Diaphragmatic Fatigue and Breathing Pattern during Weaning from Mechanical Ventilation in COPD Patients*

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The medium-term outcome of weaning from mechanical ventilation in COPD patients is not easy to anticipate because a respiratory fatigue may eventually develop. We evaluated the diaphragmatic function and the breathing pattern during 40 weaning trials on 15 patients ventilated after acute respiratory failure. We formed two groups according to the success (group B, n = 18) or failure (group A, n = 19) of the medium-term attempt (group A/less than 10 hours; group B/more than 12 hours). Provided the patients showed the classic weaning criteria (tidal volume >5 ml/kg, respiratory frequency <30 breaths per minute, PaO₂ >50 mm Hg), the study of the breathing pattern did not allow differentiation between the groups. However, the transdiaphragmatic pressure (Pdi) and the Pdimax, which gave an indication of the power of diaphragm contraction, dropped early in the group that could not stand weaning, with an increase in the Pdi/Pdimax ratio. In addition, this same group showed a diaphragmatic dysfunction attested for by a frequent negative gastric pressure associated with or shortly preceded by an abdominal paradoxic motion.

Weaning from mechanical ventilation is a high risk period for the patient with chronic obstructive pulmonary disease (COPD). A short-term failure is easily detected through clinical investigation or blood gas analysis. Early prediction in long term ability to sustain spontaneous breathing is not so easy. In daily practice, it requires identification of direct pulmonary signs and indirect extrapulmonary signs. The latter may consist of a nutritional evaluation, the existence of an underlying infection, or a latent affection of other organs. Direct respiratory signs are much more difficult to evaluate and usually indicate a respiratory muscle fatigue. The added inspiratory load induced by weaning from mechanical ventilation may cause muscle exhaustion leading to ventilatory failure and acute hypercapnia.¹³

The assessment of diaphragmatic contractility cannot be measured directly, but a good indication can be found by measuring transdiaphragmatic pressure during spontaneous breathing¹⁴ and its relation to maximum transdiaphragmatic pressure (Pdi/Pdimax).⁵ Moreover, as diaphragm contraction happens mainly during the inspiratory phase, the respiratory effort increases as the ratio of inspiration time to total cycle time (T₁/Ttot) increases.⁸

The purpose of this study was to evaluate some measurements of the respiratory muscular function and of the breathing pattern to find out whether changes could give an indication about the medium-term outcome of weaning from mechanical ventilation. We selected a homogeneous group of COPD patients who had been artificially ventilated for acute respiratory failure, and had successfully borne a two-hour weaning period without any sign of exhaustion.

Materials and Methods

Patients

Fifteen patients (11 men, four women) were included in the study of 40 weaning attempts. They ranged from 55 to 72 years old (mean age ± SD = 63.1 ± 6.1 years), weighed 49 to 75 kg, and all had a medical history of COPD, confirmed in ten patients by respiratory function tests performed from one to four months before or after the acute respiratory failure (Table 1). For all patients, respiratory failure was caused by bacterial exacerbation of COPD confirmed by local and/or general bacteriologic samples. None of the patients showed any sign of thromboembolism and only tracheotomized patients were selected. Mechanical ventilation lasted 8 ± 3 days.

When weaning was performed, the patients' condition was stable

Table 1—Lung Function Parameters and Blood Gas Data for Ten Patients with COPD*

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Mean ± SD</th>
</tr>
</thead>
<tbody>
<tr>
<td>VC (% predicted)</td>
<td>47.9 ± 6.2</td>
</tr>
<tr>
<td>TLC (% predicted)</td>
<td>121 ± 37.7</td>
</tr>
<tr>
<td>FEV₁ (% predicted)</td>
<td>31.1 ± 9.3</td>
</tr>
<tr>
<td>FEV₁/VC (%)</td>
<td>36 ± 10</td>
</tr>
<tr>
<td>PaO₂ (mm Hg)</td>
<td>57 ± 8</td>
</tr>
<tr>
<td>PaCO₂ (mm Hg)</td>
<td>52 ± 5</td>
</tr>
<tr>
<td>pH (units)</td>
<td>7.38 ± 0.04</td>
</tr>
<tr>
<td>SaO₂ (%)</td>
<td>88 ± 5</td>
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</table>

*These values were recorded from one to four months before or after the acute respiratory failure. Definition of abbreviations: VC = vital capacity; TLC, total lung capacity; FEV₁, forced expiration volume in 1 second.

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and afebrile. During completion of the study, the treatment (minidose subcutaneous heparin and erythromycin) was not interrupted. No other drug was given. All patients gave their informed consent.

Methodology

A Hans-Budolph one-way valve system was connected to the tracheotomy cannula and allowed to separate the inspiratory and the expiratory flows. A Draeger spirometer set out on the expiratory side measured ventilation per minute (V(min)), expiratory frequency (f), and tidal volume (VT). A Lill-type pneumotachograph connected to a differential pressure transducer measured the inspiratory flow. Another transducer measured pressure in the airway (Paw).

The Pdi was the result of the difference between gastric (Pga) and esophageal (Pes) pressures measured on the gastric and esophageal balloons with the system of Milic-Emili et al:7 the esophageal balloon, filled with 0.4 ml of air, was inserted into the middle-third of the esophagus and used as a pleural pressure index (Ppl). The gastric balloon, containing 2 ml of air, was placed 65 cm from the nostrils and reflected the intra-abdominal pressure (Pga). The relation between Pga and Pdi reflected the diaphragm effectiveness in the inspiratory process. The Pdimax was obtained, after clamping the airway during the end-expiratory phase, by asking the patient to reduce the pressure as much as possible while he could "see" his effort on a monitor in front of him (Mueller's experiment visualizing effort). We calculated the transpulmonary pressure at functional residual capacity (FRC) by the difference between Paw and Pes.

The occlusion pressure at 100 ms (P0.1) was measured with the classic technique:8 obstruction of the inspiratory circuit with a balloon, the patient being unable to see or prevent it. The different curves were monitored and recorded on an oscilloscope. We could then calculate the inspiratory time (T1), the expiratory time (T2), and the total cycle time (Ttot).

Blood gases were analyzed using a semi-automatic device.

Procedure

Weaning trial was interrupted when one of the following conditions was not respected: VT=5 mL/kg, f<30 breaths/min, PaO2>50 mm Hg. We included in the study the patients who had borne these conditions for two hours. Then, we took a series of five measurements of Pga, Pes, Pdi, Pdimax, P0.1. VT with the patients in a constant half-supine position. The mean inspiratory flow rate (V/Ttot), T1/T2, and Pdi/Pdimax were calculated from these values. A clinical study together with hourly measurements of Vt, f, and blood gas analysis enabled us to evaluate the weaning trial. If the patients had to be ventilated again, we took a second series of measurements before confronting them again. The time limit (TL) was defined as the duration of the weaning trial, plus the two initial hours of the period of selection. Statistical analysis of data was performed using Student's t-test. All values are given as the mean ± SD.

Results

We formed two separate weaning groups as follows: group A (n = 19), consisting of the patients connected again before the tenth hour; and group B (n = 18), consisting of the patients still weaned after 12 hours. Three weaning trials were not included in the study because they were interrupted between the tenth and twelfth hour. The two groups did not differ, neither blood gas analysis readings at the beginning of the study nor in ventilation duration (8.1±2.8 days vs 7.8±3.2 days).

Table 2 shows the various values of the breathing pattern and diaphragmatic function as recorded and calculated after a two-hour actual weaning period. The data recorded were easily reproducible and consist of the average worked out from five different values. The comparison of the breathing pattern in both groups showed no significant difference as regards Vmin, Vt, f, Pes, VT/tot, PaO2, PaCO2 or pH. Only the ratio T1/Ttot was significantly lower in group A (p<0.01) because of the reduction of inspiratory time.

On the other hand, there was a major difference between the indices of diaphragmatic function:

(1) The transdiaphragmatic pressure was significantly lower in group A (p<0.05) with a lower Pdimin in the same group (p<0.05) so that the transdiaphragm...
Group B values. There is no negative value in group B.

Mechanical pressure expressed as a function of transdiaphragmatic maximum pressure Pdi/Pdimax was higher in group A (p<0.001) (Table 2). With a Pdi/Pdimax limit of 0.4, 16 out of 18 weaning attempts in group B showed a ratio lower than 0.4, while 13 out of 19 attempts in group A showed a ratio higher than 0.4 (Fig 1).

(2) There was a different diaphragmatic function in group A as the Pga was significantly lower than that of group B (p<0.001) (Table 2). A negative value (16/19 in group A) showed either paradoxical ventilation or a flattened diaphragm, which was not easy to diagnose clinically. There was no negative value in group B (Fig 2).

The results before connecting group A to mechanical ventilation again are given in Table 3. The breathing pattern (Fig 3) was as expected: hypoventilation with rapid shallow breathing, drop in the mean inspiratory flow rate, and changes in blood gas data. The Pdi/Pdimax ratio increased again because of the collapse of Pdimax. The Pga remained negative.

Table 3—Breathing Pattern, Diaphragmatic Function and Blood Gas Data in Group A When Connected Again to Mechanical Ventilation

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Mean ± SD</th>
<th>p Values</th>
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<tbody>
<tr>
<td>Vmin, L/min</td>
<td>6.08 ± 0.1</td>
<td>p&lt;0.001</td>
</tr>
<tr>
<td>VT, ml</td>
<td>160 ± 9</td>
<td>p&gt;0.001</td>
</tr>
<tr>
<td>f, breaths/min</td>
<td>3.6 ± 4.2</td>
<td>p&lt;0.001</td>
</tr>
<tr>
<td>Ti, s</td>
<td>0.550 ± 0.08</td>
<td>p&lt;0.001</td>
</tr>
<tr>
<td>Ti/Ttot</td>
<td>0.340 ± 0.01</td>
<td>p&lt;0.001</td>
</tr>
<tr>
<td>VT/TV, ml/s</td>
<td>2.50 ± 1.8</td>
<td>p&lt;0.001</td>
</tr>
<tr>
<td>P01, cm H2O</td>
<td>7 ± 4.1</td>
<td>NS</td>
</tr>
<tr>
<td>Pdi/Pdimax</td>
<td>0.370 ± 0.11</td>
<td>p&lt;0.001</td>
</tr>
<tr>
<td>Pga, cm H2O</td>
<td>-6.1 ± 1.5</td>
<td>p&lt;0.001</td>
</tr>
<tr>
<td>PaO2, mm Hg</td>
<td>38 ± 7</td>
<td>p&lt;0.001</td>
</tr>
<tr>
<td>PaCO2, mm Hg</td>
<td>75 ± 9</td>
<td>p&lt;0.001</td>
</tr>
<tr>
<td>pH, units</td>
<td>7.31 ± 0.04</td>
<td>p&lt;0.01</td>
</tr>
</tbody>
</table>

*The values are compared with those of the same group registered after a two-hour weaning period. Comparisons are made with Student’s paired t-test.

Discussion

Our study brings out the following two important findings: (1) on patients with COPD disconnected from mechanical ventilation and showing no sign of respiratory failure within two hours, the values of Vmin, VT/Ti, Pga, pH, PaO2, and PaCO2 did not provide any clue as to the final success or failure of medium-term weaning (ten hours); and (2) due to the low value of the Pdimax, the Pdi/Pdimax ratio was higher on the group that failed to be weaned within ten hours. In addition, that same group showed a negative Pga in 16/19 trials, which never occurred in the other group.

In a previous paper,10 we showed that the patients who had to be reconnected to mechanical ventilation within ten hours showed no initial difference in their breathing pattern compared with the others. Only later, and particularly after two hours, did changes occur that suggested a quicker deterioration of the pulmonary mechanical condition. On the present study, the differences between our groups after two hours were not really significant except for a shorter Ti/Ttot ratio (p<0.01), a result probably due to a central type adaptation to compensate for the imposed extra-load.11 On the contrary, the signs of diaphragmatic dysfunction occur earlier and are easily exposed, but their meaning is less clear. The Pdi, ie, the difference between abdominal and pleural pressures, is a measure of diaphragmatic efficiency4,6 but needs a good technique in order to avoid misinterpretation;8,10,13 the Pga may be increased by the contraction of abdominal muscles: we took great care of our patients’ total relaxation during measurements, and only the inspiratory values of Pga and Pdi were recorded. Besides, evaluation of results is quite difficult in COPD patients because of airway obstruction and distension. Obstruction causes a lapse between swings in Ppl and Pga and measuring Pdi as the difference between the

*Figure 2. Levels of Pga in the two groups of weaning trials. Note the significant difference between group A (weaning time <10 hours) and group B (weaning time >12 hours). Mean Pga (± SD) is significantly lower in group A: 16/19 trials in group A show a negative value. There is no negative value in group B.*

*Figure 3. Reconstructed spiromgrams (mean ± SD) of group A (triangles) and group B (stars), after two hours of weaning trial. Group (squares) stands for the values in group A when connected again to mechanical ventilation.*
maximal values gives a wrong result. The error was lessened in our study as we recorded Pdi in real-time and measurements were made simultaneously. Distention reduces Pdi because of a flattening diaphragm with shortened fibers, so that it works on an ineffective portion of its length-tension curve. Therefore, Pdi may be underestimated, not only because of its volume-dependent character, but also because of the shape of the diaphragm. Moreover, Pdi varies over a wide range among individuals, a variation not related to fatigue but to a strong recruitment of the intercostal and accessory inspiratory muscles. For that reason, the Pdi was brought to the level of the Pdimax evaluated during a maximal inspiratory maneuver (Mueller), the patient receiving, on a monitor, visual feedback of the effort developed. This method turned out to be the surest and the most easily reproducible.

In our study, the group who had to be connected again to mechanical ventilation within ten hours showed a low Pdi and a still lower Pdimax; the values were even lower at the end of the weaning period, which may be due to such factors as decrease in central respiratory drive, diaphragm atrophy, hyperinflation, or alteration of the contractility.

A central depression cannot be held responsible because of the high level of Pao2 recorded in both groups. Besides, this has been confirmed by other workers studying acute respiratory failure in the COPD patient. Diaphragm atrophy may arise in patients submitted to prolonged mechanical ventilation. That may account for the initial reduction of Pdimax, and therefore, the increased ratio of Pdi/Pdimax, but however true for certain patients, this could not explain the differences between our two groups which were not that different in regard to the average duration of mechanical ventilation and the nutritional status. Moreover, a given patient may change groups within 24 hours, and his diaphragm condition would probably not undergo a drastic change in so short a delay.

A different level of pulmonary hyperinflation for each group would be a much more plausible theory but difficult to confirm without a direct measurement of the functional residual capacity. Intermittent positive pressure ventilation is, in itself, a cause of hyperinflation which may be aggravated by weaning, especially in COPD patients for whom hyperinflation is a pre-existing condition. Several of our findings in group A may certainly be due to a more important distention than in group B. Therefore, the decrease in Pdimax could be an indicator of a bad condition of the diaphragmatic function, the diaphragm having to work more (increase of Pdi/Pdimax) with less efficiency (decrease of Pdi). Then, the bad condition of the diaphragm function was a major element causing fatigue and might as such account for the failure of the weaning trial in group A.

We cannot confirm here the alteration of diaphragmatic contractility during weaning with our methods. Indeed, diaphragmatic contractility is defined as the Pdi produced in response to a given level of stimulation, which may be measured by the Pdi/frequency curve recorded at different levels of phrenic stimulation. However, several authors have demonstrated the electromyographic evidence of inspiratory muscle fatigue using the ratio HI/LO of the rectified and integrated signals in patients who failed to wean from the ventilator. Moreover, Roussos et al have shown that a Pdi greater than 40 percent of the Pdimax cannot be tolerated indefinitely without fatigue. Our findings agree with a diaphragmatic fatigue existing as early as two hours after the beginning of the weaning period because the patients in group A exhibited a significantly higher Pdi/Pdimax ratio, not related to an increased Pdi (on the contrary, it was lower than group B's) but rather a lower Pdimax. Whatever the reason why the Pdimax decreased after two hours in group A (hyperinflation and/or alteration of diaphragm contractility), the resulting increase in the ratio Pdi/Pdimax caused the diaphragm to be much less fatigue-resistant. Nevertheless, fatigue would account much more easily than hyperinflation alone for the level of Pga recorded in group A. Regarding Pga overestimating Pab, our findings indicate a constant and often remarkable, negative abdominal pressure during inspiration, probably a symptom of abdominal paradoxic motion, which when undetected at the time of measurements, will show about an hour later. This paradoxic motion usually means poor prognosis in regards to the outcome of weaning. Thus, in a study where the diaphragmatic EMG was recorded during the weaning trial, the decrease in the ratio HI/LO was accompanied or followed by a paradoxic motion during inspiration, a clinical sign of fatigue.

After a two-hour weaning period, the blood gas parameters were not significantly different in the two groups, but group A showed a progressive respiratory acidemia and hypoxemia. The etiologic factors were probably multiple: increase in dead-space ventilation, heterogeneity of ventilation/perfusion ratio, and increase in production of carbon dioxide. Then, hypoxemia, hypercapnia, and acidosis joined their deleterious effects on diaphragmatic contractility, and fatigue was accentuated.

In conclusion, the failure of medium-term weaning trial in the COPD patient shows a definite diaphragmatic dysfunction two hours after the beginning of the weaning period. Neither the respiratory pattern nor the blood gas data allows a clear distinction between these patients and those who will stand the weaning trial over the ten following hours. Our data give no clue as to the origin of the dysfunction. It might
be diaphragmatic fatigue eased and worsened by a drastic hyperinflation, classic in these patients. For all cases, the recording, two hours after the beginning of the weaning trial, of a null or negative Pga during inspiration (together or without an abdominal paradox movement) or of a Pdi/Pdmax ratio over 40 percent, is undoubtedly of poor prognosis as regards the medium term outcome of weaning.

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