Open, Noninvasive Ventilation Using a 1-Lb Ventilator, Oxygen, and a Low Profile Mask Improves 6 MWT Distances in Advanced COPD

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Introduction: Loss of mobility occurs with advanced COPD and heralds reduced quality of life and increased health care utilization. The current standard of care for treating activity limitation caused by COPD is pulmonary rehabilitation, which is effective in improving mobility and exertional tolerance. However, pulmonary rehabilitation may not restore normal exercise tolerance in advanced COPD, and disease progression eventually leads to worsening functional limitation. Available ventilation systems either dramatically reduce quality of life, or are not suitable for ambulatory use, and thus are not a practical solution to treat activity limiting dyspnea in COPD. There is an urgent need for research into additional therapeutic options that minimize functional impairment in advanced COPD.

To address this important unmet need, we previously conducted a non-significant risk trial with a pre-commercial, prototype mask and wearable ventilator system. In that trial, use of the ventilator system was comfortable for most patients. In addition, patients using the test ventilation system showed a mean increase in 6MWT distance of 24 meters, while patients with a baseline walk distance of ≤ 300 meters improved 44 meters on average. These trial results were reported at the 2010 ATS conference.1 Here we report on a follow-up trial where we studied the same wearable 1-lb ventilator system featuring a refined mask designed for regular ambulatory use (Figure 1). The noninvasive open ventilation (NOIV™) mask and ventilator system (Breathe Technologies, San Ramon, CA) has received FDA clearance for home and institutional use. The ventilator system delivers an external, pressurized oxygen source and utilizes proprietary NOIV™ technology. We hypothesized that this ventilator system would be well tolerated by patients in a pulmonary rehabilitation setting and would improve 6MWT distances to a similar extent as the previously tested prototype.

NOIV™ Test System Compared to Alternative Therapies Using a Lung Simulation Model

In bench tests using an IngMar Medical ATS-5000 simulator, the NOIV™ system provides substantial augmentation of tidal volumes and oxygen concentration using lung test conditions that model COPD (Figures 2 & 3).

Non-invasive Open Ventilation (NOVEL) 2 Study Overview:
Study Hypothesis: The ventilator system will be well-tolerated for 1 hour of use.
Study Design: Open-label, cross over in 34 patients previously enrolled in a pulmonary rehabilitation program. Four pulmonary rehab centers. Use of a low-profile, open-mask based interface in conjunction with a wearable 1-lb ventilator (Breathe Technologies) and oxygen tank. For the control walk, oxygen use was 5.9 pm, or the patient's oxygen Rx for exertion - whichever was greater.
Key Inclusion/Exclusion Criteria: COPD patients with FEV< 60% of predicted. Oxygen prescription of ≥ 2 L/min and < 8 Lpm at exertion. Able to complete 6MWT on standard oxygen therapy. No signs of acute illness.
Study Endpoints: Patient tolerance and device function while at rest, and with exertion.

Conclusion: Study results show that the NOIV™ system was well tolerated on patients at both rest and exertion. No adverse events were reported.

- Mean 6MWT distance across the full study population (n=34) improved by 34.1 meters using NOIV™ therapy.
- Patients with low baseline 6MW distance < 300 meters (n=13) showed a substantially higher mean improvement of 73.3 meters.
- Patients with baseline 6MW distances > 300 meters (n=21) showed a mean improvement of 9.8 meters.

Future Directions: Given that the majority of study subjects tolerated NOIV™ therapy for at least one hour of continuous use, future studies should test patient tolerance for longer periods of exposure. Additionally, there is much promise for this therapy to improve exercise capacity. Future studies with NOIV™ therapy should measure the effect on patients in other key patient outcomes, such as in performing activities of daily living (ADLs) or in quality of life measurements. Finally, the system has shown promise, in both this study and a prior study, for patients with COPD. There is a potential to study increased exercise tolerance with NOIV™ therapy in patients with other types of lung disease, such as ILD.

References:

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Table 1: Patient Characteristics in NOVEL 2 Trial

<table>
<thead>
<tr>
<th>Patient Characteristic</th>
<th>Mean</th>
<th>SD</th>
<th>Range</th>
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<tbody>
<tr>
<td>Age (y)</td>
<td>66.8</td>
<td>5.6</td>
<td>55-79</td>
</tr>
<tr>
<td>Body Mass Index (BMI)</td>
<td>27.7</td>
<td>6.1</td>
<td>15.7-36.6</td>
</tr>
<tr>
<td>FEV1 % Predicted</td>
<td>33.9</td>
<td>11.7</td>
<td>7.6-60</td>
</tr>
<tr>
<td>RV in % Predicted</td>
<td>77.0</td>
<td>80.1</td>
<td></td>
</tr>
<tr>
<td>FEV1/FVC Ratio % Predicted</td>
<td>0.37</td>
<td>0.76</td>
<td></td>
</tr>
<tr>
<td>O2 Sat at Rest (bp)</td>
<td>23.5</td>
<td>0.97</td>
<td>0.00-4.00</td>
</tr>
<tr>
<td>O2 Re during Exertion (bp)</td>
<td>3.21</td>
<td>1.25</td>
<td>2.00-6.00</td>
</tr>
</tbody>
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Male/Female %          | 59/41 |     |

(n=15) | (n=21) |

Results 1: Patient Reaction to Test Ventilator Indicates Long-term Use Potential
Among study participants, 2/3 of the subjects reported improved comfort or equivalent improvement over their nasal cannula during their 6MWT's.

Results 2: Test NOIV™ System Improves 6MWT Distance without Changing Other Metrics
In bench tests using an IngMar Medical ATS-5000 simulator, the NOIV™ system provides substantial augmentation of tidal volumes and oxygen concentration using lung test conditions that model COPD (Figures 2 & 3).

Results 3: Substantial Increase in 6MWT Distance in Patients Walking < 300 m at Baseline