The Clinical Impact of New Long-Term Oxygen Therapy Technology

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Long-term oxygen therapy (LTOT) improves survival for patients afflicted with severe chronic obstructive pulmonary disease and may also reduce the incidence of repeat hospitalization due to exacerbations. When properly dosed and titrated, LTOT has also been shown to improve exercise tolerance, thereby enhancing the overall health-related quality of life for this growing patient population. Equipment used to provide LTOT is undergoing a radical transformation, with newer delivery devices offering a sharp contrast to older, more traditional home oxygen equipment. This newer approach to providing LTOT— commonly referred to as "non-delivery technology"—affords LTOT users unprecedented freedom, since they are no longer dependent on home-care providers for repeat deliveries to replenish or replace depleted oxygen contents. Instead, non-delivery LTOT equipment is self-sufficient and able to provide all of the oxygen needed to meet both stationary and ambulatory requirements. However, several models of the newer LTOT equipment have certain operational and performance limitations. Accordingly, in order to preclude unintended desaturation with newer LTOT devices, each patient must undergo an individualized pulse-oximetry titration study by a knowledgeable and experienced respiratory therapist to ensure optimum dosing under all conditions of use. *Key words: long-term oxygen therapy, LTOT, chronic obstructive pulmonary disease, COPD, oxygen-conserving technology, portable oxygen concentrator.* [Respir Care 2009;54(8):1100–1111. © 2009 Daedalus Enterprises]

Introduction

Long-term oxygen therapy (LTOT) is the administration of low-flow supplemental oxygen that traditionally is administered at doses of 1–4 L/min. When appropriately prescribed and correctly used, LTOT has been shown to improve survival in patients afflicted with severe chronic hypoxemia secondary to chronic obstructive pulmonary disease (COPD).[1-5] Aside from minimizing the sequelae associated with untreated chronic hypoxemia (eg, pulmonary hypertension, cor pulmonale, congestive heart failure), LTOT has also been shown to confer a modest but definite enhancement in neuropsychological function in patients with longstanding hypoxemic COPD.[6-8] In terms of maximum benefit, studies have confirmed that continuous oxygen ($\geq$ 15 h/d) is superior to intermittent or nocturnal LTOT.[2] More recently, in a re-analysis of data from the landmark 1980 Nocturnal Oxygen Therapy Trial, Petty and Bliss discovered that those subjects using continuous LTOT who also reported high daily walking activity, seemed to derive maximum benefit over others (both nocturnal and continuous users) reporting low daily walking activity.[9]

An economic benefit is likewise derived from LTOT. Effective treatment of chronic hypoxemia reduces exacerbations, which, more often than not, translate into costly and often life-threatening re-hospitalizations.[10] The value of LTOT as a standard of care for severe chronic hypoxemia is evidenced by its inclusion in the current Global Initiative for Chronic Obstructive Lung Disease (GOLD) Guidelines, an evidenced-based international document detailing how COPD should be diagnosed, staged, managed, and, perhaps most importantly, prevented.[11]

The therapeutic objective of LTOT is to relieve chronic hypoxemia. This is typically accomplished by the administration of a prescribed dose of supplemental oxygen administered via nasal cannula, although LTOT can also be administered via a transtracheal oxygen catheter.[12,13] LTOT is usually not administered via oxygen face masks, since these devices require a minimum flow rate of 8 L/min to reduce the likelihood of rebreathing of exhaled CO_2.[14] The clinical goal of LTOT is to elevate the patient's fraction of inspired oxygen (F_{IO_2}) such that the P_{aO_2} is maintained $\geq$ 60 mm Hg or, correspondingly, to maintain an arterial oxygen saturation $\geq$ 90%.[15] When blood oxygen levels fall and remain precipitously below those values for a sustained period of time, serious cardiovascular consequences are observed, most notably pulmonary hypertension with resultant right-heart failure.[16] It has been suggested that the survival benefit observed with sustained use of LTOT is related in part to the amelioration of pulmonary hypertension.[17] It is estimated that there are currently more than 1.3 million Americans receiving LTOT.[18] As the number of patients diagnosed with COPD is expected to double in the next 7–10 years, the demand for LTOT is certain to increase as well.[19-21]

Traditional Long-Term Oxygen Therapy Systems

Stationary Systems

When LTOT is prescribed, it is intended to be used continuously. Most COPD patients spend the majority of their time in and around their home, where LTOT is traditionally provided using one of 2 types of large stationary system: a standard oxygen concentrator, or a liquid-oxygen (LOX) system.[22] To facilitate movement in and about the home environment, patients can be connected to their stationary system with up to 50 feet of supply tubing. Should there be cause to ambulate beyond that distance, either within the home or out into the community, a portable oxygen device will be required if LTOT is to remain uninterrupted.

Oxygen concentrators, electrically powered devices weighing 35–50 pounds, employ air-separation technology and are capable of delivering up to 6 L/min of concentrated oxygen ($\geq$ 85%), although there are now several models of concentrators capable of providing up to 10 L/min. When properly dosed, concentrated oxygen has proven to be more than sufficient to achieve the desired clinical goal of elevating and maintaining the $P_{aO_2} \geq$ 60 mm Hg. Oxygen concentrators are easy to operate and require minimal maintenance by the patient, although they do require an uninterrupted source of household electrical current. In that regard, sustained disruptions of electrical power, as experienced during severe weather or other natural disasters, are problematic.

By contrast, the main component of a LOX stationary system is a large base unit (referred to as a "dewar"), which is a specially designed "thermos-type" container that stores oxygen in its liquid state at −273°F. Through controlled evaporation, LOX is converted to United States Pharmacopoeia grade gaseous oxygen, which is in turn delivered to the patient at the prescribed liter flow.[22] However, as oxygen contents are depleted, the dewar requires periodic refilling by the home-care provider. Since the procurement, storage, and transportation of LOX requires special equipment and compliance with additional regulatory requirements, these systems are not considered to be as cost-effective or as convenient as an oxygen concentrator. However, LOX systems do offer one important advantage, most notably for those LTOT patients who spend a large amount of time beyond the confines of their stationary system, as will be described shortly. Figure 1 illustrates a standard oxygen concentrator and a LOX stationary system.

Portable Systems

When patients must leave their home for a few hours (eg, to visit their physician or to shop for groceries), LTOT should not be interrupted. Accordingly, as part of their LTOT prescription, patients are also provided a small, portable oxygen-delivery system to complement their stationary system.[22] As with stationary systems, there are also 2 traditional ways to provide portable LTOT.

Fig. 1. Left: Standard oxygen concentrator. (Courtesy of Invacare, Elyria, Ohio.) Right: Two liquid-oxygen (LOX) dewars. (Courtesy of Caire Medical, Ball Ground, Georgia.)

The most common approach is the use of small, lightweight aluminum gaseous-oxygen cylinders (size M-6) that are usually carried or, if need be, can easily be pulled on a cart. However, with smaller cylinders, especially if they are light enough to be carried, there is the tradeoff of limited oxygen capacity. For instance, a patient with an LTOT prescription of 2 L/min will deplete an M-6 cylinder having a total capacity of 164 L of gaseous oxygen in little more than one hour. One way to extend the amount of time away from the stationary system would be to use a larger vessel, such as an aluminum E cylinder having a capacity of 622 L of gaseous oxygen. At 2 L/min, a full E cylinder would last approximately 5 hours. However, an E cylinder with cart and regulator weighs in excess of 20 pounds, making this portable system unwieldy and extremely difficult to maneuver. This contrasts sharply to the aforementioned M-6 cylinder, which, including regulator, weighs less than 5 pounds and is easily carried.

The second option for providing traditional ambulatory oxygen is to couple the aforementioned stationary LOX dewar with a smaller, portable LOX container that the patient can refill from the stationary dewar prior to ambulation. In the past this has been the main advantage of LOX systems, especially for those patients who spend a great deal of the day away from home (ie, several hours a day on 2–3 or more days per week). Since the home-care provider needs to refill the stationary LOX base unit approximately every 10–14 days, this traditional portable option is considered to be more cost-effective for high ambulatory patients. However, many LTOT patients, especially the very frail elderly, have difficulty refilling the portable LOX canister. Figure 2 illustrates a small lightweight gaseous-oxygen cylinder with carrying case and a refillable portable LOX device.

Oxygen-Conserving Technology

A major drawback of both of the traditional continuous-flow LTOT portable systems is the limited amount of time the patients could be away from their stationary system. The introduction of oxygen-conserving technology in the mid-1980s for both gaseous oxygen and LOX portable systems offered a creative solution.[23] Rather than delivering oxygen continuously, an oxygen-conserving device (OCD), which is an integral part of the oxygen regulator, dispenses oxygen only intermittently. Instead of continuous flow, an OCD intermittently delivers a pre-set volume or bolus of oxygen, which is measured in mL per breath. The bolus is delivered in response to the patient's inspiratory effort (or demand), as detected through the nasal cannula. The bolus is delivered during the first 60% of the patient's inspiratory portion of the breathing cycle.[24-25] Hence, oxygen is not flowing—and thus is not being wasted—during the remainder of each breathing cycle. Because the delivered dose of oxygen via intermittent bolus is different from the physician's continuous-flow prescription, a separate prescription is required whenever an OCD is substituted.

OCDs allow patients to spend considerably more time away from the stationary system than continuous flow. However, the actual length of time a particular cylinder or LOX canister will last with an OCD is a function of: cylinder/canister size and capacity, the model of OCD being used, and the patient's respiratory rate.[26]

Titrating Patients to Oxygen-Conserving Devices

An important consideration when using any oxygen-conserving technology is to ensure that the delivered bolus of oxygen is sufficient to maintain the same degree of oxygen saturation that was attained with the physician's original continuous-flow prescription. A common misperception is that a numerical setting on a particular OCD (eg, 1, 2, 3) is equivalent to the numerical settings on an oxygen flow meter. They are not at all equivalent.[27,28] The numerical settings on an oxygen flow meter denote L/min of continuous flow, whereas

Fig. 2. Left: Standard portable gaseous-oxygen cylinder with oxygen-conserving device. (Courtesy of Western Medical, Westlilake, Ohio.) Right: Refillable portable liquid oxygen canister. (Courtesy of Caire Medical, Ball Ground, Georgia.)

the numerical settings on an OCD indicate the relative sizes of the delivered boluses. Adding further confusion, a numerical setting of 2 on one particular model of OCD will deliver a bolus of oxygen that may be larger or smaller than a setting of 2 on a model from a different manufacturer. Further, the bolus waveform will be different for each model. Unfortunately, product performance standardization is lacking and confusion reigns.[26]

This gives rise to a major clinical concern that patients may inadvertently be at risk for desaturation if an unsuspecting clinician simply sets the numerical setting on an OCD to that of the continuous-flow prescription. For example, a patient with an LTOT prescription of 2 L/min may, in fact, maintain adequate oxygenation when using a particular model OCD set at 2 while resting in the sitting position, which could only be ascertained via pulse oximetry. In this example, the OCD would be described as providing "functional" or "clinical" equivalency to the continuous-flow prescription, but only under the condition of rest while in the sitting position. Should this patient move to a different activity level, such as casual walking or even structured exercise, then functional equivalency might be achieved only when the OCD is set at 3, perhaps 4, or possibly never, again as could only be determined via pulse oximetry. Further, should a different model of OCD be placed on this same patient under similar conditions, the numerical setting(s) used for the former OCD, in all likelihood, would not necessarily provide the same degree of oxygenation when selected on the replacement model.

The importance of the need to use pulse oximetry to individually titrate each individual when initially placed on an OCD is underscored by recommendation 5 from the Sixth Long-Term Oxygen Therapy Consensus Conference, held in August 2005, which states, "All patients who are provided an intermittent-flow device (which is one category of oxygen-conserving device) must be clinically evaluated and titrated to the intermittent flow required by the specific device being employed, in order to ensure optimal oxygen delivery for that individual patient during rest and during routine activities of daily living."[29] This recommendation was later reaffirmed and included in the August 2007 revised clinical practice guideline for Oxygen Therapy in the Home or Alternate Site Health Care Facility, developed and published by the American Association for Respiratory Care.[30]

Limitations of Traditional Portable Systems

While traditional portable LTOT systems employing OCD technology have been used effectively for the past 3 decades, one important issue remains: the amount of time a patient may be away from their stationary system is limited. The length of time of an excursion will be determined by the amount of oxygen contents (gaseous or liquid) contained in the portable device, and the frequency of excursions will be limited by the available supply of oxygen contents in the

home. Since one of the biggest fears LTOT patients have is "running out of oxygen," ambulation is somewhat limited with traditional LTOT systems. Patients are always mindful of the need to return home to their stationary system before their portable supply is depleted. There are also issues associated with the continuing need to contact the home-care provider to schedule home deliveries to obtain the needed refills, and the anxiety of not knowing if the delivery will occur in time for their next ambulatory excursion, planned or otherwise. The net effect is that spontaneous ambulation beyond the confines of the stationary system is not always possible, and concerns over the availability of sufficient portable oxygen often becomes a disincentive to ambulation in general.

Home oxygen providers are likewise dealing with their own uncertainties regarding the need for frequent home deliveries to replenish depleted oxygen contents. Their concerns are driven in part by economic imperatives as well as by newer clinical insights. In terms of economics, recent Medicare policies and cuts in reimbursement levels for LTOT equipment are cause for concern.[31] Since one of the major uncompensated costs that home oxygen providers encounter is repeat home deliveries to replace depleted contents, there is growing concern that the frequency of such deliveries will need to be further curtailed.

At the same time, there is growing evidence that patients with COPD who perform a relatively high level of physical activity in their daily life on a sustained basis have a substantially reduced risk of readmission due to an exacerbation.[32] It appears that regularly scheduled extended excursions out of the home into and around the community are not only clinically advantageous, but add significantly to the overall quality of life for this patient population.[33] Further, the scientific evidence of the clinical, psychological, and economic advantages of having COPD patients participate in a formal pulmonary rehabilitation program continues to grow.[34-36] For many COPD patients, successful participation in a pulmonary rehabilitation program entails the need for ample portable oxygen, especially when structured walking exercise is attempted.[37] Any disruption to the unencumbered access to unlimited portable oxygen quickly becomes a deterrent to subsequent participation. Fortunately, we are now witnessing a veritable explosion of new technology for providing both stationary and ambulatory LTOT that contrasts sharply with the older, more traditional equipment developed and used during the late 20th century.

New Long-Term Oxygen Therapy Technology

Non-Delivery Long-Term Oxygen Therapy Systems

This newer, 21st-century LTOT technology has been described variously as "non-delivery" or "delivery-less," due to

Fig. 3. Left: Concentrator that transfills a gaseous cylinder. (Courtesy of Invacare, Elyria, Ohio.) Right: Liquefier that transfills liquid oxygen canister. (Inspired Technology, North Huntington, Pennsylvania).

the fact that the home-care provider no longer has to make periodic home deliveries to replenish depleted gaseous or LOX contents.[27] A non-delivery LTOT device is self-sustaining—capable of producing ample oxygen to effectively provide for both stationary and ambulatory needs. This new approach makes the LTOT user relatively self-sufficient in terms of in-home use, ambulation (both within and outside of the home), mobility, and overall lifestyle. Home oxygen providers are also finding that non-delivery LTOT technology can be a very cost-effective alternative to the expense of maintaining traditional stationary and portable systems with repeat home deliveries.

Concentrators That Transfill.   Non-delivery systems are either novel variations or scaled versions of traditional oxygen concentrators. One approach is the use of a standard oxygen concentrator, which, when coupled with an external pressure booster, can transfill a small, lightweight portable cylinder with pressurized concentrated oxygen. One particular system goes even further and transfills a small LOX-like canister with liquefied concentrated oxygen. Regardless of which of these novel transfilling approaches is used, patients are able to reuse the cylinder/canister, which has an integral OCD, for their ambulatory needs. When they return home, it's a simple matter of attaching the empty cylinder/canister for refilling, and in several hours they are ready for their next excursion. However, this approach to non-delivery technology does have its limitations. Since patients must return home each day, they are essentially tied to their home stationary unit. Further, these units are entirely too heavy to be transported outside of the home. Figure 3 illustrates non-delivery systems that are able to provide in-home transfilling of gaseous-oxygen cylinders or LOX-type canisters.

Portable Oxygen Concentrators

Portable oxygen concentrators (POCs) represent another non-delivery approach to providing LTOT. POCs are scaled versions of standard concentrators, and there are 2 types: POCs that can deliver oxygen only in the pulse-dose mode, and those capable of delivering oxygen in either the continuous-flow or pulse-dose mode. All POCs are lightweight, user friendly, esthetically pleasing, and easily transportable. POCs can be powered by standard household alternating current, direct current (available in motor vehicles), or by a rechargeable battery. Thus, POCs afford LTOT patients a heretofore unavailable luxury: the freedom to go wherever they want, whenever they want, and however they prefer to travel, including aboard commercial aircraft.[38,39]

Pulse-dose-only POCs are the lightest in weight (5–10 pounds), but the trade-off is a limitation on how much therapeutic oxygen (ie, $\geq 85\%$) they are able to produce in one minute's time. The maximum oxygen production capabilities of existing pulse-dose POCs range from 480 mL/min to 1,040 mL/min, thus limiting their operation to pulse-dose delivery only, similar to what was described previously with OCDs. However, while the OCDs were intended to be used only during ambulation, pulse-dose-only POCs are increasingly being promoted as effective for providing both stationary and ambulatory LTOT. This raises important questions about the effectiveness and safety of providing all LTOT via intermittent bolus delivery on a 24-hours-a-day, 7-days-a-week basis especially since the 2 landmark studies that demonstrated the survival benefit of LTOT used continuous flow delivery.[2,3] Clearly, further research is needed to demonstrate that the same outcomes can be attained using pulse-dose-only delivery devices. Figure 4 illustrates several POCs that can only operate in the pulse-dose delivery mode.

A POC with higher oxygen production capabilities can operate in either the continuous-flow mode (0.5–3 L/min) or in the pulse-dose mode during ambulation, to conserve battery life. The more robust oxygen production capabilities of this non-delivery device (3,000 mL/min) offers clinicians more options over pulse-dose-only POCs when providing LTOT on a 24-hours-a-day, 7-days-a-week basis. A POC with higher oxygen production capabilities is slightly heavier than pulse-dose-only POCs (17 pounds vs 5–10 pounds), and unlike certain pulse-dose POCs, cannot be carried with a shoulder strap. However, it can be easily lifted into and out of an automobile with an integral handle and is easily pulled on a wheeled cart. Of interest is a recent study that compared patients' exercise capacity when they carried their portable oxygen system or used a wheeled cart.[40] Patients performed significantly better on a 6-min walk test and had a better Borg score when they pulled their portable oxygen system than when they carried

Fig. 4. Four models of pulse-dose-only portable oxygen concentrator. (Courtesy of (A) Respironics, Murrysville, Pennsylvania; (B) Invacare, Elyria, Ohio; (C) Inogen, Goleta, California; and (D) AirSep, Buffalo, New York.)

the same system, suggesting that carrying a portable oxygen system might not be appropriate for all patients, regardless of the weight of the device. At this writing, there is only one POC capable of operating in either the continuous-flow or pulse-dose mode (Fig. 5). No doubt as non-delivery technology continues to evolve, we will see further additions to this type of LTOT device.

Table 1 lists common operational and performance parameters of commonly available POCs.

The Long-Term Oxygen Therapy Continuum

As with traditional oxygen equipment, it is important that a non-delivery LTOT system, whatever the design, provide ample protection from desaturation, regardless of a patient's type or intensity of activities of daily living. One way to frame this important requirement is to think of LTOT as a treatment intervention that must be effective across a continuum of activities that each patient experiences throughout every day (personal communication, Ron F Richard, SeQual Technologies, San Diego, California, April 2008). Individual oxygen requirements vary for each patient as they move back and forth across the LTOT continuum, as depicted in Figure 6.

At one end of the continuum we have sedentary use, where the majority of daily LTOT use occurs. At this point in the continuum, patients are typically at home, generally resting and occasionally performing various, non-stressful domiciliary activities of daily living such as personal hygiene, meal preparation, and possibly even light housekeeping. Systemic oxygen demand is at its lowest at this point on the continuum, and, accordingly, the amount of supplemental oxygen required to ensure adequate saturation is likewise at its lowest.

Fig. 5. This portable oxygen concentrator can operate in either continuous-flow (0.5–3 L/min) or pulse-dose mode (settings 1–6). (Courtesy of SeQual Technologies, San Diego, California.)

However, when temporarily transitioning to the activity portion of the continuum, there are a range of activities, from casual walking to participation in structured pulmonary rehabilitation, that contribute to an increase in systemic oxygen demand. The increased oxygen demand is in direct response to the intensity and frequency of activity and often results in a concomitant increase in the patient's respiratory rate. Thus, any ambulatory LTOT device used during activity must be capable of providing sufficient therapeutic oxygen to meet the higher systemic demands, as well as responding to increased respiratory rates if arterial desaturation is to be avoided. When desaturation does occur with a certain activity type or intensity, patients typically cease performing that activity due to the distress of the accompanying dyspnea.

Oxygenation requirements during sleep may also be different from what is required during rest or activity. Although the neuro-chemical control of breathing during sleep

Table 1. Performance Characteristics of Several Models of Portable Oxygen Concentrator

Model	Company	Weight (lb)	Maximum Oxygen Production (mL/min)	Flow Settings	Pulse Settings	Maximum Bolus Size (mL)	Maximum F_{IO_2} at 20 breaths/min
FreeStyle	AirSep, Buffalo, New York	6	480	NA	1–3	26	0.27 at setting 3
Inogen One	Inogen, Goleta, California	10	750	NA	1–5	26	0.29 at setting 5
XPO_2	Invacare, Elyria, Ohio	7	900	NA	1–5	42	0.24 at setting 5
EverGo	Respironics, Murraysville, Pennsylvania	10	1,050	NA	1–6	36	0.32 at setting 6
Eclipse 2	SeQual Technologies, San Diego, California	17	3,000	0.5–3.0 L/min	1–6	96	0.42 at setting 6

F_{IO_2} = fraction of inspired oxygen
NA = not available
(Adapted from References 26 and 28.)

is the same for COPD patients as it is for normal subjects, there is diminished responsiveness and blunted sensitivity with COPD.[41,42] This leads to a higher incidence of nocturnal desaturation, especially in those patients with more advanced disease, who are prone to periods of transient hypoventilation with resultant alveolar gas-exchange dysfunction.[43] Such episodes of desaturation, not unexpectedly, are most profound during periods of rapid-eye-movement (REM) sleep.[44-46] To help mitigate nocturnal desaturation in COPD patients receiving LTOT, in 1995 the American Thoracic Society promulgated guidelines suggesting that the oxygen dose should be increased by 1 L/min over the regular prescription during periods of extended exercise and sleep.[47] A similar recommendation appeared 15 years earlier in the Nocturnal Oxygen Therapy Trial.[2] However, more recent studies cast doubt on this recommendation when they were unable to show nocturnal desaturation was an absolute in every COPD patient using LTOT.[48,49] Nonetheless, it is still good clinical practice to confirm that the prescribed dose for daytime LTOT is sufficient to prevent exercise and/or sleep induced desaturation.

It should be noted that there is a subset of patients who, in addition to COPD, also have obstructive sleep apnea syndrome as a comorbid condition. The presence of both conditions is now commonly referred to as *overlap syndrome*.[50,51] Not surprisingly, the degree of nocturnal desaturation is even more profound in patients with overlap syndrome, and in this patient population effective treatment must also include, in addition to LTOT, a nightly regimen of positive-airway-pressure therapy.[52]

The last point on the LTOT continuum is altitude, essentially those instances where a decrease in atmospheric pressure results in a lower partial pressure of inspired oxygen. The most common example of this would be patients who permanently reside at a higher elevation (eg, Denver at 5,280 ft), as well as those who occasionally travel to altitude in a personal or commercial motor vehicle for business or pleasure. It would also include those COPD patients who take advantage of the new United States Department of Transportation policy requiring United States air carriers to permit approved POCs to be brought aboard a commercial aircraft for in-flight use.[38,39] In each of the above situations, depending on the degree of chronic hypoxemia, there may be a need for a higher dose of delivered oxygen than would otherwise be the case at sea level, but this would need to be determined on a case-by-case basis.

In summary, the systemic oxygen needs of patients vary as they transition back and forth across the LTOT continuum. It is therefore important that any non-delivery device used to provide both stationary and ambulatory LTOT be capable of providing sufficient concentrated oxygen in the dose required to protect the patient from desaturation.

Oxygen as a Controller Medication

Whether it is United States Pharmacopoeia grade, as is most often found in institutional settings, or concentrated,

Sedentary ⟷ **Activities** ⟷ **Sleep** ⟷ **Altitude**

Stationary use	Moderate ambulation	Nocturnal	Residing at altitude
Domiciliary ADLs	Scheduled walking	desaturation	Traveling to altitude
	Structured exercise	OSA	Air travel

Fig. 6. The long-term oxygen therapy continuum. The primary clinical objective is to ensure adequate oxygenation/saturation ($S_{pO_2} \geq 90\%$) across the entire LTOT continuum *at all times*.

as is largely used in home care, oxygen is a drug. Accordingly, the United States Food and Drug Administration, regardless of care setting, requires that oxygen be dispensed only upon the written order of a licensed physician. Additionally, state pharmacy boards likewise require that the storage, dispensing, and maintenance of oxygen equipment be controlled and do so by imposing strict personnel requirements and facility standards for home-care providers. Clearly, it is the position of both the Food and Drug Administration and state pharmacy boards that the unauthorized or inappropriate use of oxygen and oxygen-delivery equipment has the potential to result in real harm or injury to the public.

LTOT is a controller medication, and in this respect is no different than any other inhaled medication prescribed to manage chronic respiratory symptoms of bronchoconstriction or airway inflammation. Physicians prescribe LTOT to control the symptom of chronic hypoxemia.

The dosing of oxygen in the hospital setting for COPD patients recovering from an exacerbation is well controlled and closely monitored. Specific therapeutic goals are defined, with the goal of in-patient oxygen therapy to prevent tissue hypoxia and to preserve cellular oxygenation.[15] Typically, the flow rate is adjusted to maintain a $P_{aO_2} \geq 60$ mm Hg or an arterial oxygen saturation $\geq 90\%$. The device setting is easily monitored by noting the setting on the flow meter connected to the oxygen source. The delivered dose of supplemental oxygen in turn elevates the F_{IO_2}, which ultimately determines the oxygen partial pressure in the alveolar gas-exchange areas. Since it is difficult to measure with precision the actual inhaled F_{IO_2}, especially when using a low-flow oxygen-delivery system such as a nasal cannula, the degree of arterial oxygen saturation is most often used as a surrogate indicator.[53,54] Accordingly, the liter flow is titrated up or down depending on the patient's response to therapy, as determined via pulse oximetry.

As the patient's condition improves and preparations are made for discharge, the decision to continue oxygen therapy is made based upon the severity of the disease state, and, most importantly, the degree of chronic hypoxemia. Assuming the patient meets the requisite clinical and laboratory criteria, arrangements are made for LTOT. The prescribed dose for LTOT is usually a reflection of the liter flow the patient received up to the time of discharge.

Optimum Long-Term Oxygen Therapy Dosing

Regrettably, there is still no definitive data on what constitutes the optimum dose for LTOT. For years, continuous flow has long been held to be the accepted standard, and, as such, 2 L/min was ordered (and is continuing to be ordered) for the majority of patients starting

LTOT.[24,26] In terms of physiologic response, the focus has been on maintaining the P_{aO_2} at or slightly above 60 mm Hg or the arterial oxygen saturation at or slightly above 90%.[15] Whether or not these physiologic values are optimally therapeutic has never been firmly established, leading one preeminent pulmonary researcher to recently lament that, "we are remarkably casual in clinical practice about how we assign supplemental oxygen dose."[54] However, the availability of newer analytical technology, specifically the latest generation of highly accurate and reliable portable pulse oximeters, provides a useful tool to determine optimum dosing.

The actual targets for optimum arterial oxygen saturation levels for stable chronic hypoxemia remain to be empirically determined for each position on the LTOT continuum. However, a recent study evaluating the ability of 4 ambulatory oxygen systems to protect against exercise-induced desaturation gives rise to an interesting "what if" scenario.[55] Subjects in that study ($n = 39$) were randomly oxygenated for 5 min on each of the 4 devices being evaluated before undergoing a 6-min walk test to assess functional exercise capacity. While the reported mean pre-walk saturation measured via pulse oximetry (S_{pO_2}) was 95%, the actual saturation values ranged from 88% to 100%, indicating that while some of the subjects were saturated to the high 90% range, others were saturated only to levels at the lower end of the range (88–90%). While those authors did not specifically target a set pre-walk saturation level, there did not appear to be any adverse effects for those subjects who did achieve a pre-walk saturation level well into the high 90% range. Of interest is that 44% of the subjects were unable to complete the entire 6-min walk test. The reported mean walking time was 4.6 min, the mean post-walk S_{pO_2} was 88% (range 70–99%), and the mean pre-walk versus post-walk difference in oxygen saturation range was $6 \pm 4\%$ to $7 \pm 5\%$.[55] In essence, the data suggest that all four of the tested devices failed equally in their ability to protect the subjects from exercise-induced desaturation. One wonders what the results of the study (distance walked relative to the level of desaturation) would have been had each of the subjects been specifically titrated to a pre-walk saturation of 95–96% on each of the 4 modalities tested and the stabilization period was for a minimum of 15 min, versus the 5 min period used in the study? The validity of this conjecture remains to be empirically determined.

Effect of Increased Respiratory Rate on Fraction of Inspired Oxygen

As mentioned, continuous-flow delivery has historically been the accepted standard for low-flow supplemental oxygen therapy.[24,26] When using LTOT equipment that provides continuous flow, the home-care provider (most often

a respiratory therapist [RT]) sets the flow meter at the prescribed setting. In this scenario the set liter flow is readily identifiable. However, a bench study that looked at 2 L/min oxygen flow and the effect of increased respiratory rate on oxygen concentration found that the measured F_{IO_2} dropped when the respiratory rate increased.[56] The prevailing explanation for this finding is that as the respiratory rate increases, the inspiratory time is shortened, reducing the amount of oxygen inhaled per breath.[26] Another possible contributing factor is that a decrease in inspiratory time might also result in a higher flow of inhaled ambient air, causing further dilution of the F_{IO_2}.

As observed with continuous oxygen flow, when a patient is using a pulse-dose-only POC and their respiratory rate increases, there is the possibility that the delivered F_{IO_2} will decrease. A more recent bench study compared the relative F_{IO_2} observed with oxygen flow at 2 L/min to that obtained with 4 pulse-dose-only POCs (also set at 2) at varying respiratory rates.[57] Figure 7 demonstrates the drop in the F_{IO_2} observed with continuous flow (as reported in the aforementioned bench study), but also reveals a similar drop in the measured F_{IO_2} in 3 of the 4 pulse-dose-only POCs tested under conditions of increases in the simulated respiratory rate. This finding suggests that certain pulse-dose-only POCs, due to their limited capacity for therapeutic oxygen production, may not always be able to maintain the purity of concentrated oxygen ($\geq 85\%$) in the face of significant increases in the patient's respiratory rate.

Another concern over the limited oxygen production capabilities of certain POCs is when these devices are used aboard a commercial airliner where internal cabin pressure is equivalent to 8,000–10,000 feet. Since the number of LTOT patients using this mode of transportation is expected to increase substantially, it is important that any POC used during air travel is able to protect the integrity of the F_{IO_2} to maintain adequate oxygenation. Having the oxygen requirements of a patient exceed the therapeutic oxygen production capacity of a particular model of POC (eg, as may happen with a low dose pulse-only POC[28]) could result in suboptimal oxygen dosing.

Since current lung simulators cannot accurately model the complex interaction of physiology and respiratory mechanics that ultimately determines actual oxygen delivery, the results of in-vitro studies do not universally translate to what would be observed in vivo. However, bench studies are useful to alert clinicians to issues that should not be ignored, and in this particular case that would be the effect that increases in the respiratory rate might have on the inhaled F_{IO_2}.

Regrettably, the lack of standardization that we saw previously during the discussion of OCDs has carried over to POCs. For example, a selected numerical setting on the control panel of a POC, while an indicator of the bolus size
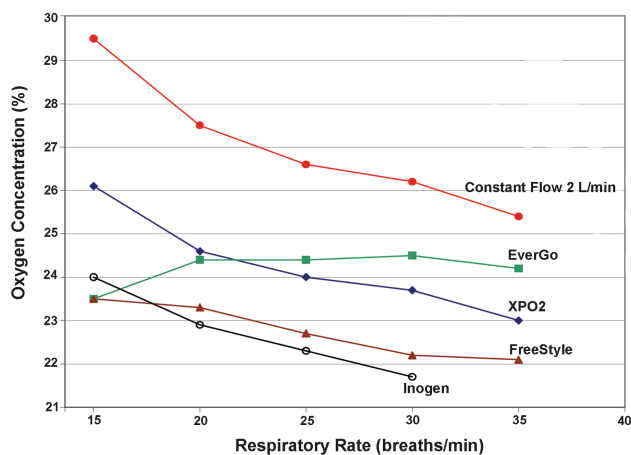

Fig. 7. Effect of breathing frequency on fraction of inspired oxygen with continuous flow at 2 L/min, with 4 pulse-dose-only portable oxygen concentrators at the numerical setting of 2. (Adapted from Reference 57.)

does not specifically denote the actual bolus size in mL. Instead, the home-care therapist must consult product literature to try to figure out the actual bolus size per numerical setting. Since it is the *volume* of the pulse dose, not the pulse dose *setting*, that ultimately determines the therapeutic dose (ie, the F_{IO_2}), in a perfect world each numerical setting on the control panel of all POCs would depict the delivered bolus size of oxygen in mL.

The difficulty in quickly discerning the delivered dose at each numerical setting on a POC underscores the importance of having a titration study done by a knowledgeable and experienced clinician whenever an LTOT patient is first connected to a pulse-dose-only POC, or when a continuous-flow POC is first being used in the pulse-dose delivery mode. Subsequent reassessments should also be considered to ensure that the selected pulse-dose settings remain effective, especially once the patient has been using the newer device for several days following discharge from an acute hospital stay. The frequency of such reassessments is best determined by the home-care therapist and should be guided by the patient's rate of recovery from the exacerbation and their subsequent response to the selected settings as they transition back and forth across the LTOT continuum.[58]

Role of the Respiratory Therapist With New Long-Term Oxygen Therapy Technology

One of the unfortunate legacies of home-care services in the United States is that formal recognition of and reimbursement for RTs is lacking. This is due in large measure to the fact that when the Medicare program was launched in the mid-1960s, the profession itself was barely 20 years old and only just beginning to establish itself as an important allied health profession. Over the past several de-

cades, several attempts to redress this oversight have been, regrettably, unsuccessful. Nonetheless, as part of its long-standing commitment to ensure timely access to quality respiratory care services by those afflicted with chronic respiratory conditions, the American Association for Respiratory Care continues its efforts to gain reasonable recognition and fair reimbursement for the contribution that RTs render in all post-acute-care settings. Until such time that these efforts are successful, the formidable costs associated with having RTs employed by home-care companies will continue to be recouped under payments received under the durable-medical-equipment benefit under Medicare Part B.

The major challenge is that the Medicare durable-medical-equipment benefit reimburses home-care providers only for the purchase or rental of prescribed medical equipment. In fact, Medicare manuals detailing eligibility and coverage criteria for the Part B durable-medical-equipment benefit specifically state that services provided by an RT are not reimbursable. However, over the last 30 years, reimbursement rates for LTOT equipment were sufficient enough to allow most home-care providers to more than cover the costs associated with having RTs on staff. The services and care that home-care RTs provided, while uncompensated directly, resulted in better utilization of all prescribed respiratory equipment, including the safe and effective introduction of newer technology, most notably in LTOT and devices used for the diagnosis and treatment of sleep disorders.

Unfortunately, recent reductions in Medicare monthly reimbursement rates for LTOT equipment, coupled with a newly implemented 36-month payment cap, has reawakened longstanding concerns about the continued viability of RTs in home care.[31] In some respects, while undertaken to control escalating health-care expenditures and to take advantage of plummeting acquisition costs for standard oxygen concentrators, various Medicare initiatives over the years have, albeit unintentionally, reduced a prescribed therapeutic intervention to commodity status. There is decidedly more emphasis on LTOT equipment at the expense of focusing instead on more important clinical and patient outcomes.

This gives rise to a serious concern with respect to the growing demand for new, non-delivery LTOT technology, which by all accounts will eventually become the way of the future. Non-delivery LTOT technology, while clearly offering great economic and clinical advantages to home-care providers, patients, and prescribers alike, is not completely free of unintended adverse consequences. If not properly interfaced with each patient by a knowledgeable and experienced clinician using pulse oximetry to confirm oxygen saturation levels are therapeutic, the potential for serious under-treatment is real. Indeed, the benefits reported from the use of LTOT are observed only with the successful and sustained correction of hypoxemia.[59] Furthermore, the under-prescribing, under-utilization, and inadequate titration of LTOT has been identified as a significant risk factor for COPD exacerbations and exercise-induced hypoxia.[60,61] Accordingly, RTs, in spite of the economic hurdles faced by home-care providers, are essential for the safe and proper transition to non-delivery LTOT technology, and, for that matter, for the continued effective use of traditional LTOT equipment. One can only hope that home-care providers continue to appreciate the value of having RTs on staff to provide the care and services the vulnerable COPD patient population requires for optimum disease management.

At the same time, RTs in all care settings need to ensure that COPD patients requiring LTOT have the equipment that best suits their respective needs, especially as the clinical value of scheduled ambulation and/or structured exercise without concomitant oxygen desaturation continues to be reaffirmed. To that end, RTs in the home-care setting must remain current with all of the latest LTOT technology, inclusive of the operational and performance capabilities (and limitations) of all available devices. For their part, hospital-based therapists should spend time with their home-care colleagues to keep abreast of the latest LTOT technology and of which options are readily available. In turn, home-care therapists should regularly visit their hospital colleagues to share information about successful outcomes observed when new LTOT technology is used optimally. Lastly, RT in all practice settings should never pass on any opportunity to ensure that patients with a chronic respiratory disease remain adherent to all prescribed controller medications, including LTOT. The clinical and economic impact of non-adherence with prescribed respiratory controller medications and devices is staggering and, in addition to recidivism, contributes to a substantial waste of precious health care resources.[62]

Summary

The availability of new, non-delivery LTOT technology has ushered in a new era for COPD patients requiring supplemental oxygen to manage chronic hypoxemia. Non-delivery technology represents a new paradigm for home-care providers, but the technology comes at a time when there is still a huge installed base of traditional LTOT equipment. Home-care providers are therefore faced with a real dilemma to try to maintain—in the face of continuing reimbursement cuts and caps—an existing process that is heavily dependent on repeat and costly home deliveries to replenish depleted oxygen contents, or to begin the transition to the more patient-centric, cost-effective, non-delivery process. While the new non-delivery technology certainly has its advantages, the higher capital acquisition costs associated with any newer technology cannot be ig-

nored. Each home-care provider will eventually have to determine if non-delivery technology does indeed represent a viable, cost-effective option. If the answer is yes, then the next decision will be to determine which specific technology will provide the best clinical and economic outcomes. Adding to the decision-making dilemma is the fact that patients themselves are now learning about non-delivery technology through other channels (eg, from fellow LTOT users or the Internet), and many prefer the new-found freedom that comes with having a single, self-sustaining and easily transportable oxygen-delivery device. Patients are now starting to request the newer technology from their home-care providers, and sometimes the requests are brand-specific.

However, not every patient can be effectively oxygenated with every type of non-delivery device. Accordingly, home-care providers deciding to transition to non-delivery technology must carefully evaluate which system will provide the greatest flexibility to the largest number of their patients. This will require a careful review of the existing devices, with special attention paid to the actual delivered dose (whether in L/min or mL/breath) and degree of oxygenation provided by each device at each numerical setting.[27,28] Again, in the words of one preeminent pulmonary researcher, "It is good clinical practice to titrate oxygen dose *with the device the patient will be using,* at rest, during exercise, and during sleep."[54]

Along these lines, instead of continuing to use the traditional prescription indicating so many L/min, the timing could not be more opportune for prescribing physicians to henceforth consider writing orders for LTOT that would direct the "RT to titrate LTOT" to a specific saturation target.[63] Such an approach to prescribing LTOT would ensure that each patient was properly interfaced with their oxygen equipment by an acknowledged expert and that the determined delivered dose(s) would be based upon each patient's individual needs as dictated by their respective life-style and activities of daily living across the entire LTOT continuum. Further, fulfilling a "titrate to saturate" prescription by way of a standing protocol would be equally advantageous.[64,65] RTs have long been using a protocol-directed approach to providing care in the hospital setting, and the time to extend this patient-centric approach to the home-care setting could not be better.[66] Moreover, this would be the same whether one is using the older traditional systems or one of the newer non-delivery technologies. In either case, the goal should be the same: to ensure that adequate oxygenation is provided at times and at all points across the LTOT continuum. Our patients deserve no less.

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