Refillable Oxygen Cylinders May Be an Alternative for Ambulatory Oxygen Therapy in COPD*

Antoine Cuvelier, MD; Jean-François Nuir, MD, FCCP; Nadia Chakroun, MD; Jérôme Aboab, MD; Gabriella Onea, MD; and Daniel Benhamou, MD

Study objectives: To compare, in clinical conditions, the efficacy of refillable oxygen cylinders (O2-HFs) in improving oxygenation and exercise capacity of patients with COPD during a 6-min walking test.

Design: Prospective randomized study with a cross-over design.

Setting: A university teaching hospital.

Patients: Ten patients with COPD, in a stable state and previously treated with long-term domiciliary oxygen therapy. Baseline characteristics were as follows: age, 65 ± 7 years; PaO2 on room air, 55.4 ± 6.3 mm Hg; PaCO2 on room air, 46.2 ± 7.4 mm Hg; FEV1/vital capacity, 47 ± 7%; and FEV1, 30 ± 7% of predicted value (mean ± SD).

Design: All patients performed three successive 6-min walking tests, the first test in room air and the other tests in a randomized order with either a conventional oxygen cylinder (O2-C) or an O2-HF.

Measurements and results: The fraction of inspired oxygen (FiO2) delivered by O2-HFs was significantly lower than the FiO2 delivered by O2-Cs (94.2 ± 2.6% vs 98.8 ± 4.9%, p = 0.02). Mean O2-HF and O2-C weights before the walking tests were similar (3,510 ± 251 g and 3,770 ± 142 g, respectively; p = 0.09). Mean transcutaneous oxygen saturation was similarly improved with both oxygen delivery systems. Mean distances with O2-C (373.5 ± 81 m) and O2-HF (375 ± 97 m) were not different but significantly improved, as compared with room air (334.5 ± 90 m; p = 0.03 and 0.02, respectively). Dyspnea sensations were similar for the three tests.

Conclusion: O2-HFs are as efficient as O2-Cs for performing short-term exercises. Because of a lower cost, pressurizing units may be worthwhile for improving ambulatory oxygen therapy and pulmonary rehabilitation programs. (CHEST 2002; 122:451–456)

Key words: COPD; exercise; oxygen inhalation therapy; rehabilitation

Abbreviations: FiO2 = fraction of inspired oxygen; O2-C = conventional oxygen cylinder; O2-HF = refillable oxygen cylinder; SaO2 = arterial oxygen saturation; VC = vital capacity

At the beginning of the 1980s, long-term oxygen therapy was shown to significantly improve long-term survival of hypoxemic patients with COPD.1,2 The duration of oxygen therapy during both daytime and nighttime is a key factor in improving survival among patients with COPD and chronic respiratory failure. It is generally accepted that compliance to treatment should be at least 15 h/d,1–3 and two prospective studies4,5 demonstrated the importance of ambulatory oxygen devices for improving this compliance in COPD patients. Pépin and Barjhoux4 showed that ambulatory oxygen supplies may lead to a threefold increase of probability to perform oxygen therapy for > 15 h/d. Vergeret and Brambilla5 demonstrated that oxygen use during the day was significantly higher if an ambulatory device was provided to the patient.

To maintain mobility and quality of life, oxygen therapy has to be simple to use and carry. Because concentrators are not portable, ambulatory oxygen therapy is performed with gaseous cylinders or the more expensive liquid oxygen devices. Pressurizing units that are able to fill up oxygen cylinders from concentrators have been recently developed. Thus, refill cylinders could therefore represent a new alternative for improving overall oxygen therapy.
while reducing costs of production and delivery. To the best of our knowledge, no prior similar studies were dedicated to this equipment. This study was designed to compare, in real clinical conditions, the efficacy of refilled oxygen cylinders (O2-HFs) in improving oxygenation and exercise capacity of patients with COPD during a 6-min walking test.

**Materials and Methods**

**Patients**

Patients with COPD defined according to American Thoracic Society criteria were prospectively included in the study. All patients had to be in a stable state, already treated at home with long-term oxygen therapy, and able to perform walking tests. The study was performed in the ambulatory division of our department, which is devoted to ambulatory follow-up of patients with chronic respiratory insufficiency. Inclusion criteria were PaO2 at rest and on room air ≥ 60 mm Hg, FEV1 of < 55% of predicted value, FEV1/VC of < 65%, previously documented oxygen desaturation at rest (arterial oxygen saturation [SaO2] < 90% on room air) and a stable clinical state for at least 3 months prior to inclusion. Patients with PaO2 > 60 mm Hg in room air but with a previous demonstration of significant desaturation during exercise were also included in the study. All patients gave informed consent to participate in the study, after they received information on the objectives and interest of the study. The protocol was approved by our local university ethical committee.

**Materials**

The pressurizing unit that was used is a domiciliary oxygen supply equipped with a compressor that fills up an oxygen cylinder from a standard oxygen concentrator (HomeFill system; Invacare; Elyria, OH). The compressor fills up portable D-sized cylinders (O2-HF) with oxygen-enriched air under a 140-bar pressure; in comparison, commercial oxygen cylinders (O2-Cs) are filled under a 200-bar pressure. The O2-HF is linked to the compressor with a dedicated valve, and a manometer controls the filling of the cylinder. The fraction of inspired oxygen (FiO2) delivered by the compressor was permanently controlled by an oxygen-concentration sensor (SensO2; Invacare). The compressor automatically stops when the cylinder is filled up or if the oxygen concentration is < 85%. At rest, the patient can use the concentrator simultaneously with the working compressor, but the flow to the patient will always remain priority as compared with the flow to the compressor. Filling time of a D-sized O2-HF is approximately 2 h, although longer if the patient is using the concentrator simultaneously. O2-HF autonomy is about 140 min, with an average flow of 2 L/min.

**Study Design**

A prospective randomized study with cross-over design, double dummy, and single blind was performed. Each patient performed a reference 6-min walking test carrying a new O2-C with nasal prongs but breathing room air (the cylinder was voluntarily switched off during this first 6-min walking test). If significant desaturation was observed, the patient was then randomized into the study and performed two successive 6-min walking tests while inhaling oxygen with either an O2-HF or an O2-C. All three tests were separated by 60-min rest periods. In order to have similar conditions for the three walking tests, we used the same model of D-sized oxygen cylinders (Air Liquide Santé; Taema, France). All cylinders had an identical appearance.

All 6-min walking tests were performed under supervision of a trained respiratory therapist in a 10-m corridor, in the second half of the morning. Just before each test, the O2-HF's were completely filled up by the medical team. Walking tests with the O2-C and the O2-HF were performed with a same oxygen flow of 2 L/min. When 6-min walking tests in room air were not tolerated, they were then carried out on 1 L/min of oxygen and the following tests performed with 3 L/min of oxygen. Transcutaneous SaO2 and cardiac frequency were recorded each minute during all the tests with a portable oximeter (Nonin 8500; Nonin; Plymouth, MN) and secondly recorded on a printer. Oxygen concentrations were measured at the beginning of each walking test with an oxygen sensor (Oxy 2100; CFPO; Paris, France). Cylinder weights were also measured at the beginning of each walking test with a 0.1-kg sensitivity scale. Dyspnea at rest and after exercise was measured with a Borg scale. Twelve patients agreed to participate in the study. Two patients were excluded because a severe dyspnea obliged them to stop one of the three walking tests before the end. Data from 10 patients were available for analysis.

**Statistical Analysis**

Statistical data were obtained with software (GB-Stat 6.5; Dynamic Microsystems; Silver Spring, MD). Paired data were analyzed by the Wilcoxon rank test, and nonpaired data were analyzed by the Mann-Whitney test. Each test was considered as significant if p values ≤ 0.05. Equivalence of the two oxygen delivery devices was defined by a SaO2 difference of < 1.5%. The sample size was calculated with software (nQuery; Statistical Solutions; Saugus, MA). For an equivalence hypothesis, 23 patients are needed for a study power of 80% and an α significance level at 0.05. Because of a cross-over design and a mean correlation of 0.5, the final required number of patients was 10.

**Results**

Ten patients with COPD (9 men and 1 woman; mean age, 65 ± 7 years) were included in the study. Mean FEV1 was 0.84 ± 0.14 L (30 ± 7% of predicted value), FEV1/VC was 47 ± 7%, total lung capacity was 5.89 ± 1.64 L (98 ± 27% of predicted value), and residual volume was 3.86 ± 1.32 L (144 ± 73% of predicted value). Room air arterial blood gases in a stable state showed a PaO2 of 55.4 ± 6.3 mm Hg and a PaCO2 of 46.2 ± 7.4 mm Hg. All individual data are reported in Table 1. All patients were previously treated with long-term oxygen therapy (between 1.5 L/min and 3 L/min), and three patients were also treated with noninvasive mechanical ventilation at home (patients 2, 5, and 8). Three patients had basal PaO2 > 60 mm Hg in room air but were previously documented as having significant desaturation when walking and were treated by long-term oxygen therapy.

At the beginning of the study, FiO2 measured
from O2-HFs was significantly lower than with O2-Cs (94.24 ± 2.56% vs 98.85 ± 4.89%, respectively; p = 0.025). The mean O2-HF weight before walking tests was 3,510 ± 251 g, and the mean O2-C weight was 3,770 ± 142 g. This difference was not significant (p = 0.09).

Individual data are reported in Figure 1. Transcutaneous SaO2 with either O2-C or O2-HF was better than in room air. Both walking tests under oxygen were performed with a 2 L/min flow except for patient 8, who performed O2-C and O2-HF walking tests with a 3 L/min flow because of severe dyspnea on room air. Mean SaO2 values with O2-C and O2-HF were very similar throughout the walking tests (Table 2). With the exception of one value at 6 min, there was a significant improvement of SaO2 at each minute of the tests with oxygen (O2-C or O2-HF) as compared with room air.

No significant individual cardiac intolerance (bradycardia or tachycardia) was observed. Mean cardiac frequencies were very similar under each condition (Fig 2). A slight increase of mean cardiac frequencies was due to the reflex tachycardia during the tests.

Mean walking distance in room air was 334.5 ± 90 m. This distance was significantly increased when performed with either O2-C (373.5 ± 81 m, p = 0.03) or O2-HF (375 ± 97 m, p = 0.02). No statistical difference was found between distances performed under oxygen either with O2-C or O2-HF (Fig 3).

At basal conditions, the Borg scale showed a mean

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Table 1—Clinical Characteristics of the Patients in the Study*

<table>
<thead>
<tr>
<th>Patient No.</th>
<th>Age, yr</th>
<th>FEV1, L (%)</th>
<th>VC, L (%)</th>
<th>FEV1/VC, %</th>
<th>TLC, L (%)</th>
<th>RV, L (%)</th>
<th>PaO2, mm Hg</th>
<th>PaCO2, mm Hg</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>64</td>
<td>0.76 (24)</td>
<td>1.92 (49)</td>
<td>40</td>
<td>7.14 (116)</td>
<td>5.22 (22)</td>
<td>46.6</td>
<td>46.3</td>
</tr>
<tr>
<td>2</td>
<td>67</td>
<td>0.9 (43)</td>
<td>1.80 (69)</td>
<td>50</td>
<td>4.71 (96)</td>
<td>3.69 (164)</td>
<td>53.3</td>
<td>42.8</td>
</tr>
<tr>
<td>3</td>
<td>76</td>
<td>0.7 (28)</td>
<td>1.50 (44)</td>
<td>47</td>
<td>6.94 (112)</td>
<td>3.75 (122)</td>
<td>60.1</td>
<td>38.3</td>
</tr>
<tr>
<td>4</td>
<td>69</td>
<td>0.87 (35)</td>
<td>1.72 (55)</td>
<td>51</td>
<td>6.19 (116)</td>
<td>4.47 (206)</td>
<td>47.3</td>
<td>56.1</td>
</tr>
<tr>
<td>5</td>
<td>59</td>
<td>0.94 (32)</td>
<td>2.22 (61)</td>
<td>42</td>
<td>8.46 (138)</td>
<td>6.24 (253)</td>
<td>55.6</td>
<td>58.3</td>
</tr>
<tr>
<td>6</td>
<td>57</td>
<td>0.6 (20)</td>
<td>1.20 (30)</td>
<td>53</td>
<td>3.95 (61)</td>
<td>2.46 (111)</td>
<td>60.8</td>
<td>46.1</td>
</tr>
<tr>
<td>7</td>
<td>59</td>
<td>1.13 (34)</td>
<td>3.44 (78)</td>
<td>33</td>
<td>7.64 (123)</td>
<td>4.20 (179)</td>
<td>66.1</td>
<td>42.2</td>
</tr>
<tr>
<td>8</td>
<td>60</td>
<td>0.74 (26)</td>
<td>1.54 (41)</td>
<td>48</td>
<td>5.24 (86)</td>
<td>3.70 (164)</td>
<td>57.1</td>
<td>36.4</td>
</tr>
<tr>
<td>9</td>
<td>61</td>
<td>0.76 (25)</td>
<td>2.04 (51)</td>
<td>52</td>
<td>3.60 (57.5)</td>
<td>1.56 (71.8)</td>
<td>57.8</td>
<td>42.4</td>
</tr>
<tr>
<td>10</td>
<td>78</td>
<td>0.91 (35)</td>
<td>1.66 (48)</td>
<td>55</td>
<td>4.98 (76)</td>
<td>3.32 (122)</td>
<td>48.8</td>
<td>53.6</td>
</tr>
<tr>
<td>Mean</td>
<td>65</td>
<td>0.84 (30)</td>
<td>1.90 (53)</td>
<td>47</td>
<td>5.89 (98)</td>
<td>3.86 (144)</td>
<td>55.4</td>
<td>46.2</td>
</tr>
<tr>
<td>SD</td>
<td>7.36</td>
<td>0.14 (7)</td>
<td>0.61 (14)</td>
<td>7</td>
<td>1.64 (27)</td>
<td>1.32 (73)</td>
<td>6.3</td>
<td>7.4</td>
</tr>
</tbody>
</table>

*TLC = total lung capacity; RV = residual volume.
†Helium residual volume assessment; otherwise, plethysmographic assessment.

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Figure 1. Individual values of transcutaneous SaO2 (%) during exercise. RA = room air.
dyspnea score of 3.3 ± 1.5. This value did not significantly change after the walking tests; mean dyspnea scores after walking tests in room air were not different from walking tests with either O₂-C or O₂-HF (Fig 4).

**Discussion**

**Our Results**

The purpose of our study was to evaluate the pressurizing unit in a realistic situation, like an exercise test. We show that O₂-Cs and O₂-HFs may provide a similar level of oxygenation on a short-term basis during a 6-min walking test. Although our data were obtained from a population of patients with COPD with different degrees of pulmonary impairment, individual SaO₂ curves displayed identical trends for the three walking tests. These original data show that SaO₂ improvements are equivalent with both oxygen supplies and, therefore, demonstrate a similar performance between O₂-HFs and O₂-Cs. Noteworthy, these results were obtained in spite of a lower filling gas pressure (140 bars) and a slightly lower FIO₂ (94.24 ± 2.56%) in O₂-HFs as compared to O₂-Cs (200 bars and 98.85 ± 4.89%, respectively). It is not sure that such a difference may be of clinical relevance, at least on a short-term basis. In fact, the actual average FIO₂ received by the patients does not differ significantly when considering the entraining room air via the Venturi effect. As previously described in most studies from the literature,7,8 we found an increase of mean distances performed under oxygen as compared with room air, and this improvement was similar with either oxygen device. Moreover, our patients had variable dyspnea improvements with oxygen but without any difference between both oxygen supplies. We suggest that performances (mean distances, dyspnea score) achieved through the walking tests are similar with both oxygen devices, mainly because both type of cylinders have similar weights. Overall, pressurizing units allow easy use of effective oxygen cylinders, at least on a short-term basis.

**Technical Advantage of Pressurizing Units**

As a source of ambulatory oxygen, O₂-HFs may be an alternative to portable O₂-Cs and liquid oxygen devices. Few clinical studies have compared the

<table>
<thead>
<tr>
<th>Time</th>
<th>SaO₂ (%) Room Air</th>
<th>SaO₂ (%) O₂-C</th>
<th>SaO₂ (%) O₂-HF</th>
<th>p Value† Room Air vs O₂-C</th>
<th>p Value† Room Air vs O₂-HF</th>
<th>p Value† O₂-C vs O₂-HF</th>
</tr>
</thead>
<tbody>
<tr>
<td>Baseline</td>
<td>84.8 ± 4.05</td>
<td>90.6 ± 3.81</td>
<td>90.5 ± 2.92</td>
<td>0.0051</td>
<td>0.0051</td>
<td>0.9594</td>
</tr>
<tr>
<td>1 min</td>
<td>81.8 ± 3.94</td>
<td>86.8 ± 3.58</td>
<td>86.7 ± 2.67</td>
<td>0.0051</td>
<td>0.0125</td>
<td>0.9326</td>
</tr>
<tr>
<td>2 min</td>
<td>80.9 ± 5.24</td>
<td>85.4 ± 3.75</td>
<td>85.3 ± 4.27</td>
<td>0.0077</td>
<td>0.0166</td>
<td>0.9442</td>
</tr>
<tr>
<td>3 min</td>
<td>79.8 ± 6.00</td>
<td>85.0 ± 3.89</td>
<td>86.4 ± 4.24</td>
<td>0.0166</td>
<td>0.0051</td>
<td>0.2135</td>
</tr>
<tr>
<td>4 min</td>
<td>79.5 ± 5.25</td>
<td>85.6 ± 4.65</td>
<td>86.9 ± 4.41</td>
<td>0.0051</td>
<td>0.0051</td>
<td>0.03</td>
</tr>
<tr>
<td>5 min</td>
<td>81.6 ± 5.54</td>
<td>85.4 ± 4.62</td>
<td>85.9 ± 4.51</td>
<td>0.0093</td>
<td>0.0051</td>
<td>0.398</td>
</tr>
<tr>
<td>6 min</td>
<td>79.7 ± 5.03</td>
<td>86.0 ± 4.67</td>
<td>86.3 ± 5.56</td>
<td>0.077</td>
<td>0.0051</td>
<td>0.4838</td>
</tr>
</tbody>
</table>

*Data are presented as mean ± SD. Data are provided for each minute of the tests.
†Statistical analysis performed with Wilcoxon rank test.
relative advantages of gaseous and liquid oxygen for portable use in patients with COPD. Comparing both devices in a prospective controlled study, Vergeret and Brambilla did not find any difference in total ambulatory oxygen use, and observed that compliance to long-term oxygen therapy was improved whatever the ambulatory system used. Other authors highlighted a slight preference for a liquid oxygen system because the oxygen lasted longer, filling was easier, and the canister was easier to carry. However, substitution of gaseous oxygen by liquid oxygen therapy for all hypoxemic COPD patients is not medically justified, and is not largely available in most countries for economic reasons. Used with either liquid or gaseous sources, oxygen-conserving devices may provide significant savings and enhance patient autonomy, during either exercise or sleep.

O2-HFs may be of significant help in order to enable exercise in hypoxemic patients. Supplemental oxygen in patients with COPD with exercise-induced hypoxemia has been shown to be associated with improvement of exercise tolerance and dyspnea. At home or during rehabilitation, oxygen may be delivered for the relief of short episodes of dyspnea either before, during, or after exercise. Such practices have been shown to be beneficial for symptomatic relief of dyspnea. O2-HFs may be a good compromise at home, since ambulatory patients will be able to manage their physical autonomy without the constraints of oxygen home delivery and with overall decreasing costs. On a long-term basis, savings on home delivery expenses should ameliorate the initial high costs of the pressurizing units. Similarly, O2-HFs should be important to respiratory care departments in order to lower the costs of exercise testing and walking tests.

**Conclusion**

In conclusion, when used in clinical conditions and in spite of a slightly lower FIO2 delivered, our study showed that O2-HFs improve Sao2 as well as O2-Cs,
at least on a short-term basis. This new technology may facilitate exercise testing and enhance the feasibility of pulmonary rehabilitation programs.

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