The Effect of Corticosteroids on Inspiratory Muscle Performance in Humans*

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Functional alterations in the inspiratory muscles were evaluated in patients receiving corticosteroids for diseases other than respiratory. Inspiratory muscle strength, as expressed by the maximal inspiratory mouth pressure (Pimax), and inspiratory muscle endurance (PmPeak/Pimax), using a pressure threshold breathing device, were evaluated in eight patients with normal pulmonary and inspiratory muscle functions (two patients with rapidly progressive glomerulonephritis, two with glomerulonephritis with minimal changes, two with idiopathic thrombocytopenic purpura, and two with subacute thyroiditis). There was a gradual decrease in both inspiratory muscle strength and endurance following corticosteroid administration. After 8 weeks of treatment PmPeak/Pimax decreased from 84.4 ± 2.4 to 67.9 ± 3.1 percent (p < 0.001), while inspiratory muscle strength dropped from 128.9 ± 9.6 to 96.5 ± 7.4 cm H2O (p < 0.005). Gradual steroid dosage tapering resulted in marked improvement in both strength and endurance; the inspiratory muscle strength rose significantly to 112.2 ± 8.1 cm H2O (p < 0.0005) when steroid treatment was stopped, and even more significantly 6 months later (to 123.1 ± 8.1 cm H2O [p < 0.0001]), and the PmPeak/Pimax rose to 60.6 ± 3.4 percent (p < 0.001) and to 74.7 ± 3.2 percent (p < 0.0001), respectively. We conclude that corticosteroids have a significant deteriorating effect on respiratory muscle function in humans. This weakness is reversible while tapering steroid dosage. Steroid therapy should be reconsidered in patients with underlying lung disease.

(Chest 1993; 104:1788-91)

FVC = forced vital capacity; Pimax = maximal inspiratory mouth pressure; PmPeak = peak pressure; PmPeak/Pimax = inspiratory muscle endurance

Corticosteroids in high doses and for prolonged periods are frequently used in the treatment of many pulmonary diseases.1,2 Steroid-induced myopathy is a well-known clinical entity in patients treated with high doses of corticosteroids.3 However, little attention has been paid to the effects of chronic administration of corticosteroids on respiratory muscle function, although this question is of great potential relevance to patients already suffering from respiratory disorders.4 Several studies have been performed in order to provide definitive information on the effects of chronic administration of corticosteroids on respiratory muscle function in patients with respiratory diseases.5,6 However, it is impossible to separate the effects of steroid therapy from the effects of the underlying diseases in these patients.

Therefore, we examined 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

Clinical Data

A group of 8 patients, 4 men and 4 women, with ages ranging from 17 to 33 years were studied. All were consecutive patients who received corticosteroids for diseases other than respiratory and 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 pulmonary function tests.
3. Normal respiratory muscle function tests.
4. Not taking any medications.

The patients' 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 to complete withdrawal within 6 weeks.

Tests

All measurements were made with the subject seated in a high-back chair to keep posture constant. All tests were performed before and every 2 weeks after the administration of corticosteroids and up to 3 months. Tests were then repeated following complete withdrawal of the drug and 6 months later.

Spirometry: The forced vital capacity (FVC) and the FEV1 were measured three times on a computerized spirometer (Compact, Vitalograph, Buckingham, England), and the best trial was reported.

Inspiratory Muscle Strength: Inspiratory muscle strength was assessed by measuring the maximal inspiratory mouth pressure (Pimax), at residual volume, 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 (PmPeak/Pimax), a device similar to that proposed by Nickerson and Keens was used. Subjects inspired through a two-way Hans-Budolph valve, the inspiratory port of which 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-gram 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).

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Table 1—Characteristics of Patients Included in the Study*

<table>
<thead>
<tr>
<th>Subject</th>
<th>Sex</th>
<th>Age, yr</th>
<th>Indication†</th>
<th>Steroid Dose, mg/d</th>
<th>FEV₁, %</th>
<th>FVC, %</th>
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</thead>
<tbody>
<tr>
<td>1</td>
<td>M</td>
<td>17</td>
<td>RPGN</td>
<td>90</td>
<td>104</td>
<td>110</td>
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<tr>
<td>2</td>
<td>F</td>
<td>26</td>
<td>ITP</td>
<td>60</td>
<td>100</td>
<td>94</td>
</tr>
<tr>
<td>3</td>
<td>M</td>
<td>24</td>
<td>MCGN</td>
<td>60</td>
<td>94</td>
<td>98</td>
</tr>
<tr>
<td>4</td>
<td>M</td>
<td>31</td>
<td>RPGN</td>
<td>90</td>
<td>105</td>
<td>107</td>
</tr>
<tr>
<td>5</td>
<td>F</td>
<td>29</td>
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<td>89</td>
<td>97</td>
</tr>
<tr>
<td>6</td>
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<td>60</td>
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<tr>
<td>7</td>
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<td>25</td>
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<td>101</td>
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<tr>
<td>8</td>
<td>F</td>
<td>33</td>
<td>ITP</td>
<td>60</td>
<td>92</td>
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</tbody>
</table>

Mean ± SEM 25.5 ± 2.0 61.3 ± 7.4 99.6 ± 2.7 102.2 ± 2.2

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

Statistical Analysis

Comparisons of the posttreatment versus pretreatment values of respiratory muscle performance in the eight patients were carried out using the two-way repeated measures analysis of variance.

RESULTS

Spirometry data for the subjects before treatment are also presented in Table 1. There was no difference between the posttreatment and pretreatment values in regard to the FEV₁/FVC ratio relationship. However, there was a small but significant decrease, from 99.6 ± 2.7 to 94.6 ± 1.8 (mean ± SEM [p<0.01]) in FEV₁ (percentage of predicted normal values) and from 102.2 ± 2.2 to 90.6 ± 2.4 (p<0.001) in the FVC (percentage of predicted normal values) following treatment.

The results of the individual inspiratory muscle function are shown in Figures 1 and 2. All subjects had normal inspiratory muscle strength, as expressed by the Pmax at residual volume (126.9 ± 9.6 cm H₂O) and PmPeak/Pmax as expressed by the relationship between PmPeak and the Pmax (84.4 ± 2.4 percent), before treatment. Following administration of corticosteroids, there was a gradual decrease in both inspiratory muscle strength and endurance, although the rate of decrease was not identical. Two weeks after the initiation of treatment, a significant drop in PmPeak/Pmax was already observed (from 84.4 ± 2.4 to 67.9 ± 3.1 percent [p<0.001]), while inspiratory muscle strength was still reserved at this point and showed a significant drop only at the end of the 4th week of treatment (from 126.9 ± 9.6 to 109.4 ± 10.3 cm H₂O [p<0.005]).

At the end of the 8 weeks of treatment, inspiratory muscle performance reached the lowest values. Mean inspiratory muscle strength dropped to as low as

![Figure 1](http://journal.publications.chestnet.org/pdfaccess.ashx?url=/data/journals/chest/21678/)

**Figure 1.** Inspiratory muscle strength, as expressed by the Pmax at residual volume before steroid treatment, after 8 weeks of treatment (left) and following tapering steroid dosage and 6 months after complete withdrawal of the drug (right).
86.5 ± 7.4 cm H2O (p < 0.0001), while the PmPeak/Pimax decreased to 38.9 ± 2.4 percent (p < 0.0001). Following gradual reduction of the steroid dose, the patients regained both strength and endurance; the inspiratory muscle strength rose significantly to 112.2 ± 8.1 (p < 0.0005) when steroid treatment was stopped, and rose even more significantly 6 months later to 123.1 ± 8.1 [p(0.0001)], as shown in Figure 1. The inspiratory muscle endurance rose to 60.6 ± 3.4 percent (p < 0.001) and to 74.7 ± 3.2 percent (p < 0.0001), respectively, as seen in Figure 2. At this point in time, the values of both strength and endurance statistically were not different from baseline values.

**DISCUSSION**

In this report, we present eight patients with normal lung and respiratory muscle function, with diseases other than respiratory, who developed severe inspiratory muscle weakness during treatment with high doses of corticosteroids. Tapering the steroid dosage down was clearly associated with regained inspiratory muscle strength and endurance.

The reduction in PmPeak/Pimax, after 2 weeks of treatment was striking when compared with the reserved inspiratory muscle strength at this point in time. Glycogen depletion and lactate accumulation are usually associated with reduced muscle endurance.12 Although glycogen depletion was not observed, after 2 weeks, in corticosteroid-treated animals, lactate levels were significantly elevated in the diaphragms of the animals.13 It is possible that the increased lactate accumulation may have played a role in the reduced endurance at this point in time, while the strength was still normal. A number of previous studies have shown the myopathic effects of corticosteroids on respiratory muscle function in animals.15-16 Ferguson and colleagues13 found that the histologic changes in the diaphragm were associated with no change in diaphragmatic strength but with a fall in PmPeak/Pimax. These studies show that steroids may affect respiratory muscles and that myopathy may occur after treatment for 2 weeks or even less. However, there may be species differences in susceptibility to steroid myopathy, and these results are not necessarily applicable to humans.

Several studies have examined the effects of corticosteroids on respiratory muscle function in humans. Bowyer and colleagues6 found that those patients who showed a marked reduction in hip flexor strength also had reduced inspiratory muscle strength. Melzer and Souhrada7 described four obese patients with steroid-dependent bronchial asthma and inspiratory muscle weakness. However, in a previous study by Weiner et al,17 it was shown that hyperinflation adversely affects the performance of the inspiratory muscles, in patients with asthma; therefore, the reduction in peak inspiratory mouth pressure may have been due, either partly or completely, to factors other than steroid therapy. There also are anecdotal reports on inspiratory and expiratory muscle weakness following steroid treatment.18 However, in the vast majority of the cases, respiratory muscle weakness developed following treatment with a combination of steroids and muscle relaxants.19-21

On the other hand, Picado and coworkers3 compared patients who had steroid-dependent bronchial asthma with age- and sex-matched patients who had asthma but were not taking oral steroids. There was no significant difference in respiratory muscle perform-
ance between the two patient groups. However, a training effect of the inspiratory and expiratory muscle could have masked respiratory muscle weakness due to steroid myopathy in the prednisone group. Another explanation for the lack of muscle weakness complaints in these asthmatic subjects might be the fact that these patients usually were treated with low doses of steroids. Therefore, although these human studies provide important information, they do not clarify the effects of steroid therapy per se on respiratory muscle function in humans.

In a recent study, Wang and colleagues have found, in 16 normal volunteers, that prednisone in moderate dosage administered for 2 weeks had no significant effect on respiratory muscles in humans. However, corticosteroids in higher doses and for longer periods of time are frequently used in the treatment of many pulmonary diseases, and the results of the study by Wang et al are not necessarily applicable to higher doses or longer durations of treatment.

Our study shows that patients who receive high-dose steroids for several weeks may develop inspiratory muscle weakness, which seems to be reversible following withdrawal of the drug. We were able to isolate the effects of corticosteroids on inspiratory muscle performance from those effects contributed to the underlying disease, by choosing patients who had no pulmonary disease and who had normal pulmonary and respiratory muscle function.

Whether similar changes might be observed in patients treated with lower doses of corticosteroids needs to be determined. However, if such changes are encountered frequently, the use of systemic corticosteroids should be limited in patients already suffering from respiratory disease.

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