

Specific Inspiratory Muscle Training in Patients With Mild Asthma With High Consumption of Inhaled β_2 -Agonists*

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Background: It has been known for many years that there are variations between asthmatic patients in terms of their perception of breathlessness during airway obstruction.

Study objective: To investigate the relationship between β_2 -agonist consumption and the score of perception of dyspnea, in mild asthmatics, and the relationship between the effect of specific inspiratory muscle training (SIMT) on the score of perception of dyspnea and β_2 -agonist consumption in "high perceivers."

Methods: Daily β_2 -agonist consumption was assessed during a 4-week run-in period in 82 patients with mild asthma. Patients with a mean β_2 -agonist consumption of > 1 puff/d ("high consumers") then were randomized into two groups: one group of patients received SIMT for 3 months; the other group of patients was assigned as a control group and received sham training. Inspiratory muscle strength and perception of dyspnea were assessed before patients entered the study, following the 4-week run-in period, and after completing the training period.

Results: Following the 4-week run-in period, 23 high-consumer patients (mean $[\pm \text{SEM}]$ β_2 -agonist consumption, 2.7 ± 0.4 puffs/d) were detected. The mean Borg score during breathing against resistance was significantly higher ($p < 0.05$) in the patients with high β_2 -agonist consumption than in the subjects with low mean β_2 -agonist consumption. Following SIMT, the mean maximal inspiratory pressure increased significantly from 94.1 ± 5.1 to 109.7 ± 5.2 cm H_2O ($p < 0.005$) in the training group. The increase in inspiratory muscle strength was associated with a statistically significant decrease in the mean Borg score during breathing against resistance ($p < 0.05$) as well as in the mean daily β_2 -agonist consumption.

Conclusions: We have shown that patients with mild asthma, who have a high β_2 -agonist consumption, have a higher perception of dyspnea than those with normal consumption. In addition, SIMT was associated with a decrease in perception of dyspnea and a decrease in β_2 -agonist consumption. (CHEST 2000; 117:722-727)

Key words: high consumption of inhaled β_2 -agonists; inspiratory muscle training; perception of dyspnea

Abbreviations: PEFR = peak expiratory flow rate; P_{max} = maximal inspiratory pressure; P_m = mouth pressure; RV = residual volume; SIMT = specific inspiratory muscle training

In the management of bronchial asthma, the subject's perception of dyspnea serves as one of the most important indexes used to guide treatment. It is well documented that in patients with asthma there is a considerable variation in the severity of breathlessness for any particular degree of airflow obstruction.¹ The factors underlying this variability are still to be explored. Previous studies have shown that among those factors that can affect the perception of dyspnea related to bronchoconstriction are changes

in lung volumes, speed of bronchoconstriction, anxiety level, duration of asthma, and age.²⁻⁵ Other influences include attitudes, expectations, and personality traits.^{6,7}

The perception of airway obstruction is blunted in many patients with asthma.^{1,4-6,8} Such a decreased perception of dyspnea may result in undertreatment of asthma, delay modification in treatment,⁹ and even may predispose patients to fatal asthma attacks.¹⁰ On the other hand, some patients who are "high perceivers" become very distressed with relatively minor changes in bronchoconstriction,¹ and may use β_2 -agonists unnecessarily.

Studies investigating dyspnea suggest that, at least in part, it is perceived by the patient as respiratory

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Manuscript received February 2, 1999; revision accepted October 21, 1999.

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muscle effort.^{11,12} In addition, a number of studies have been carried out in order to correlate dyspnea and respiratory muscle performance. It is well documented that the degree of breathlessness subjectively reported by the patients is related to the activity and strength of the inspiratory muscles.^{13,14}

In the present study, β_2 -agonist consumption was used to detect patients who are "high consumers" among patients with mild asthma. The mean score of perception of dyspnea was also high in these patients. Then the effect of specific inspiratory muscle training (SIMT) on the score of perception of dyspnea and β_2 -agonist consumption was investigated in those patients who were high perceivers.

MATERIALS AND METHODS

Eighty-two patients, 46 men and 36 women, with mild, stable asthma ($FEV_1 > 80\%$ of predicted normal values on at least two visits) attending an outpatient clinic were recruited for the study. All satisfied the American Thoracic Society definition of asthma, with symptoms of episodic wheezing, cough, and shortness of breath responding to bronchodilators and reversible airflow obstruction documented in at least one previous pulmonary function study.¹⁵ All subjects were in stable clinical condition, and their symptoms were controlled by their primary physicians with β_2 -agonists, only as required.

Study Design

All patients were studied during a 4-week run-in period and were required to be compliant with the recording of pre-bronchodilator consumption morning peak expiratory flow rates (PEFRs) and daily β_2 -agonist consumption in a diary card. The information on the diary card was verified by a respiratory therapist daily by phone and once weekly by a personal visit. Patients with recorded PEFR $< 80\%$ of their best value were excluded from the study.

After the 4-week run-in period, the study subjects were separated into two groups: one group of patients had a mean β_2 -agonist consumption of > 1 puff/d (high consumers); the other group had a mean β_2 -agonist consumption of ≤ 1 puff/d (normal consumers). The groups were defined arbitrarily before the study began. Inspiratory muscle strength and perception of dyspnea then were measured. The subjects who were high consumers comprised the study group and were randomized into two groups: one group received SIMT (group A) for 3 months; the other group was assigned to be a control group and received sham training (group B). β_2 -agonist consumption again was recorded in diary cards during the last 4 weeks of the training. Patients again were told to take β_2 -agonists only when needed and were not told that the aim of the training was to reduce β_2 -agonist consumption. Inspiratory muscle strength and perception of dyspnea then were measured once again. In all the patients, we performed several practice tests before the baseline value was recorded in order to correct possible training and learning effects. All the data were collected by the same person, who was blinded to the training group designation, as were the patients themselves, who were also blinded to the mode of treatment.

Tests

Spirometry: The FVC and the FEV_1 were measured three times on a computerized spirometer (Compact; Vitalograph;

Buckingham England), and the best trial is reported. Bronchodilators were withheld 12 h before spirometry testing.

Inspiratory Muscle Strength: Inspiratory muscle strength was assessed by measuring the maximal inspiratory pressure (P_{imax}) at residual volume (RV), as previously described by Black and Hyatt.¹⁶ The value obtained from the best of at least three efforts was used.

Perception of Dyspnea: The sensation of dyspnea was measured while the subject breathed through a device similar to that proposed by Nickerson and Keens.¹⁷ Subjects inhaled through a two-way valve (Hans-Rudolph; Fridengen, Germany), the inspiratory port of which was connected to a chamber and plunger to which weights could be added externally. The subjects breathed against progressive resistance, at 1-min intervals, in order to achieve a mouth pressure (P_m) of 0 (no resistance), 5, 10, 20, and 30 cm H₂O. After breathing for 1 min in each inspiratory load, in a protocol similar to the one that has been described previously by Kikuchi et al,¹⁰ the subjects rated the sensation of difficulty in breathing (dyspnea) using a modified Borg scale.¹⁸ This scale is a linear scale of numbers ranking the magnitude of difficulty in breathing, ranging from 0 (none) to 10 (maximal).

Training Protocol: Subjects in both groups trained daily for a period of 3 months, six times a week, with each session consisting of 0.5 h of training. The subjects received SIMT with a threshold inspiratory muscle trainer (Threshold Inspiratory Muscle Trainer; Healthscan; Cedar Grove, NJ). The subjects started breathing at a resistance level equal to 15% of their P_{imax} for 1 week. The resistance then was increased incrementally, 5 to 10% each session, to reach 60% of their P_{imax} at the end of the first month. SIMT then was continued for the next 2 months at 60% of their P_{imax} and was adjusted every week to the new P_{imax} achieved. Patients in group B received sham training with the same device but trained with no resistance.

Data Analysis

The results are expressed as the mean \pm SEM. Correlations were assessed by calculating Spearman correlation coefficients. Comparisons of lung function inspiratory muscle strength and dyspnea score were carried out using the two-way, repeated-measures analysis of variance.

RESULTS

Six patients had each recorded at least one decrease in the PEFR (to $< 80\%$ of their highest value) and were excluded from the study.

Following the 4-week run-in period, the remaining 76 subjects were separated into two groups: one group comprised 23 patients (15 men and 8 women) with a mean β_2 -agonist consumption of > 1 puff/d (defined as high consumers; mean \pm SEM, 2.7 ± 0.4 puffs/d); the other group comprised 53 patients with a low mean β_2 -agonist consumption of ≤ 1 puff/d (mean \pm SEM, 0.4 ± 0.1 puffs/d) who were excluded from the next stage of the study. There were no differences between the groups in age, baseline FEV_1 values, or P_{imax} (Table 1).

The mean Borg score during breathing against resistance was significantly higher ($p < 0.05$) in the patients with high β_2 -agonist consumption (Borg score, 0.2, 2.0, 3.6, 4.3, and 5.3 when breathing

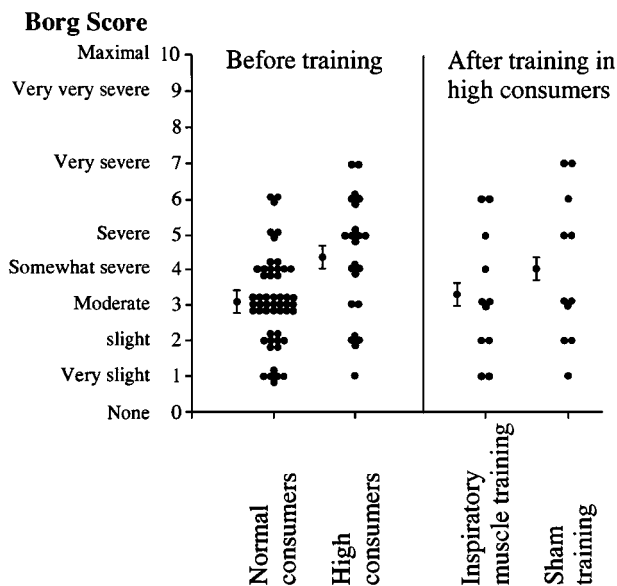


FIGURE 1. Perception of dyspnea (Borg score) during breathing against resistance that creates a negative pressure of 20 cm H₂O, in the patients with mild asthma who are high consumers and normal consumers, before training and in the training and control subgroups of the high consumers, following the training period.

against 0, 5, 10, 20, and 30 cm H₂O, respectively) than in the subjects with normal mean β_2 -agonist consumption (Borg scores, 0.3, 1.3, 2.0, 3.1, and 3.8, respectively).

The Borg scores of individual patients during breathing with resistance to create a Pm of 20 cm H₂O are shown in Figure 1. We have chosen the value of 20 cm H₂O, as did Kikuchi et al,¹⁰ because this is a moderate load that may be encountered daily

Table 1—Subject Characteristics*

Characteristics	Daily β_2 -agonist consumption, puff	
	> 1 (n = 23)	≤ 1 (n = 53)
Age, yr	34.0 ± 2.8	37.3 ± 3.1
Sex		
Male	15	27
Female	8	26
Baseline FEV ₁ , % predicted	90.8 ± 2.1	91.6 ± 2.2
P _{imax} , cm H ₂ O	96.0 ± 3.7	91.0 ± 4.0
Daily β_2 -agonist, puffs	2.7 ± 0.4	0.4 ± 0.1

*Values are given as mean ± SEM.

by asthmatic patients. The mean score for the patients with high β_2 -agonist consumption was significantly higher than that for the normal consumers (4.3 ± 0.4 vs 3.1 ± 0.2, respectively; $p < 0.01$).

In the second stage of the study, the 23 high consumers were randomized into two groups: 12 patients comprised the study group and received SIMT (group A); 11 patients were assigned to the control group and received sham training (group B). One patient was dropped from the study group because of the exacerbation in his asthma, so we report here the results of the remaining 22 patients. The effect of the training on inspiratory muscle strength is shown in Figure 2. All patients in the training group showed an increase in inspiratory muscle strength, as assessed by measuring the P_{imax} at RV. The mean P_{imax} increased significantly from 94.1 ± 5.1 to 109.7 ± 5.2 cm H₂O ($p < 0.005$). The mean P_{imax} remained unchanged in the control group that received sham training (97.6 ± 5.1 and 98.1 ± 5.3 cm H₂O, respectively).

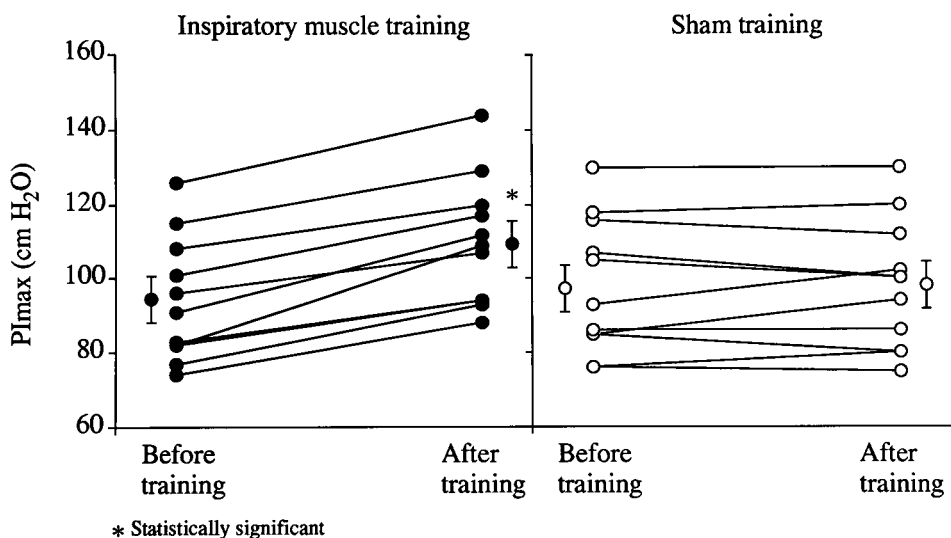


FIGURE 2. Inspiratory muscle strength, as expressed by the P_{imax} at RV, before and following 3 months of training, in the training and control subgroups of high consumers.

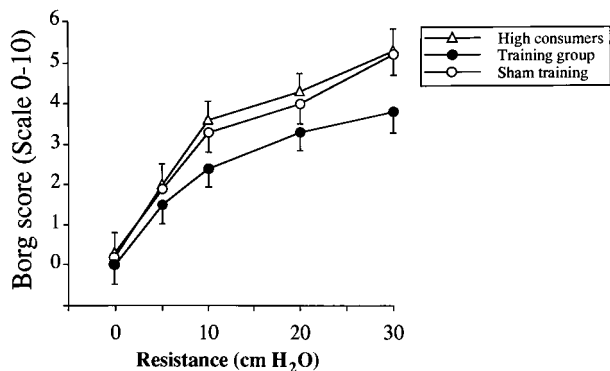


FIGURE 3. Mean (\pm SEM) perception of dyspnea (Borg score) during breathing against resistance in the high consumers before training, and in the training and control subgroups of the high consumers following the training period. There was no difference between the normal consumer patients and the training group following the training.

The increase in inspiratory muscle strength was associated with a statistically significant decrease in the mean Borg score during breathing against resistance in the study group (Borg score, 0.2, 1.5, 2.4, 3.3, and 3.8 when breathing against 0, 5, 10, 20 and 30 cm H₂O, respectively) but not in the control group (Borg score, 0.3, 1.9, 3.3, 4.0, and 5.2, respectively; $p < 0.05$) (Fig 3). The individual changes in Borg scores during breathing with resistance to create a Pm of 20 cm H₂O also decreased significantly in the study group but not in the control group (Fig 4).

The mean daily β_2 -agonist consumption in the 23 high consumers was 2.7 ± 0.4 puffs/d (range, 1.4 to

5.6 puffs) before training. There was no difference in consumption between the 11 patients in the study group and the 11 patients in the control group (2.6 ± 0.4 and 2.8 ± 0.8 puffs/d, respectively). However, during the last 4 weeks of training there was a significant decrease in the mean daily β_2 -agonist consumption in the training group (2.6 ± 0.4 to 1.6 ± 0.4 puffs/d; $p < 0.001$) but not in the control group (2.8 ± 0.3 to 2.9 ± 0.4 puffs/d; $p = 0.17$). This decrease was significant, although it remained higher than what we defined as normal consumers.

DISCUSSION

In this study, we have shown that patients with mild asthma who are high β_2 -agonist consumers have higher perceptions of dyspnea than do normal consumers. In addition, SIMT was associated with a decrease in the perception of dyspnea in these high perceivers and a decrease in β_2 -agonist consumption. It is of interest that although the perception-of-dyspnea curve became similar to the curve of the normal consumers, the drop in β_2 -agonist consumption was, although significant, not to the level of what we have defined as normal consumption.

The perception of dyspnea is critical, but it presents a paradox to patients with airway obstruction. On one hand, it limits daily activity and impairs quality of life, but, on the other hand, it provides a warning of deterioration.

It has been shown that there is a close relationship between the sensation of breathlessness and respiratory muscle force both in healthy subjects and in

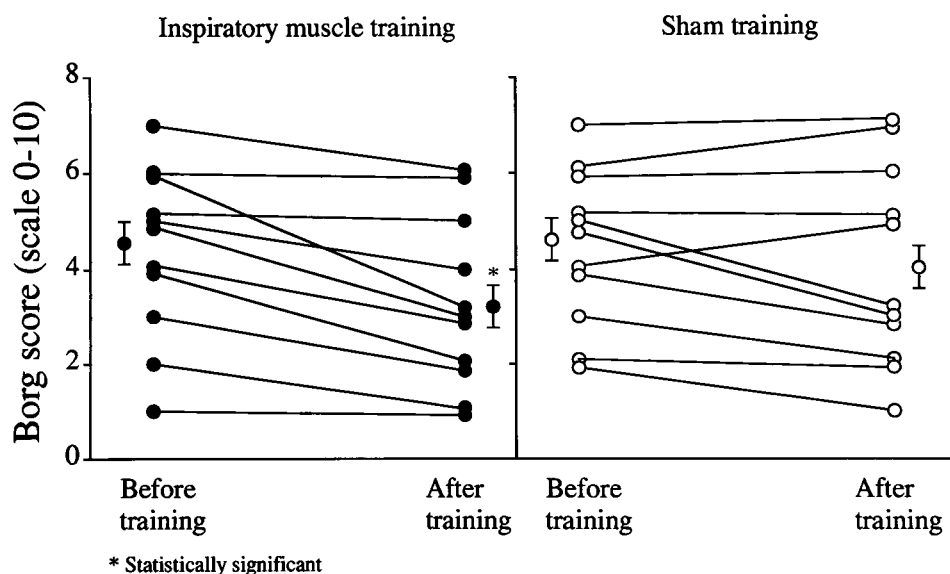


FIGURE 4. The individual changes in Borg scores during breathing against resistance that creates a negative pressure of 20 cm H₂O in the high consumers following the training period.

patients with COPD who have severe lung function impairment.^{11–13,19} The respiratory muscles, like other skeletal muscles, can be trained,^{20,21} resulting in significant improvement in respiratory muscle performance. This increase in respiratory muscle performance was associated with a decrease in the sensation of breathlessness in patients who had COPD with a pretraining respiratory muscle weakness.¹⁹

Patients with asthma usually are assumed to have normal respiratory muscle performance. Although asthma patients are exposed to airway obstruction and hyperinflation, which by itself adversely affects the inspiratory muscles by forcing them to operate in an inefficient part of the force-length relationship, these conditions are probably opposed by the training effect of breathing through increased airway resistance. However, it already has been demonstrated, in healthy subjects with normal respiratory muscle performance, that the perceived magnitude of added ventilatory loads can be reduced by resistive training that is aimed at increasing inspiratory muscle strength.²² In another study,¹ Burdon and colleagues have found that asthmatic subjects who frequently develop acute airflow obstruction acquire a degree of tolerance that reduces the perception of dyspnea.

In a previous study performed by us,²³ inspiratory muscle training resulted in a decrease in β_2 -agonist consumption in patients with moderate asthma. The perception of dyspnea was not measured in this study.

Many factors may be responsible for the considerable variations in the perception of dyspnea for any particular degree of airflow obstruction in asthmatic patients; the efficiency and performance of the inspiratory muscles, the length-tension relationship of the system, the cooperation of the various muscle groups in generating force, the frequency and timing of force generation, and the variation in the psychological response.^{24,25}

It has been shown already that temporal adaptation is responsible for some of the variability in breathlessness experienced by asthmatic subjects.¹ Patients with prolonged exposure to airflow obstruction were less breathless for any given reduction in FEV₁ than those with normal FEV₁. The asthmatic patients in our training group passed two processes that might contribute to the decrease in their perception of breathlessness and decreased β_2 -agonist consumption: (1) temporal adaptation by the exposure to increased airway resistance that might mimic airflow obstruction; and (2) inspiratory muscle training that increased the inspiratory muscle strength known to reduce the perceived magnitude of breathlessness, at least in healthy subjects.

A decreased perception of breathlessness is poten-


tially dangerous in patients with asthma, because the severity of an exacerbation of asthma may be underestimated. On the other hand, high perception carries with it the possibility of a decrease in quality of life and the usage of unnecessary, and sometimes dangerous, β_2 -agonists.

Our study shows that even in patients with mild asthma there is a wide variation in the magnitude of the sensation of dyspnea. Those who are high perceivers also consume relatively high doses of β_2 -agonists. SIMT seems to reduce both the perception of dyspnea and β_2 -agonist consumption. We believe that SIMT is safe, at least in patients with mild asthma, without producing the possible result of an exaggerated ablation of the perception of dyspnea. The clinical significance of our short-term study is not yet clear and needs to be elucidated in long-term follow-up studies in asthmatic patients.

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Chest 2000;117:722-727
DOI: 10.1378/chest.117.3.722

This information is current as of February 16, 2006

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