Pilot Study of a New Device to Titrate Oxygen Flow in Hypoxic Patients on Long-Term Oxygen Therapy

Serena Cirio FT and Stefano Nava MD

BACKGROUND: The O2 Flow Regulator (Dima, Bologna, Italy) is a new automated oxygen regulator that titrates the oxygen flow based on a pulse-oximetry signal to maintain a target $S_pO_2$. We tested the device’s safety and efficacy. METHODS: We enrolled 18 subjects with chronic lung disease, exercise-induced desaturation, and on long-term oxygen therapy, in a randomized cross-over study with 2 constant-work-load 15-min cycling exercise tests, starting with the patient’s previously prescribed usual oxygen flow. In one test the oxygen flow was titrated manually by the respiratory therapist, and in the other test the oxygen flow was titrated by the O2 Flow Regulator, to maintain an $S_pO_2$ of 94%. We measured $S_pO_2$ throughout each test, the time spent by the respiratory therapist to set the device or to manually regulate the oxygen flow, and the total number of respiratory-therapist titration interventions during the trial. RESULTS: There were no differences in symptoms or heart rate between the exercise tests. Compared to the respiratory-therapist-controlled tests, during the O2 Flow Regulator tests $S_pO_2$ was significantly higher (95 ± 2% vs 93 ± 3%, $P = .04$), significantly less time was spent below the target $S_pO_2$ (171 ± 187 s vs 340 ± 220 s, $P < .001$), and the O2 Flow Regulator tests required significantly less respiratory therapist time (5.6 ± 3.1 min vs 2.0 ± 0.1 min, $P = .005$). CONCLUSIONS: The O2 Flow Regulator may be a safe and effective alternative to manual oxygen titration during exercise in hypoxic patients. It provided stable $S_pO_2$ and avoided desaturations in our subjects. Key words: long-term oxygen therapy; oxygen; COPD; $S_pO_2$; oximetry; exercise test. [Respir Care 2011;56(4):429–434. © 2011 Daedalus Enterprises]

Introduction

Long-term oxygen therapy (LTOT) has been a standard treatment for patients with COPD and chronic respiratory failure since the 1970s, when it was found that LTOT can improve survival.$^1,2$ Indications for LTOT are accepted worldwide, and international guidelines recommend LTOT if the patient’s resting $P_{aO_2}$ is < 55 mm Hg, or 55–59 mm Hg if there is evidence of right-atrial enlargement, congestive heart failure, and high hematocrit (> 55%).$^3,5$ There is overall agreement that a $P_{aO_2} > 60$ mm Hg is the goal of LTOT, to enhance peripheral oxygenation.$^6,7$ The indications for LTOT in patients with exercise-induced desaturation are still controversial. Some studies have found an $S_pO_2$ drop despite supplemental oxygen during mild exercise, sleep, and usual activities of daily living.$^8-10$ Recent guidelines on pulmonary rehabilitation emphasize the importance of COPD patients, including those with chronic respiratory failure, maintaining an active life, and an exercise program for the muscles of ambulation is

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Serena Cirio FT is affiliated with the Pulmonary and Critical Care Unit, Fondazione Salvatore Maugeri, Istituto di Ricovero e Cura a Carattere Scientifico, Istituto Scientifico di Pavia, Italy. At the time of this research, Stefano Nava MD was also affiliated with the Pulmonary and Critical Care Unit, Fondazione Salvatore Maugeri, IRCCS, Istituto Scientifico di Pavia, Italy. He is now affiliated with Pneumologia e Terapia Intensiva Respiratoria, Dipartimento Cardio-Toraco-Vascolare, Policlinico Sant’Orsola-Malpighi, Bologna, Italy.

Ms Cirio has disclosed a relationship with Vivisol. Dr Nava has disclosed no conflicts of interest.

Correspondence: Stefano Nava MD, Pneumologia e Terapia Intensiva Respiratoria, Policlinico Sant’Orsola-Malpighi, via Massarenti n.9, Bologna 40138 Italy, E-mail: stefano.nava@aosp.bo.it.

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recommended as a main component of pulmonary rehabilitation.11

Different types of exercise produce different levels of desaturation,12-14 so the commonly prescribed fixed oxygen flow, which is usually titrated at rest, may not meet every patient’s need. It would be preferable, therefore, to regulate the oxygen flow according to the patient’s actual, changing need. A new automatic O2 flow-regulator device, the O2 Flow Regulator (Dima, Bologna, Italy, distributed by Vivisol, Monza, Italy) was recently released (Fig. 1). Its primary function is to titrate the oxygen flow rate based on a pulse-oximetry signal, to maintain a target $\text{SpO}_2$.

We conducted a pilot randomized crossover study to evaluate the safety and efficacy of the O2 Flow Regulator, compared to usual manual oxygen flow titration.

**Methods**

**Patients**

We recruited 18 consecutive clinically stable COPD patients on LTOT from the patients attending a pulmonary rehabilitation program. The inclusion criteria were hypoxia at rest ($P_{aO_2} < 55 \text{ mm Hg on room air}$) and exercise-induced desaturation when using their usual prescribed oxygen flow. The usual oxygen flow is prescribed based on a mean $S_{pO_2} \approx 88\%$ during a 6-min walk test, and reassessment the next day during a 15-min constant-exercise cycle-ergometer test, at the same oxygen flow. We excluded patients who had chronic heart failure or any other cardiopathy, atrial fibrillation, neurological disease, or difficulty in cycling; who needed an O2 flow of $> 6 \text{ L/min at rest}$; whose carboxyhemoglobin was $> 4\%$; or whose methemoglobin was $> 1\%$. This study was approved by the Comitato Etico Centrale of Fondazione Salvatore Maugeri, and we obtained written informed consent from each subject.

**Study Design**

The study was a randomized controlled crossover trial. In each subject, during 2 standardized 15-min cycling tests, we measured $\text{SpO}_2$, respiratory therapist (RT) time (to set or adjust the devices), and the total number of RT interventions. On 2 consecutive days, each subject performed, in random order, and using the same oxygen source (portable liquid oxygen cylinder, filled and calibrated before every test, with a maximum flow rate of 6 L/min), the exercise test with an individualized stable work load that was selected on the basis of 2 previous exercise tests that determined the maximum exercise load the patient could sustain without needing to pause, while using their prescribed oxygen flow. During the tests the patients were monitored continuously with a 3-lead electrocardiogram and pulse oximetry (Pulsox-3iA, Konica Minolta Sensing, Ramsey, New Jersey) with a finger probe. A priori we chose a target $S_{pO_2}$ of 94%.15 The randomization order was decided with opaque sealed envelopes.

**O2 Flow Regulator**

The O2 Flow Regulator was developed to automatically titrate the O2 flow to maintain a constant $S_{pO_2}$ (Fig. 2). It is placed in line between an oxygen source and the user. Once the clinician sets the target $S_{pO_2}$, the device should be able to maintain it, increasing or decreasing the flow for any $S_{pO_2}$ variation above or below the target. A microprocessor continuously reads the $S_{pO_2}$ signal; if $S_{pO_2}$ is lower than the target, it rapidly opens the flow valve (2 L change over 30 s) to increase oxygen delivery. If $S_{pO_2}$ exceeds the target, the valve slowly closes (0.5 L change over 30 s) to reduce the flow.

**Protocol**

Each subject performed 2 exercise tests: one in which the RT manually titrated the oxygen flow (the RT-controlled test), and one in which the O2 Flow Regulator titrated the oxygen flow (the O2 Flow Regulator test) un-
under the supervision of the same RT. During the RT-controlled test, to simulate the behavior of the O₂ Flow Regulator, the RT titrated the oxygen flow rate every one minute, as necessary to achieve the target SpO₂, with the same flow-change rates as the O₂ Flow Regulator.

We measured dyspnea and leg fatigue with the modified Borg scale, every minute. The oximeter calculated the mean SpO₂ during the test and the time spent with SpO₂ < 94%.

We counted the number of RT interventions (titrations) during the RT-controlled test. An observer naïve to the protocol used a stopwatch to measure the RT time during the RT-controlled test, and, during the O₂ Flow Regulator test, to measure the RT time to set the O₂ Flow Regulator (ie, set the target SpO₂ and alarms, and check the battery and memory card).

**Statistical Analysis**

We used a paired t test to compare the data from the exercise tests. Data are presented as mean ± SD. A P < .05 was considered statistically significant.

**Results**

Table 1 shows the cohort’s mean age, PₐO₂, PₐCO₂, pH, baseline SpO₂, and nadir SpO₂ during exercise. All the patients tolerated well the experimental procedures and completed both tests. There was no statistical differences in dyspnea, leg fatigue, heart rate, or oxygen saturation at rest between the RT-controlled tests and O₂ Flow Regulator tests (Table 2). Dyspnea, leg fatigue, and heart rate increased similarly. Mean SpO₂ was significantly higher during the O₂ Flow Regulator tests (95 ± 2% vs 93 ± 3%, P = .04).

Figure 3 shows typical SpO₂ traces from a representative patient during both the RT-controlled test and the O₂ Flow Regulator test. Figure 4 shows the amount of time the subjects spent below the target SpO₂. Overall, the O₂ Flow Regulator tests had significantly less time below the target SpO₂ (171 ± 187 s vs 341 ± 220 s, P < .001). During the O₂ Flow Regulator tests only 2 of the 18 subjects had SpO₂ decrease to < 90%, and those desaturation periods were < 30 s.

Figure 5 illustrates the number of manual titrations during the RT-controlled tests. The mean RT time was significantly greater in the RT-controlled tests (5.6 ± 3.7 min vs 2.0 ± 0.1 min, P = .005).

**Discussion**

The major international guidelines and position papers on prescription of LTOT are based either on resting or exertional SpO₂, usually assessed during the 6-min walk test. However, at home some LTOT patients have severe desaturations during sleep or activities of daily living, that are not necessarily revealed during the 6-min walk test. This suggests that the oxygen flow should be constantly titrated. We found the O₂ Flow Regulator safe and effective in meeting the target SpO₂. The O₂ Flow Regulator tests had significantly less time below the target SpO₂ (171 ± 187 s vs 341 ± 220 s, P < .001). During the O₂ Flow Regulator tests only 2 of the 18 subjects had SpO₂ decrease to < 90%, and those desaturation periods were < 30 s.

There are several reasons an in-line oxygen flow regulator may be useful in LTOT patients. First, studies have found that, when reevaluating patients’ LTOT requirement after the initial prescription, many patients no longer meet the LTOT eligibility criteria or that they need to have the oxygen flow reduced, mostly because they were recovering from an exacerbation. The O₂ Flow Regulator can decrease the oxygen flow to zero if the target SpO₂ is being met without oxygen flow, which is particularly important.
in patients with hypercapnia, because increasing $P_{aO_2}$ in a patient with hypercapnic respiratory failure causes deleterious changes to alveolar ventilation and gas exchange, which worsens acidosis, and increases morbidity and mortality.19

Second, it has been suggested that long-term rehabilitation programs may be useful in COPD patients, with or without chronic respiratory failure.11 Among the various rehabilitation activities, high-intensity training is more effective in improving exercise capacity, and supplemental oxygen increases exercise ability, allowing higher exercise intensity, in COPD patients without resting hypoxemia who desaturate during exercise.20 This highlights the importance of oxygen flow titration for these patients during rehabilitation at home, especially considering that their clinical status may deteriorate.

Third, few studies have recorded $S_pO_2$ over a 24-hour period in COPD patients, either receiving LTOT or not, and both groups manifest severe desaturations during sleep and activities of daily living.8-10 Walking is usually associated with the lowest mean $S_pO_2$ and with the highest number of desaturations, which are particularly severe in some individuals. However, eating, washing, house-work, dressing, and even watching television are activities of daily living that are associated with frequent desaturations, in certain cases even worse than during walking. Some patients may spend > 30% of the day with $S_pO_2$ below 90%.8-10 These desaturation episodes are dangerous, because they may transiently increase the mean pulmonary arterial pressure, which may be one of the main causes of chronic pulmonary hypertension in COPD patients (ie, out of proportion) with otherwise moderate but not severe airflow obstruction.21 Therefore, continuous oxygen flow titration is needed to avoid desaturations that cannot be predicted on the basis of a simple exercise test in the hospital.

Fourth, development or worsening of hypoxemia during sleep is well documented in COPD patients and is associated with cardiac arrhythmia and, eventually, pulmonary hypertension.22 Nocturnal desaturation also occurs in approximately a quarter of COPD patients with diurnal $P_{aO_2}$ > 60 mm Hg, and is not necessarily evaluated with nocturnal oximetry.23 Indeed, even in the case of this evaluation, the first step is to perform the examination without oxygen, and then to repeat it with oxygen. With the O2 Flow Regulator, both tests could be performed in one night, because if $S_pO_2$ remains above the target 90%, the O2 Flow Regulator will not deliver any oxygen, which could be eventually added in case of desaturation, as established by the algorithm. In this case important information will be available for the clinician to set the appropriate oxygen flow.

Last, as clearly illustrated in the present study, the O2 Flow Regulator may save RT time when an exercise program should be set for a COPD patient, and at the same time make the appropriate adjustments in the case a clinician is not present.

Limitations

Our selection of a 15-min constant-work-rate test may be criticized, but compared to the incremental maximal, symptom-limited testing induces more severe hypoxemia and therefore would have resulted in substantially fewer patients qualifying for LTOT.14 Cutaneous oxygen saturation measurement (ie, pulse oximetry) has several advan-
tages in the estimation of arterial oxyhemoglobin, but also some disadvantages: it is less accurate than direct measurement of arterial blood, particularly in patients with carboxyhemoglobin or methemoglobin. However, we excluded such individuals. The target $S_pO_2$ we chose (94%) may be considered too high in usual clinical practice, and a lower $S_pO_2$ may also be acceptable.

Conclusions

The $O_2$ Flow Regulator safely and effectively titrated oxygen flow during a constant-work-load exercise test, and may save RT time during pulmonary rehabilitation exercise. We see potential for the $O_2$ Flow Regulator in many daily life situations where the oxygen flow should be reduced or augmented. Safety and patient satisfaction with the $O_2$ Flow Regulator need to be examined in a larger prospective study.

REFERENCES


