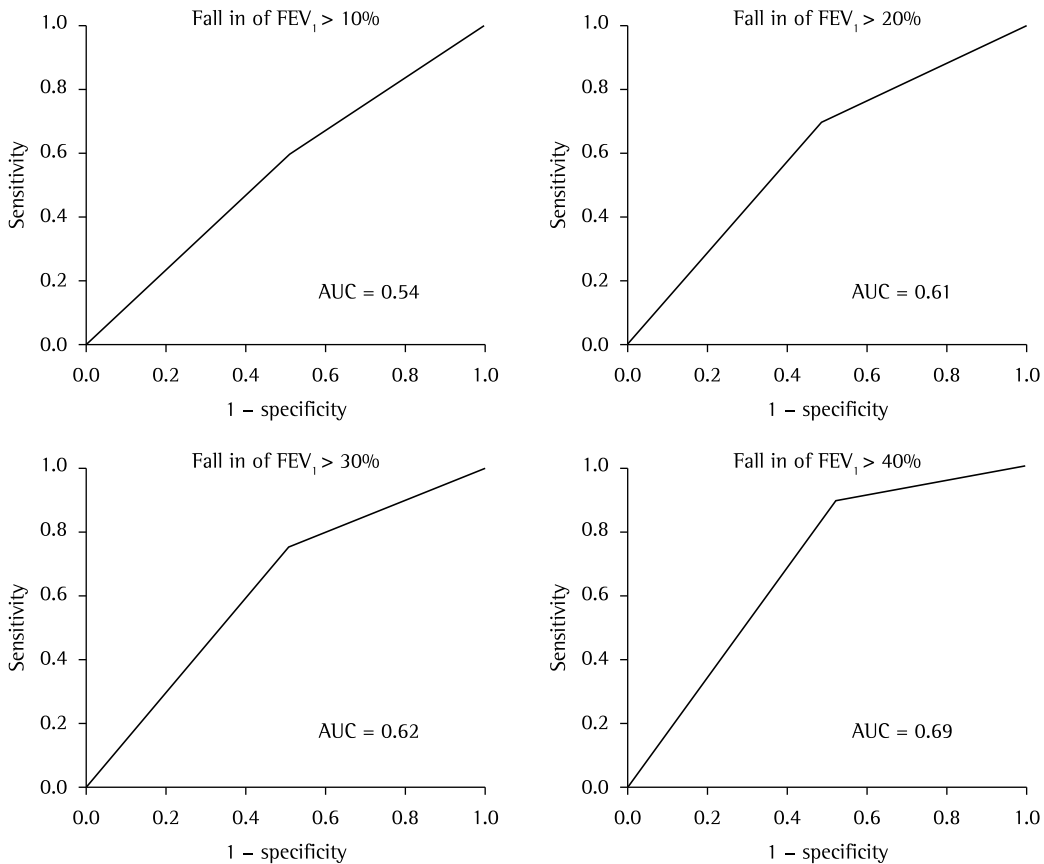


Figure 2 - ROC curves to determine the sensitivity and specificity of the word labeled visual analog dyspnea scale in identifying the degree of obstruction, as measured by the fall in FEV₁ at various cut-off points. AUC: area under the curve.

dyspnea. However, our participants were, on average, of normal weight.

Individuals with severe asthma can have an impaired perception of dyspnea, since the intrinsic positive end-expiratory pressure due to hyperinflation is one of the most important loads during exercise.⁽²³⁾ This phenomenon has also been identified during methacholine challenge testing.⁽²⁴⁾ Therefore, it is crucial to highlight that the majority of the children and adolescents in our sample had stable asthma, in which expiratory flow limitation and lung hyperinflation rarely occur.⁽²⁵⁾

The perception of dyspnea should be analyzed during asthma attacks. According to one group of authors, the Pediatric Dyspnea Scale, which is scored from 1 to 7, should be used as a tool to help guide discharge decisions.⁽²⁶⁾

All of the children and adolescents in our sample had physician-diagnosed asthma and were using anti-inflammatory agents, both of

which have been shown to have the potential to improve the perception of dyspnea,⁽²⁷⁻²⁹⁾ although we did not observe that. In addition, the dyspnea scale we employed showed constant sensitivity and specificity values for the percentage of fall in FEV₁, regardless of the cut-off point applied.

It is of note that we asked the participants to rate only the sensation of dyspnea. Various post-exercise sensations, caused by physical discomfort, might have influenced the perceived dyspnea score. In the absence of other explanations, exercise-induced dyspnea is often labeled as a manifestation of asthma; however, one group of authors reported that, during exercise, patients with exercise-induced dyspnea but without asthma coughed more and had more airway symptoms than did healthy controls, even though the spirometry values remained unchanged.⁽³⁰⁾

Another potential limitation of the word labeled visual analog dyspnea scale employed

in the present study is its tight range of possible scores, resulting in a lack of precision when compared with the Borg scale, which is a ten-point scale and therefore more accurate. In addition, the percentage fall in FEV₁ was positively associated with the presentation of the disease, which allowed the word labeled visual analog dyspnea scale to be tested in children and adolescents with different levels of impairment in FEV₁.

We found that the dyspnea scale employed in the present study had acceptable discriminatory power, which allowed us to study the association between perception of dyspnea and intensity of EIB. However, our results cannot be generalized to the day-by-day variability in bronchoconstriction seen in asthma patients.

In conclusion, the children and adolescents with asthma evaluated in our study scarcely perceived their dyspnea, as determined by a word labeled visual analog dyspnea scale, during an EIB test. It is important to focus on possible methods to improve the perception and knowledge of the symptoms of asthma in this population.

References

1. Lima RG, Pastorino AC, Casagrande RR, Sole D, Leone C, Jacob CM. Prevalence of asthma, rhinitis and eczema in 6 - 7 years old students from the western districts of São Paulo City, using the standardized questionnaire of the "International Study of Asthma and Allergies in Childhood" (ISAAC)-phase IIIB. *Clinics (Sao Paulo)*. 2007;62(3):225-34.
2. Solé D, Melo KC, Camelo-Nunes IC, Freitas LS, Britto M, Rosário NA, et al. Changes in the prevalence of asthma and allergic diseases among Brazilian schoolchildren (13-14 years old): comparison between ISAAC Phases One and Three. *J Trop Pediatr*. 2007;53(1):13-21.
3. Solé D, Wandalsen GF, Camelo-Nunes IC, Naspitz CK; ISAAC - Brazilian Group. Prevalence of symptoms of asthma, rhinitis, and atopic eczema among Brazilian children and adolescents identified by the International Study of Asthma and Allergies in Childhood (ISAAC) - Phase 3. *J Pediatr (Rio J)*. 2006;82(5):341-6.
4. McFadden ER Jr, Kiser R, DeGroot WJ. Acute bronchial asthma. Relations between clinical and physiologic manifestations. *N Engl J Med*. 1973;288(5):221-5.
5. Palmer KN, Kelman GR. Pulmonary function in asthmatic patients in remission. *Br Med J*. 1975;1(5956):485-6.
6. Turcotte H, Corbeil F, Boulet LP. Perception of breathlessness during bronchoconstriction induced by antigen, exercise, and histamine challenges. *Thorax*. 1990;45(12):914-8.
7. Lavietes MH, Ameh J, Cherniack NS. Dyspnea and symptom amplification in asthma. *Respiration*. 2008;75(2):158-62.
8. Chetta A, Gerra G, Foresi A, Zaimovic A, Del Donno M, Chittolini B, et al. Personality profiles and breathlessness perception in outpatients with different gradings of asthma. *Am J Respir Crit Care Med*. 1998;157(1):116-22.
9. Teeter JG, Bleecker ER. Relationship between airway obstruction and respiratory symptoms in adult asthmatics. *Chest*. 1998;113(2):272-7.
10. Lansing RW, Moosavi SH, Banzett RB. Measurement of dyspnea: word labeled visual analog scale vs. verbal ordinal scale. *Respir Physiol Neurobiol*. 2003;134(2):77-83.
11. Scott J, Huskisson EC. Graphic representation of pain. *Pain*. 1976;2(2):175-84.
12. Global Initiative for Asthma. Global Strategy for Asthma Management and Prevention. Bethesda: National Institutes of Health, National Heart, Lung, and Blood Institute; 2006.
13. Anderson SD, Argyros GJ, Magnussen H, Holzer K. Provocation by eucapnic voluntary hyperpnoea to identify exercise induced bronchoconstriction. *Br J Sports Med*. 2001;35(5):344-7.
14. Polgar G. Pulmonary function testing for pediatric chest diseases. *Pediatr Ann*. 1977;6(8):526-39.
15. McFadden ER Jr. Exercise-induced airway obstruction. *Clin Chest Med*. 1995;16(4):671-82.
16. Bierman CW, Spiro SG, Petheram I. Characterization of the late response in exercise-induced asthma. *J Allergy Clin Immunol*. 1984;74(5):701-6.
17. Peiffer C, Marsac J, Lockhart A. Chronobiological study of the relationship between dyspnoea and airway obstruction in symptomatic asthmatic subjects. *Clin Sci (Lond)*. 1989;77(3):237-44.
18. Kikuchi Y, Okabe S, Tamura G, Hida W, Homma M, Shirato K, et al. Chemosensitivity and perception of dyspnea in patients with a history of near-fatal asthma. *N Engl J Med*. 1994;330(19):1329-34.
19. Bijl-Hofland ID, Cloosterman SG, Folgering HT, Akkermans RP, van Schayck CP. Relation of the perception of airway obstruction to the severity of asthma. *Thorax*. 1999;54(1):15-9.
20. Catellier P, Turcotte H, Deschesnes F, Boulet LP. Changes in lung volumes and poor perception of bronchoconstriction-induced respiratory symptoms. *Ann Allergy Asthma Immunol*. 1998;81(4):315-21.
21. Pianosi P, Smith CP, Almudevar A, McGrath PJ. Dalhousie dyspnea scales: Pictorial scales to measure dyspnea during induced bronchoconstriction. *Pediatr Pulmonol*. 2006;41(12):1182-7.
22. Teixeira CA, Dos Santos JE, Silva GA, de Souza ES, Martinez JA. Prevalence of and the potential pathophysiological mechanisms involved in dyspnea in individuals with class II or III obesity. *J Bras Pneumol*. 2007;33(1):28-35.
23. Barreiro E, Gea J, Sanjuás C, Marcos R, Broquetas J, Milic-Emili J. Dyspnoea at rest and at the end of different exercises in patients with near-fatal asthma. *Eur Respir J*. 2004;24(2):219-25.
24. Loughheed MD, Fisher T, O'Donnell DE. Dynamic hyperinflation during bronchoconstriction in asthma: implications for symptom perception. *Chest*. 2006;130(4):1072-81.
25. Boczkowski J, Murciano D, Pichot MH, Ferretti A, Pariente R, Milic-Emili J. Expiratory flow limitation in

- stable asthmatic patients during resting breathing. *Am J Respir Crit Care Med.* 1997;156(3 Pt 1):752-7.
26. Khan FI, Reddy RC, Baptist AP. Pediatric Dyspnea Scale for use in hospitalized patients with asthma. *J Allergy Clin Immunol.* 2009;123(3):660-4.
27. Boulet LP, Turcotte H, Cartier A, Milot J, Côté J, Malo JL, et al. Influence of beclomethasone and salmeterol on the perception of methacholine-induced bronchoconstriction. *Chest.* 1998;114(2):373-9.
28. Boulet LP, Turcotte H. Lung hyperinflation, perception of bronchoconstriction and airway hyperresponsiveness. *Clin Invest Med.* 2007;30(1):2-11.
29. Costa Mdo R, Oliveira MA, Santoro IL, Juliano Y, Pinto JR, Fernandes AL. Educational camp for children with asthma. *J Bras Pneumol.* 2008;34(4):191-5.
30. Ternesten-Hasséus E, Johansson EL, Bende M, Millqvist E. Dyspnea from exercise in cold air is not always asthma. *J Asthma.* 2008;45(8):705-9.

About the authors

Patrícia Bueno Lima

Biologist. Department of Internal Medicine, Division of Pulmonology, Federal University of São Paulo, São Paulo, Brazil.

Ilka Lopes Santoro

Affiliate Professor. Department of Internal Medicine, Division of Pulmonology, Federal University of São Paulo, São Paulo, Brazil.

Lilian Ballini Caetano

Staff Physician. Department of Internal Medicine, Division of Pulmonology, Federal University of São Paulo, São Paulo, Brazil.

Anna Lúcia de Barros Cabral

Staff Physician. Darcy Vargas Public Hospital, São Paulo, Brazil.

Ana Luisa Godoy Fernandes

Associate Professor. Department of Internal Medicine, Division of Pulmonology, Federal University of São Paulo, São Paulo, Brazil.