Workstation 3: The addition of non-invasive ventilation during exercise training in COPD patients

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AIMS

Exercise intolerance in lung diseases is the consequence of a complex interplay of different factors. While several of these factors are susceptible of improvement by specific interventions, we will to focus in this Workshop on the potential role of non-invasive ventilation as one of the so called ergogenic aids to usual training, specifically related to the population of COPD. In particular, the potential benefits of non-invasive ventilation during a rehabilitation course including training will be reviewed.

- Discuss the role of non-invasive ventilation as a potential ergogenic aid to exercise in COPD
- Report the clinical available evidence to train severe COPD patients assisted by non-invasive techniques during a rehabilitation course
- Discuss the actual limitations of such a strategy in this population
- To identify patients that may benefit from NIV during pulmonary rehabilitation
- To practically initiate NIV in the clinical context of the “COPD” patient with regard to optimal interface, mode of ventilation and settings for exercise and nocturnal use
- To identify equipment options that facilitate the use of NIV for pulmonary rehabilitation

SUMMARY

Severe COPD individuals experience limitation during exercise due to several factors involving ventilation and gas exchange.

Recent research has pointed out potential ergogenic aids to improve exercise performance in such patients. These may act at different pathophysiological mechanisms i.e. unloading the respiratory system, reducing the ventilatory demand \[1\], and increasing the arterial oxygen content \[2\].

Training peripheral muscles by adding non-invasive ventilatory aid may potentially help to prolong exercise time and to increase exercise intensity \[3\]. Indeed, the intensity of training is crucial to achieve a true physiologic effect. However, in severe severe COPD, exertional dyspnea and leg fatigue could impede to maintain intensity of training for enough time to yield such effect \[2\].

However, there has also been speculation that the addition of non-invasive ventilation applied at night in addition to pulmonary rehabilitation alone improves outcome. In this situation non-invasive ventilation is applied via a nasal mask or pillow or full face mask with the aims of decreasing breathlessness, correcting ABG’s and improving sleep quality. Garrod et al., \[4\] showed an increase in walking distance in COPD patients who underwent a pulmonary rehabilitation program. However, this was not reproduced by Schonhofer and co-workers\[5\] when measured by cycle ergonometry. Indicating the non-invasive ventilation alone may not have a drastic effect on cycle endurance. A later study following patients up for 2 years showed that the addition of non-invasive ventilation in this
situation improved HRQOL, dyspnoea, gas exchange, exercise tolerance and decreased the lung function decline [6].

Non-invasive ventilation can be applied during exercise via a nasal pillows, nasal mask, full face mask or mouthpiece with the aim of providing enough pressure to match the patients peak inspiratory flow. Using non-invasive ventilation during exercise has been shown to unload the respiratory muscles [7, 8], improve gas exchange [9], potentially improve dyspnea perception [1, 9] and prolong exercise duration [10-13].

Clinical studies in COPD patients have clarified a potential role for this ergogenic aid during training course, especially for the most severe and symptomatic individuals, unable to maintain exercise intensity. Notwithstanding, results are still contradictory (See table below). Three meta-analysis, two on physical training with non-invasive ventilation [14, 15] and the one on nocturnal non-invasive ventilation in stable COPD [16], using exercise performance as an outcome. All have concluded that larger randomised controlled trials are warranted as this area requires more in-depth analysis. However, the joint ATS/ERS key concepts and advances in pulmonary rehabilitation statement [17] identifies non-invasive ventilation used as an adjunct to PR augments the effects of the exercise program. The effect is more pronounced in severe COPD and that the greatest benefit appears when higher pressures are used. They also conclude that as non-invasive ventilation is “difficult and labour intensive” it may only be feasible in specialist units.

Major barriers to using non-invasive ventilation as an adjunct to pulmonary rehabilitation include, lack of confidence around the ventilator along with what pressures to use, portability of the ventilators, battery length time and weight of the equipment. Simple things like walking aid trolleys and file carriers can help to overcome the issue of weight and portability (see pictures below) or exercising on a treadmill or exercise bike. With regard to what pressures to use it would seem that high pressures [9, 10] produce a more favourable outcome and that supplementary oxygen therapy is warranted[18]
<table>
<thead>
<tr>
<th>Study</th>
<th>Subjects</th>
<th>COPD Severity</th>
<th>Training / exercise test</th>
<th>Study details</th>
<th>Mask</th>
<th>Ventilator mode</th>
<th>Pressure cmH₂O</th>
<th>Major outcomes</th>
</tr>
</thead>
<tbody>
<tr>
<td>Johnson 2002</td>
<td>39</td>
<td>Severe</td>
<td>Treadmill</td>
<td>RCT: NIV vs. heliox vs. usual training</td>
<td>Nasal</td>
<td>Bilevel</td>
<td>IPAP 8-12 EPAP 2</td>
<td>↑ in exercise training time in NIV group</td>
</tr>
<tr>
<td>Bianchi 2002</td>
<td>33</td>
<td>Mild to moderate</td>
<td>Cycling</td>
<td>RCT: PAV vs. usual training</td>
<td>Nasal and face mask</td>
<td>PAV</td>
<td>6.6 (VA 2.2L) 3.5 (FA 1.6L per s)</td>
<td>Improvements in peak work rate, dyspnoea In both groups</td>
</tr>
<tr>
<td>Hawkins 2002</td>
<td>19</td>
<td>Severe</td>
<td>Cycling</td>
<td>RCT: PAV vs. usual training</td>
<td>Face mask</td>
<td>PAV</td>
<td>12.7 (VA 1.5L) 3.6 (FA 0.7L per s)</td>
<td>↑ mean training time in NIV group</td>
</tr>
<tr>
<td>Reuveny 2005</td>
<td>24</td>
<td>Moderate to severe</td>
<td>Treadmill</td>
<td>RCT: NIV vs. usual training</td>
<td>Face mask</td>
<td>Bilevel</td>
<td>IPAP 7-10 EPAP 2</td>
<td>Greater ↑ in training intensity in NIV group</td>
</tr>
<tr>
<td>Van ‘t Hul 2006</td>
<td>29</td>
<td>Moderate to severe</td>
<td>Cycling</td>
<td>RCT: NIV vs. sham NIV</td>
<td>Mouthpiece and nose clip</td>
<td>IPS</td>
<td>10</td>
<td>↑ SWT distance and cycle endurance</td>
</tr>
<tr>
<td>Toledo 2007</td>
<td>18</td>
<td>Moderate to severe</td>
<td>Treadmill</td>
<td>RCT: NIV vs. usual training</td>
<td>Nasal</td>
<td>Bilevel</td>
<td>IPAP 10-15 EPAP 4-6</td>
<td>↑ VO2 max at peak in NIV group</td>
</tr>
<tr>
<td>Cotes 2003</td>
<td>14</td>
<td>Moderate to severe</td>
<td>Cycling</td>
<td>Alternate allocation NIV vs. usual training</td>
<td></td>
<td>Bilevel</td>
<td>IPAP ? EPAP 4-8</td>
<td>Peak VO2 max higher in NIV group</td>
</tr>
<tr>
<td>Kyroussis 2000</td>
<td>5</td>
<td>Severe</td>
<td>Exhaustive treadmill</td>
<td>With and without NIV</td>
<td>Face mask</td>
<td>PS</td>
<td>?</td>
<td>NIV led to substantial unloading of the respiratory muscle pump</td>
</tr>
<tr>
<td>Dreher 2007</td>
<td>20</td>
<td>Very severe</td>
<td>6 min walking distance</td>
<td>Randomized crossover: with and without NIV and supplementary O2</td>
<td>Nasal</td>
<td>PS and bilevel</td>
<td>Average PS = 29 and PEEP 4 (high intensity NIV)</td>
<td>NIV led to ↑ walking distance, ↑ oxygen levels and ↓ dyspnoea</td>
</tr>
<tr>
<td>Dolmage 1997</td>
<td>10</td>
<td>Moderate to severe</td>
<td>Cycling 60-70% maximum</td>
<td>Randomized crossover:</td>
<td>PAV</td>
<td>VA 6cm H₂O/L 3.6 (FA 3cmH₂O/L per s) CPAP 5cmH₂O</td>
<td>PAV + CPAP increased cycle endurance time</td>
<td></td>
</tr>
<tr>
<td>Study Authors</td>
<td>Subjects (n)</td>
<td>COPD Severity</td>
<td>Training / exercise test</td>
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<tr>
<td>Van 't Hul 2004[10]</td>
<td>45</td>
<td>Severe</td>
<td>Cycling 75% maximum</td>
<td>Randomized crossover: Mouthpiece and nose clip</td>
<td>PS</td>
<td>IPS of 5 and IPS of 10</td>
<td>IPS of 10 cmH2O led to ↑ exercise endurance</td>
<td></td>
</tr>
<tr>
<td>Garrod 2000[4]</td>
<td>45</td>
<td>Moderate to severe</td>
<td>PR ISWT</td>
<td>RCT: usual training and NIV at night + usual training</td>
<td>Bilevel</td>
<td>IPAP 13-24 EPAP 4-6</td>
<td>NIV and PR led to ↑ ISWT distance</td>
<td></td>
</tr>
<tr>
<td>Schonhofer 2008[5]</td>
<td>35 COPD 24 respiratory failure</td>
<td>Moderate</td>
<td>Cycling 75% maximum</td>
<td>NI</td>
<td>Bilevel</td>
<td>?</td>
<td>No improvement seen in COPD group</td>
<td></td>
</tr>
<tr>
<td>Walker 2015[18]</td>
<td>15</td>
<td>Severe to very severe</td>
<td>6 minute walking distance</td>
<td>Randomised crossover: supplementary oxygen vs. NIV</td>
<td>Bilevel</td>
<td>High intensity</td>
<td>NIV without supplementery O2 in hypoxic, hypercapnic COPD patients led to ↓ distance walked and a ↓ PaO2 compared to oxygen therapy alone</td>
<td></td>
</tr>
<tr>
<td>Duiverman 2011[6]</td>
<td>66</td>
<td>Moderate to severe</td>
<td>PR: cycling, walking and IMT</td>
<td>Outcomes: 6 minute walking distance</td>
<td>Bilevel</td>
<td>Mean±SD IPAP 23±4 EPAP 6±2 BPM 18±3</td>
<td>Non invasive ventilation and PR ↑HRQOL, ↑mood, ↑gas exchange, ↑exercise tolerance, ↓dyspnoea, and a decreased decline in lung function rate</td>
<td></td>
</tr>
</tbody>
</table>

Adapted from: Piper and Menadue, Breathe, 2009 [22]. This table summarises some but not all of the studies in this area.
Practicalities of NIV and Walking

From: Dreher M, Storre JH, Windisch W. ERJ. 2007 [9].

From: Dr Miguel Gonclaves, Porto.
Case Study

John is a 72 year old male with a clinical diagnosis of COPD, has a FEV1 15% predicted. John lives with his wife and is totally reliant on her in his activities of daily living. He uses non invasive ventilation (NIV) at night due to severe hypercapnia with a daytime PaCO$_2$ of 8.9kPa and a PaO$_2$ of 6.7kPa. He uses NIV via a nasal pillows system. His current setting is IPAP 32 cmH$_2$O, EPAP 8cmH$_2$O, BPM 15 and a target volume 650mls. He also requires 3L O$_2$ to be entrained.

John attended clinic with his wife and his main complaint was the fact that he had lost all independence.

John underwent exercise testing (6 minute walking distance) in 3 conditions on liquid oxygen, on NIV and NIV in conjunction with oxygen. The results are tabulated below.

<table>
<thead>
<tr>
<th></th>
<th>Distance walked (m)</th>
<th>Initial SpO$_2$ (%)</th>
<th>Final SpO$_2$ (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Liquid O$_2$</td>
<td>110</td>
<td>91</td>
<td>62</td>
</tr>
<tr>
<td>NIV</td>
<td>140</td>
<td>97</td>
<td>73</td>
</tr>
<tr>
<td>NIV+O$_2$</td>
<td>190</td>
<td>94</td>
<td>92</td>
</tr>
</tbody>
</table>

Due to the increased walking distance and preserved oxygen saturation it was recommended that John walk with NIV and oxygen therapy (See picture 1 below).

Picture 1

John and his wife, John is mobilizing with his ventilator and oxygen

However, Due to the weight of of the ventilator and oxygen and relatively low battery life of the ventilator he was unable to mobilise far. John also found that wearing nasal pillow the whole time
made his face sore and he also found that the pressures delivered on the ventilator were not always enough to off load the work of breathing.

Johns ventilator was changed to one that had a longer battery life. The mode of ventilation was changed to mouthpiece ventilation. Most importantly all the equipment was secured onto a trolley which enabled him to mobilise independently (See picture 2 and 3).

**Picture 2**

![Picture 2](image)

**Picture 3**

![Picture 3](image)

Johns initial use of his ventilator went from night time use and a short period in the middle of the day to 24/7 use (See figure 1). But, as Johns ventilator dependence increase his exercise tolerance and distance that he was able to walk increased. He also was able to achieve social independence and was back out meeting his friends.
This figure shows a ventilator download for hours of use. Note initially the nocturnal use and short periods in the day to near 24/7 usage. Ventilator usage is shown by the green bars.

**Acknowledgement:** Photos and ventilator download were provided by Miguel Gonçalves, Porto.

**REFERENCES**


SUGGESTED READING

1. To ensure a basic understanding of the principles of NIV and how to initiate and modify settings: ERS Practical Handbook of Noninvasive Ventilation. Simonds AK, editor: European Respiratory Society; 2015 2015-09-01 00:00:00. 320

Online Resources

1. To ensure a basic understanding of the principles of NIV and how to initiate and modify settings: ERS NIV Simulation Program, http://www.ers-education.org/e-learning/simulators.aspx

Online congress and ERS School presentations

1. The use of NIV during rehabilitation, P. Wijkstra (Groningen, The Netherlands)
2. Annual Congress 2013 –Non-invasive ventilation and airway structure and function
3. ERS School Course on Noninvasive Positive Pressure Ventilation, Hanover 2012
4. NIV in rehabilitation, T. Kohnlein (Hannover, Germany)

EVALUATION

1. Non-invasive ventilation during training in the COPD population should be indicated
   a. Almost never
   b. Always
   c. On a individual basis in the most severe and disabled individuals
   d. None of the previous

2. Main mechanisms by which non-invasive ventilation may increase the exercise load are:
   a. Reduction of mechanical load of respiratory system
   b. Improvement of gas exchange
   c. Reduction of respiratory muscles activity
   d. All of the previous

3. Quality of life following a training course with supplemental non-invasive ventilation in COPD may turn
   a. Always better
   b. Never better
   c. Potentially better
   d. Better in the best performing patients
4. What interface should be used when exercising on NIV?
   I. Nasal mask
   II. Full face mask
   III. Mouthpiece ventilation
   IV. Nasal pillows

   Answer one choice from below
   a. All of the above
   b. None of the above
   c. I, III and IV
   d. I, II and IV

5. You decide to initiate your patient on NIV to enhance their exercise capacity. You decide to use a ventilator with a good battery life. You initiate your patient on a bilevel ventilator with an IPAP 15 cmH2O, EPAP 4 cmH2O a respiratory rate of 15bpm with 2L O2 entrained. You start walking them and they complain of breathlessness. What do you do?
   a. Increase EPAP to 6 cmH2O
   b. Increase the IPAP to 20 cmH2O
   c. Decrease the respiratory rate to 10bpm
   d. Increase the inspiratory trigger

6. What equipment is required when preparing to perform rehabilitation with NIV for a COPD patient for the first time?
   I. Portable ventilator with good battery life
   II. Supplementary oxygen therapy
   III. High IPAP
   IV. Walking aid trolley
   V. Pulse oximeter

   Answer one choice from below:
   a. I, II, III, V
   b. I, II, IV, V
   c. II, III, IV, V
   d. ALL OF THE ABOVE