Inspiratory Muscle Training During Treatment With Corticosteroids in Humans*

Paltiel Weiner, MD; Yair Azgad, MSc; and Margalit Weiner PhD

In a previous study performed by us, functional alterations in the inspiratory muscles were evaluated in patients receiving corticosteroids for diseases other than respiratory. We have shown that patients who received high-dose steroids for several weeks developed inspiratory muscle weakness that was reversible following withdrawal of the drug treatment. The present study was designed to evaluate the ability of specific inspiratory muscle training (SIMT) to prevent the effects of a therapeutic dosage of corticosteroids on inspiratory muscle function in patients receiving the drug for diseases other than pulmonary, with no underlying respiratory or muscular disease. Twelve patients, 5 men and 7 women, with ages ranging from 19 to 41 years, who received corticosteroids for diseases other than respiratory were recruited into two groups: 6 patients were assigned to the control group and got sham training and 6 patients received SIMT while receiving corticosteroids in a single-blind group-comparative trial. In both groups, there was no difference between the post-treatment and pretreatment values as regard to the FEV₁/FVC relationship. However, in the control group but not in the training group, there was a small but significant decrease, from 99.2 ± 3.0 to 94.3 ± 2.8 (mean ± SEM, p<0.01) in FEV₁ (percent of predicted normal values) and from 103.5 ± 4.0 to 88.7 ± 3.1 (p<0.001) in the FVC, following treatment. All subjects had normal inspiratory muscle strength, as expressed by the maximal inspiratory mouth pressure (PImax) at residual volume, and inspiratory muscle endurance as expressed by the relationship between peak pressure and the PImax before treatment. Following administration of corticosteroids, there was a gradual decrease in both inspiratory muscle strength (from 117.5 ± 9.4 to 80.5 ± 3.3 cm H₂O, p<0.005) and endurance (from 82.7 ± 2.6 to 40.2 ± 1.7%, p<0.001) in the control group. On the contrary, despite corticosteroid therapy, there were no significant changes in the inspiratory muscle function in the patients whose inspiratory muscles were specifically trained. We conclude that corticosteroids have a significant deteriorating effect on respiratory muscle function in humans. This weakness is preventable by using SIMT during corticosteroid treatment.

(Chest 1995; 107:1041-44)

PImax= maximal inspiratory mouth pressure; RV = residual volume; SIMT = specific inspiratory muscle training

Key words: inspiratory muscle training; corticosteroid treatment

In a recent study,¹ we have shown that patients who received high-dose steroids for several weeks developed inspiratory muscle weakness, which seemed to be reversible following withdrawal of the drug treatment. We were able to eliminate some of the problems that limit the interpretation of the impact of corticosteroids on inspiratory muscle performance by choosing patients with no underlying pulmonary disease and with normal pulmonary and respiratory muscle function.

A number of studies have been carried out to correlate dyspnea and respiratory muscle performance. It was well documented that the intensity of breathlessness is related to the activity and the strength of the inspiratory muscles.² ³

Corticosteroids in high doses and for prolonged periods are frequently used in the treatment of many pulmonary diseases,⁴ ⁵ but the adverse effect of the drug on the respiratory muscles might be of great potential relevance to patients already suffering from dyspnea due to their respiratory disorder.⁶

It is well established that respiratory muscles can be trained, even in healthy subjects, like other skeletal muscles, and several reviews have been published dealing with ventilatory muscle training.⁷ ⁸⁻¹¹

We hypothesized that specific inspiratory muscle training (SIMT) would prevent steroid-induced inspiratory muscle weakness and dyspnea in patients with no underlying pulmonary disorder.

This study was designed to evaluate the ability of SIMT to prevent the effects of a therapeutic dosage of corticosteroids on inspiratory muscle function in patients receiving the drug for diseases other than pulmonary with no underlying respiratory or muscular disease.

Methods

Twelve consecutive patients, 5 men and 7 women, with ages...
Table 1—Characteristics of Patients Included in the Study*

<table>
<thead>
<tr>
<th>Subject/Sex/Age, yr</th>
<th>Indication</th>
<th>Steroid Dose, mg/d</th>
<th>FEV₁, %</th>
<th>FVC, %</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Group A</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>1/F/41</td>
<td>ITP</td>
<td>80</td>
<td>100</td>
<td>120</td>
</tr>
<tr>
<td>2/F/22</td>
<td>ITP</td>
<td>60</td>
<td>108</td>
<td>104</td>
</tr>
<tr>
<td>3/M/34</td>
<td>RPGN</td>
<td>60</td>
<td>100</td>
<td>91</td>
</tr>
<tr>
<td>4/M/35</td>
<td>RPGN</td>
<td>90</td>
<td>91</td>
<td>97</td>
</tr>
<tr>
<td>5/F/24</td>
<td>ST</td>
<td>60</td>
<td>90</td>
<td>103</td>
</tr>
<tr>
<td>6/M/19</td>
<td>MCGN</td>
<td>90</td>
<td>106</td>
<td>106</td>
</tr>
<tr>
<td>Mean ± SEM</td>
<td>29.2 ± 3.4</td>
<td>73.3 ± 6.1</td>
<td>99.2 ± 3.0</td>
<td>105.5 ± 4.0</td>
</tr>
<tr>
<td><strong>Group B</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>1/F/28</td>
<td>ITP</td>
<td>80</td>
<td>94</td>
<td>99</td>
</tr>
<tr>
<td>2/F/36</td>
<td>ITP</td>
<td>60</td>
<td>100</td>
<td>104</td>
</tr>
<tr>
<td>3/M/20</td>
<td>MCGN</td>
<td>60</td>
<td>104</td>
<td>97</td>
</tr>
<tr>
<td>4/M/21</td>
<td>RPGN</td>
<td>90</td>
<td>98</td>
<td>104</td>
</tr>
<tr>
<td>5/F/40</td>
<td>ST</td>
<td>40</td>
<td>88</td>
<td>92</td>
</tr>
<tr>
<td>6/F/22</td>
<td>MCGN</td>
<td>60</td>
<td>109</td>
<td>101</td>
</tr>
<tr>
<td>Mean ± SEM</td>
<td>21.8 ± 3.4</td>
<td>65.0 ± 7.2</td>
<td>98.5 ± 3.0</td>
<td>99.5 ± 1.9</td>
</tr>
</tbody>
</table>

*All lung function data are expressed as percentage of predicted normal values. RPGN = rapidly progressive glomerulonephritis; MCGN = minimal changes glomerulonephritis; ST = subacute thyroiditis; ITP = idiopathic thrombocytopenic purpura.

ranging from 19 to 41 years, who received corticosteroids for diseases other than respiratory, were recruited into two groups: 6 patients were assigned to the control group (group A) and got sham training, while 6 patients received SIMT (group B) while receiving corticosteroids in a single-blind group-comparative trial (Table 1). The patients had to meet the following criteria: (1) no history or evidence of any respiratory, cardiovascular, allergic, neuromuscular, rheumatologic, or endocrine disease, or any disease that might impair muscle function; (2) normal results of pulmonary function tests; (3) normal results of respiratory muscle function tests; and (4) not taking any medications.

The patient characteristics are summarized in Table 1. Subjects were treated with high doses of corticosteroids (prednisone, 1 to 1.5 mg/kg/d) for 8 weeks when doses were tapered down, up to complete withdrawal within 6 weeks.

**Tests**

All measurements were made with the subject seated in a high-backed chair to keep posture constant. All tests were performed before and every 2 weeks after the administration of corticosteroids, and up to 8 weeks.

**Spirometry:** The forced vital capacity (FVC) and the forced expiratory volume in 1 s (FEV₁) were measured three times on a computerized spirometer (Compact, Vitalograph, Buckingham England) and the best trial is reported.

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

**Inspiratory Muscle Endurance:** To determine inspiratory muscle endurance, a device similar to that proposed by Nickerson and Keens was used. Subjects inspired through a two-way valve (Hans-Rudolph) whose inspiratory port was connected to a chamber and plunger to which weights could be added externally. Inspiratory threshold load was then increased by the progressive addition of 25- to 100-g weights at 2-min intervals, as was previously described by Martyn and coworkers, until the subjects were exhausted and could no longer inspire. The pressure achieved with the heaviest load (tolerated for at least 60 s) was defined as the peak pressure (PmPeak).

**Training Protocol:** Subjects of both groups trained five times a week, each session consisting of 30 min of training, while receiving corticosteroids. The training was performed under the supervision of a physiotherapist. Both groups received the same attention and adjustment in medications and were managed equally during the training period.

In the SIMT group, subjects started to train with a resistance equal to 15% of their Plmax, and the resistance was then increased incrementally to 60% of their Plmax, through the first month. The SIMT was then continued at 60% of the Plmax. The level of load was adjusted every week according to the new measurements of the Plmax achieved by the patients. Patients in group A breathed through the same trainer with no resistance. The subjects received either SIMT or a sham training with a threshold inspiratory muscle trainer (Threshold Inspiratory Muscle Trainer, Healthscan, NJ).

Patients in both groups were highly motivated and highly compliant with the training. Even the control patients continued using the sham training to the end of the study. However, most of the patients in the control group became gradually aware of the fact that they were using a sham device, but there was no interaction between the two groups.

**Data Analysis**

The paired t tests were used to compare posttreatment with respect to pretreatment values. The analysis of variance was carried out to compare changes exhibited by the two groups.

**RESULTS**

Spirometry data for the two groups before treatment are also presented in Table 1. In both groups, there was no difference between the posttreatment and pretreatment values with regard to the FEV₁/FVC relationship. However, in the control group but not in the training group, there was a small but significant decrease, from 99.2 ± 3.0 to 94.3 ± 2.8 (mean ± SEM, p<0.01) in FEV₁ (percentage of predicted normal values) and from 103.5 ± 4.0 to 88.7 ± 3.1 (p<0.001) in the FVC (percentage of predicted normal values) following treatment (Fig 1).

The results of the individual inspiratory muscle functions are shown in Figures 2 and 3. All subjects had normal inspiratory muscle strength, as expressed by the Plmax at RV (117.5 ± 9.4 cm H₂O for group...
A and 106.7 ± 7.6 cm H₂O for group B) and inspiratory muscle endurance as expressed by the relationship between P₂₀Peak and the PImax (82.7 ± 2.6% and 79.5 ± 3.0%, respectively), before treatment.

Following administration of corticosteroids, there was a gradual decrease in both inspiratory muscle strength (from 117.5 ± 9.4 to 80.5 ± 3.3 cm H₂O, p<0.005) and endurance (from 82.7 ± 2.6 to 40.2 ± 1.7%, p<0.001) in the control group, although the rate of decrease was not identical. The decrease in endurance was already detected after 2 weeks of corticosteroid therapy, while the decrease in strength was noted only 4 weeks following the initiation of treatment. On the contrary, despite corticosteroid therapy, there was no significant change in the inspiratory muscle function in the patients whose inspiratory muscles were specifically trained.

**DISCUSSION**

In this study, six patients with normal lung and respiratory muscle function, with diseases other than respiratory, developed severe inspiratory muscle weakness during treatment with high doses of corticosteroids. This weakness was preventable by using SIMT during corticosteroid treatment in another six patients.

A number of previous studies have shown the myopathic effects of corticosteroids on respiratory
In a study recently performed by us, we reported that administration of corticosteroids to eight patients with normal lung and respiratory muscle function, for 8 weeks, resulted in a moderate reduction in inspiratory muscle strength (from 126.9±9.6 to 86.5±7.4 cm H₂O, p<0.0001) and striking reduction in endurance (from 84.4±2.4 to as low as 38.9±2.4%, p<0.0001). A number of studies have been carried out to correlate dyspnea and respiratory muscle performance. It was well documented that the intensity of breathlessness is related not only to the activity, but also to the strength of the inspiratory muscles. 2-4 Corticosteroids in high doses and for prolonged periods are frequently used in the treatment of many pulmonary diseases, 19-21 and the potential myopathic effect of the drug on the respiratory muscles, as was observed in our study, is of great relevance to patients, like patients with COPD already suffering from dyspnea due to their underlying respiratory disorder. In addition, asthmatic patients treated with long-term corticosteroids might be disadvantaged during asthma attacks when the increased work of breathing demands further muscle effort. In such cases, the potential benefits of corticosteroids on lung function may be overshadowed by their negative effect on inspiratory muscle function.

It has been shown previously that the inspiratory muscles can be trained for both strength and endurance in normal subjects, 11 quadruplegics, 22 patients with cystic fibrosis, and patients with COPD. 23-25 The new threshold inspiratory muscle trainers are designed to provide a specific, constant workload that is independent of variations in inspiratory flow rate. In two previous studies, we were able to demonstrate that all patients who trained with threshold trainer were able to increase their inspiratory muscle strength and endurance. 26,27 The present study clearly shows that inspiratory muscle training abolished completely the adverse effect of the corticosteroids on the inspiratory muscles. Corticosteroids play a major role in the treatment of COPD, asthma, and other pulmonary diseases, some of them already being characterized by inspiratory muscle weakness and dyspnea. In such cases, to prevent the adverse effect of the drug, SIMT might be recommended along with the treatment.

REFERENCES