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

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Study objectives: **To compare, in clinical conditions, the efficacy of refilled oxygen cylinders (O_2-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; Pa_{O_2} on room air, 55.4 ± 6.3 mm Hg; Pa_{CO_2} on room air, 46.2 ± 7.4 mm Hg; FEV_1/vital capacity, 47 ± 7%; and FEV_1, 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 (O_2-C) or an O_2-HF.**
Measurements and results: **The fraction of inspired oxygen (F_{IO_2}) delivered by O_2-HFs was significantly lower than the F_{IO_2} delivered by O_2-Cs (94.2 ± 2.6% vs 98.8 ± 4.9%, p = 0.02). Mean O_2-HF and O_2-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 O_2-C (373.5 ± 81 m) and O_2-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: **O_2-HFs are as efficient as O_2-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: F_{IO_2} = fraction of inspired oxygen; O_2-C = conventional oxygen cylinder; O_2-HF = refilled oxygen cylinder; Sa_{O_2} = 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 studies[4,5] demonstrated the importance of ambulatory oxygen devices for improving this compliance in COPD patients. Pépin and Barjhoux[4] showed that ambulatory oxygen supplies may lead to a threefold increase of probability to perform oxygen therapy for > 15 h/d. Vergeret and Brambilla[5] 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, refilled cylinders could therefore represent a new alternative for improving overall oxygen therapy

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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 (O_2-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[6] 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 Pa_{O_2} at rest and on room air $\leq$ 60 mm Hg, FEV_1 of $<$ 55% of predicted value, FEV_1/vital capacity (VC) of $<$ 65%, previously documented oxygen desaturation at rest (arterial oxygen saturation [Sa_{O_2}] $<$ 90% on room air) and a stable clinical state for at least 3 months prior to inclusion. Patients with $Pa_{O_2} > 60$ 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 (O_2-HF) with oxygen-enriched air under a 140-bar pressure; in comparison, commercial oxygen cylinders (O_2-Cs) are filled under a 200-bar pressure. The O_2-HF is linked to the compressor with a dedicated valve, and a manometer controls the filling of the cylinder. The fraction of inspired oxygen (FIO_2) 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 O_2-HF is approximately 2 h, although longer if the patient is using the concentrator simultaneously. O_2-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 O_2-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 O_2-HF or an O_2-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 O_2-HFs were completely filled up by the medical team. Walking tests with the O_2-C and the O_2-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 Sa_{O_2} 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 sensibility 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 were $\leq$ 0.05. Equivalence of the two oxygen delivery devices was defined by a Sa_{O_2} 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 or 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 $\pm$ 7 years) were included in the study. Mean FEV_1 was 0.84 $\pm$ 0.14 L (30 $\pm$ 7% of predicted value), FEV_1/VC was 47 $\pm$ 7%, total lung capacity was 5.89 $\pm$ 1.64 L (98 $\pm$ 27% of predicted value), and residual volume was 3.86 $\pm$ 1.32 L (144 $\pm$ 73% of predicted value). Room air arterial blood gases in a stable state showed a Pa_{O_2} of 55.4 $\pm$ 6.3 mm Hg and a Pa_{CO_2} of 46.2 $\pm$ 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 Pa_{O_2} $>$ 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, FIO_2 measured

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

Patient No.	Age, yr	FEV_1, L (%)	VC, L (%)	FEV_1/VC, %	TLC, L (%)	RV, L (%)	Pa_{O_2}, mm Hg	Pa_{CO_2}, mm Hg
1	64	0.76 (24)	1.92 (49)	40	7.14 (116)	5.22 (22)	46.6	46.3
2	67	0.9 (43)	1.80 (69)	50	4.71 (96)	3.69 (164)	53.3	42.8
3	76	0.70 (28)	1.50 (44)	47	6.94 (112)	3.75 (122)	60.1	38.3
4	69	0.87 (35)	1.72 (55)	51	6.19 (116)	4.47 (206)	47.3	56.1
5	59	0.94 (32)	2.22 (61)	42	8.46 (138)	6.24 (283)	55.6	58.3
6	57	0.64 (20)	1.20 (30)	53	3.95 (61)†	2.46 (111)	60.8	46.1
7	59	1.13 (34)	3.44 (78)	33	7.64 (123)	4.20 (179)	66.1	42.2
8	60	0.74 (26)	1.54 (41)	48	5.24 (86)†	3.70 (164)	57.1	36.4
9	61	0.76 (25)	2.04 (51)	52	3.60 (57.5)	1.56 (71.8)	57.8	42.4
10	78	0.91 (35)	1.66 (48)	55	4.98 (76)†	3.32 (122)	48.8	53.6
Mean	65	0.84 (30)	1.90 (53)	47	5.89 (98)	3.86 (144)	55.4	46.2
SD	7.36	0.14 (7)	0.61 (14)	7	1.64 (27)	1.32 (73)	6.3	7.4

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

from O_2-HFs was significantly lower than with O_2-Cs (94.24 ± 2.56% vs 98.85 ± 4.89%, respectively; p = 0.025). The mean O_2-HF weight before walking tests was 3,510 ± 251 g, and the mean O_2-C weight was 3,770 ± 142 g. This difference was not significant (p = 0.09).

Individual data are reported in Figure 1. Transcutaneous Sa_{O_2} with either O_2-C or O_2-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 O_2-C and O_2-HF walking tests with a 3 L/min flow because of severe dyspnea on room air. Mean Sa_{O_2} values with O_2-C and O_2-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 Sa_{O_2} at each minute of the tests with oxygen (O_2-C or O_2-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 O_2-C (373.5 ± 81 m, p = 0.03) or O_2-HF (375 ± 97 m, p = 0.02). No statistical difference was found between distances performed under oxygen either with O_2-C or O_2-HF (Fig 3).

At basal conditions, the Borg scale showed a mean

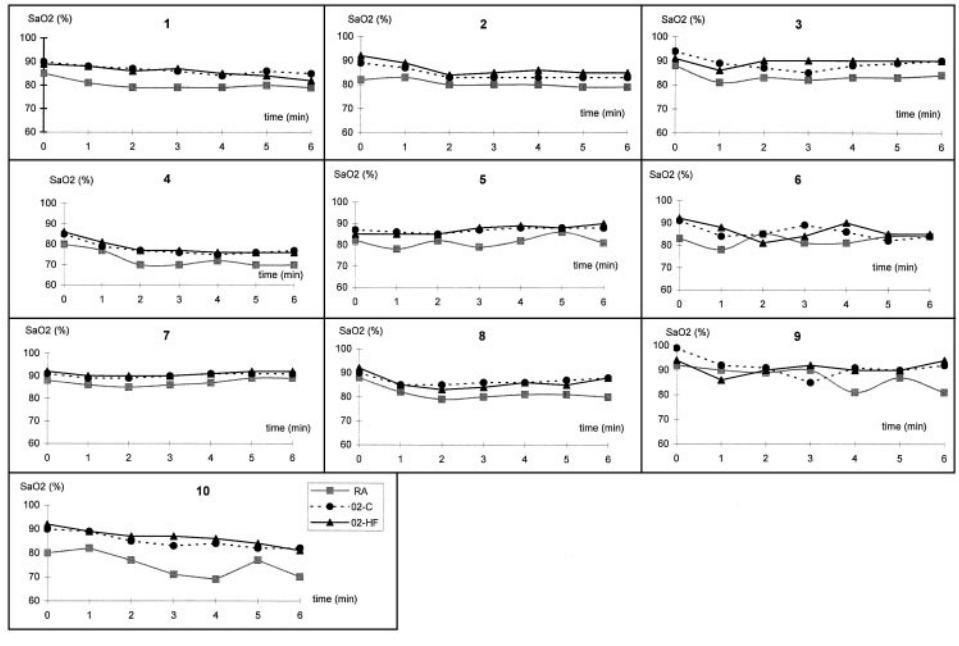

FIGURE 1. Individual values of transcutaneous Sa_{O_2} (%) during exercise. RA = room air.

Table 2—*Mean Sao_2 During Walking Tests (n = 10)

Time	Sao_2 (%), Room Air	Sao_2 (%), O_2-C	Sao_2 (%), O_2-HF	p Value† Room Air vs O_2-C	p Value† Room Air vs O_2-HF	p Value† O_2-C vs O_2-HF
Baseline	84.8 ± 4.05	90.6 ± 3.81	90.5 ± 2.92	0.0051	0.0051	0.9594
1 min	81.8 ± 3.94	86.8 ± 3.58	86.7 ± 2.67	0.0051	0.0125	0.9326
2 min	80.9 ± 5.24	85.4 ± 3.75	85.3 ± 4.27	0.0077	0.0166	0.9442
3 min	79.8 ± 6.00	85.0 ± 3.89	86.4 ± 4.24	0.0166	0.0051	0.2135
4 min	79.5 ± 5.25	85.6 ± 4.65	86.9 ± 4.41	0.0051	0.0051	0.03
5 min	81.6 ± 5.54	85.4 ± 4.62	85.9 ± 4.51	0.0093	0.0051	0.398
6 min	79.7 ± 5.93	86.0 ± 4.67	86.3 ± 5.56	0.077	0.0051	0.4838

*Data are presented as mean ± SD. Data are provided for each minute of the tests.
†Statistical analysis performed with Wilcoxon rank test.

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 O_2-C or O_2-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 O_2-Cs and O_2-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 Sao_2 curves displayed identical trends for the three walking tests. These original data show that Sao_2 improvements are equivalent with both oxygen supplies and, therefore, demonstrate a similar performance between O_2-HFs and O_2-Cs. Noteworthy, these results were obtained in spite of a lower filling gas pressure (140 bars) and a slightly lower Fio_2 (94.24 ± 2.56%) in O_2-HFs as compared to O_2-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 Fio_2 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, O_2-HFs may be an alternative to portable O_2-Cs and liquid oxygen devices. Few clinical studies have compared the

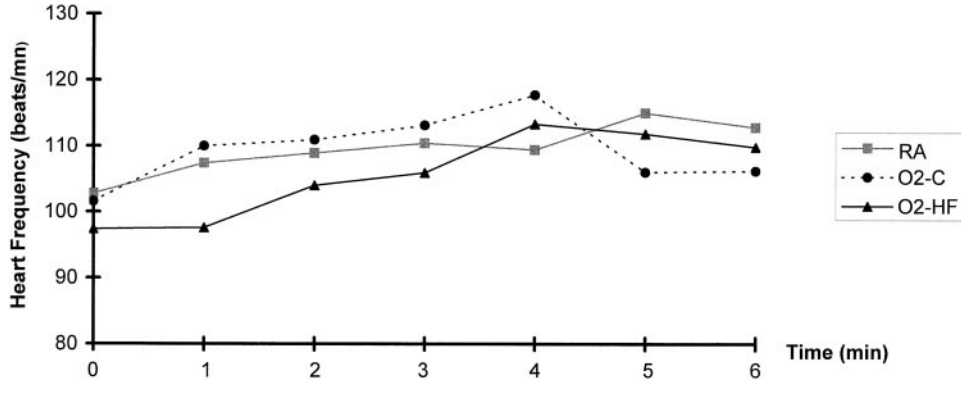

Figure 2. Mean cardiac frequencies during walking tests performed (n = 10). See Figure 1 legend for expansion of abbreviation.

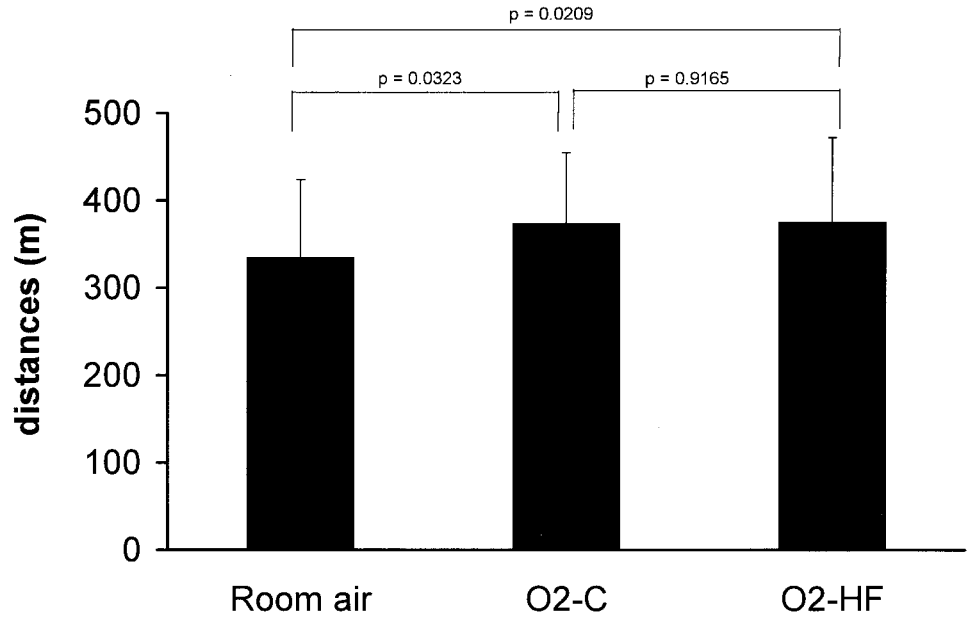

FIGURE 3. Mean distances during walking tests. Statistical analysis was performed using the Wilcoxon rank test.

relative advantages of gaseous and liquid oxygen for portable use in patients with COPD.[5,9] Comparing both devices in a prospective controlled study, Vergeret and Brambilla[5] 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.[10] 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.[11] Used with either liquid or gaseous sources, oxygen-conserving devices may provide significant savings[7,12] and enhance patient autonomy, during either exercise or sleep.[8,13]

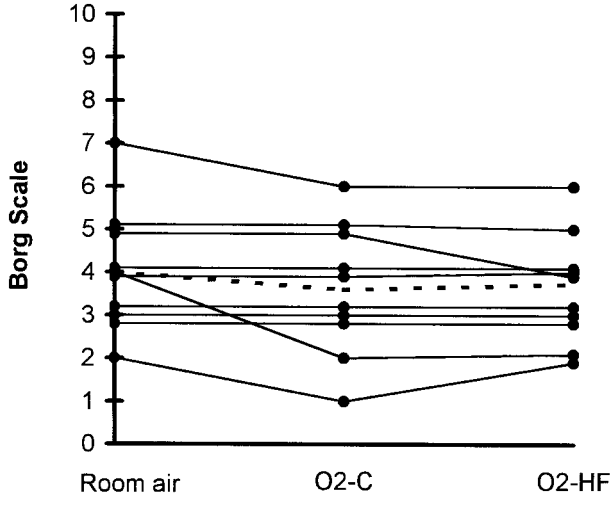

FIGURE 4. Quantification of dyspnea sensations during exercise.

O_2-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.[14,15] 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.[11,15] O_2-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, O_2-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 FIO_2 delivered, our study showed that O_2-HFs improve SaO_2 as well as O_2-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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References

1 Nocturnal Oxygen Therapy Trial Group. Continuous or nocturnal oxygen therapy in hypoxemic chronic obstructive lung disease: a clinical trial. Ann Intern Med 1980; 93:391–398
2 Medical Research Council Working Party. Long term domiciliary oxygen therapy in chronic hypoxic pulmonale complicating chronic bronchitis and emphysema. Lancet 1981; 1:681–686
3 Tarpy SP, Celli BR. Long-term oxygen therapy. N Engl J Med 1995; 333:710–714
4 Pépin JL, Barjhoux C. Long-term oxygen therapy at home: compliance with medical prescription and effective use of therapy. Chest 1996; 109:1144–1150
5 Vergeret J, Brambilla C. Portable oxygen therapy: use and benefit in hypoxaemic COPD patients on long-term oxygen therapy. Eur Respir J 1989; 2:20–25
6 American Thoracic Society. Standards for the diagnosis and care of patients with chronic obstructive pulmonary disease. Am J Respir Crit Care Med 1995; 152:S77–S120
7 Garrod R, Bestall JC, Wedzicha JA. Evaluation of pulsed dose oxygen delivery during exercise in patients with severe chronic obstructive pulmonary disease. Thorax 1999; 54: 242–244
8 Roberts CM, Bell J. Comparison of the efficacy of a demand oxygen delivery system with continuous low flow oxygen in subjects with stable COPD and severe oxygen desaturation on walking. Thorax 1996; 51:831–834
9 Lilker ES, Karnick A, Lerner L. Portable oxygen in chronic obstructive lung disease without hypoxemia and cor pulmonale: a controlled double-blind crossover study. Chest 1975; 68:236–241
10 Lock SH, Blower G, Prynne M, et al. Comparison of liquid and gaseous oxygen for domiciliary portable use. Thorax 1992; 47:98–100
11 Calverley PMA. Supplementary oxygen therapy in COPD: is it really useful? Thorax 2000; 55:537–538
12 Tiep BL. Portable oxygen systems. In: Tiep BL, ed. Portable oxygen therapy. New York, NY: Futura Publishing Company, 1991
13 Cuvelier A, Muir JF, Czernichow P, et al. Nocturnal efficiency and tolerance of a demand oxygen delivery system in COPD patients with nocturnal hypoxemia. Chest 1999; 116: 22–29
14 Garrod R, Paul EA, Wedzicha JA. Supplemental oxygen during pulmonary rehabilitation in patients with COPD with exercise hypoxaemia. Thorax 2000; 55:539–543
15 Killen JWW, Corris PA. A pragmatic assessment of the placement of oxygen when given for exercise induced dyspnea. Thorax 2000; 55:544–546