Benefits of an Oxygen Reservoir Cannula versus a Conventional Nasal Cannula during Exercise in Hypoxemic COPD Patients: A Crossover Trial

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Key Words
Chronic obstructive pulmonary disease · Long-term oxygen therapy · Oxymizer · Nasal cannula

Abstract

Background: The Oxymizer® is a special nasal cannula that provides a higher luminal diameter in combination with an incorporated oxygen (O₂) reservoir. It is assumed that a higher O₂ concentration can be delivered breath by breath in order to increase oxygenation.

Objective: We aimed to investigate the effects of the Oxymizer on endurance time in comparison to a conventional nasal cannula (CNC).

Methods: Forty-three patients with severe chronic obstructive pulmonary disease (COPD, age 60 ± 9 years, FEV₁ 37 ± 16% pred.) and indications for LTOT were recruited during pulmonary rehabilitation for this cross-over study. After an initial maximal incremental cycle test, all patients performed 4 cycling endurance time tests at 70% of their peak work rate (twice with the Oxymizer and twice with a CNC, in reverse order).

Results: The endurance time was significantly higher when patients cycled while using the Oxymizer in comparison to while using the CNC [858 ± 754 vs. 766 ± 652 s; between-group difference 92 s (95% confidence interval 32–152), p < 0.001]. In addition to a longer cycling duration, O₂ saturation at isotime was significantly higher with the Oxymizer (93.5 ± 5.4 vs. 90.4 ± 5.3%; p = 0.027). Furthermore, there was a positive correlation (r = 0.427, p = 0.002) between the O₂ flow rate and improvements in the constant work rate test, showing greater improvements in favor of the Oxymizer in patients with a higher demand for O₂ (≥4 liters/min).

Conclusion: We show that O₂ delivery via the Oxymizer is superior to a CNC with regard to endurance capacity and oxygenation during exercise in patients with severe COPD. It seems that patients with a higher demand for O₂ (≥4 liters/min), in particular, may benefit more from the use of the Oxymizer.

Background

Long-term oxygen (O₂) therapy (LTOT) is clearly indicated and recommended as a part of routine clinical practice in patients with hypoxemic chronic obstructive pulmonary disease (COPD) [1, 2]. The benefits of LTOT in patients with COPD are well known. LTOT reduces hospitalizations and the risk of comorbidities and prolongs survival [3, 4]. The rationale for supplemental O₂ during exercise in hypoxemic COPD patients is related to improved peripheral muscle oxygenation [5] and exercise capacity [6] as well as decreased symptoms of dyspnea [7], possibly allowing them to train at higher intensities [8]. However, the ideal kind of O₂ application has not yet been clarified [9]. The most popular device in clinical practice
is the conventional nasal cannula (CNC). The Oxymizer® device (Inovo Inc., Fla., USA) was first developed in the early 1980s. It contains a flow-reducing $O_2$ reservoir within the cannula (fig. 1). The pendant is covered within a hard, plastic, circle-shaped chamber and is worn in a sternal position under or on top of the clothing. The Oxymizer pendant stores $O_2$ during exhalation and delivers an enriched $O_2$-bolus in addition to continuous flow upon inhalation. Thus patients’ oxygenation may be improved [10] and/or $O_2$ flow rates can be decreased without compromising the level of oxygenation [11]. Up to now, most studies have investigated the effects of the initial, less-sophisticated version of the Oxymizer; in the late 1980s, they were limited by small sample sizes and/or examined patients’ oxygenation only at rest [11–16]. We aimed to investigate the potential benefits of the advanced Oxymizer in comparison to a CNC during exercise in an adequately powered sample size of hypoxemic patients with COPD.

**Methods and Materials**

**Patients**

All patients admitted for a 3-week inpatient pulmonary rehabilitation program with spirometry-proven COPD (Global Initiative for Obstructive Lung Disease stage IV) and on established LTOT (a flow rate $\geq 2$ liters/min at rest or during activity) were eligible for participation in the study. They were included after giving their written informed consent. Exclusion criteria consisted of common known absolute and relative contraindications for cardiopulmonary exercise testing [17].

**Study Design**

Consecutive patients admitted to our pulmonary rehabilitation program (content described elsewhere) [18] between March 2012 and December 2013 were invited to participate in this randomized cross-over study. Due to the study design, it was not possible to blind patients and the investigators who performed the constant work rate tests (CWRTs) to the $O_2$ device. However, the researchers who performed the final data analyses were blinded to group allocation as the intervention type was encoded by numbers.

To start, all patients performed a standardized, symptom-limited incremental cycle test (Cardiomed Bike, Proxomed Medical, Alzenau, Germany), beginning at 25 W, with an increase of 10 W/min until exhaustion [17]. Patients were highly encouraged to reach their maximal work rate. Peak work rate (PWR) was defined as the highest work rate that subjects were able to maintain for the previous 60 s. The next day, the patients consecutively performed a sequence of 4 cycling CWRTs at 70% of their initial PWR [19]. On day 1 and 2 after the incremental cycle test, patients performed 1 CWRT using a CNC or the Oxymizer after 24 h in random order. One week later, they repeated the 2 CWRTs again on 2 consecutive days at the same work load using CNC and Oxymizer in reverse order (see online suppl. fig.1; for all online suppl. material, see www.karger.com/doi/10.1159/000368165).

Before each CWRT, patients were instructed to cycle as long as possible at their given work load and at $\geq 50$ revolutions/min. Patients were told to inhale through the nose and to exhale using pursed-lips breathing, if possible. Settings of the cycle ergometer like seat height or handlebar position were noted and were kept the same for all tests. Before each CWRT, patients initially rested for 10 min sitting on the bicycle while breathing $O_2$ via the nasal cannula that was used during the test. Patients then were motivated every minute by encouragements from the investigator like ‘Well done’, ‘try to go on’ and ‘Perfect, you can make it’ to ensure that external motivation at each CWRT was similar. If patients were able to cycle for $>30$ min, intensity was then increased by 10 W every 5 min until exhaustion.

This study was approved by the Bavarian Ethics Committee (ID12019) and listed in the Clinical Trials Registry (www.clinicaltrials.gov; NCT01713413).

**Hypothesis**

Our primary hypothesis was that, in comparison to CNC, the use of the Oxymizer by hypoxemic COPD patients during CWRT will prolong endurance time to a clinically relevant amount.

**Randomization Procedure**

Allocation concealment was administered by a computer-generated randomization procedure using permuted blocks with a length of 6 numbers and a 1:1 ratio which was revealed after the pa-
tient was included in the study. The decision to accept or reject a participant was made with no knowledge of the next assignment in the sequence.

**Outcomes and Measurements**

The primary outcome parameter was endurance time achieved during CWRT. Partial pressure of O$_2$ (PaO$_2$), partial pressure of carbon dioxide (PaCO$_2$) and symptoms of dyspnea and leg fatigue at the end of CWRT were determined as secondary outcome parameters. PaO$_2$ and PaCO$_2$ were assessed by blood gas analysis (ABL 820, Radiometer GmbH, Willich, Germany) taken from the hyperemic earlobe. 'Isotime' was defined as the duration of the shortest CWRT between the tests with the Oxymer and the CNC. Values for heart rate and O$_2$ saturation (SpO$_2$) at isotime were retrospectively determined by analyzing the continuously recorded data of the SenTec® device (SenTec AG, Thierwil, Switzerland), with patients being linked to the device via an ear clip during all CWRTs.

The first blood gas analyses were made at rest while the patient was sitting on the cycle ergometer. During the CWRT, patients were asked to give a brief signal when they come close to exhaustion, so the investigator could prepare to take the second blood gas measurement in the last seconds of cycling. Before and directly at the end of the CWRT, patients were asked to rate the intensity of dyspnea and leg fatigue on the modified Borg scale (0–10) [20]. Lung function was measured on admission by Master Screen Body Plethysmograph (Jaeger, Wuerzburg, Germany) in accordance with ATS guidelines [21]. To determine fat-free mass index, body composition was measured by NutriGuard MS (Data Input Body Composition, Pöcking, Germany).

**Sample Size Calculation**

To detect a minimal important difference of 105 s at the CWRT [22] between the two types of O$_2$ application, assuming a standard deviation of 238 s, a statistical power of 80% and a risk for a type 1 error (α) <5%, a sample size of 43 patients in total would be needed.

**Statistical Analysis and Missing Data**

Data are presented as mean and standard deviation or mean and 95% confidence interval (CI) unless otherwise stated. Mean values of both CWRTs with CNC and the Oxymer were taken for final analysis, respectively. Since all values were normally distributed, intragroup comparison was carried out by using a paired Student t test. An unpaired t test was used to analyze normally distributed subgroups between the ‘Lowflower’ and ‘Highflower’ group (see online suppl. table 1). The level of significance was set at p ≤ 0.05. Missing data were treated as follows. Blood gas samples were invalid in 3 patients at the end of the CWRT with the CNC and in 2 patients during Oxymer use, respectively. These 5 patients were excluded from the secondary outcome analysis of capillary blood gases at the end of the CWRT. All other data were available. Data analysis was performed using PASW Statistics v18.0 (Chicago, Ill., USA). Figures were designed by GraphPad Prism v5 (San Diego, Calif., USA).

**Results**

Forty-five patients were enrolled in this study. After the first CWRT, 2 patients quit the study at their own request because the study design was too stressful for them. In total, 43 patients completed all test procedures and were finally analyzed. Baseline characteristics of the study population are shown in table 1.

Patients were able to significantly increase their endurance time during the CWRT by 92 s (95% CI 32–152, p = 0.003) when using the Oxymer instead of a CNC (fig. 2), and the average O$_2$ flow rate was 3.6 ± 1.3 liters/min. Ox-

**Table 1. Baseline characteristics**

<table>
<thead>
<tr>
<th>Parameters</th>
<th>Values</th>
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<tbody>
<tr>
<td>Number of patients</td>
<td>43</td>
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<tr>
<td>Age, years</td>
<td>60.1±8.9</td>
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<tr>
<td>Female, n (%)</td>
<td>21 (49)</td>
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<tr>
<td>BMI, kg/m$^2$</td>
<td>24.9±5.3</td>
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<td>BODE index</td>
<td>5.1±1.9</td>
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<tr>
<td>CAT score</td>
<td>22.8±6.3</td>
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<tr>
<td>FFMI</td>
<td>19.0±3.1</td>
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<td>Drugs on admission, n (%)</td>
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<tr>
<td>LABA</td>
<td>41 (95)</td>
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<td>LAMA</td>
<td>35 (81)</td>
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<tr>
<td>Theophyllin</td>
<td>5 (12)</td>
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<tr>
<td>ICS</td>
<td>38 (88)</td>
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<tr>
<td>Oral corticosteroids</td>
<td>6 (14)</td>
</tr>
<tr>
<td>O$_2$-demand at rest, l/min</td>
<td>1.9±1.3</td>
</tr>
<tr>
<td>O$_2$-demand during activity or exercise, l/min</td>
<td>3.6±1.3</td>
</tr>
<tr>
<td>PaO$_2$ at rest breathing room air, mm Hg</td>
<td>55.8±5.9</td>
</tr>
<tr>
<td>PaCO$_2$, at rest breathing room air, mm Hg</td>
<td>41.7±7.5</td>
</tr>
<tr>
<td>PaO$_2$ at rest breathing O$_2$ with the CNC, mm Hg (O$_2$ flow rate 2.5±0.8 liters/min)</td>
<td>72.5±14.3</td>
</tr>
<tr>
<td>PaCO$_2$ at rest breathing O$_2$ with the CNC, mm Hg (O$_2$ flow rate 2.5±0.8 liters/min)</td>
<td>41.3±7.1</td>
</tr>
<tr>
<td>PaO$_2$ at rest breathing O$_2$ with the OXY, mm Hg (O$_2$ flow rate 2.5±0.8 liters/min)</td>
<td>78.1±18.0*</td>
</tr>
<tr>
<td>PaO$_2$ at rest breathing O$_2$ with the OXY, mm Hg (O$_2$ flow rate 2.5±0.8 liters/min)</td>
<td>41.2±7.7</td>
</tr>
<tr>
<td>PWR, W</td>
<td>67±23</td>
</tr>
<tr>
<td>70% PWR, W</td>
<td>48±19</td>
</tr>
<tr>
<td>FEV$_1$, liters</td>
<td>1.1±0.6</td>
</tr>
<tr>
<td>FEV$_1$, % pred.</td>
<td>37.5±16.9</td>
</tr>
<tr>
<td>TLC, liters</td>
<td>8.9±1.6</td>
</tr>
<tr>
<td>TLC, % pred.</td>
<td>146.9±28.0</td>
</tr>
<tr>
<td>RV, liters</td>
<td>6.2±1.7</td>
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<tr>
<td>RV, % pred.</td>
<td>283.6±82.6</td>
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<tr>
<td>DLCO, % pred.</td>
<td>29±14</td>
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</table>

**BODE index** = BMI obstruction/dyspnea/exercise capacity index; CAT = COPD assessment test; DLCO = diffusion capacity factor of the lung for carbon monoxide; FFMI = fat-free mass index; ICS = inhaled corticosteroids; LABA = long-acting β2 agonists; LAMA = long-acting antimuscarinic agents; OXY = Oxymer; RV = residual volume; TLC = total lung capacity. *p < 0.05 significantly different to PaO$_2$ at rest breathing O$_2$ via the CNC.
Oxygenation was also higher with the Oxymizer at rest ($\text{PaO}_2$ 78.1 ± 18.0 vs. 72.5 ± 14.3 mm Hg, $p = 0.029$), at isotime ($\text{SpO}_2$ 93.5 ± 5.4 vs. 90.4 ± 5.3%, $p = 0.027$; fig. 3) and at the end of the CWRT ($\text{PaO}_2$ 64.8 ± 11.4 vs. 61.5 ± 10.0 mm Hg, $p < 0.0001$). However, there was no significant difference at rest or at the peak of CWRT regarding heart rate, $\text{pPaCO}_2$, symptoms of dyspnea or leg fatigue between the two $\text{O}_2$ application forms (table 2).

For a subgroup analysis, we classified the patients into 4 groups regarding their $\text{O}_2$ flow rates (2, 3, 4 or 5–6 l).

**Table 2.** Changes in outcomes during CWRT with the use of a CNC or the Oxymizer

<table>
<thead>
<tr>
<th></th>
<th>CNC (n = 43)</th>
<th>Oxymizer (n = 43)</th>
<th>Difference (95% CI)</th>
<th>$p$</th>
<th>Estimated effect size (Cohen’s $d^a$)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Primary outcome</strong></td>
<td></td>
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</tr>
<tr>
<td>Endurance time, s</td>
<td>766±652</td>
<td>858±754</td>
<td>92 (32–152)</td>
<td>0.003</td>
<td>0.13</td>
</tr>
<tr>
<td><strong>Secondary outcomes</strong></td>
<td></td>
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<td></td>
</tr>
<tr>
<td>HR at rest before CWRT, bpm</td>
<td>86±11</td>
<td>86±13</td>
<td>0 (–2–2)</td>
<td>0.933</td>
<td>0.00</td>
</tr>
<tr>
<td>HR at isotime, bpm</td>
<td>114±15</td>
<td>112±15</td>
<td>–2 (–6–10)</td>
<td>0.631</td>
<td>–0.13</td>
</tr>
<tr>
<td>HR at end of CWRT, bpm</td>
<td>112±14</td>
<td>113±16</td>
<td>1 (–0–3)</td>
<td>0.138</td>
<td>0.06</td>
</tr>
<tr>
<td>$\text{SpO}_2$ at rest before CWRT, %</td>
<td>97.3±1.7</td>
<td>97.8±1.6</td>
<td>0.5 (–0.8–0.8)</td>
<td>0.017</td>
<td>0.50</td>
</tr>
<tr>
<td>$\text{SpO}_2$ at isotime, %</td>
<td>90.4±5.3</td>
<td>93.5±5.4</td>
<td>2.5 (0.0–5.1)</td>
<td>0.027</td>
<td>0.54</td>
</tr>
<tr>
<td>$\text{SpO}_2$ at end of CWRT, %</td>
<td>90.3±5.3</td>
<td>91.0±6.2</td>
<td>0.7 (0.1–1.4)</td>
<td>0.070</td>
<td>0.18</td>
</tr>
<tr>
<td>$\text{PaO}_2$ at rest before CWRT, mm Hg</td>
<td>72.5±14.3</td>
<td>78.1±18.0</td>
<td>5.6 (0.6–10.5)</td>
<td>0.029</td>
<td>0.31</td>
</tr>
<tr>
<td>$\text{PaO}_2$ at end of CWRT, mm Hg</td>
<td>61.5±10.0</td>
<td>64.8±11.4</td>
<td>3.3 (1.6–4.9)</td>
<td>&lt;0.0001</td>
<td>0.29</td>
</tr>
<tr>
<td>$\text{PaCO}_2$ at rest before CWRT, mm Hg</td>
<td>38.7±9.0</td>
<td>38.5±8.6</td>
<td>–0.2 (–2.4–2.0)</td>
<td>0.819</td>
<td>0.00</td>
</tr>
<tr>
<td>$\text{PaCO}_2$ at end of CWRT, mm Hg</td>
<td>45.3±10.4</td>
<td>44.7±9.7</td>
<td>–0.6 (–1.6–0.4)</td>
<td>0.487</td>
<td>0.00</td>
</tr>
<tr>
<td>Dyspnea at rest before CWRT, Borg scale</td>
<td>2.6±1.8</td>
<td>2.6±1.8</td>
<td>0.0 (–0.3–0.2)</td>
<td>0.797</td>
<td>0.00</td>
</tr>
<tr>
<td>Dyspnea at end of CWRT, Borg scale</td>
<td>7.0±1.0</td>
<td>6.9±1.8</td>
<td>–0.1 (–0.4–0.2)</td>
<td>0.390</td>
<td>0.00</td>
</tr>
<tr>
<td>Leg fatigue at rest before CWRT, Borg scale</td>
<td>2.9±1.7</td>
<td>2.8±1.8</td>
<td>–0.1 (–0.3–0.3)</td>
<td>0.934</td>
<td>0.00</td>
</tr>
<tr>
<td>Leg fatigue at end of CWRT, Borg scale</td>
<td>6.8±1.9</td>
<td>6.7±2.0</td>
<td>–0.1 (–0.5–0.2)</td>
<td>0.433</td>
<td>0.00</td>
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</table>

Values are mean ± SD unless otherwise stated. bpm = Beats per min; HR = heart rate.

$^a$ 0.2 = small effect size, 0.4 = medium effect size, 0.8 = large effect size.
Effects of the Oxymizer in Hypoxemic COPD Patients

Fig. 4. Additional benefit of the Oxymizer on endurance time during the CWRT in comparison to with a CNC in 43 COPD patients depending on their individual amount of O₂ supplementation in liters/min (*p < 0.05).

Table 3. Differences in outcomes of CWRTs in ‘O₂-Lowflower’ and ‘O₂-Highflower’ patients using a CNC or the Oxymizer

<table>
<thead>
<tr>
<th></th>
<th>‘O₂-Lowflower’ (n = 21)</th>
<th>Intragroup difference (95% CI)</th>
<th>‘O₂-Highflower’ (n = 22)</th>
<th>Intragroup difference (95% CI)</th>
<th>Between-group difference (95% CI)</th>
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<tbody>
<tr>
<td><strong>Primary outcome</strong></td>
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<tr>
<td>Endurance time, s</td>
<td>530±406</td>
<td>550±455</td>
<td>20 (–37–75)</td>
<td>991±765</td>
<td>1,153±868</td>
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<tr>
<td></td>
<td>CNC</td>
<td>OXY</td>
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<tr>
<td><strong>Secondary outcomes</strong></td>
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<tr>
<td>HR at isotime, bpm</td>
<td>116±14</td>
<td>111±12</td>
<td>5±7*</td>
<td>112±17</td>
<td>112±16</td>
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<tr>
<td>HR at end of CWRT, bpm</td>
<td>110±12</td>
<td>111±13</td>
<td>1 (–2–2)</td>
<td>114±16</td>
<td>116±18</td>
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<tr>
<td>SpO₂ at isotime, %</td>
<td>90.3±5.4</td>
<td>92.9±4.9</td>
<td>2.6±2.1**</td>
<td>90.5±6.9</td>
<td>94.0±5.9</td>
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<tr>
<td>SpO₂ at end of CWRT, %</td>
<td>92.1±3.2</td>
<td>93.0±3.6</td>
<td>0.9 (–0.1–1.9)</td>
<td>88.5±6.4</td>
<td>89.0±7.5</td>
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<tr>
<td>PaO₂ at end of CWRT, mm Hg</td>
<td>64.9±9.2</td>
<td>69.0±9.9</td>
<td>4.1 (1.4–6.9)**</td>
<td>57.8±9.8</td>
<td>60.1±11.4</td>
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<tr>
<td>PaCO₂ at end of CWRT, mm Hg</td>
<td>46.3±9.8</td>
<td>45.7±9.0</td>
<td>(–0.6–2.1–0.9)</td>
<td>44.2±11.2</td>
<td>43.7±10.6</td>
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<tr>
<td>Dyspnea at end of CWRT, Borg scale</td>
<td>7.1±1.9</td>
<td>6.8±1.8</td>
<td>(–0.3–0.6–0.1)</td>
<td>6.9±1.9</td>
<td>6.9±1.8</td>
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<tr>
<td>Leg fatigue at end of CWRT, Borg scale</td>
<td>7.1±1.7</td>
<td>6.9±1.8</td>
<td>(–0.2–0.3–0.2)</td>
<td>6.4±2.0</td>
<td>6.4±2.1</td>
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</table>
| Values are means ± SD unless otherwise stated. bpm = Beats per min; HR = heart rate. *p < 0.05, **p < 0.01, ***p < 0.001.

a 2–3 liters/min; b 4–6 liters/min.

online suppl. table 1). Patients classified as ‘O₂-Highflower’ significantly improved their endurance time by 162 s (95% CI 61–261 s, p < 0.01) when using the Oxymizer. In contrast, ‘O₂-Lowflower’ patients were not able to improve their endurance time with the Oxymizer (table 3). Nevertheless, at the end of the CWRT, the Oxymizer had significantly increased PaO₂ in all patients independently of low or high O₂ flow rates (table 3).

No adverse event or any other unexpected incident occurred during the study.

Discussion

In this study, patients were able to increase endurance time during the CWRT significantly by 12% when using the Oxymizer instead of a CNC. However, this is equivalent to a benefit of 92 s which is still below the expected MID of 105 s [22]. The superiority of breathing O₂ via the Oxymizer was consistent between test 1 and test 2 as well as between test 3 and test 4 (see online suppl. fig. 2). Dividing the study population into ‘O₂-Highflowers’ and ‘O₂-Lowflowers’, we found that only ‘O₂-Highflower’ patients were able to improve endurance time to a clinically relevant extent (by 162 s) by using the Oxymizer. Studies that have investigated the effects of a bronchodilator inhalation therapy (over 3–4 weeks) versus placebo report...
ed improvements of 67 [23], 93 [24] and 111 [25] s in the exercise endurance time. That a simple device like the Oxymizer can improve exercise endurance to a similar or even larger extent than bronchodilator inhalation is an interesting finding. Especially in very disabled patients with advanced COPD and the need for LTOT, the Oxymizer could be an easy and safe approach to improve exercise endurance and oxygenation. Oxygenation was significantly higher with the Oxymizer than with CNC at isotime. Since isotime can be seen as a reliable parameter in interventional trials, this represents a worthwhile finding of this study. Furthermore, at peak exercise of the CWRT, hypoxemia (PaO₂ <60 mm Hg) was prevalent in 18/43 individuals (42%) when using CNC and in only 12/43 (28%) when using the Oxymizer. However, regardless of low or high O₂ flow rates, the Oxymizer increased oxygenation at rest and during exercise significantly above the level reached by the CNC. In ‘O₂-Highflowers’, in particular, the Oxymizer was successful in keeping the mean PaO₂ level >60 mm Hg upon completion of CWRT, but it dropped below this threshold with CNC. This could reveal a meaningful benefit towards better oxygenation in daily life.

It must be noted that these results were obtained during a cycling task and may therefore not be directly transferred to other activities of daily living. Another point of clinical relevance is whether there is a different response between the two O₂ delivery systems regarding symptoms of dyspnea during activity. Although patients cycled longer with the Oxymizer, their dyspnea ratings at peak CWRT were at a comparable level. Unfortunately, we did not record sensations of dyspnea at isotime to support this relevance.

A recently published study by Marti et al. [26] investigated the effects of an Oxymizer versus a CNC in a cross-over study design during the 6-minute walking test (6MWT) in 28 patients with COPD (age 66 ± 9 years and FEV₁ 31 ± 11% pred.). O₂ supplementation via Oxymizer and CNC were similarly effective in correcting exercise-induced hypoxemia during the 6MWT in comparison to room air. During the test, an average SpO₂ of ≥90% was reached in 86 and 79% of the patients with the Oxymizer and CNC, respectively. However, use of the Oxymizer did not result in any further increase of 6MWT distance compared to the CNC (347 ± 10 vs. 352 ± 11 m, p = n.s.). This finding diverges from ours, and may perhaps be explained by the self-paced nature of the 6MWT in comparison to a CWRT.

Adherence is an aspect that could further complicate the use of an Oxymizer in the ‘real life’ of patients. Acceptance of the Oxymizer was once investigated in a small study including 21 patients over a 1-month period; a former version of the Oxymizer which was made out of stiffer and less comfortable plastic material than the current one was evaluated [11]. Although patients successfully maintained their SpO₂ level despite a 3-fold reduction in the rate of O₂ flow, 9/21 patients (43%) abandoned the Oxymizer due to discomfort.

Our study has several strengths. Firstly, it was adequately powered to detect a clinically relevant difference between the use of a CNC and the Oxymizer during a CWRT in subjects with COPD. Secondly, the CWRT is an approved, valid method for assessing endurance capacity in patients with COPD with highly significant intraclass correlation coefficients (≥0.85) between test and retest (p < 0.001) [19]. Thirdly, the cross-over design used in this study can be considered a useful strategy for eliminating the potential bias of fatigue or variable daily conditions between the CWRTs.

However, this study also reveals some limitations: the chosen intensity of 70% of PWR during the CWRTs overall for patients might have been too low as there was a wide range in endurance time. A higher cycling intensity or a more progressive test protocol might have resulted in more homogeneous results. Furthermore, whether a patient’s breathing pattern during the CWRTs was via the nose or mouth was not recorded, and so the efficacy of O₂ intake was not precisely detectable. We wanted to investigate a ‘real life’ situation of providing O₂ via two different types of nasal cannula. We believe that the differences in influence of the individual breathing pattern may have been negligible.

Conclusions

To our knowledge, this is the first study which showed that O₂ delivery via the Oxymizer is superior to a CNC with regard to improved exercise endurance time and oxygenation (at rest, at isotime and at peak exercise) during cycling in hypoxemic patients with COPD. It seems that patients with O₂ flow rates of ≥4 liters/min, in particular, may benefit the most from the use of an Oxymizer during exercise training. Thus, this device may thus be used to improve endurance capacity in very disabled patients. Future studies are needed to evaluate if exercise intensity during endurance training can be further increased and if improvements in exercise capacity are superior when O₂ supplementation is provided via an Oxymizer.
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References


22 Casaburi R: Factors determining constant work rate exercise tolerance in COPD and their role in dictating the minimal clinically important difference in response to interventions. COPD 2005;2:131–136.


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