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Comparing supplementary oxygen benefits from a portable oxygen concentrator and a liquid oxygen portable device during a walk test in COPD patients on long-term oxygen therapy

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Summary
Background: Differences in oxygen delivery between portable oxygen concentrators (POC) and liquid oxygen (LO) portable units, pose a question if POCs are equally effective as LOs in reducing exercise-induced hypoxaemia.
Design: Randomized, single-blind clinical trial.
Patients: Thirteen COPD patients (means: age 66±11 year, FEV_1 35.2±13.7% predicted) and respiratory failure (means: PaO_2 52±5 mmHg, $PaCO_2$ 51.3±7.5 mmHg).
Methods: All patients underwent a series of 6-min walk tests (6 MWT) carried out in random order among one of the three devices: POC, LO cylinder and cylinder with compressed air (CA). Oxygen supplementation was 3 lpm for LO and an equivalent to 3 lpm in a pulse flow system for POC.
Results: The mean SpO_2 was equally improved at rest: 92.9±2.8% with POC and 91.7±2.0% with LO compared to CA—87.8±2.7% (POC and LO vs. CA $p<0.05$). POC and LO significantly improved oxygenation during 6 MWT (mean SpO_2 was 84.3±5% and 83.8±4.2%, respectively) compared to breathing CA—77.6±7.4%, $p<0.05$. Mean 6 MWT distance increased with LO (350±83 m) and POC (342±96 m) when compared to CA (317±84 m), however, these differences were not statistically significant. Dyspnoea score assessed at the end of the exercise (Borg scale) was significantly lower when breathing oxygen (4.2±1.2 with POC and 4.1±1.7 with LO vs. 5.4±1.9 with CA, $p<0.05$).

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Conclusions: Effectiveness of oxygen supplementation from a POC did not differ from the LO source during 6 MWT in COPD patients with respiratory failure. Oxygen at 3 lpm flow was not sufficient to prevent hypoxaemia during strenuous exercise.

Introduction

Long-term domiciliary oxygen therapy (LTOT) is one of a very few medical procedures that prolong life of patients with respiratory failure.[1,2] More than 2 million people benefit from this form of treatment worldwide. A majority of them use oxygen concentrators (OC) as a source of oxygen. OCs remain the most economic way to provide oxygen at home. To comply with physician prescription to breathe oxygen for more than 15 h per day, patients using OCs are forced to stay at home and to limit their outdoor activities.

Liquid oxygen (LO) overcomes that inconvenience by combining a large stationary unit with a small portable canister allowing the patient to leave home and to enjoy outdoor activities while using supplementary oxygen.

A less efficient combination is the use of an OC at home and pressurized oxygen in small lightweight cylinder for ambulation. Need for frequent refilling and cumbersome logistics make this source less convenient although less expensive than LO. Now, portable gas cylinders can also be safely refilled from a uniquely constructed oxygen concentrator.[3]

Recently, a new ambulatory source of oxygen—portable oxygen concentrator (POC)—has become available. Lightweight, battery operated, systems with an integrated oxygen-conserving device (OCD) provide a mobile oxygen source for a few hours use. Oxygen flow is set up as an equivalent of continuous oxygen flow per minute. There are no published reports on the effectiveness of oxygen supply provided by POCs.

The aim of the study was to determine if a POC is as effective as LO in reducing exercise-induced hypoxaemia in severe COPD patients on LTOT.

Materials and methods

Subjects

Fifteen patients with COPD undergoing LTOT were included in the study. COPD was diagnosed using GOLD criteria.[4] Eligibility for LTOT was based on the ATS/ERS guidelines: $PaO_2 \leqslant 55$ mmHg or PaO_2 56–60 mmHg and the ECG or radiographic evidence of pulmonary hypertension or polycythaemia with haematocrit $\geqslant 55\%$.[5] Exclusion criteria included: refusal to participate in the study, important comorbidities (e.g. limiting angina, musculoskeletal disability and malignancy), recent (within 8 weeks) exacerbation of COPD. The protocol of the study was explained to each subject, and signed informed consent was obtained from all patients. The study protocol was approved by the Institutional Ethics Committee.

Study design

Investigations were performed in an outpatient clinic. All subjects underwent a series of five 6-min walk tests (6 MWT). Tests were performed in a 30-m corridor in accordance with the ATS guidelines.[6] To minimize effect of learning, first two sessions of 6 MWT were conducted as training sessions and involved breathing air and carrying a 3.5 kg weight, corresponding to the weight of portable oxygen delivery devices. The last three sessions of 6 MWT were performed with one of three tested devices: POC (4.6 kg; LifeStyle AirSep, Buffalo, NY, USA), LO cylinder (3.3 kg; FreeLOX, Taema, France) and a cylinder with compressed air (CA) (3.3 kg). The subjects carried the devices themselves during the tests. Oxygen supplementation was 3 lpm for LO and an equivalent to 3 lpm for POC. Three liters flow was set on the CA cylinder. The order of testing devices was randomly assigned. The subjects were not aware of what type of oxygen delivery system they were testing. Each 6 MWT was administered on separate visits several days apart. Before each test, all subjects were allowed to rest for 30 min breathing room air. Then arterial blood was taken for blood gas analysis. Next, while resting, the subjects were given oxygen or air supplementation from one of the tested devices. After 10 min, blood pressure, heart rate and dyspnoea level were measured; the last one using the Borg scale.[7] Next, the subjects performed the walk test. Arterial blood oxygen saturation (SpO_2) and pulse rate were monitored continuously with a pulse oximeter (Pulsox-3Li, Minolta, Osaka, Japan). The oximeter recorded the SpO_2 and pulse rate every 5 s. As soon as the walk test was completed blood pressure, heart rate and dyspnoea level were measured again.

Data analysis

Statistical analysis was performed using Statistica 7.1 data analysis software system (StatSoft Inc.). Results are given as mean $\pm$ SD, unless stated otherwise. Friedman's ANOVA by ranks followed by post hoc sign tests were used to analyse differences between POC, LO and CA breathing. A p-value < 0.05 was considered to be statistically significant.

Results

Patient characteristics

In total, 13 patients completed the study (seven men and six women; mean age 66 $\pm$ 11 years). One patient developed exacerbation of COPD during the study and one patient refused to participate. Their mean FEV_1 was 0.79 $\pm$ 0.27 l (35.2 $\pm$ 13.7% of predicted), FEV_1/VC was 51.8 $\pm$ 11.3%,

Table 1 Demographic and clinical data of 13 study participants.

Variables	
Males/females, *n*	7/6
Age, years	66±11
BMI, kg/m^2	27.2±4.9
FEV_1% pred.	35.2±13.7
FEV_1%FVC	51.8±11.3
RV%TLC	70±12
PaO_2, mmHg	52.5±5
$PaCO_2$, mmHg	51.3±7.5
Prescribed oxygen flow in resting condition, lpm	1.7±0.7

Data are presented as mean±SD, unless otherwise stated.
Definition of abbreviations:
lpm—litres per minute; BMI—body mass index; FEV_1—forced expiratory volume in one second; FEV_1/FVC—forced expiratory volume in 1 s to forced expiratory volume ratio; RV/TLC—residual volume to total lung capacity ratio; PaO_2—partial pressure of oxygen in arterial blood; $PaCO_2$—partial pressure of carbon dioxide in arterial blood.

residual volume (RV) was 5.1±2 l (232±98% of predicted), RV/TLC was 70±12%. Resting arterial blood gases at room air showed a PaO_2 of 52.5±5 mmHg and a $PaCO_2$ of 51.3±7.5 mmHg. Demographic and clinical data of study participants are shown in Table 1.

Walking distance

During two training walk tests, subjects covered 305±91 and 315±92 m, respectively (p = NS). The results of both tests corresponded very closely to the distance covered during the proper test when breathing CA—317±84 m. Better results were obtained when patients were using LO—350±83 m or POC—342±96 m. However, differences between oxygen and air breathing were not significant.

Breathlessness during walk tests

The level of dyspnoea while resting before the tests was similar, ranging from 1.5±1.3 before the test with CA, to 1.6±1.4 for LO and 1.6±1.7 for POC. Breathlessness at the end of exercise was significantly lower while breathing oxygen (4.2±1.2 for POC and 4.1±1.7 for LO) than while breathing room air (5.4±1.9, $p<0.05$).

Efficacy of oxygen supplementation

Both oxygen devices assured good oxygenation at rest: the mean SpO_2 was 92.9±2.8% with POC and 91.7±2.0% using LO, while on air SpO_2 was 87.8±2.7% (POC and LO vs. CA $p<0.05$). The mean value of SpO_2 during the 6 MWT was 84.3±5% and 83.8±4.2% (p = NS) for POC and LO, respectively, while during air breathing SpO_2 fell to 77.6±7.4% (POC and LO vs. CA $p<0.05$). There were no significant differences in oxygenation between POC (SpO_2 81.5±8%) and LO (SpO_2 80.9±7.1%) at the end of the tests.

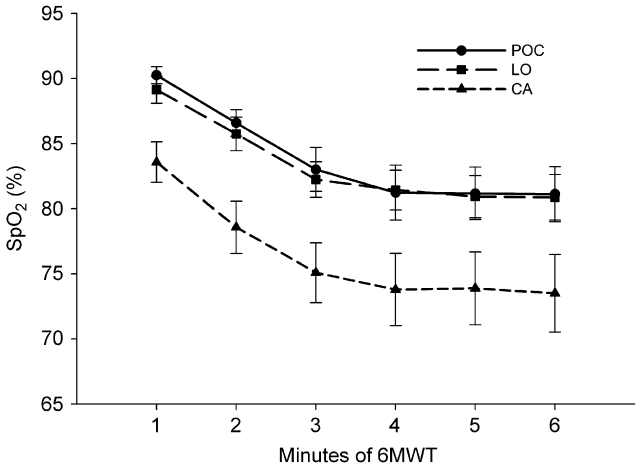

Figure 1 Mean SpO_2 at each minute of 6 MWT for the 13 subjects with tested devices. Data are presented as mean±SE.

The SpO_2 after the CA tests was 73.2±10.7%, which was significantly lower than SpO_2 after 6 MWTs with oxygen devices ($p<0.05$).

Comparison of desaturation time

SpO_2 below 90%, 88%, 85% and 80% during 6 MWT demonstrated that the POC provided slightly better oxygenation than LO. However, the differences were very small and insignificant. The desaturation time was significantly shorter during oxygen breathing than during air breathing. For example, time of 6 MWT spent in desaturation below 88% was present during 59±36% of time during the test with POC, 71±25% for LO ($p = 0.08$) and 87±27% for CA (POC and LO vs. CA, $p<0.05$) and time of test spent in desaturation below 80% was 21±26% for POC, 29±32% for LO ($p = 0.38$) and 49±37% for CA ($p<0.05$).

The same pattern of SpO_2 decrease during 6 MWT was observed with all three devices. There was a steep decline in SpO_2 during the first 3 min of 6 MWT followed by a plateau towards the end of the test (Figure 1). However, SpO_2 at the end of each minute was lower during air breathing than during oxygen breathing from both sources ($p<0.05$).

Discussion

The need of oxygen supplementation during ambulation in COPD patients on LTOT has already been identified by Barach[8] and Cotes and Gilson[9] in the middle of the 20th century. Those needs were fulfilled by the development of portable units with LO and gaseous compressed oxygen. At the end of the 20th century high-pressure cylinders refilled from oxygen concentrators were constructed.[3] In 2002, first POC was introduced, followed by several other models.[10] However, there are no publications about their efficacy apart from congress abstracts.[11–13] We believe that our study is the first one comparing a new device with a well-established source of ambulatory oxygen. We compared POC to a LO portable unit. Both devices are designated to supply oxygen during ambulation. The principal question was: Is POC equally effective in reducing exercise-induced desaturation in patients with respiratory failure? In spite of

significant differences in oxygen delivery between the two devices compared, results of our study showed no statistically significant differences in oxygenation between POC and portable LO. The mean SpO_2 during the whole test, as well as SpO_2 measured in the end of the test and at each consecutive minute of the test were almost equal for both devices. Despite no significant differences, most measured variables were slightly higher for POC than for the portable LO. The improvement of oxygenation using LO and POC was significantly better when compared with air breathing. Supplemental oxygen had no significant influence on the distance covered during 6 MWT. Although the distance increased by 25 m with POC and 33 m with LO, this improvement did not reach level of statistical significance ($p = 0.09$). This may be an effect of limited number of studied subjects (type 2 error). Both devices significantly reduced breathlessness at the end of exercise.

Differences between devices

There are two principal differences between POCs and LOs. First, a POC does not provide 100% oxygen. The concentration of oxygen ranges between 85% and 95% depending on flow rate. The higher flow, the lower concentration of oxygen, while LOs give pure, 100% oxygen at any flow. Second, the LO portable unit tested in our study gave continuous oxygen flow while the POC delivered oxygen in pulses. POCs do not store oxygen, but produce it continuously. To conserve oxygen and decrease the weight of equipment, a POC has a built-in OCD. The bolus of low volume oxygen is delivered to airways only during inspiration.

The amount of oxygen delivered by OCDs is expressed as ''equivalent'' to continuous flow. But in fact the equivalency is not a universal value. The OCDs differ in volume and time of oxygen delivery at the same flow setting, which cause the differences in FiO_2.[14]

OCD in POC tested in our study (''Impulse Elite'') is the pulse-type device. It releases fixed bolus of oxygen with the beginning of each breath which is advantageous, while it was shown that delivered FiO_2 depends on oxygen volume delivered in the first 0.6 s of inhalation.[15] At the setting of 3 lpm, used in our investigation, the bolus according to manufacturer is 26.25 cm^3. The total amount of inhaled oxygen per minute depends on bolus amount and number of breaths. This pattern of oxygen delivery raises important issues. The main question is does it provides adequate oxygenation, particularly during exercise?

Comparison of pulse-dose and continuous flow

There are very few studies comparing both systems of oxygen delivery. Bliss et al.[14,15] using lung models suggest that pulse-dose system could be more effective than continuous flow in delivery of oxygen during exercise. On the other hand, Gallegos and Shigeoka[16] proved in theoretical model that POCs may under-treat hypoxaemia, especially during exercise mainly because of low oxygen concentration and low bolus volume.

The studies on patients with respiratory failure also gave controversial results. Roberts et al. compared the efficacy of a demand oxygen delivery system to continuous flow. In both systems 100% oxygen was used. The results showed that the demand oxygen delivery system was less effective. However, either of the systems was able to prevent desaturation.[17] Lewarski et al. compared compressed concentrator gas (93% O_2) delivered via OCD to continuous flow of 100% oxygen. They found no statistically significant differences in SpO_2 between the two methods used.[11] Cuvelier et al. performed a similar study comparing concentrator-refilled vs. conventional pressurized oxygen cylinder, both without OCD. Even with the differences in FiO_2 delivery ($94.2 \pm 2.6\%$ vs. $98.8 \pm 4.9\%$, $p = 0.02$) the mean transcutaneous oxygen saturation showed similar improvement with both devices.[3]

In spite of the higher weight of POC of about 1 kg, which must have increased the work performed by patients, our study has revealed identical improvement in oxygenation during exercise. That data can suggest that lighter models of POC may be more effective during ambulation in patients on long-term oxygen therapy.

How many lpm are needed by hypoxaemic COPD patients during exercise?

It is well known that the oxygen flow preventing desaturation at rest is not effective during exercise. ERS/ATS recommendations advise augmentation of oxygen flow during exercise. The mean oxygen flow prescribed for our patients in resting condition was 1.7 ± 0.7 lpm. Our study showed that continuous flow or equivalent to 3 lpm of oxygen, which correspond approximately to doubling resting dose, was not preventing hypoxaemia during strenuous exercise. However, it may be sufficient during less vigorous activities of daily life. Case et al. investigated oxygenation in hypoxaemic COPD patients during rehabilitation activities. Each patient was titrated to a POC setting that yielded the $SpO_2 > 90\%$ during exercise. They found that both a POC with the setting of 4.7 ± 0.5, which is equivalent to lpm, and a continuous flow LO with a mean flow of 3.9 ± 1.3 lpm, provided sufficient oxygenation: SpO_2 93% and 91%, respectively.[12] McCoy et al. tested three models of POC on six COPD oxygen-dependent patients. The devices were titrated to oxygen supplementation at rest for tested subjects. During self-paced 10-min walk there was no significant desaturation. In two patients a decrease of SpO_2 to 89% was noted. There were no differences between three tested POCs.[13]

Conclusions

With rapid technological development more new medical equipment becomes available including POCs. Our results suggest that the effects of oxygen supplementation with POCs did not differ from the LO portable units during 6 MWT in walking distance and SpO_2. It appears that POCs may be safely used for ambulatory oxygen treatment. Our data suggests that doubling the dose of oxygen flow at rest, was not sufficient to prevent hypoxaemia during strenuous exercise and rather three-fold increase of oxygen flow should be prescribed.

Conflict of interest statement

Authors had no direct, indirect or potential conflict of interest in the course of this study. Both tested devices, portable oxygen concentrator and system of liquid oxygen, were rented from local distributor. All authors of the manuscript are researchers at the Medical University of Warsaw and have no financial or other connection with the equipment provider.

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