The relationship among inspiratory muscle strength, the perception of dyspnea and inhaled beta₂-agonist use in patients with asthma

Paltiel Weiner MD, Rasmi Magadle MD,
Marinella Beckerman MD, Noa Berar-Yanay MD

P Weiner, R Magadle, M Beckerman, N Berar-Yanay. The relationship among inspiratory muscle strength, the perception of dyspnea and inhaled beta₂-agonist use in patients with asthma. *Can Respir J* 2002;9(5):307-312.

BACKGROUND: It is well documented that the perception of dyspnea (POD), subjectively reported by patients, is related to the activity and strength of the inspiratory muscles, and influences the use of 'as needed' beta₂-agonists.

STUDY OBJECTIVE: To investigate the relationship among the increase in inspiratory muscle strength after specific inspiratory muscle training, beta₂-agonist consumption and the POD in patients with persistent, mild to moderate asthma.

METHODS: Inspiratory muscle strength, daily beta₂-agonist consumption and the POD were measured in 30 patients with mild to moderate asthma. Patients were then randomly assigned to two groups: one group received specific inspiratory muscle training until an increase of more than 20 cm H₂O was reached, and one group was a control group and received sham training. Inspiratory muscle strength, the POD and daily beta₂-agonist

consumption were assessed during and after the training period.

RESULTS: There was no good correlation between the baseline maximal inspiratory pressure and the POD, or between the baseline maximal inspiratory pressure and the mean daily beta₂-agonist consumption. However, there was a significant correlation between the POD and the mean daily beta₂-agonist consumption. The increase in inspiratory muscle strength after the inspiratory muscle training was closely correlated with the decrease in the POD ($P < 0.001$) and the decrease in beta₂-agonist consumption ($P < 0.001$).

CONCLUSIONS: The present study shows that, in patients with mild to moderate, persistent asthma, there is a correlation between the POD and the mean daily beta₂-agonist consumption. When the inspiratory muscles are strengthened, there is a significant decrease in the POD and in beta₂-agonist consumption.

Key Words: *Inspiratory muscle strength; Inspiratory muscle training; Perception of dyspnea*

Résumé à la page suivante

Department of Medicine A, Hillel-Yaffe Medical Center, Hadera, Israel

Correspondence and reprints: Dr Paltiel Weiner, Department of Medicine A, Hillel Yaffe Medical Center, Hadera, Israel 38100.

Telephone +011-972-6-6304527, fax +011-972-6-6304522, e-mail weiner@hillel-yaffe.health.gov.il

Le lien entre la force musculaire inspiratoire, la perception de dyspnée et le recours aux β_2 -agonistes chez les asthmatiques

HISTORIQUE : Il est bien documenté que la perception de dyspnée (PDD), déclarée subjectivement par les patients, est reliée à l'activité et à la force des muscles inspiratoires et qu'elle influence le recours aux β_2 -agonistes consommés « au besoin ».

OBJECTIF DE L'ÉTUDE : Explorer le lien entre l'augmentation de la force musculaire inspiratoire après un entraînement précis de la force des muscles inspiratoires, la consommation de β_2 -agonistes et la PDD chez les patients atteints d'asthme persistant moyen à modéré.

MÉTHODOLOGIE : La force musculaire inspiratoire, la consommation quotidienne de β_2 -agonistes et la PDD ont été mesurées chez 30 patients atteints d'asthme bénin à modéré. Les patients ont été divisés aléatoirement entre deux groupes : l'un a reçu un entraînement précis des muscles inspiratoires jusqu'à l'atteinte d'une augmentation de l' H_2O de

plus de 20 cm, et l'autre, représentant le groupe témoin, a reçu un entraînement bidon. La force musculaire inspiratoire, la PDD et la consommation quotidienne de β_2 -agonistes ont été évaluées pendant et après la période d'entraînement.

RÉSULTATS : Il n'existait aucune bonne corrélation entre la pression inspiratoire maximale de base et la PDD, ou entre la pression inspiratoire maximale de base et la consommation quotidienne moyenne de β_2 -agonistes. Cependant, on remarquait une importante corrélation entre la PDD et la consommation quotidienne moyenne de β_2 -agonistes. L'accroissement de la force musculaire inspiratoire après l'entraînement des muscles inspiratoires était relié de près à la diminution de la PDD ($P < 0,001$) et à la diminution de la consommation de β_2 -agonistes ($P < 0,001$).

CONCLUSIONS : La présente étude démontre que, chez les patients atteints d'une asthme persistant bénin à modéré, il existe une corrélation entre la PDD et la consommation quotidienne moyenne de β_2 -agonistes. Lorsque les muscles inspiratoires sont renforcés, on remarque une diminution considérable de la PDD et de la consommation de β_2 -agonistes.

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 still have to be explored. Previous studies have shown that among factors that can affect the perception of dyspnea (POD) 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).

Studies investigating dyspnea suggest that it, at least in part, is perceived to be respiratory muscle effort (8-9). In addition, a number of studies have been carried out to correlate dyspnea and respiratory muscle performance. It is well documented that the degree of breathlessness, subjectively reported by patients, is related to the activity and strength of the inspiratory muscles (10-11).

The POD is very important in patients with asthma. On one hand, it serves as one of the most important indexes used to guide treatment, especially in the modification of treatment, and on the other hand, it influences the use of 'as-needed' β_2 -agonists.

In a recent study, Weiner et al (12) showed that, in patients with mild asthma and high β_2 -agonist consumption, specific inspiratory muscle training (SIMT) was associated with a decrease in the POD and a decrease in β_2 -agonist consumption.

In the present study, we expanded the previous research (12) and investigated patients with more severe asthma and with various PODs. We hypothesized that there are relationships between inspiratory muscle strength, the POD and β_2 -agonist consumption, and that SIMT results in increased inspiratory muscle strength that is associated with a decreased POD and β_2 -agonist consumption. Therefore, our specific aim was to investigate the relationship among the POD, inspiratory muscle strength and β_2 -agonist consumption before and after SIMT in patients with persistent, mild to moderate asthma.

PATIENTS AND METHODS

Thirty consecutive patients (13 female and 17 male patients) with persistent, mild to moderate asthma attending the Asthma Outpatient Clinic (Hadera, Israel) were recruited for the study. All the patients satisfied the American Thoracic Society definition of asthma, having 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 (13). All of the patients had mild to moderate asthma (defined by a forced expiratory volume in 1 s [FEV₁] greater than 60% of predicted normal values). All subjects were treated by their primary physicians with inhaled corticosteroids (budesonide 400 to 800 μ g/day or fluticasone dipropionate 200 to 500 μ g/day) and β_2 -agonists as required. Their characteristics are summarized in Table 1.

Study design

All patients were studied during a two-week run-in period for stability confirmation, and were required to record their prebronchodilator morning peak expiratory flow rates and daily β_2 -agonist consumption on a diary card. The information on the diary card was verified daily by phone and weekly during a personal visit by a respiratory therapist. After the two-week run-in period, inspiratory muscle strength and the POD were measured in all subjects.

In the second stage of the study, the subjects were randomly assigned to one of two groups: a group that received SIMT (group A) or a control group that received sham training (group B). β_2 -agonist consumption was again recorded on diary cards during the week after each stage during the training period. Inspiratory muscle strength was assessed weekly. When an increase in the inspiratory muscle strength of 5, 10, 15 and 20 cm H_2O was achieved, the POD was also measured. The training was designed to end when the inspiratory muscle strength of each individual subject increased by greater than 20 cm H_2O over the base-

line value in the study group and after 12 weeks in the control group.

In all the patients, several practice tests were performed before the baseline value was taken to correct possible training and learning effects. All the data were collected by the same individual, who was blinded to the training group, as well as by the patients themselves, who were also blinded to the mode of training.

Tests

Spirometry: The forced vital capacity (FVC) and the FEV₁ were measured three times on a computerized spirometer (Compact, Vitalograph, United Kingdom), and the best trials were reported. The data were acceptable when the two largest FVC and FEV₁ values were within 0.2 L of each other. Bronchodilators were withheld for 12 h before spirometry.

Inspiratory muscle strength: Inspiratory muscle strength was assessed by measuring the maximal inspiratory mouth pressure (PI_{max}) at residual volume (RV), as previously described by Black and Hyatt (14). The value obtained from the best of at least three efforts was used. The data were acceptable when the two highest PI_{max} values were within 5% of each other.

POD: The POD was measured while the subject breathed through a device similar to that proposed by Nickerson and Keens (15). Subjects inspired through a two-way Hans-Rudolph valve whose inspiratory port was connected to a chamber and plunger to which weights could be added externally, imposing an inspiratory threshold load. The subjects breathed against progressive loads, at 1 min intervals, to achieve mouth pressures of 0 (no resistance), 5, 10, 20 and 30 cm H₂O. After breathing for 1 min at each inspiratory load, the subjects rated the sensation of difficulty in breathing (dyspnea) using a modified Borg scale (16). The Borg 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 once per day, six days per week; each session consisted of 0.5 h of training. The subjects received SIMT with a threshold inspiratory muscle trainer (Threshold Inspiratory Muscle Trainer, USA). The subjects started breathing at loads equal to 15% of their PI_{max} for one week. The load was then increased incrementally by 5% to 10% at each session to reach 60% of their PI_{max} at the end of the first month. The SIMT was then continued at 60% of their PI_{max}, which was adjusted every week to the new PI_{max} achieved. The intense training (up to 60% of their PI_{max}) and the longevity of the training (30 min/day) provided both strength and endurance training. Patients in group B received sham training with the same device, but without the diaphragm and with no loads.

Data analysis

The results are expressed as mean $\pm$ SEM. Correlations were assessed by calculating Spearman correlation coefficient.

TABLE 1

Characteristics of subjects in a study investigating the relationship among the perception of dyspnea, inspiratory muscle strength and beta₂-agonist consumption before and after specific inspiratory muscle training in patients with persistent, mild to moderate asthma

	Training group n=15	Control group n=15
Age	39.7 $\pm$ 5.0	37.1 $\pm$ 4.8
Baseline FEV ₁ (% of predicted)	78.6 $\pm$ 2.9	76.4 $\pm$ 2.4
PI _{max} (cm H ₂ O)	92.1 $\pm$ 5.6	86.4 $\pm$ 5.3
Daily beta ₂ -agonist use (puffs/day)	3.4 $\pm$ 0.8	3.1 $\pm$ 0.9
Borg score (sum)	12.4 $\pm$ 0.8	12.1 $\pm$ 0.8

FEV₁, Forced expiratory volume in 1 s; PI_{max}, Maximal inspiratory mouth pressure. All values are mean $\pm$ SEM

patients. Comparisons of lung function, inspiratory muscle strength and dyspnea score were carried out using the two-way, repeated measures ANOVA.

RESULTS

There was no significant difference between the study group and the control group in age, FEV₁, inspiratory muscle strength as assessed by measuring the PI_{max} at RV, POD and mean daily beta₂-agonist consumption during the two-week run-in period (Table 1). It should be mentioned that, although all the patients were treated regularly by their primary physician with inhaled corticosteroids, they still used beta₂-agonists, on average, three times per day.

There was no good correlation between the baseline PI_{max} and the POD, nor between the baseline PI_{max} and the mean daily beta₂-agonist consumption. However, there was a significant correlation between the POD (Borg score) and the mean daily beta₂-agonist consumption ($R^2=0.526$, $P<0.01$) (Figure 1).

After the two-week run-in period, the 30 patients were randomly assigned to one of two groups: 15 patients (nine male and six female patients) comprised the study group and received SIMT (group A), and 15 patients (eight male and seven female patients) were assigned to the control group and received sham training (group B).

Two patients dropped out of the study group, one due to an exacerbation, and one to a lack of compliance, and four patients dropped out of the control group after becoming aware of the sham training.

All of the patients in the training group showed a gradual increase in inspiratory muscle strength, as was assessed by measuring the PI_{max} at RV. The patients reached the goal of a greater than 20% increase in the PI_{max} over baseline values within 16 to 25 weeks.

The mean PI_{max} increased significantly from 92.1 $\pm$ 5.6 cm H₂O to 111.5 $\pm$ 6.2 cm H₂O ($P<0.005$) after the training period. The mean PI_{max} remained almost unchanged in the control group, which received sham training.

Figure 1) The relationship between the perception of dyspnea (Borg score) during breathing against loads and the maximal inspiratory mouth pressure (PI_{max}) (top left), between the Borg score and β_2 (β_2)-agonist consumption (top right), and between the PI_{max} and β_2 -agonist consumption (bottom)

Figure 2) The relationship between the increase in the maximal inspiratory mouth pressure (PI_{max}) and the decrease in dyspnea (Borg score) after specific inspiratory muscle training

(86.4 ± 5.3 cm H₂O to 85.1 ± 5.4 cm H₂O), and the difference between the two groups was highly significant ($P < 0.005$). The increase in inspiratory muscle strength was associated with a gradual decrease in the mean Borg score during breathing against resistance in the study group, but not in the control group ($P < 0.05$). There was a close correlation ($P < 0.001$) between the increase in PI_{max} and the decrease in mean Borg score during breathing against resistance (Figure 2).

Figure 3) The relationship between the increase in the maximal inspiratory mouth pressure (PI_{max}) and the decrease in the β_2 (β_2)-agonist consumption after specific inspiratory muscle training

There was also a close correlation ($P < 0.001$) between the increase in PI_{max} and the decrease in mean β_2 -agonist consumption in the training group (Figure 3), but not in the control group.

In addition, there was also a close correlation ($P < 0.001$) between the decrease in the mean Borg score during breathing against resistance and the decrease in mean β_2 -agonist consumption in the training group (Figure 4), but not in the control group.

The mean $\pm$ SEM FVC and the mean FEV₁ remained almost unchanged after the training period in both groups.

DISCUSSION

In the present study, we showed that, in patients with persistent, mild to moderate asthma, there was a significant correlation between the POD and the mean daily β_2 -agonist consumption. It was also shown that the inspiratory muscles can be trained in these patients. The increase in inspiratory muscle strength was closely correlated with the decrease in the POD and the decrease in β_2 -agonist consumption.

Dyspnea probably results from a mismatch between central respiratory motor activity and incoming afferent information from receptors in the airways, lungs, respiratory muscles and chest wall structures (17). Dyspnea occurs when the subject faces heightened ventilatory demand, when ventilatory impedance increases, and when breathing pattern change, when there are blood gas and respiratory muscle abnormalities (18).

In many patients with asthma, there is not a good correlation between the severity of breathlessness and the degree of airflow obstruction (1), probably because of the many factors that influence the POD.

One may wonder whether the threshold loading test is the optimal one to use to evaluate the POD. The POD for asthma is usually studied during spontaneous attacks or during bronchoprovocation with smooth muscle agonists like histamine and methacholine. These studies have the advantages of mimicking faithfully mechanical derangements, sensations and qualitative aspects of dyspnea during a spontaneous asthmatic attack (19), and the bronchoconstriction is easily reversible. However, despite a close linear relationship between the decrease in FEV_1 and the increase in the POD, there is a considerable variation in the severity of breathlessness for any particular degree of airflow obstruction (1). Measuring the POD during external mechanical loading (resistive, elastic or threshold) less accurately simulates the mechanical characteristics of an asthma attack (20). However, it was previously shown that the imposed inspiratory threshold load is a good predictor for explaining the variability of the perceived dyspnea (21). In addition, this test is easy to perform and is highly reproducible.

There is a close relationship between the sensation of breathlessness and respiratory muscle force, both in normal subjects and in patients with chronic obstructive pulmonary disease and severe lung function impairment (9,10,19). Inspiratory muscle training was associated with decreased dyspnea in patients with COPD and pretraining respiratory muscle weakness (19), and in patients with mild asthma and high β_2 -agonist consumption but normal respiratory muscle strength (12). Inspiratory muscle training was evaluated in patients with various other respiratory disorders such as neuromuscular disorders (20) and cystic fibrosis (21), and in elite athletes (22), with favourable results.

Patients with asthma are usually assumed to have normal respiratory muscle performance. Although they are exposed to airway obstruction and hyperinflation, which, by themselves, adversely affect the inspiratory muscles by forcing them to operate in an inefficient part of the force-length relationship, this is probably opposed by the training effect of breathing through increased airway resistance (1). However, it has already been demonstrated in normal subjects with normal respiratory muscle performance that the perceived magnitude of added ventilatory loads can be reduced by resistance training aimed at increasing inspiratory muscle strength (23).

The patients with asthma in our training group underwent two processes that might have contributed to the decrease in their perception of breathlessness and decreased β_2 -agonist consumption:

- Temporal adaptation by the exposure to increased airway resistance that may mimic airflow obstruction. It has been already shown that temporal adaptation is responsible for some of the variability in breathlessness experienced by subjects with asthma (1). Patients with prolonged exposure to airflow obstruction were less breathless for any given reduction in the FEV_1 than those with a normal FEV_1 .

Figure 4) The relationship between the decrease in dyspnea (Borg score) and the decrease in the β_2 (β_2)-agonist consumption after specific inspiratory muscle training

- Inspiratory muscle training that increased the inspiratory muscle strength known to reduce the perceived magnitude of breathlessness (24-26).

The close relationship between the increase in the PI_{max} and the POD in the training group confirms that, as in normal subjects, strengthening the inspiratory muscles is associated with a reduction in the sensation of breathlessness.

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

Decreased perception of breathlessness is potentially dangerous in patients with asthma, because the severity of an exacerbation of asthma may be underestimated. However, a high perception of breathlessness carries with it the possibility of a decrease in quality of life and the use of unnecessary β_2 -agonists.

Our study emphasizes the important role that the inspiratory muscles play in the POD in patients with asthma. It shows that the performance of the inspiratory muscles can be improved by training, even when there is no pretraining weakness. This improvement is significantly correlated with a decrease in the sensation of breathlessness, and therefore, with a decrease in β_2 -agonist consumption. We believe that SIMT is safe, at least in patients with mild to moderate asthma who are 'high perceivers' and consume relatively high doses of β_2 -agonists, not carrying with it the possibility of exaggerated ablation of the POD. The clinical significance of our short term study is not yet clear and needs to be elucidated in long term follow-up studies in patients with asthma.

REFERENCES

- Burdon JG, Juniper EF, Killian KJ, Hargreave FE, Campbell EJ. The perception of breathlessness in asthma. *Am Rev Respir Dis* 1982;126:825-8.
- Orehek J, Beaupre A, Badier M, Nicoli MM, Delpierre S. Perception of airway tone by asthmatic patients. *Bull Eur Physiopathol Respir* 1982;18:601-7.
- D'Amours P, Cormier Y, Boulet LP, et al. Lung hyperinflation is a major determinant of dyspnea in histamine-induced asthma. *Chest* 1989;96:247S. (Abst)
- Altose MD. Dyspnea. In: Simmons DH, ed. *Current Pulmonology*. Chicago: Year Book Medical Publishers, 1986:199-226.
- Connolly MJ, Crowley JJ, Charan NB, Nielson CP, Vestal RE. Reduced subjective awareness of bronchoconstriction provoked by methacholine in elderly asthmatic and normal subjects as measured on a simple awareness scale. *Thorax* 1992;47:410-3.
- O'Donnell DE, Webb KE. Breathlessness in patients with severe chronic airflow limitation: physiologic correlations. *Chest* 1992;102:824-31.
- Morgan AD, Peck DF, Buchanan DR, McHardy GJ. Effect of attitudes and beliefs on exercise tolerance in chronic bronchitis. *Br Med J (Clin Res Ed)* 1983;286:171-3.
- Killian KG, Campbell EJM. Dyspnea and exercise. *Ann Rev Physiol* 1983;44:465-79.
- Killian KG, Jones NL. The use of exercise testing and other methods in the investigation of dyspnea. *Clin Chest Med* 1984;5:99-108.
- Jones GL, Killian KJ, Summers E. The sense of effort, oxygen cost, and pattern of breathing associated with progressive elastic loading to fatigue. *Fed Proc* 1984;42:1420. (Abst)
- Killian KJ, Gandevia SC, Summers E, Campbell EJ. Effect of increased lung volume on perception of breathlessness, effort, and tension. *J Appl Physiol* 1984;57:686-91.
- Weiner P, Berar-Yanay N, Davidovich A, Magadle R, Weiner M. Specific inspiratory muscle training in patients with mild asthma, with high consumption of inhaled β_2 -agonists. *Chest* 2000;117:722-7.
- Standards for the diagnosis and care of patients with chronic obstructive pulmonary disease (COPD) and asthma. This official statement of the American Thoracic Society was adopted by the ATS Board of Directors, November 1986. *Am Rev Respir Dis* 1987;136:225-44.
- Black LF, Hyatt RE. Maximal respiratory pressures: Normal values and relationship to age and sex. *Am Rev Respir Dis* 1969;99:696-702.
- Nickerson BG, Keens TG. Measuring ventilatory muscle endurance in humans as sustainable inspiratory pressure. *J Appl Physiol* 1982;52:768-72.
- el-Manshawi A, Killian KJ, Summers E, Jones NL. Breathlessness during exercise with and without resistive loading. *J Appl Physiol* 1986;61:896-905.
- Schwartzstein RM, Manning HL, Weiss JW, Weinberger SE. Dyspnea: a sensory experience. *Lung* 1990;168:185-99.
- Dyspnea. Mechanisms, assessment, and management: a consensus statement. American Thoracic Society. *Am J Respir Crit Care Med* 1999;159:321-40.
- Lougheed MD, Lam M, Forkert L, Webb KA, O'Donnell DE. Breathlessness during acute bronchoconstriction in asthma. Pathophysiologic mechanisms. *Am Rev Respir Dis* 1993;148:1452-9.
- Kelsen SG, Prestel TF, Cherniack NS, Chester EH, Deal EC Jr. Comparison of the respiratory responses to external resistive loading and bronchoconstriction. *J Clin Invest* 1981;67:1761-8.
- Chen RC, Yan S. Perceived inspiratory difficulty during inspiratory threshold and hyperinflationary loadings. *Am J Respir Crit Care Med* 1999;159:720-7.
- Patessio A, Rampulla C, Fracchia C, et al. Relationship between the perception of breathlessness and inspiratory resistive loading: report on a clinical trial. *Eur Respir J* 1989;7(Suppl):587s-591s.
- Koessler W, Wanke T, Winkler G, et al. 2 years' experience with inspiratory muscle training in patients with neuromuscular disorders. *Chest* 2001;120:765-9.
- de Jong W, van Aalderen WM, Kraan J, Koeter GH, van der Schans CP. Inspiratory muscle training in patients with cystic fibrosis. *Respir Med* 2001;95:31-6.
- Volianitis S, McConnell AK, Koutedakis Y, McNaughton L, Backx K, Jones DA. Inspiratory muscle training improves rowing performance. *Med Sci Sports Exerc* 2001;33:803-9.
- Redline S, Gottfried SB, Altose MD. Effects of changes in inspiratory muscle strength on the sensation of respiratory force. *J Appl Physiol* 1991;70:240-5.