Comparison of BiPAP Nasal Ventilation and Ventilation via Iron Lung in Severe Stable COPD*

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The effects of noninvasive ventilators on COPD remain controversial because of their obscure mechanisms. A randomized crossover study, using iron lung and positive pressure nasal ventilation (BiPAP) each for 40 min, was performed in 11 stable patients with severe COPD. Throughout the study, we monitored surface EMGdi, EMGst, ECG, \( \text{SaO}_2 \), \( \text{ETCO}_2 \), and the movements of RC and AB. Afterwards the data were replayed to calculate \( V_T, RR, PB, V_T/T_i, i\text{EMG}_st \), and phase angle. No statistically significant improvement was found in view of the above parameters. However, the percentage of \( i\text{EMG}_st \) change after 40-min BiPAP ventilation, compared with the baseline, was much more significant in patients with FEV, below 0.55 L than those with FEV, above 0.55 L (\( n = 4.7 \), \( i\text{EMG}_st \) vs 62.93 percent ± 23.27 percent vs 32.45 percent ± 42.79 percent, \( p = 0.0056 \)). \( i\text{EMG}_st \) correlated significantly with FEV, during BiPAP ventilation (\( p < 0.05 \), \( r = 0.59 \)). We conclude that the \( i\text{EMG}_st \) during short-term BiPAP ventilation correlates with the severity of the disease.

Respiratory muscle fatigue may contribute to exercise limitation and respiratory failure in patients with severe chronic obstructive pulmonary disease (COPD). Conventional mechanical ventilation has been successful in supporting ventilation and resting the respiratory muscles when severe respiratory muscle fatigue or failure occurs, but severe complications may ensue from repeated and long-term endotracheal intubation.

Noninvasive ventilators such as the iron lung, pneumowrap, or positive pressure ventilation via a nasal or face mask can spare the complications of artificial airways. These ventilators have successfully improved the alveolar ventilation in patients with neuromuscular diseases or thoracic deformities. However, their efficacy in patients with severe COPD remains controversial. Strumpf and coworkers found that long-term nocturnal nasal ventilation had no obvious effect on gas exchange, respiratory muscle strength, exercise endurance, or dyspnea rating in COPD patients. Nava and coworkers showed that negative pressure ventilation could induce respiratory muscle rest in similar patient groups. However, Belman and coworkers demonstrated that positive ventilation was much more effective than negative pressure ventilation in reducing diaphragmatic activity. According to our experience in BiPAP ventilation, COPD patients in acute exacerbation tended to get used to the ventilator more quickly than those in stable condition. Therefore, we hypothesize that the effects of noninvasive ventilators are correlated with the disease severity.

Using a randomized crossover design, this study aims to assess and compare the short-term effects of noninvasive ventilators on respiratory muscle activity, respiratory drive, respiratory muscle strength, gas exchange, and thoracoabdominal asynchrony (TAA) in patients with severe COPD.

Materials and Methods

Patients

Eleven male patients were included in the study. All had a previously documented diagnosis of COPD and met the following criteria: (1) FEV, below 1.1 L; (2) being stable for at least 1 week; and (3) the ability to tolerate the supine position for at least 2 h. The study protocols were approved by the ethical research committee of our hospital. All the patients gave their informed consent prior to the study.

Measurements

All patients underwent flow-volume examination (Sensormedics 2450, Anaheim, Calif) and arterial blood gas (ABG) analysis on room air (Radiometer ABL 3, Copenhagen, Denmark) before the study. Maximum inspiratory pressure (Pimax) and maximum expiratory pressure (Pemax) of mouth were also measured using a mouthpiece with a small airleak that was connected to a differential aneroid pressure transducer (Coulbourn T41-05, Lehigh Valley, Pa). All the experiments were conducted in a well-isolated room. Recording devices were set up as in Figure 1. Oxygen saturation (\( \text{SaO}_2 \)) was monitored by a pulse oximeter (Ohmeda Biox 3700, Englewood, Colo). End-tidal \( \text{CO}_2 \) (\( \text{ETCO}_2 \)) was monitored continu-

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BiPAP Nasal Ventilation vs Iron Lung in COPD (Lien et al)
A

B

FIGURE 1. Rib cage (RC) and abdomen (AB) motion plotted against each other (with time as an implicit variable) in a Lissajous figure. The ratio of s/m is an index of thoracoabdominal asynchrony. For phase angle $0<\phi<90$, $s = m/\cos\phi$; For $90<\phi<180$, $s = m/\sin\phi$, where $s = m/\cos\phi$. Left (A), The clockwise direction of the loop indicates that RC expansion precedes AB expansion during inspiration (from reference 21, with permission). Right (B), An example of the Lissajous figure from one breath of one of our patients.

Deep breath was to confirm the optimal positions of the electrodes. The integrated EMG activity of sternocleidomastoid muscle (iEMGst) showed gradual improvement from rest to 40 min after BiPAP ventilation.
inductive plethysmography (Respigraph, Respitrace Corporation, Miami Beach, Fla). Two recording bands were placed around the middle RC, ie, 10 cm above xyphoid process, and around the AB just above the umbilical line, respectively.

**Signal Analysis**

The signals from the EtCO₂ monitor, pressure transducer, respiratory inductive plethysmography, ECG, and EMG amplifier/filters passed through an analog to digital converter (Coulbourn L25-12) to a personal computer. With the help of software (CODAS, Coulbourn), the signals were displayed throughout the study and recorded for 1 min every 10 min. During recording, the same signals were simultaneously displayed and recorded on a strip chart recorder (Multi-Graphic Recording System, Coulbourn R14-18).

**Figure 3.** Left (A), Phase angle, EMGdi, and EMGst showed insignificant and highly variable change during rest and BiPAP ventilation of different duration. Right (B), Similar findings were noted during iron lung ventilation. Values represent mean ± SD.

**Figure 4.** (Left (A), These figures demonstrate insignificant changes in VT, VT/Ti, and RR between rest and BiPAP ventilation of different duration. Right (B), Similar findings were noted during iron lung ventilation. Values represent mean ± SD.
Table 1—Characteristics of 11 Patients With Severe COPD

<table>
<thead>
<tr>
<th></th>
<th>Average</th>
<th>SD</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sex</td>
<td>All male</td>
<td></td>
</tr>
<tr>
<td>Age, yr</td>
<td>69</td>
<td>5</td>
</tr>
<tr>
<td>FEV₁, L</td>
<td>0.71</td>
<td>0.21</td>
</tr>
<tr>
<td>FEV₁, % pred</td>
<td>28</td>
<td>9</td>
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<tr>
<td>FVC, L</td>
<td>2.01</td>
<td>0.53</td>
</tr>
<tr>
<td>FEV₁/FVC</td>
<td>0.35</td>
<td>0.05</td>
</tr>
<tr>
<td>PaCO₂*</td>
<td>45.1</td>
<td>10.8</td>
</tr>
<tr>
<td>PaO₂*</td>
<td>66.3</td>
<td>13.7</td>
</tr>
<tr>
<td>pH*</td>
<td>7.44</td>
<td>0.05</td>
</tr>
</tbody>
</table>

*Room volume arterial blood gases.

Tidal volume (Vr) was measured using the sum signal from the respiratory inductive plethysmograph that was calibrated with a spirometer (Gould, Cleveland, Ohio) before study. Respiratory rate (RR) and inspiratory time (Ti) were calculated on a breath-by-breath basis from the sum signal.

The signals of RC and AB were replayed to form "Lissajous figures" (Fig 1) on software (Lotus version 2). A "phase angle," θ, was calculated as an index of TAA = θ̅ which can be measured from a Lissajous figure, in which AB and RC motion are plotted on the x and y axis, respectively, with time as an implicit variable (Fig 1a).

Figure 1b shows an example of the Lissajous figure from one breath of one of our patients. The width of the "loop" is an index of asynchrony and is quantified by dividing the width of the figure at mid-RC excursion (m) by the width of the figure at the extremes of AB excursion (s). When θ̅ = 0°, m = s/2; for 90° < θ̅ < 180°, θ̅ = 0° – μ, where μ = m/s.

The integrated diaphragmatic EMG (iEMGdi) was calculated during inspiration using software developed by Belman et al. The EMG of sternocleidomastoid muscle (iEMGst) was directly rectified and integrated without kicking out the QRS activity because the cardiac electrical activity was negligible on the neck.

Protocol

After the recording devices were carefully set up, the patient rested in the supine position for 10 min. The data were recorded on both personal computer and strip chart recorders, using those obtained in the last minute as a baseline. Afterward, the patients were randomized to either positive nasal ventilation via BiPAP (Respiromics, Monroeville, Pa) or iron lung (Emerson, Cambridge, Mass) ventilation for 40 min. During ventilatory support, the data were recorded for 1 min every 10 min. Pmax and Pmax were measured again immediately after the ventilatory support. After resting for 10 min, the patient was shifted to the other ventilatory support for another 40 min. The data were also recorded for 1 min every 10 min. During BiPAP ventilation, spontaneous (S) mode was used with IPAP around 10 cm H₂O and EPAP at 2 cm H₂O as the patient could tolerate. The pressure level of the iron lung was set around 20 cm H₂O without causing any discomfort. The rate of the iron lung was set around 18 cycle/min, which can be adjusted according to the comfort of patients.

Subsequently, the patient rested for another 10 min to obtain the last baseline data that were recorded again in the last minute. Pmax and Pmax were measured again. Throughout the study, the signals of EMG, ECG, and respiratory movements were displayed on the monitor of the personal computer.

Statistics

One-way analysis of variance for repeated measures was used to compare the values during spontaneous breathing, BiPAP, and iron lung. Student's t test was used to compare the ΔEEMGst, pulmonary function, and ABG between the patients with FEV₁ below 0.55 L and those with FEV₁ above 0.55 L. Simple linear regression was used to evaluate the correlation between FEV₁ and ΔEEMGst. Differences were considered statistically significant when p < 0.05. All results are reported as mean ± SD.

Results

The characteristics of 11 patients are demonstrated in Table 1. All were male with an average age of 69 ± 5 years. Average FEV₁ was 0.71 ± 0.21 L (28 percent ± 9 percent of predicted values). Mild hypoxemia (PaO₂, 66 ± 13.7 mm Hg) and minimal hypercapnea (PaCO₂, 45.1 ± 10.8 mm Hg) were noted in ABG on room air.

Response to BiPAP

Figure 2 shows an example of the recorded tracings from one of our patients. Deep breath tracings were used to confirm the optimal position of the electrodes. The EMG activities were suppressed gradually with the use of BiPAP. However, the result was not constant for other patients. Data of the EMG activities of both diaphragm and sternocleidomastoid muscles are displayed in Figure 3a, which shows no significant difference between the baseline and those obtained 40 min after the use of BiPAP. The change of phase angle was also insignificant. The changes of Vr, Vr/Ti, and RR were also insignificant (Fig 4a).

Before and 40 min after BiPAP, there was also no significant change in pulse rate (88.1 ± 11.2/min vs 86.3 ± 10.0/min), ETCO₂ (36.3 ± 13.4 mm Hg vs 35.5 ± 9.3 mm Hg), or SaO₂ (95.1 ± 2.3 percent vs 95.6 ± 2.0 percent).

Pmax and Pmax were not improved after the use of BiPAP for 40 min either (−49.0 ± 20.0 cm H₂O vs −48.6 ± 37.5 cm H₂O and 65.4 ± 24.5 cm H₂O vs 66.4 ± 24.4 cm H₂O).

When the FEV₁ of the patients was below 0.55 L,
the reduction in iEMGst was quite obvious after the use of BiPAP for 40 min (Fig 5). Conversely, the EMG was not suppressed or even increased in some patients when the FEV1 was above 0.55 L (Fig 5). The difference of ΔiEMGst between these two groups was statistically significant (−62.93 percent ± 23.27 percent vs 32.45 percent ± 42.79 percent, p = 0.0056). The comparison of patient age, pulmonary function, and ABG between these two groups was demonstrated in Table 2. Furthermore, the correlation between FEV1 and ΔiEMGst was statistically significant (Fig 6, r = 0.59, p <0.05).

Response to Iron Lung

The iEMGdi and iEMGst did not change significantly after the use of the iron lung for 40 min (Fig 3B). Unlike BiPAP, no significant correlation between pulmonary function and the change in EMG activities could be found. The change in phase angle was not significant either. There were insignificant changes in VT, Vt/Ti, and RR (Fig 4B).

There were also no significant changes in pulse rate

**Table 2—Comparison of Pulmonary Function and Arterial Blood Gases (ABC) Between the Patients With FEV1 Above 0.55 L and Those With FEV1 Below 0.55 L**

<table>
<thead>
<tr>
<th>Patient No.</th>
<th>Patients With FEV1 &gt;0.55 L</th>
<th>Patients With FEV1 &lt;0.55 L</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age, yr</td>
<td>70 ± 5</td>
<td>68 ± 2</td>
<td>NS†</td>
</tr>
<tr>
<td>FEV1, L</td>
<td>0.84 ± 0.15</td>
<td>0.47 ± 0.03</td>
<td>0.0006</td>
</tr>
<tr>
<td>FEV1, % pred</td>
<td>34.3 ± 7.6</td>
<td>19.5 ± 1.3</td>
<td>0.0017</td>
</tr>
<tr>
<td>FVC, L</td>
<td>2.29 ± 0.44</td>
<td>1.53 ± 0.24</td>
<td>0.0190</td>
</tr>
<tr>
<td>FEV1/FVC</td>
<td>0.37 ± 0.05</td>
<td>0.32 ± 0.03</td>
<td>NS</td>
</tr>
<tr>
<td>PaCO2*</td>
<td>39.6 ± 6.2</td>
<td>54.6 ± 9.5</td>
<td>0.0256</td>
</tr>
<tr>
<td>PaO2*</td>
<td>65.1 ± 10.9</td>
<td>68.3 ± 15.6</td>
<td>NS</td>
</tr>
<tr>
<td>pH*</td>
<td>7.46 ± 0.06</td>
<td>7.42 ± 0.02</td>
<td>NS</td>
</tr>
</tbody>
</table>

*Room air ABG.
†NS = not significant (p>0.05).

Study Limitations

In this study, we used surface electrodes to record EMGdi. Doubt could be raised that the EMG might be contaminated by the activities of intercostal or abdominal muscles; nevertheless, this kind of contamination can be negligible in both normal subjects and COPD patients.2,10,24,25 Actually, good correlation between surface and esophageal EMG has been described by several studies.10,27

To minimize the discomfort of the patients and the consequent influence on the study, we did not record esophageal or transdiaphragmatic pressures (Pdi). However, the excellent correlation found between pressure time integral (PTI) and iEMGdi (r = 0.88 by Belman et al11 and r = 0.801 by Rochester et al27) strongly supported the use of iEMGdi to reflect the diaphragmatic activity in our study. In addition, the study of Rochester and coworkers27 also showed similar correlation between peak Pdi and iEMGdi (r = 0.818).

Thoracoabdominal asynchrony has long been regarded as a sign of respiratory muscle fatigue, for example, as seen during weaning from mechanical ventilation.2 Although this concept has been challenged by Tobin et al28 and Pourriat et al29 it still reflects a condition in which the load on the inspiratory muscles is on the increase.30,32 Since one of the goals of the ventilators is to unload the respiratory muscles, it is reasonable to use TAA as a parameter in assessing the effects of mechanical ventilation. Allen and coworkers22 have successfully used "phase angle" derived from the time lag between AB and RC motion to reflect TAA in pediatric patients with airflow obstruction. They found that substantial TAA existed and improvement in TAA was closely linked to the improvement in lung mechanics. A similar study done by Sivan and coworkers33 also evidenced a strong association between the degree of stridor and the degree of TAA in children. In adult patients with stable COPD, phase angle and inspiratory asynchrony index were also used to reflect TAA.31

Response to BiPAP

We could not find statistically significant improvements in iEMGst, iEMGdi, phase angle, VT, Vt/Ti, RR, PR, ETCO2, SaO2, Pimax, and Pmax after the use of BiPAP. This result agreed with that of Strumpf.
et al\textsuperscript{19} but contradicted other investigations.\textsuperscript{11,18,20} The differences in the disease severity may be the underlying reason. Since our study excluded patients with orthopnea because of the use of iron lung in supine position, subjects had to be those with less severe COPD. The patients in the study of Carrey and coworkers\textsuperscript{20} did have much higher PaCO\textsubscript{2} level than our patients had (58 vs 45 mm Hg). Some other studies done in patients with acute exacerbation of COPD using nasal or face mask showed a tendency toward less intubation during hospitalization.\textsuperscript{31,34} This also supports the assumption that disease severity could influence the effects of mask ventilation. Further support comes from our finding that the patients with lower FEV\textsubscript{1} had more obvious reduction in iEMGst. The correlation was statistically significant. The data in Table 2 showed that PaCO\textsubscript{2} was significantly higher (\textit{p} = 0.0256) and FVC was also much lower (\textit{p} = 0.0199) in patients with FEV\textsubscript{1} below 0.55 L than those with FEV\textsubscript{1} above 0.55 L. All three parameters, \textit{ie}, FEV\textsubscript{1}, FVC, and PaCO\textsubscript{2}, are crucial in reflecting ventilatory function. This suggests that the effect of BiPAP correlates with ventilatory function impairment in patients with severe and stable COPD.

During the initial setting of BiPAP, most of our patients seemed unable to tolerate an IPAP of more than 10 cm H\textsubscript{2}O. Acclimation and practice seemed also to be important factors during nasal ventilation, frequently mentioned in negative pressure ventilation (NPV).\textsuperscript{10,11,19} This observation is supported by the study of Strumpf and coworkers\textsuperscript{9} in which 7 of 19 patients dropped out due to intolerance of the nasal mask. In our experience during BiPAP ventilation, it usually took naive patients several hours to several days to adapt to higher levels of pressure support. Conversely, patients in acute exacerbation tended to become accustomed to the ventilator more quickly.

In the preliminary report of Ambrosino and coworkers,\textsuperscript{14} 2-h use of BiPAP showed marked improvements in ABG, ventilatory pattern (VE, VT, RR), and iEMGdi. Twenty-two cm H\textsubscript{2}O of IPAP was used in their study, whereas only 10 cm H\textsubscript{2}O of IPAP was used in our study. If we could use higher pressure support longer in patients with more severe disease, the result might be different.

\textit{Response to Iron Lung}

Our study did not find any significant changes in phase angle, iEMGdi, iEMGst, VT, RR, VT/TI, SaO\textsubscript{2}, tCO\textsubscript{2}, PR, Pimax, or Pmax after 40-min use of iron lung. This result was similar to that of Belman and coworkers,\textsuperscript{11} but contradicted those of Nava et al\textsuperscript{10} and Rodenstein et al.\textsuperscript{19} In the study of Nava and coworkers, the iEMGdi reduced significantly after 10 min of pneumowrap when the negative pressure was above −15 cm H\textsubscript{2}O. In the study of Rodenstein and coworkers,\textsuperscript{19} a short run (5 min) of a tank ventilator did not reduce iEMGdi, but longer ventilatory support (20 to 60 min) did decrease iEMGdi by 20 percent. They suggested that acclimation and learning effect might play an important role in the initial 5 to 20 min when NPV was used in a naive patient. Conversely, our result did not show any progressive reduction in iEMGdi during 40 min of iron lung ventilation (Fig 6).

To answer whether a 40-min period is still too short for patients to adapt to the iron lung, further investigation with longer ventilatory support is needed.

The effect of long-term intermittent NPV has also been studied in patients with severe COPD. The investigation by Zibrak and coworkers\textsuperscript{15} observed no clinically significant improvements in pulmonary function, ABG, respiratory muscle strength, or exercise endurance after the use of poncho wrap. The activities of respiratory muscles were not documented in their study during NPV. Eleven of their 20 patients dropped out because of intolerance to the ventilator. This problem was not encountered in our study because patients with orthopnea had been excluded. In addition, the use of the iron lung in our study was believed to be more efficient than other NPV\textsuperscript{26,25} including poncho wrap, and might have better patient’s acceptance. Celi and coworkers\textsuperscript{17} had similar findings that long-term intermittent pulmowrap together with pulmonary rehabilitation did no better than a rehabilitation program alone in the improvements of FEV\textsubscript{1}, Pdimax, TTDi, and endurance time. However, one of their patients, who had severe hypercapnea, did improve. Cropp and DiMarco\textsuperscript{13} also found that patients with the highest PaCO\textsubscript{2} tended to benefit most from NPV. Because of the relatively small number of patients included in these studies, including ours, a subgroup of patients who had more severe disease and would have responded favorably to the NPV might have been excluded inadvertently leading to the conflicting results from different investigators.\textsuperscript{10,12,13,16}

\textbf{Conclusions}

For stable patients with severe COPD using short-term BiPAP or iron lung, we concluded the following: (1) ventilatory pattern (TAA), gas exchange, or respiratory muscle strength was not significantly improved; (2) ventilatory drive and activities of respiratory muscles were not significantly suppressed; (3) the suppression of sternocleidomastoid muscle activity during short-term BiPAP ventilatory support correlated significantly with the severity of the disease.

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