

Automated Oxygen Flow Titration to Maintain Constant Oxygenation

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BACKGROUND: One century after the introduction of the oxygen flow meter into clinical practice, we have developed a device, FreeO₂, that automatically titrates the oxygen flow delivered to spontaneously breathing patients, with the aim of maintaining a stable S_{pO₂}. We evaluated this system in healthy subjects during induced hypoxemia. **METHODS:** Hypoxemia was induced in 10 healthy subjects while breathing a gas mixture of variable F_{IO₂} (air + nitrogen). Each subject performed 3 hypoxemic challenges with the addition, in a random order, of either: air with constant flow (1.5 L/min); oxygen with constant flow (1.5 L/min); or automatic oxygen flow titration. Subjects were blinded to the intervention. Oxygen flow, S_{pO₂}, end-tidal CO₂, respiratory rate, and heart rate were recorded every second. The primary outcome was the time with S_{pO₂} between 92% and 96%. **RESULTS:** The S_{pO₂} target (92–96%) was achieved a median of 26.0%, 36.8%, and 66.5% (*P* < .001) of the time with air, constant oxygen, and automated oxygen titration, respectively. Severe oxygen desaturations (S_{pO₂} < 88%) were respectively observed at a median of 33.7%, 12.7%, and 0.4% of the time (*P* < .001). Hyperoxia was present a median of 4.1%, 39.1%, and 14.5% of the time (*P* < .001). Tachycardia was present with air and with constant oxygen flow, but not while using automated oxygen titration. These results were obtained with a mean and maximal oxygen flow of 1.3 L/min and 7.6 L/min with the automated titration. **CONCLUSIONS:** In this model of induced hypoxemia, the FreeO₂ system that automatically titrates the oxygen flow was more efficient at maintaining the S_{pO₂} target, while ensuring a statistically significant reduction in the rates of severe hypoxemia and hyperoxia, in comparison with air or constant oxygen flow. These beneficial results were obtained with less oxygen, in comparison to a constant oxygen flow. *Key words:* oxygen therapy; closed-loop; automation; respiratory failure; COPD; hypoxemia; desaturation; hyperoxia. [Respir Care 2012;57(8):1254–1262. © 2012 Daedalus Enterprises]

Introduction

Oxygen therapy is widely used at home, during pre-hospital transport, and in many hospital departments.¹ Currently, more than one million patients are receiving long-term oxygen therapy (LTOT) in the United States, which represents an annual cost of 1.8 billion dollars.² Only considering the pre-hospital setting, 2 million oxygen treatments have been delivered annually in England.³ World-

wide, including home care, hospital, and pre-hospital transport, tens of millions of people are receiving oxygen therapy each year.

Hypoxemia is frequently encountered in COPD.⁴ It is responsible for a reduction in exercise tolerance⁵ and causes various complications related to chronic hypoxemia in advanced stages of this disease, namely: pulmonary hyper-

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Drs Lellouche and L'Her are co-inventors of the FreeO₂ system and have disclosed relationships with Oxynov. This research was partly supported by the Canadian Foundation for Innovation Leaders Opportunity Fund and by Fonds de Recherche en Santé du Québec.

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tension, right heart failure, polycythemia, and increased mortality.⁶ When patients with COPD experience chronic hypoxemia at rest, LTOT has been shown to reduce complications and mortality.^{2,7,8}

However, the oxygen flow in patients with LTOT is not always optimal. Patients' needs are variable during the day,⁹ and episodes of oxygen desaturation may occur in nearly half of the patients during the night,¹⁰ as well as during daily activities, despite the use of LTOT.¹¹ Oxygen supplementation is usually delivered using fixed flows throughout the day and night. Although adjusting oxygen flow is recommended to improve overall oxygenation during daily living, particularly during exercise and sleep,¹² most clinicians are reluctant to have patients adjust their own oxygen therapy.

Similarly, oxygen therapy during exacerbation of COPD is not optimally prescribed.³ Excessive oxygen flow in these patients can be harmful, and several authors have demonstrated that hyperoxia can induce hypercapnia in patients with severe COPD.¹³⁻¹⁵ Despite the recommendations,¹⁶ the known clinical consequences of oxygen-induced hypercapnia,¹⁷ and the negative impact of hypercapnia on patient outcome,¹⁸ it has been shown that the vast majority of patients hospitalized for exacerbations of chronic respiratory disease receive oxygen at high flows.³

For all these reasons, tailoring oxygen therapy to the needs of patients is desirable. Adjustments in oxygen flow should meet several objectives:

- Minimize episodes of desaturation
- Avoid excessive oxygen administration that may be responsible for respiratory acidosis
- Customize the oxygen flow to patient's needs, especially during activity and sleep

In other populations, such as acute coronary syndrome or traumatic brain injury, there are also risks associated with oxygen desaturation^{19,20} and hyperoxia.²¹⁻²³

Closed-loop adjustment of oxygen administration based on S_{pO_2} may help optimize oxygen therapy and improve patient safety. FreeO₂ is a newly developed device that automatically adjusts closed-loop oxygen flow to spontaneously breathing patients, with the aim of maintaining stable S_{pO_2} at all activity levels. The aim of the current study was to evaluate this system in a model of induced hypoxemia in healthy subjects. We hypothesized that continuous automatic adjustment of oxygen flow would maintain subjects within the oxygenation target.

Methods

We conducted a blinded randomized controlled crossover study in 10 healthy subjects during induced hypox-

QUICK LOOK

Current knowledge

Oxygen therapy is widely used at home, in the hospital, and in other treatment facilities. During oxygen therapy, hypoxemia and hyperoxemia may occur with changes in patient activity and breathing pattern. Hypoxemia during oxygen therapy may limit patient activity and result in adverse events.

What this paper contributes to our knowledge

Closed-loop control of low-flow oxygen resulted in fewer episodes of hypoxemia, reduced oxygen use, and more time spent at the oxygen saturation target, compared to a single predetermined flow.

emia (hypoxic challenge). The study was conducted in a single center (Centre de Recherche de l'Institut Universitaire de Cardiologie et de Pneumologie de Québec). Each subject underwent, in random order, 3 hypoxic challenges, each time receiving through nasal cannulae one of the following: air delivered at a fixed flow; oxygen delivered at a fixed flow; or oxygen flow automatically titrated by the tested device (Fig. 1). The subjects were blinded to the gas delivered.

The study was approved by the local ethics committee, and a signed consent was obtained from each healthy subject. Exclusion criteria for healthy volunteers were cardiac or respiratory disease, epilepsy, any chronic disease requiring medication, or pregnancy.

Evaluated Device: Automated Oxygen Titration (FreeO₂)

The authors are co-inventors of the evaluated device and have founded a research and development company to develop automated systems for respiratory support. This system automatically adjusts the administered oxygen flow using a closed-loop algorithm, based on physiological data, and provides continuous monitoring of respiratory parameters in spontaneously breathing patients. The main parameter taken into account is the S_{pO_2} , which continuously feeds the algorithm at a rate of one value per second. A proportional integral controller adjusts the oxygen flow delivered by a mass-flow controller from 0 to 20 L/min (flow accuracy ± 0.1 L/min), with the aim of maintaining the S_{pO_2} within a predefined target that can be set by the clinician. The tested device provides continuous flow delivery. The algorithm uses the end-tidal CO₂ (P_{ETCO_2}) and respiratory rate mainly as monitoring data and as alarm thresholds. The prototype used in this study was the first version of the device with reduced monitoring capacity, and with the first version of the proportional integral con-

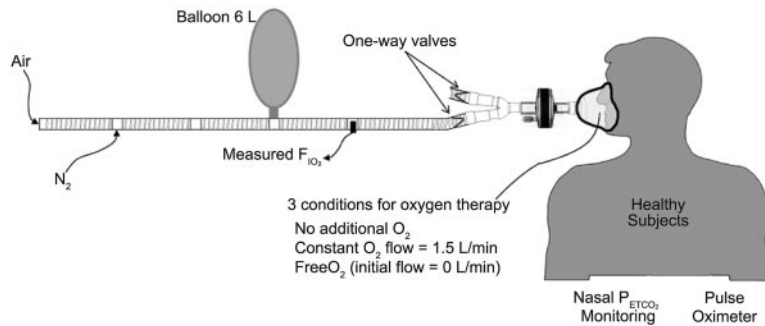


Fig. 1. Model to induce hypoxemia in healthy subjects and to compare 3 conditions for oxygen therapy. The hypoxemic challenge was induced by progressively reducing the F_{IO_2} from 0.21 to 0.07, then rising up to 0.21. The variations of F_{IO_2} were achieved by delivering a mixture of air and nitrogen, with progressive increase then decrease of the nitrogen flow. The challenge was stopped if the S_{pO_2} decreased below 84%. The first F_{IO_2} steps (0.21 and 0.15) lasted 2 minutes, and then the F_{IO_2} was progressively decreased by 0.01 during one minute until 0.07 unless the S_{pO_2} decreased below 84%. The hypoxemic challenge was performed under 3 different conditions, by nasal cannulae in each subject, in random order: air, constant oxygen flow at 1.5 L/min, and automated oxygen titration (FreeO₂ with initial flow set at 0 L/min). End-tidal CO₂ (P_{ETCO_2}), respiratory rate, S_{pO_2} , heart rate, and oxygen flow were continuously recorded with the FreeO₂ device. The system was set in a monitoring mode for air and constant oxygen conditions.

troller. The system was developed in collaboration with the Department of Electronic and Informatics Engineering at Laval University, Québec, and is pending patent.

Induced Hypoxemia Model: Hypoxemic Challenge

We developed a model of induced hypoxemia in healthy subjects, as previously described.²⁴ This model consisted of breathing a mixture of air and nitrogen. Air was initially administered through a mask, at a constant flow of 15 L/min, followed by progressive increase in nitrogen flow, in order to induce mild hypoxia (gradual decrease of the F_{IO_2} from 0.21 to a minimum of 0.07). Inspired F_{IO_2} was continuously monitored by an oxygen analyzer (5800, Hudson RCI, Temecula, California) within the circuit, and several predefined amounts were delivered in a step-wise fashion (F_{IO_2} of 0.21, 0.15, 0.13, 0.12, 0.11, 0.10, 0.09, 0.08, and 0.07). The pace for the F_{IO_2} reduction was constant and predefined. However, if the S_{pO_2} was below or equal to 84%, the lowest levels of inspired oxygen were not delivered and the F_{IO_2} was gradually raised to 0.21, again using the same predefined steps.

The predefined safety rules for the hypoxic challenge were the following. S_{pO_2} was continuously monitored using a pulse oximeter (N600X, Nellcor, Covidien, Boulder, Colorado) in addition to the pulse oximeter (OEM, Nonin, Plymouth, Minnesota) embedded in the tested device. F_{IO_2} decrease was to be stopped if S_{pO_2} measured by the N600X was below 84%. If very severe desaturation occurred ($S_{pO_2} < 80\%$), the study was to be stopped and the subject returned to ambient air plus oxygen breathing, to achieve a rapid return to an $S_{pO_2} > 95\%$.

The study was conducted in a research laboratory of the Institut Universitaire de Cardiologie et de Pneumologie de Québec, and during all measurements at least one intensive care physician was present.

Air or Oxygen Administration

All subjects received the air/nitrogen mixture (hypoxic challenge) and were blinded to the following 3 interventions administered in random order:

- Air at a fixed flow of 1.5 L/min
- Oxygen at a fixed flow of 1.5 L/min
- Oxygen flow automatically titrated by the tested device (with the aim of maintaining a constant S_{pO_2} at 94%)

Measurements

The F_{IO_2} level of the delivered air/nitrogen mixture was monitored continuously. Using the FreeO₂ device's monitoring capabilities, the following data were recorded each second: S_{pO_2} , P_{ETCO_2} , respiratory rate, heart rate, and oxygen flow. The tested device was connected during all 3 experimental conditions, to record the values entering the system, but the option for automated oxygen adjustment was not activated for the fixed flow air and oxygen conditions.

Statistics

The primary end point of the study was the percentage of time within the S_{pO_2} target zone (92–96%). The secondary outcomes were the percentage of time with moderate desaturation ($S_{pO_2} < 92\%$ and $> 88\%$), severe desaturation ($S_{pO_2} < 88\%$), and hyperoxia ($S_{pO_2} > 96\%$). The minimum F_{IO_2} achieved was also recorded.

The number of subjects was set at 10, a sample size felt to be sufficient to verify that the O₂ flow controlling algorithm responded well to its goals. Descriptive statistics, including means, standard deviations, and medians with interquartile ranges were used to describe the subjects and synthesize data. We used the Friedman test and performed

Table. Impact of Oxygen Administration on S_{pO_2} , Heart Rate, and Respiratory Rate During the Hypoxemic Challenge

	Air (1.5 L/min)	Constant Oxygen (1.5 L/min)	Variable Flow (FreeO ₂)	<i>P</i> *
% of time with $S_{pO_2} > 96\%$	4.1 (2.1–7.6)	39.1 (25.1–43.2)	14.5 (8.6–19.0)	< .001
% of time with $S_{pO_2} 92\text{--}96\%$	26.0 (23.1–27.5)	36.8 (31.0–43.4)	66.5 (63.5–74.1)	< .001
% of time with $S_{pO_2} 88\text{--}91\%$	33.3 (22.6–36.9)	14.6 (12.6–16.5)	16.6 (11.2–17.4)	< .001
% of time with $S_{pO_2} < 88\%$	33.7 (30.6–40.7)	12.7 (10.0–14.0)	0.4 (0.00–5.2)	< .001
Minimum S_{pO_2} , %	76.5 (75.3–78.8)	79 (78.3–81.0)	86.5 (84.3–87.8)	.003
Minimum inspired oxygen step delivered, %	11 (10.3–12.0)	8 (8–9)	7 (7–7)	< .001
Heart Rate, beats/min				
Median (25–75th interquartiles)	80 (77–83)	77 (76–80)	75 (74–77)	.02
Minimum–maximum	69–93	71–91	70–80	.08†
Δ	24	20	10	.031
Respiratory Rate (breaths/min)				
Median (25–75th interquartiles)	9.0 (7.8–10.3)	8.1 (6.9–9.7)	8.8 (8.1–10.1)	.79
Minimum–maximum	6–16.1	4.9–17.3	5.4–17.5	
Δ	10.1	12.4	12.1	.11
Median oxygen flow	0	1.5	1.0 (0–2.6)	
Maximum oxygen flow	0	1.5	5.8 (5.6–6.6)	

Data are median (interquartile range), except where otherwise noted.
 * *P* values are for the Friedman test.
 † Comparison for the maximal heart rate.
 NA = not applicable

pairwise comparisons using the Wilcoxon test to compare the percentage of time within the oxygenation target, with moderate desaturation, severe desaturation, and hyperoxia within the 3 conditions. We considered statistically significant *P* values < .05.

Results

Ten healthy subjects were included in the study (7 women, 3 men). Mean age was 25.5 ± 5.5 years, and mean body mass index was 24.7 ± 4.0 kg/m². All the subjects completed the study.

Oxygenation Target, Hypoxemia, and Hyperoxia

The percentage of time within the predefined oxygenation target ($92 \leq S_{pO_2} \leq 96\%$) increased with automated oxygen titration (Table, Fig. 2).

The percentage of time with severe desaturation ($S_{pO_2} < 88\%$) decreased with automated oxygen titration (*P* < .001). The percentage of time with hyperoxia ($S_{pO_2} > 96\%$) also decreased with automated oxygen titration (*P* < .001).

Completed F_{IO_2} Steps During the Hypoxemia Challenge

With automated oxygen titration, all the subjects were able to complete the hypoxemic challenge, reaching the minimal F_{IO_2} that was planned according to the protocol (0.07) (Fig. 3). Only one subject could attain the minimum F_{IO_2} level (0.07) with constant oxygen, and none were able to reach this step with air. The minimum S_{pO_2} levels were

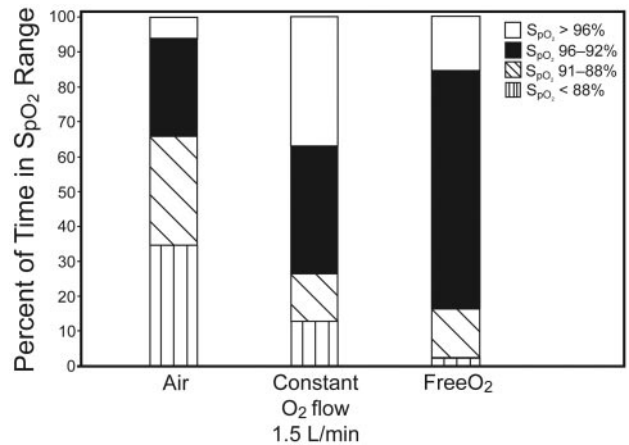


Fig. 2. Percentage of time within the predefined S_{pO_2} ranges during the 3 tested conditions (air, constant oxygen flow, and FreeO₂). The percentage of time in the oxygenation target was higher and the percentage of time with severe desaturation ($S_{pO_2} < 88\%$) was lower with automated oxygen titration. The percentage of time with hyperoxia was higher with constant oxygen flow.

$77.9 \pm 2.4\%$ with air, $80.1 \pm 1.6\%$ with constant oxygen flow, and $86.8 \pm 1.7\%$ with automated oxygen titration (*P* = .003).

Impact on Heart and Respiratory Rate

Automated titration of oxygen reduced the frequency and severity of tachycardia. The impact on respiratory rate was minimal and not statistically significant (Table, and Fig. 4).

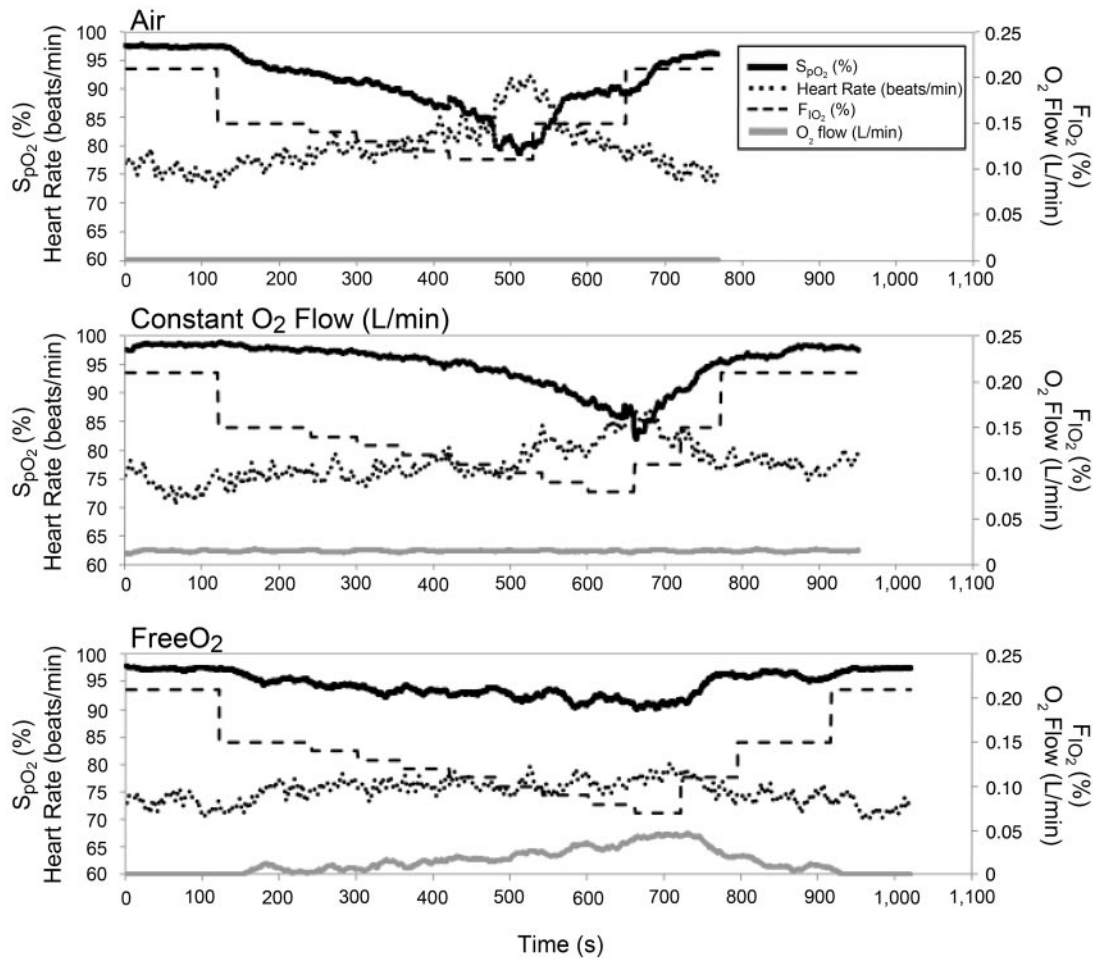


Fig. 3. Mean values of S_{pO₂}, oxygen flow, and heart rate for the 10 subjects at different stepwise decreasing and increasing F_{IO₂} levels. With air and oxygen at constant flows, the desaturation was marked and tachycardia occurred, while with the FreeO₂ system the S_{pO₂} did not decrease and tachycardia did not occur. The mean levels of F_{IO₂} attained were 0.11, 0.084 and 0.07 with air, constant flow, and FreeO₂ respectively.

Oxygen Flows

The beneficial effects on S_{pO₂} with automated titration of oxygen were obtained with a mean reduction in oxygen flow of 1.27 L/min, when comparing equivalent F_{IO₂} steps with constant oxygen flow. This represents an overall 15% reduction in O₂ flows, compared to the constant oxygen flow. Maximum administered oxygen flow was 7.2 L/min with the automated titration.

Discussion

This study is the first evaluation of FreeO₂, a device developed within our institution, which automatically adjusts the oxygen flow in order to maintain a stable S_{pO₂} level (set at 94% in the present study). The study was conducted in healthy subjects with induced hypoxia. We compared this closed-loop system to administration of air and to the administration of oxygen at a constant

flow (1.5 L/min) during hypoxemic challenges. We demonstrated that with automated oxygen titration:

- The predefined oxygenation target ($92\% \leq S_{pO_2} \leq 96\%$) was better maintained.
- Severe desaturation ($S_{pO_2} < 88\%$) was less frequent.
- Periods with hyperoxia ($S_{pO_2} > 96\%$) were decreased.
- Episodes of tachycardia were less, in comparison with air or constant oxygen flow (see Table and Figs. 2–5).
- Also, these results were obtained with 15% less oxygen consumption, in comparison with a constant oxygen flow.

In this specific model, the automatic titration of oxygen flow was shown to be feasible, and several physiological advantages were demonstrated, in comparison with fixed flow oxygen or air. The primary end point was to maintain sub-

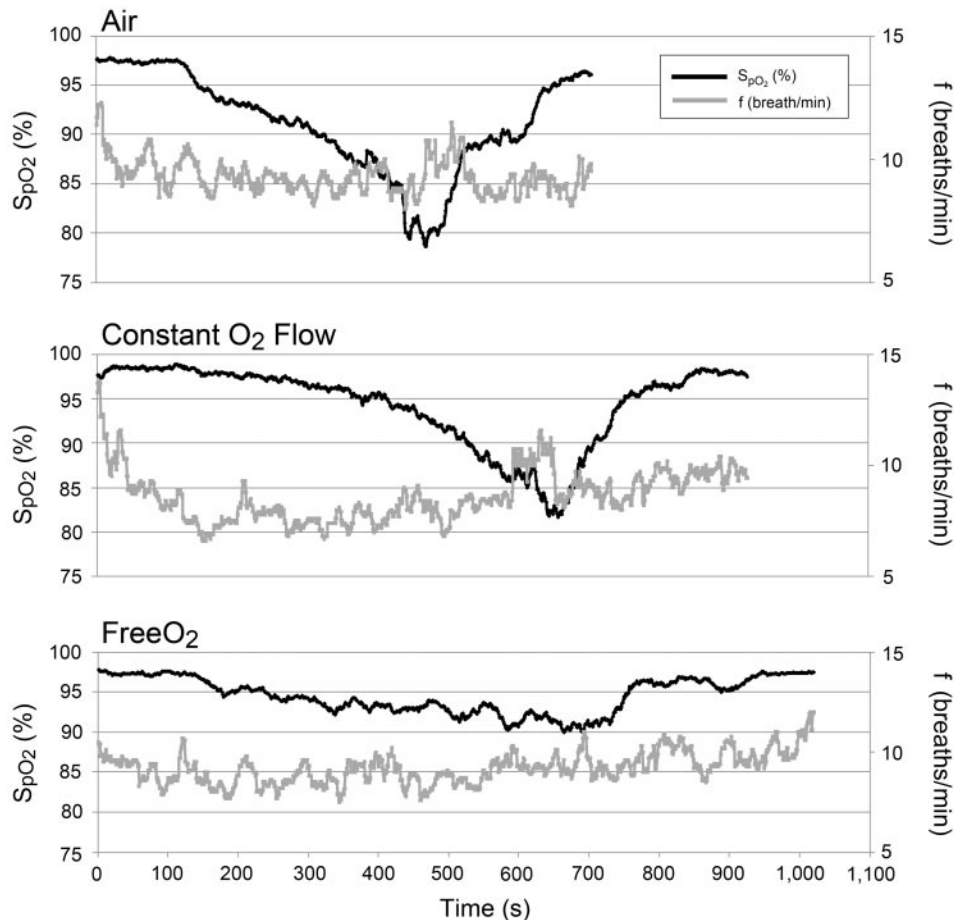


Fig. 4. Mean variations of the respiratory rate (f) during the hypoxemic challenge during the 3 tested conditions.

jects within a predetermined S_{pO_2} range. In daily practice, the oxygen flow is either fixed (most of the time in patients with LTOT) or manually adjusted (in the hospital setting). In patients without CO_2 retention, the minimum recommended arterial oxygen saturation (S_{aO_2}) level is 90% in patients with LTOT.¹² However, given the precision of the S_{pO_2} compared to S_{aO_2} ($\pm 2\%$ when S_{pO_2} is above 90%),²⁵ an S_{pO_2} of 92% or above ensures an S_{aO_2} above or equal to 90% in patients with white skin pigmentation.²⁶ We set the S_{pO_2} upper limit at 96%, considering the potential risks associated with hyperoxia²¹⁻²³ and the futility of maintaining high S_{pO_2} in most situations. The same target (92–96%) was also chosen in 2 studies evaluating closed-loop devices adjusting the F_{IO_2} in intubated patients.^{27,28} Our results are in line with a study by Johannigman et al, conducted in intubated adults. The closed-loop system evaluated demonstrated better control of the oxygenation, with reduced episodes of desaturation and hyperoxia, along with a reduction in oxygen use.²⁸ In a study by Clauere et al, conducted in low birth weight infants, a situation requiring strict control of the S_{pO_2} , the main advantage with the evaluated automated system was the work load reduction, with at least equivalent results on the control of oxygen-

ation.²⁷ This work load reduction is likely to exist with our tested device, but was not specifically evaluated in the present study.

The frequency of severe oxygen desaturation (S_{pO_2} below 88%) was very low (0.4%) with automated adjustment of the oxygen flow, in comparison with constant oxygen flow (12.7%) and with air (33.7%). The median minimal S_{pO_2} values were respectively 86.5%, 79%, and 76.5% (see Table). The reduction of the desaturation frequency and depth may have a physiologic impact in various clinical settings. In patients with COPD, LTOT has benefits with mortality reduction.^{7,8} However, even with oxygen supplementation, desaturations still frequently occur during the night¹⁰ as well as during daily activities.^{9,11} Some data suggest that even short periods of hypoxemia may promote adverse effects. Selinger et al demonstrated that pulmonary artery pressure and pulmonary vascular resistance significantly increased within 2.5 hours after the removal of oxygen supplementation in COPD patients.²⁹ In an animal model, Nattie and Doble have also shown that right ventricular hypertrophy can occur with as little as 2 hours of hypoxemia per day.³⁰

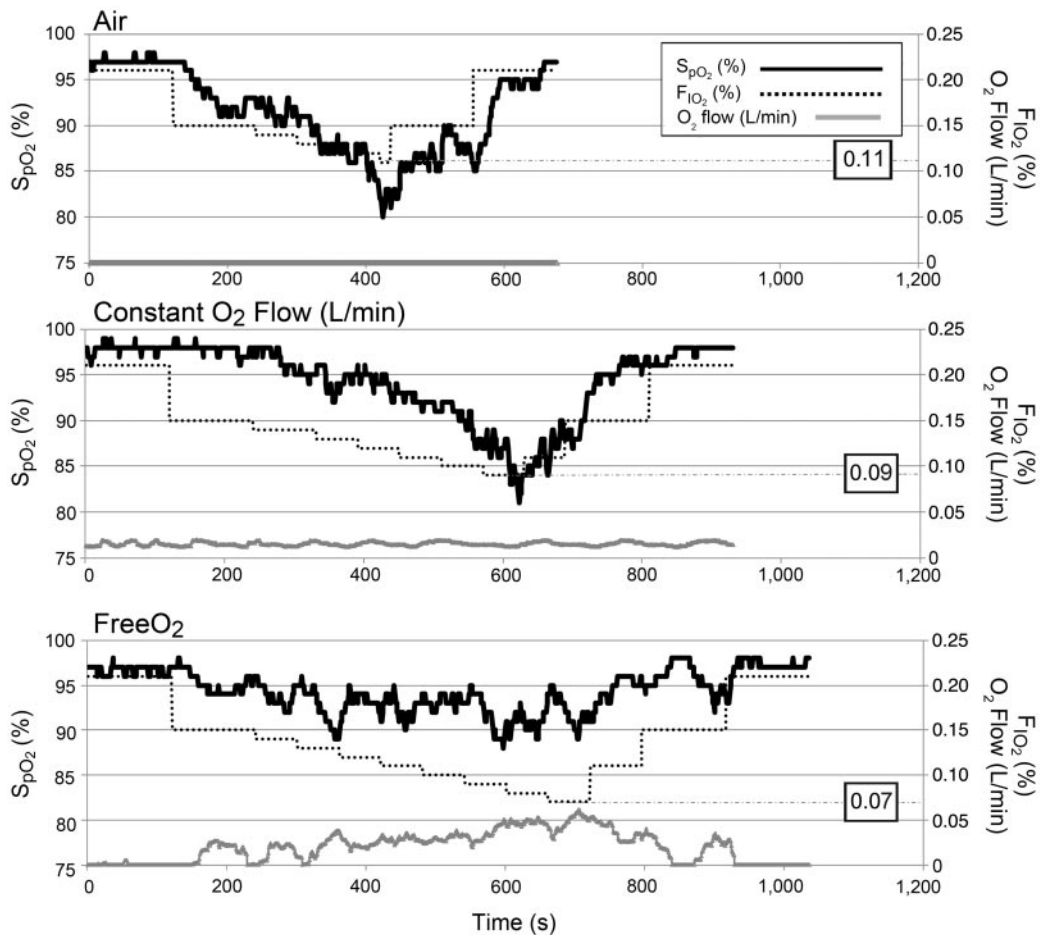


Fig. 5. S_pO₂ levels over time during the hypoxemic challenge within the 3 tested conditions for healthy subject #1. S_pO₂ levels (dark line bold) over time during the hypoxemic challenge with air (upper graph), constant oxygen (middle graph), and variable oxygen levels with FreeO₂ (bottom graph) for healthy subject 1. The F_IO₂ steps are represented by the dotted line, and oxygen flows are represented by the gray line. The F_IO₂ was increased when S_pO₂ reached 84% in healthy subjects. The desaturation occurred earlier with air, in comparison with constant flow (F_IO₂ of 0.11 vs F_IO₂ 0.09). With automated oxygen titration the minimum level of the hypoxemic challenge planned in the study, F_IO₂ = 0.07, was attained without severe desaturation.

In our study, severe desaturations were virtually absent with automated oxygen titration, as compared to 13% of the time with constant oxygen flow and 34% without oxygen (see Table and Fig. 2). In COPD patients, the reduction of severe desaturations may improve LTOT efficacy. Reduction of desaturation may also improve exercise tolerance in COPD patients, as suggested by our preliminary results.³¹

Risks associated with oxygen desaturations are also well known in other populations, such as in premature infants with neurologic deficiencies, as well as aggravation of retinopathy of prematurity induced by hyperoxia.³² The temporal link between hypoxemia and tachycardia/myocardial ischemia has also been well demonstrated in patients with coronary artery disease.²⁰ In patients with brain injury, hypoxemia increases morbidity and is considered a secondary insult that must be avoided.¹⁹

In the acute setting, cardiac complications in patients with coronary artery disease, worsening of the neurologic

condition in patients with trauma, and complications related to hypoxemia in preterm infants may be reduced by a better control of oxygenation.

In addition, excessive oxygen flow leading to hyperoxia may have deleterious effects in different populations. Although oxygen-induced hypercapnia is a well known complication in COPD patients,^{13,15} many of these patients receive high-flow oxygen during exacerbations.³ It has been shown that hyperoxia causes a significant reduction in coronary artery blood flow, with an increase in the coronary artery resistance.²¹ High oxygen flows in patients with myocardial infarction may increase the infarct size and possibly increase mortality.^{33,34} Hyperoxia may also be responsible for cerebral artery vasoconstriction,²² and in low birth weight infants, it is well demonstrated that hyperoxia is a contributing factor for retinopathy of prematurity.³⁵

In the present study the median percentage of time with hyperoxia (S_pO₂ > 96%) was 14.5% with automatic ad-

justment of the oxygen flow, compared to 39.1% under constant oxygen (see Table and Fig. 2).

Tachycardia induced by hypoxemia has been well described in several physiological studies.³⁶ In Pilling's study, episodes of oxygen desaturation in COPD patients were associated with a marked increase of the heart rate during activity, as well as during rest.⁹ In chronic respiratory failure patients, tachycardia induced by hypoxemia is greater than in healthy subjects.³⁷

Oxygen desaturation is also associated with tachycardia and myocardial ischemia in patients with coronary artery diseases.²⁰ In these patients, cardiac adverse events may be induced by increased oxygen consumption related to tachycardia.³⁸ In the present study, oxygen desaturation was associated with severe tachycardia in healthy subjects (see Fig. 3). Tachycardia occurred with constant oxygen and with air, but not with automated oxygen titration (see Table and Fig. 3).

In healthy subjects the initial response to hypoxia is an increase in tidal volume, with less effect on the respiratory rate.³⁷ On the contrary, in COPD patients with reduced ventilatory capacity, hypoxia leads to both increase of the respiratory rate and of the tidal volumes.³⁷ In the present study conducted in healthy subjects, respiratory rate was slightly increased during desaturation, but this effect, though statistically significant, was not clinically relevant (see Fig. 4). With the FreeO₂ device the respiratory rate is mainly used for monitoring purposes, and oxygen flow control does not rely on this parameter.

In our study the beneficial effects were obtained with less oxygen utilization, as compared to constant oxygen flow (see Table). Reduction of oxygen use may be advantageous in patients receiving LTOT. During medical transportation, minimization of oxygen use may also be of great importance,²⁸ due to limited supply. Another advantage of such a system is the possibility to provide to the clinicians a continuous monitoring of the respiratory pattern, including S_{pO₂}, P_{ETCO₂}, respiratory rate, oxygen needs, as well as an evaluation of minute ventilation.

Further clinical evaluation will be required to confirm that the benefits of automated oxygen titration demonstrated in this experimental model of induced hypoxemia also apply to clinical situations. Future studies are ongoing to confirm these preliminary clinical findings. The results may have been influenced by the constant oxygen flow chosen. With oxygen flows higher than 1.5 L/min, the desaturations would have occurred at a lower F_{I_{O₂}}. The percentage of time with desaturation may have been lower, but the percentage of hyperoxia would have been higher, as well as oxygen utilization. The oxygen flow used in this study is similar to usual practices in patients under LTOT.^{8,10}

In 2 recently published studies, automated titration of oxygen in COPD patients was evaluated.^{39,40} The devices were compared with either manual titration by a respira-

tory therapist during 15 min of cycling exercise³⁹ or to fixed oxygen flow in patients with LTOT at home.⁴⁰ These 2 studies showed promising results, with reduction of oxygen flow use⁴⁰ and reduced time with desaturation during exercise.³⁹ Comparative studies assessing the performance of different algorithms will be required. We are convinced that automated oxygen titration, using whatever device, will be helpful for patients receiving oxygen. However, real challenges remain, such as the instability of the controller, security issues in case of signal loss, electrical issues, and the need for an additional sensor in ambulatory patients. These potential device-related limitations require a thorough assessment to determine the real benefits for patients and for the healthcare system.

Conclusions

In conclusion, this is the first evaluation of a novel device (FreeO₂ system) whose purpose is to automatically titrate the oxygen flow in a well controlled and safe manner in an experimental model of oxygen desaturation. Compared with constant oxygen flow and with air, the system was able to better maintain the subjects in the oxygenation target, to avoid severe desaturation, and to reduce the time with hyperoxia. Moreover, there was no reflex tachycardia induced by hypoxemia, due to the reduction in desaturations with the evaluated system. These beneficial effects were obtained with less oxygen, in comparison with constant oxygen flow. Current systems to manually adjust oxygen flow use rotameter principles, a technology developed at the end of the 19th century. The first report of flow meter use by anesthesiologists was published in 1910.⁴¹ Technological improvements have allowed the use of more sophisticated devices to deliver oxygen therapy to patients, with improved efficacy and better monitoring. These automated systems may be relevant in several clinical settings, and further evaluations will be required to determine their potential impact.

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