

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

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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_{pO₂}. 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_{pO₂} of 94%. We measured S_{pO₂} 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_{pO₂} was significantly higher ($95 \pm 2\%$ vs $93 \pm 3\%$, $P = .04$), significantly less time was spent below the target S_{pO₂} (171 ± 187 s vs 340 ± 220 s, $P < .001$), and the O₂ Flow Regulator tests required significantly less respiratory therapist time (5.6 ± 3.7 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_{pO₂} and avoided desaturations in our subjects. *Key words:* long-term oxygen therapy; oxygen; COPD; S_{pO₂}; 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

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

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DOI: 10.4187/respcare.00983

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_{aO₂} 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_{aO₂} > 60 mm Hg is the goal of

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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_{pO₂} 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



Fig. 1. O₂ Flow Regulator, Dima, Bologna, Italy, which is currently only available in Italy.

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 S_{pO₂}.

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_{aO₂} < 55 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_{pO₂} ≤ 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 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 S_{pO₂}, 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_{pO₂} 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_{pO₂} (Fig. 2). It is placed in line between an oxygen source and the user. Once the clinician sets the target S_{pO₂}, the device should be able to maintain it, increasing or decreasing the flow for any S_{pO₂} variation above or below the target. A microprocessor continuously reads the S_{pO₂} signal; if S_{pO₂} is lower than the target, it rapidly opens the flow valve (2 L change over 30 s) to increase oxygen delivery. If S_{pO₂} 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-

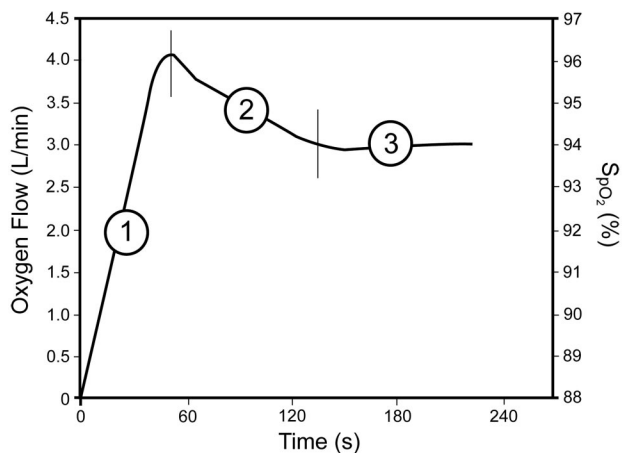


Fig. 2. O₂ Flow Regulator response to S_{pO₂} variation. At point 1, S_{pO₂} is below the target S_{pO₂}, and the O₂ Flow Regulator valve rapidly opens and increases the oxygen flow. At point 2 S_{pO₂} is above the target S_{pO₂}, and the O₂ Flow Regulator valve slowly closes and decreases the oxygen flow. At point 3 the S_{pO₂} is at the target, so the O₂ Flow Regulator maintains the current oxygen flow.

der 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 S_{pO₂}, 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 S_{pO₂} during the test and the time spent with S_{pO₂} < 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 S_{pO₂} 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, P_{aO₂}, P_{aCO₂}, pH, baseline S_{pO₂}, and nadir S_{pO₂} 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 S_{pO₂} was significantly higher dur-

Table 1. Age and Arterial Blood Values Before the Exercise Tests*

	Mean ± SD
Age (y)	69 ± 8
P _{aO₂} (mm Hg)	69 ± 9
P _{aCO₂} (mm Hg)	45 ± 8
pH	7.42 ± 0.04
Baseline S _{pO₂} (%)	95 ± 2
Nadir S _{pO₂} during 6MWT (%)	86 ± 4

* Arterial blood was sampled with the patient at rest while on his or her usual supplemental oxygen flow (mean 1.6 ± 0.4 L/min).
6MWT = 6-min walk test with the patient’s usual resting oxygen flow

ing the O₂ Flow Regulator tests (95 ± 2% vs 93 ± 3%, *P* = .04).

Figure 3 shows typical S_{pO₂} 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 S_{pO₂}. Overall, the O₂ Flow Regulator tests had significantly less time below the target S_{pO₂} (171 ± 187 s vs 341 ± 220 s, *P* < .001). During the O₂ Flow Regulator tests only 2 of the 18 subjects had S_{pO₂} 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 S_{pO₂}, usually assessed during the 6-min walk test.³⁻¹⁶ 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.¹⁷ This suggests that the oxygen flow should be constantly titrated. We found the O₂ Flow Regulator safe and effective in meeting the target S_{pO₂}. The O₂ Flow Regulator tests had significantly less time below the target S_{pO₂}. We chose our target S_{pO₂} on the basis of a study that found that an S_{pO₂} of ≥ 93% should be the objective during exercise in patients who desaturate during exercise.¹⁵

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.¹⁸ The O₂ Flow Regulator can decrease the oxygen flow to zero if the target S_{pO₂} is being met without oxygen flow, which is particularly important

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Table 2. Symptoms, Mean S_{pO_2} , and Heart Rate, at Rest and During Exercise

	At-Rest Before the RT-Controlled Test	At-Rest Before the O ₂ Flow Regulator Test	RT-Controlled Test	O ₂ Flow Regulator Test
Borg dyspnea score	0.8 ± 1.1	1.0 ± 1.2	3.2 ± 1.4*	2.9 ± 1.0*
Borg leg fatigue score	0.5 ± 1.0	0.8 ± 1.4	3.1 ± 1.5*	3.0 ± 1.8*
Heart rate (beats/min)	83 ± 10	83 ± 9	100 ± 4*	96 ± 12*
Mean S_{pO_2} (%)	92 ± 3	92 ± 3	93 ± 3†	95 ± 2‡

* At the end of the exercise test.

† Mean S_{pO_2} during the exercise test.

‡ $P = .046$

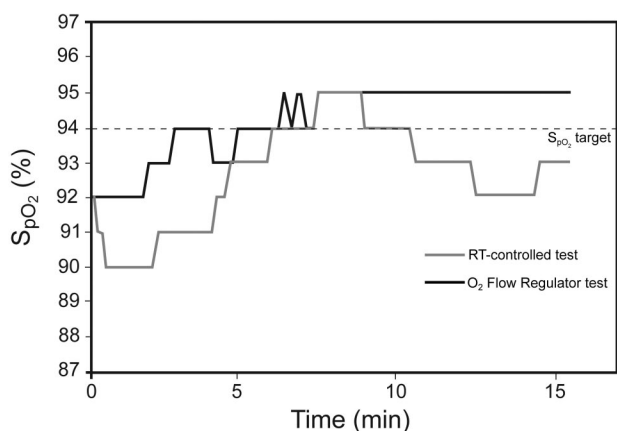


Fig. 3. Typical S_{pO_2} traces from a representative patient during exercise tests in which the supplemental oxygen flow was manually titrated by the respiratory therapist (RT) or automatically titrated by the O₂ Flow Regulator.

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,

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-

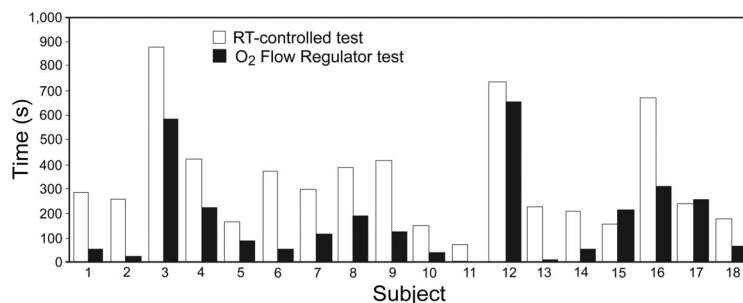


Fig. 4. Time spent below the target S_{pO_2} during exercise tests (in 18 subjects) in which the supplemental oxygen flow was manually titrated by the respiratory therapist (RT) or automatically titrated by the O_2 Flow Regulator.

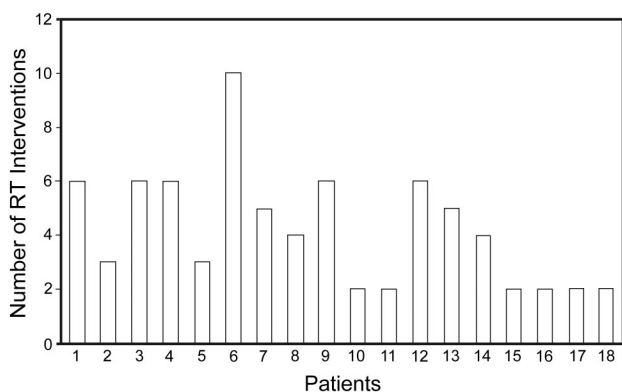


Fig. 5. Number of manual oxygen-flow titrations during exercise tests (in 18 subjects) in which the oxygen flow was manually titrated by the respiratory therapist to maintain the target S_{pO_2} .

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 > 4% or methemoglobin > 1%. However, we excluded such individuals.³ Also, the target S_{pO_2} we chose (94%)¹⁵ 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.

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