

# Influence of Gender and Inspiratory Muscle Training on the Perception of Dyspnea in Patients With Asthma\*

Paltiel Weiner, MD; Rasmi Magadle, MD; Fareed Massarwa, MD; Marinella Beckerman, MD; and Noah Berar-Yanay, MD

**Background:** Men and women respond differently to asthma.

**Patients and methods:** Maximal inspiratory mouth pressure (P<sub>imax</sub>),  $\beta_2$ -agonist consumption, and perception of dyspnea (POD) were measured in 22 women and 22 men with mild persistent-to-moderate asthma. Next, the women were randomized into two groups: those who received inspiratory muscle training and those who received sham training. The training ended when the P<sub>imax</sub> of the training group was equal to that of the male subjects. POD was then measured once again.

**Results:** Baseline P<sub>imax</sub> was significantly lower ( $p < 0.01$ ) while POD and mean daily  $\beta_2$ -agonist consumption were significantly higher in the female subjects. P<sub>imax</sub> reached the level of the male subjects at the end of the 20th week of training. The increase in the P<sub>imax</sub> was associated with a statistically significant decrease in mean daily  $\beta_2$ -agonist use and in POD to a similar level as in male subjects.

**Conclusions:** POD and mean daily  $\beta_2$ -agonist consumption in asthmatic women are significantly higher, and the P<sub>imax</sub> significantly lower, than that of their male counterparts. When the P<sub>imax</sub> of female subjects following training is equal to that in male subjects, the differences in POD and mean daily  $\beta_2$ -agonist consumption disappear. (CHEST 2002; 122:197-201)

**Key words:** influence of gender; inspiratory muscle training; perception of dyspnea

**Abbreviations:** IMT = inspiratory muscle training; P<sub>imax</sub> = maximal inspiratory mouth pressure; POD = perception of dyspnea; QOL = quality of life; RV = residual volume

Current data<sup>1</sup> suggest that there are gender differences in hospital admissions, quality of life (QOL), and use of metered-dose inhalers in patients with asthma. In adult patients with asthma, hospital admissions for women predominate, occurring at a rate approximately 2.5 times that of their male counterparts. Using the Short Form-36 questionnaire, Bousquet and colleagues<sup>2</sup> observed a better QOL score report by men than by women. Several studies<sup>3</sup> addressing the use of metered-dose inhalers have demonstrated that more rescue medications for asthma are used by women than by men. These observations were confirmed in 914 asthmatic patients in a large health maintenance organization.<sup>4</sup> Taken together, these data suggest that female patients with asthma may have a more severe form of

asthma than male patients. However, in a recent study<sup>5</sup> comparing male and female patients admitted to the hospital with asthma attacks, female patients did not have more severe asthma and did not require higher rates of admission to the ICU than male patients. If women report more symptoms and have poorer QOL than men for the same level of airflow obstruction,<sup>4,5</sup> it can be hypothesized that women perceive dyspnea differently than men. In this study, we investigated the following hypotheses: (1) women have higher perception of dyspnea (POD) than men for the same level of airflow obstruction, and therefore report more symptoms, experience poorer QOL, and use more medication; and (2) gender differences in inspiratory muscle strength are responsible for the difference in the POD.

\*From the Department of Medicine A, Hillel Yaffe, Medical Center, Hadera, Israel.

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Correspondence to: Paltiel Weiner, MD, Department of Medicine A, Hillel Yaffe Medical Center, Hadera, Israel 38100; e-mail: weiner@hillel-yaffe.health.gov.il

## MATERIALS AND METHODS

Forty-four asthmatic patients (22 women and 22 men), with mild persistent-to-moderate asthma attending the asthma clinic were recruited for the study. All patients 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.<sup>6</sup> All patients had mild-to-moderate asthma (defined by FEV<sub>1</sub> > 60% of predicted normal values). All patients were treated by their primary physician only with inhaled corticosteroids (budesonide, 400 to 800 µg/d, or fluticasone dipropionate, 200 to 500 µg/d) and β<sub>2</sub>-agonists, as required. The anti-inflammatory treatment was kept stable during the whole period of the study. Patient characteristics are summarized in Table 1.

### Study Design

All patients were studied during a 2-week run-in period for stability confirmation, and were required to record their prebronchodilator morning peak expiratory flow rates and daily β<sub>2</sub>-agonist consumption on a diary card. The information on the diary card was verified by a respiratory therapist daily by phone and weekly by personal visit. After the 2-week run-in period, inspiratory muscle strength and POD were measured in all subjects.

As asthmatic men were found to have higher mean inspiratory muscle strength, in the second stage of the study the female subjects were randomized into two groups: those who received specific inspiratory muscle training (IMT) [group A] and a control group who received sham training (group B). β<sub>2</sub>-Agonist consumption was again recorded on diary cards during the last week of each training period. Inspiratory muscle strength was measured weekly. The end point of the training was designed to be when the mean inspiratory muscle strength of the women in the training group equaled that of the male subjects. POD was then measured once again. In all patients, several practice tests were performed before the baseline value in order to correct for possible training and learning effects. All data were collected by the same person, who was blinded to the mode of training. The patients were also blinded to the mode of training. The study protocol was approved by the institutional ethics committee, and informed consent was obtained from all the subjects.

### Tests

**Spirometry:** FVC and FEV<sub>1</sub> were measured three times on a computerized spirometer (Compact; Vitalograph; Buckingham, England), before and following training, and results of the best trial were reported. Bronchodilators were withheld 12 h before spirometry.

**Inspiratory Muscle Strength:** Inspiratory muscle strength was assessed by measuring the maximal inspiratory mouth pressure (P<sub>imax</sub>) at residual volume (RV) as previously described by Black and Hyatt.<sup>7</sup> The value obtained from the best of at least three efforts was used.

**POD:** The sensation of dyspnea was measured while the

subjects breathed through a device similar to that proposed by Nickerson and Keens.<sup>8</sup> Subjects inhaled through a two-way valve (Hans Rudolph; Kansas City, MO) with an inspiratory port 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 mouth pressure of 0 (no resistance), 5, 10, 20, and 30 cm H<sub>2</sub>O. After breathing for 1 min in each inspiratory load, in a protocol similar to the one previously described by our group,<sup>9</sup> the subjects rated the sensation of difficulty in breathing (dyspnea) using a modified Borg scale.<sup>10</sup> This 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, six times a week, each session consisting of 30 min of training. The subjects received IMT with a threshold inspiratory muscle trainer (Threshold IMT; Respironics; Pittsburgh, PA). The subjects started breathing at a resistance equal to 15% of their P<sub>imax</sub> for 1 week. The resistance was then increased incrementally, 5 to 10% each session, to reach 60% of the P<sub>imax</sub> at the end of the first month. IMT was then continued at 60% of the P<sub>imax</sub>, adjusted weekly to the new P<sub>imax</sub> achieved. Patients in group B received sham training with the same device, but with no resistance.

### Data Analysis

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

## RESULTS

There was no significant difference in age or percent-predicted FEV<sub>1</sub> between female and male subjects. Inspiratory muscle strength, as assessed by measuring the P<sub>imax</sub> at RV, was significantly higher (*p* < 0.01) in the male subjects than in the female subjects (Table 1).

POD in the female group was significantly higher than that in their male counterparts (Fig 1). The mean ± SEM of the Borg score (the sum of scores achieved in each level of resistance at 0, 5, 10, 15, 20, and 30 cm H<sub>2</sub>O) was 13.1 ± 0.6 in the female group compared to 10.1 ± 0.4 in the male group (*p* < 0.005).

During the 2 weeks of follow-up, the mean daily β<sub>2</sub>-agonist consumption in the female patients was significantly higher (*p* < 0.01) than in the male patients (Table 1). There was a statistically significant correlation (*p* < 0.001) between the morning FEV<sub>1</sub> and the sum Borg score both in the female group and in the male group (Fig 2).

In the second stage of the study, the 22 women were randomized into two groups: 11 patients constituted the study group and received specific IMT,

**Table 1—Subject Characteristics\***

Characteristics	Women	Men
Subjects, No.	22	22
Age, yr	36.2 ± 3.1	37.7 ± 3.3
Baseline FEV <sub>1</sub> , % predicted	82.6 ± 2.6	80.4 ± 2.1
P <sub>imax</sub> , cm H <sub>2</sub> O	72.1 ± 4.6	107.4 ± 6.3
% predicted	84.3 ± 5.6	88.2 ± 6.1
Daily β <sub>2</sub> -agonist use, puffs/d	3.2 ± 0.6	2.0 ± 0.4
Borg score, sum	13.1 ± 0.6	10.1 ± 0.4

\*Data are presented as mean ± SEM unless otherwise indicated.

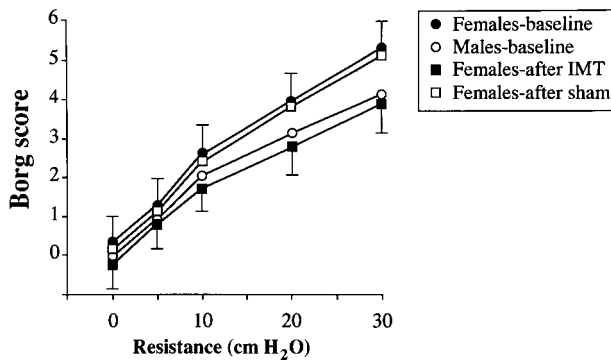


FIGURE 1. Baseline mean  $\pm$  SEM POD (Borg score) during breathing against load in the female and male groups, and following IMT in the female group.

and 11 patients were assigned to the control group with sham training. One patient from the study group and two women from the control group who became aware that they had received sham training dropped out of the study, so we report here the results of the remaining 19 patients.

The effect of the training on inspiratory muscle strength is shown in Figure 3. All patients in the training group showed a gradual increase in their inspiratory muscle strength, assessed by measuring the P<sub>imax</sub> at RV. Mean P<sub>imax</sub> increased significantly ( $p < 0.005$ , already by the end of the fourth week), compared to the control group, from  $73.1 \pm 5.1$  to  $85.0 \pm 5.6$ ,  $88.2 \pm 5.7$ ,  $93.1 \pm 6.1$ ,  $100.3 \pm 6.1$ , and  $103.9 \pm 5.9$  cm H<sub>2</sub>O, at the end of the fourth, eighth, 12th, 16th, and 20th weeks of training, respectively. At the end of the 20th week, there was no statistically significant difference between the mean P<sub>imax</sub> of the female group and that of the male group.

The mean daily  $\beta_2$ -agonist consumption in the training group was  $3.4 \pm 0.6$  puffs per day (range, 1.4 to 5.6 puffs per day) before training. There was no difference between the patients in the study group and the patients in the control group ( $3.4 \pm 0.6$  puffs per day and  $3.0 \pm 0.8$  puffs per day, respectively). However, there was a significant decrease in the mean daily  $\beta_2$ -agonist consumption in the training group (to  $2.1 \pm 0.5$  puffs per day,  $p < 0.001$ ), at the end of the training period, but not in the control group (Fig 3).

The increase in inspiratory muscle strength was associated with a statistically significant decrease in the mean Borg score during breathing against resistance ( $p < 0.05$ ) in the study group, but not in the control group. At the end of the 20th week, there was no statistically significant difference between the POD curve in the female group and that of the male group (Fig 1). There was no significant change in the FEV<sub>1</sub> following the training period in both the training and the control groups.

## DISCUSSION

The significant findings of our study are as follows: (1) for the same level of predicted FEV<sub>1</sub>, POD and mean daily  $\beta_2$ -agonist consumption in asthmatic women are significantly higher than in their male counterparts; (2) male patients have significantly higher P<sub>imax</sub> than female patients; (3) inspiratory muscles can be trained in asthmatic women to reach the same level of strength as in asthmatic men; and (4) when female patients equal their P<sub>imax</sub> to that of male patients, the differences in POD and mean daily  $\beta_2$ -agonist consumption disappear.

Our results and previous data<sup>1-4</sup> suggest that women

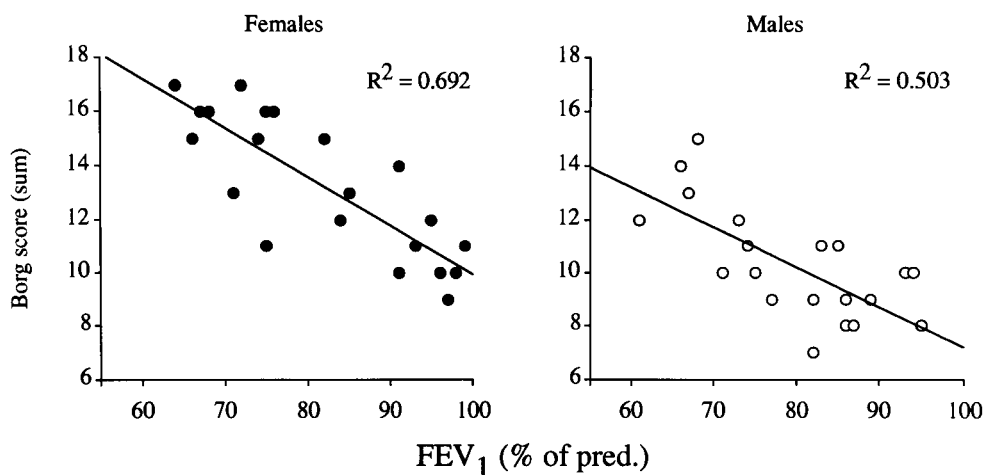


FIGURE 2. The correlation between the morning FEV<sub>1</sub> (percent predicted) and the sum Borg score both in the female patients and in the male group.

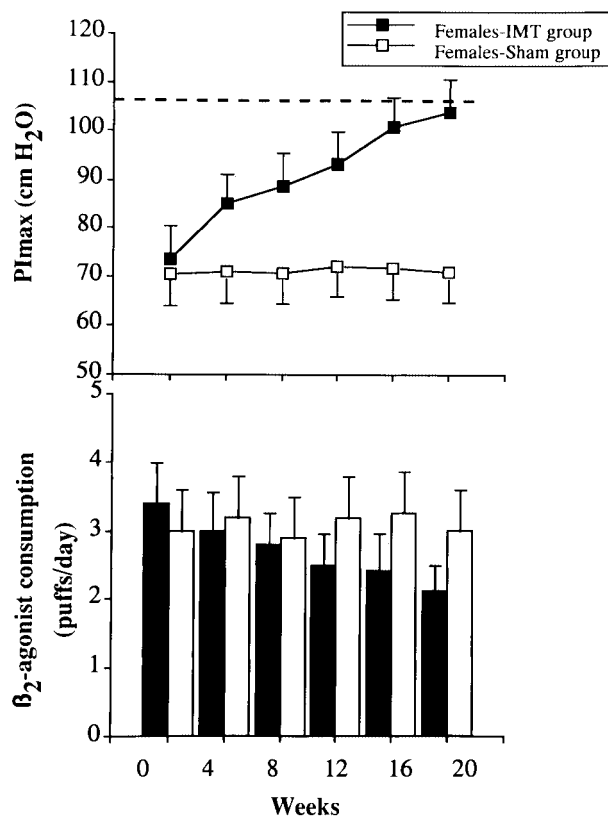


FIGURE 3. The effect of the IMT on inspiratory muscle strength, assessed by measuring P<sub>Imax</sub> at RV, and mean daily β<sub>2</sub>-agonist consumption in the female subjects before, during, and at the end of the training period.

with asthma report more symptoms, use more rescue medication, experience poorer QOL, and are admitted to the hospital more frequently than men. A possible interpretation for these findings is that women have more severe disease than men. However, in the study of Osborne and colleagues,<sup>4</sup> men had a lower prebronchodilator FEV<sub>1</sub> than women, while Trawick and colleagues,<sup>5</sup> reporting on high-risk patients admitted to the hospital, found female patients to be admitted twice as often as men, although men at hospital admission were more hypercapnic than women. In addition, once admitted, the proportion of men and women requiring intubation or the medical ICU were similar.

Another possibility for the gender differences might be due to airway hyperreactivity. However, no gender difference in airway responsiveness could be detected.<sup>11</sup>

If women seek more medical attention, use more asthma medication, and experience poorer QOL for the same level of airflow obstruction, it can be suggested that women actually experience greater discomfort to airflow obstruction than men. The fact that women report poorer QOL than men<sup>4</sup> suggests that women perceive the same level of airway obstruction differently than men.

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.<sup>12</sup> The factors underlying this variability are still to be explored. Previous studies<sup>13–16</sup> have shown that among those factors that can affect POD related to bronchoconstriction are changes in lung volume, speed of bronchoconstriction, anxiety level, duration of asthma, and age. Other influences include attitudes, expectations, and personality traits.<sup>17–18</sup> Our study shows that a gender difference may also be influential.

It has been shown that there is a close relationship between the sensation of breathlessness and respiratory muscle force, both in normal subjects and in patients with COPD with severe lung function impairment.<sup>19–22</sup> For a given resistance, men can generate greater maximal inspiratory and expiratory pressures.<sup>7</sup> Perhaps, because of this gender differential in respiratory muscle strength, women are more symptomatic than men, prompting them to use more medication and to seek more medical attention.

The respiratory muscles, like other skeletal muscles, can be trained,<sup>23,24</sup> with significant improvement in respiratory muscle performance. Our group of highly motivated female subjects trained very intensely (30 min per day, 6 days per week, at 60% of their P<sub>Imax</sub>) and showed, in fact, a marked increase (42%) in their P<sub>Imax</sub> in just 20 weeks. It was already shown by our group<sup>9</sup> that the increase in respiratory muscle performance is associated with a decrease in POD and, in addition, with a decrease in β<sub>2</sub>-agonist consumption, in patients with asthma. Rescue therapy with β<sub>2</sub>-agonists is mainly related to POD in patients with asthma. Therefore, it is not surprising that the decrease in POD was associated with a decrease in β<sub>2</sub>-agonist consumption.

Our study shows that the inspiratory muscles in women could be trained within 20 weeks to reach the same strength as in their male counterparts. This increase in inspiratory muscle strength completely concealed the gender differences in POD and β<sub>2</sub>-agonist consumption, suggesting that the gender differential in maximal inspiratory muscle strength is responsible for the fact that women are more symptomatic than men. However, other possibilities for the gender differences could not be negated in our study, and further investigations are needed to completely clarify the issue.

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