Enhancement of Exercise Performance in COPD Patients by Hyperoxia*

A Call for Research

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This essay summarizes 16 reports, published since 1956, that describe the effects of hyperoxia on exercise endurance in persons with COPD who have severe airflow obstruction (i.e., FEV₁ < 1.0 L or < 39% of predicted) and mild hypoxemia at rest (i.e., PaO₂ > 62 mm Hg or arterial oxygen saturation [SaO₂] measured by pulse oximetry of > 91%). The term hyperoxia is used because, in a proportion of study participants, oxygen administration increased exercise endurance in a dose-dependent fashion, up to a fraction of inspired oxygen of 0.5 or a flow of 100% O₂ of 6 L/min. The process appears to be dependent on an increase in PaO₂ rather than on the restoration of SaO₂ to normal levels. The results of pulmonary function tests were not predictive of response. Increased exercise performance was associated with a decrease in dyspnea, respiratory frequency, and minute ventilation. The slowing of respiratory frequency and the decrease in pulmonary air trapping likely accounted for the decrease in dyspnea. Slowing of the respiratory rate, which occurred at the expense of the retention of CO₂, is most likely due to a hyperoxia-induced decrease in chemoreceptor ventilatory drive from the aortic and carotid bodies. Research is called for to determine the following: (1) the prevalence of COPD patients who have severe airflow limitation accompanied by mild hypoxemia; (2) the proportion of these patients who show improvements in exercise performance during a test of hyperoxic exercise; and (3) whether enhanced exercise performance during a brief test translates into a meaningful increase in the ability to perform the activities of daily living.

Key words: COPD; dyspnea; exercise; oxygen inhalation therapy; physical endurance

Abbreviations: DODS = demand oxygen delivery system; FIO₂ = fraction of inspired oxygen; LTOT = long-term oxygen therapy; RVSP = right ventricular systolic pressure; SaO₂ = arterial oxygen saturation;Spo₂ = arterial oxygen saturation measured by pulse oximetry

In contrast to the evidence-based criteria for the reimbursement of LTOT, the criteria for administering and reimbursing patients for oxygen therapy during exercise were set arbitrarily, by extrapolation. The January 1996 US Medicare policy stated that oxygen therapy during exercise was not considered to be medically necessary for breathlessness. Oxygen therapy was reimbursed during exercise only if patients demonstrated hypoxemia during low-level exertion, which is relieved by oxygen administration. The specific wording is as follows:

An arterial PO₂ at or below 55 mm Hg or an arterial O₂ saturation at or below 88% taken during exercise for a patient who demonstrates an arterial PO₂ at or > 56 mm Hg, or an arterial oxygen saturation (SaO₂) at or > 89%, during the day while at rest. In this case, supplemental...
oxygen is provided for during exercise if there is evidence the use of oxygen improves the hypoxemia that was demonstrated during exercise when the patient was breathing room air.3

This essay focuses on the question of whether the peer-reviewed literature contains evidence that oxygen should be prescribed for persons with COPD to relieve dyspnea and to improve exercise performance, as well as to relieve hypoxemia. The term hyperoxia is used in this essay because the process of relieving dyspnea during exertion appears to require sufficient oxygen supplementation to result in an increase in PaO2 rather than the simple restoration of saturation to normal levels. Reports in English were sought from a National Library of Medicine PubMed search and from the bibliographies of retrieved articles in which the patients studied had COPD with severe airflow obstruction (ie, mean FEV1 < 1.0 L or < 39% of predicted) and mild resting hypoxemia (ie, mean PaO2 of > 62 mm Hg or SaO2 measured by pulse oximetry [SpO2] of > 91%). These criteria were met by 16 reports published between 1956 and 2001. Only one of these reports was a randomized controlled trial. The total number of patients studied was 173, ranging from 8 to 26 patients per report.

**Summary of Literature**

In 1956, Cotes and Gilson4 reported that portable oxygen therapy, given in a blinded fashion, usefully increased exercise performance in most of 29 patients with severe respiratory insufficiency. Twenty-eight of the 29 patients in the study had been coal miners, 18 had pneumoconiosis, and all had chronic bronchitis and emphysema. In 22 of 29 patients, walking distance on a treadmill was at least doubled when they were breathing oxygen. Studies of maximally effective oxygen concentration determined in a subset of six patients showed minimal improvement breathing 25% oxygen, showed further improvement breathing 30% and 50% oxygen, and showed no further improvement with 100% oxygen. In four patients, domiciliary oxygen permitted the performance of activities at home that would not have been possible without the use of oxygen. In a subsequent study, Cotes et al5 showed that average minute ventilation fell by 26.5% and that average cardiac output fell by 7.5% as a result of breathing oxygen during exercise.

Raimondi et al6 confirmed these results in eight men with a mean FEV1 of 0.74 L who increased their exercise endurance in response to a constant work-rate task by 35% (p < 0.005) when breathing 35% oxygen as compared with air. Vyas and colleagues7 studied the maximum duration of exercise in 12 men with a mean FEV1 of 29% of predicted values and mild resting hypoxemia (ie, mean resting PaO2, 72 mm Hg), which was measured while they were breathing air or 40% oxygen. Vyas et al found an increased exercise endurance of 12.8% (p < 0.025), which occurred at the expense of an increase in blood lactate levels and PaCO2 and a fall in pH.

Bradley and colleagues8 studied 26 men and women with severe airflow obstruction (ie, mean FEV1, 0.52 L) and mild resting hypoxemia (mean [SD] PaO2, 72.3 mm Hg [11.3 mm Hg]) while they exercised on a treadmill breathing compressed air or O2, 5 L/min by nasal prongs. Exercise endurance increased by 47% during O2 breathing, as compared with air breathing. There were no significant relationships among exercise endurance on air, oxygen breathing and rest, or exercise arterial blood gas values.

Woodcock et al9 reported studies on 10 patients with severe airflow obstruction (ie, mean FEV1, 0.71 L) and mild resting hypoxemia (ie, mean PaO2, 72.3 mm Hg). They used graduated exercise to exhaustion on a treadmill, with dyspnea measurement using an analog scale, while study participants breathed air or oxygen, 4 L/min, via cannula. Oxygen breathing resulted in a 25% mean increase in the distance walked on the treadmill (p < 0.01). The dyspnea score at 75% of the maximum treadmill distance was decreased by a mean of 24% (p < 0.02).

Stein et al10 studied nine COPD patients (mean FEV1, 0.87 L; mean PaO2, 63 mm Hg) using a graded treadmill test to maximum tolerance, breathing compressed air or 30% oxygen via a low-resistance valve. Exercise endurance was increased in eight of nine patients. This increase was achieved by a reduction in ventilatory requirements for the same workload, so that a limiting level of ventilation occurred later during incremental work. Blood lactate levels were reduced, but CO2 levels were retained.

Scano and colleagues11 studied 10 COPD subjects with somewhat less severe airflow obstruction than those in previous reports (ie, mean FEV1, 1.45 L; mean PaO2, 83.3 mm Hg). They used graded exercise to maximum on a bicycle ergometer while patients breathed air or 100% O2 through a low-resistance valved system. Total O2 consumption increased by a mean of 34% during oxygen breathing, and minute ventilation decreased. Mouth occlusion pressure at 0.1 s after onset and respiratory frequency decreased significantly during hyperoxia as compared with normoxia, suggesting a decrease in peripheral mechanical drive to respiration.

Bye and colleagues12 examined ventilatory muscle function during graded exercise to maximum on a cycle ergometer in eight COPD patients. They
showed a doubling of exercise time at constant workload, which they considered to be associated with decreased minute ventilation and evidence of decreased respiratory muscle fatigue. Criner and Celli\textsuperscript{13} studied respiratory muscle recruitment in six COPD subjects with severe airflow obstruction (ie, mean FEV\textsubscript{1}, 0.66 L) and mild hypoxemia (ie, mean PaO\textsubscript{2}, 64.5 mm Hg) while breathing air or 30% O\textsubscript{2}. They showed that exercise with O\textsubscript{2} breathing almost doubled exercise endurance time and altered respiratory muscle recruitment. While exercising while breathing O\textsubscript{2}, the diaphragm performed more ventilatory work, possibly preventing the overloading of the accessory muscles of respiration and thereby contributing to a decrease in dyspnea during exercise.

Davidson and colleagues\textsuperscript{14} assessed the effect of supplemental O\textsubscript{2} therapy on exercise performance in 17 patients with severe airflow obstruction (ie, mean FEV\textsubscript{1}, 0.79 L) and mild hypoxemia (ie, mean PaO\textsubscript{2}, 64.5 mm Hg). O\textsubscript{2}, 4 L/min, increased the mean endurance time by 59% and the 6-min walking distance by 17%. The endurance time for cycling at a constant workload was increased by 51% at an O\textsubscript{2} flow rate of 2 L/min, by 88% at 4 L/min, and by 80% at 6 L/min.

Light et al\textsuperscript{15} studied the relationship between improvement in exercise performance on O\textsubscript{2} supplementation therapy and the magnitude of hypoxic ventilatory drive in 17 patients with COPD (ie, mean FEV\textsubscript{1}, 0.99 L) and mild hypoxemia (ie, mean PaO\textsubscript{2}, 68.7 mm Hg). Identical maximal cycle ergometer exercise was carried out breathing air or 30% O\textsubscript{2}. Nine subjects increased their maximum workload, and eight subjects did not. The maximum mean exercise ventilation fell from 15.4 L/min while breathing air to 13.8 L/min while breathing 30% O\textsubscript{2} (p < 0.005). The dyspnea score while exercising fell from 8.5 while breathing air to 6.5 while breathing oxygen (p < 0.01). The measurement of hypoxic ventilatory drive was not helpful in predicting which patients would improve their exercise performance with oxygen breathing.

Dean and colleagues\textsuperscript{16} measured dyspnea scores during endurance testing on a cycle ergometer and correlated these measurements with right ventricular systolic pressure (RVSP) measured by Doppler echocardiography during a separate, supine, incremental exercise test. Tests were performed in 12 COPD patients with severe airflow obstruction (ie, mean FEV\textsubscript{1}, 0.89 L) and mild hypoxemia (ie, mean PaO\textsubscript{2}, 71 mm Hg) while the subjects breathed air or 40% O\textsubscript{2}. The duration of exercise increased from 10.3 min while breathing air to 14.2 min while breathing 40% O\textsubscript{2} (p < 0.005). Oxygen therapy delayed the rise in dyspnea scores and lowered the mean RVSP at maximum exercise from 71 to 64 mm Hg (p < 0.03).

An improvement in the duration of exercise correlated with the decrease in dyspnea (R\textsuperscript{2} = 0.66; p < 0.001), but not with the decrease in heart rate, minute ventilation, or RVSP.

Leach and colleagues\textsuperscript{17} measured exercise tolerance in 20 patients with severe COPD (ie, mean FEV\textsubscript{1}, 0.74 L) and mild hypoxemia (ie, mean PaO\textsubscript{2}, 68.7 mm Hg), and in 10 severely impaired patients with interstitial lung disease. The investigators used both an endurance walk and a 6-min walking test with patients breathing compressed air at a flow rate of 4 L/min or oxygen at 2, 4, or 6 L/min from a liquid O\textsubscript{2} source. Exercise endurance in the endurance walk at 2, 4, and 6 L/min O\textsubscript{2} was increased by 37.9%, 67.7%, and 85.0%, respectively, in comparison with that while breathing air. The exercise distance in the 6-min walk test was increased by 19.2%, 34.5%, and 36.3%, respectively, in comparison walking while breathing air. Carrying the oxygen container reduced the endurance walking distance by 22.4% and the 6-min walking distance by 14.1% in comparison with the unburdened walks. Results varied among patients but were similar in the COPD group and the interstitial lung disease group. Only among the COPD patients did desaturation while exercising have any predictive value. The authors concluded that exercise testing would be necessary to determine which patient’s exercise ability would benefit from supplemental oxygen.

O’Donnell et al\textsuperscript{18} explored the factors that might contribute to relief from dyspnea during O\textsubscript{2} administration in 11 COPD patients with severe airflow obstruction (ie, mean FEV\textsubscript{1}, 39% of predicted) and mild hypoxemia (ie, mean PaO\textsubscript{2}, 74 mm Hg). The study used exercise at approximately 50% of their patients’ incremental exercise capacity, breathing room air or 60% O\textsubscript{2} as the test. The mean PaO\textsubscript{2} value at exercise cessation was 65 mm Hg while breathing air and 226 mm Hg while breathing 60% O\textsubscript{2} (p < 0.001). While breathing 60% O\textsubscript{2}, the Borg dyspnea score/time slopes, the slope of mouth occlusion pressure at 0.1 s after onset, and blood lactate levels all fell significantly over time. Endurance time increased by 35% (p < 0.01), but the PaCO\textsubscript{2}/time did not change. The authors concluded that the relief from dyspnea was explained by reduced ventilatory demand in association with decreased lactate levels.

Somfay and colleagues\textsuperscript{19} studied 10 patients with severe COPD (ie, mean FEV\textsubscript{1}, 0.92 L) and mild hypoxemia (ie, mean SpO\textsubscript{2}, 92%, rest and 88% exercise). The endurance time on a symptom-limited incremental exercise test was increased while breathing 30% O\textsubscript{2} compared to air and increased further while breathing 50% O\textsubscript{2}, but not 75% or 100% O\textsubscript{2}. While breathing O\textsubscript{2}, in comparison with breathing air, there were significant but modest decreases in
dyspnea score, end-expiratory lung volume, end-inspiratory lung volume, minute ventilation, and breathing frequency. Improved endurance time correlated negatively with end-expiratory lung volume \((r = -0.48; \ p < 0.002)\) and with end-inspiratory lung volume \((r = -0.43; \ p < 0.005)\). The dyspnea rating decrease correlated with the decrease in respiratory frequency \((r = 0.35; \ p < 0.028)\). The authors concluded that oxygen supplementation during exercise induced a dose-dependent improvement in endurance and dyspnea, which may be partly related to decreased hyperinflation and slower breathing frequency. This effect was maximal at an inspiratory \(O_2\) concentration of 50%.

**Clinical Trial of Hyperoxic Exercise**

There has been only one double-blind, randomized, crossover trial assessing the effects of supplemental oxygen therapy during exercise on quality of life. McDonald and colleagues measured the effects of therapy with supplemental air and oxygen, at 4 L/min, on exercise performance during a step test and a 6-min walk test that were performed before and after two-week periods at home while breathing compressed air or oxygen during exercise. \(SPO_2\) and Borg dyspnea score were measured during exercise. At home, patients used gas cylinders fitted with a demand oxygen delivery system (DODS) [Oxymatic; Chad Therapeutics Inc; Chatsworth, CA] and a wheeled cart. A nasal cannula was used, and a flow of 4 L/min was used. Diary cards, which were completed every 12 h, were used to record dyspnea, cough, wheeze, and sputum production on a 4-point scale (1, none; 2, mild; 3, moderate; and 4, severe). The chronic respiratory quality-of-life questionnaire of Guyatt et al was administered at baseline, 6, and 12 weeks.

The 26 patients studied had a mean age of 73 years, severe airflow obstruction (ie, mean \(FEV_1\), 0.9 L), and mild resting hypoxemia (ie, mean \(PaO_2\), 69 mm Hg). The results of the 6-min walk tests showed an increase of 3.1 to 6.4% in distance walked from breathing air to breathing oxygen (all tests, \(p < 0.05\)). The step tests showed an increase in the number of steps from 12 to 20% (all tests, \(p < 0.05\)). Borg dyspnea scores fell slightly but not statistically significantly. Small, statistically significant improvements in dyspnea, fatigue, emotional functioning, and mastery occurred while breathing domiciliary \(O_2\) compared to baseline, however, mastery also improved significantly while breathing compressed air. There were no significant differences when the home \(O_2\) data were compared to the compressed air data. The 6-min walk test data and the step test data were similar at baseline and after the 6-week treatment period of breathing domiciliary \(O_2\) or air.

The authors concluded that although oxygen supplementation resulted in small improvements in exercise performance during both the 6-min walk test and the step test, such improvements had little effects on patients’ lives.

**Critique**

While on the whole the study was well-done, it has two serious flaws. The domiciliary oxygen was administered via a DODS (Oxymatic) at the 4 L/min setting. Roberts and colleagues compared exercise performance in subjects using the DODS Oxymatic as compared with using continuous-flow oxygen at the same flow rate. They found that use of the DODS Oxymatic produced only a small increase in walking distance, without an elevation in oxygen saturation. The results using the DODS Oxymatic were inferior to those breathing continuous-flow oxygen in most of the measured variables.

The other flaw in the study is that all patients received oxygen supplementation with only 4 L/min oxygen. A number of studies have shown that some patients require supplementation by as much as 6 L/min oxygen to obtain a maximal effect.

**The Physiology of Hyperoxic Exercise in Chronic Airflow Obstruction**

Airflow obstruction is the hallmark of COPD. Resting hyperinflation of the lungs, as indicated by increases in functional residual capacity and total lung capacity, is frequent in patients with severe COPD. Tidal breathing occurs over a less advantageous portion of the length-tension curve of the diaphragm. Work done by accessory muscles of respiration is increased. During exercise, the ventilatory muscles are unable to do the work necessary to adequately increase tidal volume. Tachypnea and a shortened expiratory phase result in air trapping. The resulting increase in pulmonary distention moves tidal breathing into an even less advantageous position on the diaphragm length-tension curve with a further shortening of the respiratory muscle fibers and a further decrease in their capacity to perform work. Diaphragmatic fatigue may occur.

Ventilation/perfusion mismatch in the lungs of persons with COPD causes hypoxemia. Many individuals with severe airflow obstruction due to COPD, whether they have mild or severe resting hypoxemia, demonstrate improved exercise performance and decreased dyspnea in a dose-dependent fashion up to a fraction of inspired oxygen (\(FiO_2\)) of 0.5 or up to a flow of 6 L/min of 100% \(O_2\) by nasal
cannula. Decreased ventilatory rates, tidal volumes, minute volumes, and inspiratory capacities frequently are observed in patients. Dyspnea is decreased.4,10,13,16,18 Oxygen administration also consistently enhances arterial blood O2 saturation and, therefore, O2 content. Cardiac output, systemic BP, and pulmonary arterial pressure are decreased.5

Maltais and colleagues24 performed a crossover trial of peak exercise while patients breathed air or oxygen (FIO2, 0.75) in 14 COPD patients. The mean (± SD) peak exercise capacity increased from 46 ± 3 W while breathing room air to 59 ± 5 W when breathing supplemental oxygen (p < 0.001). Leg blood flow, O2 delivery, and O2 uptake were greater at peak exercise while breathing O2 than while breathing air (p < 0.05). During submaximal exercise, dyspnea score and minute ventilation were significantly reduced while breathing O2 (p < 0.05), whereas leg blood flow, leg O2 uptake, and leg fatigue were similar under both experimental conditions. The improvement in peak exercise work rate correlated with the increase in peak O2 delivery (r = 0.66; p < 0.01) and peak O2 uptake for the legs (r = 0.53; p < 0.05), and with the reduction in dyspnea at isoeexercise intensity (r = 0.56; p < 0.05). The authors concluded that improvement in peak exercise capacity with oxygen supplementation could be explained by the reduction in dyspnea at submaximal exercise and by the increases in leg O2 delivery and uptake, which enabled the exercising muscles to perform more external work. The metabolic capacity of the lower limb muscles was not exhausted at peak exercise during room air breathing in these patients with COPD.

Simon and colleagues25 addressed the question of why, in some patients with COPD, a plateau in lower limb O2 uptake, O2 delivery, and blood flow occurs despite the progression of the imposed workload during cycling. In a study of 14 men with COPD, they found that in eight patients leg O2 uptake increased in parallel with total O2 uptake as the normoxic external work rate increased. In six subjects, a plateau in leg O2 uptake and blood flow occurred during exercise despite the increase in workload and total O2 uptake. These six patients also exhibited a plateau in O2 extraction during exercise. The peak exercise work rate was higher in the eight patients without a plateau than in the eight with a plateau (51 ± 10 vs 40 ± 13 W, respectively; p = 0.043). Tidal volume, minute ventilation, and dyspnea were significantly greater at submaximal exercise in patients in the plateau group compared with those in the nonplateau group. It appears that in some patients with COPD, blood flow directed to peripheral muscles and O2 extraction during exercise may be limited.

In the studies of Somfay et al19 of severely obstructed, mildly hypoxemic COPD patients, the degree of exercise enhancement produced by hyperoxia was correlated with the reduction in the ventilatory requirement for exercise. It was hypothesized that the reduction in ventilatory requirements occurred because hyperoxia resulted in decreased stimulation to ventilation from the aortic and carotid bodies and because the reduced ventilatory requirement enabled the prolongation of the time for exhalation and therefore, as the authors showed, less hyperinflation. Dynamic hyperinflation has long been postulated to be a major mechanism of exercise limitation in COPD patients.22

More recently, Somfay and colleagues26 have addressed the question of whether hyperoxic exercise can speed the dynamic response of O2 uptake and can reduce the transient lactate increase. In 10 study participants with severe COPD and mild hypoxemia, they found that the time constants for O2 uptake, heart rate, CO2 output, and minute ventilation were significantly slower than in healthy subjects. Hyperoxia decreased end-exercise ventilation in the COPD group but not in the normal group. Hyperoxia significantly slowed the kinetics of CO2 output and minute ventilation in both groups but did not increase the speed of oxygen uptake kinetics. Only small increases in blood lactate levels occurred with exercise, and this increase did not correlate with oxygen uptake kinetics. This study supported the authors’ hypothesis that the decreased ventilatory requirement for hyperoxic exercise stems from direct chemoreceptor inhibition rather than from improved muscle function.

In summary, the mechanisms of improvement of hyperoxic exercise performance in patients with severe COPD and mild hypoxemia are complex. Improvement in exercise performance is usually submaximal at an FIO2 of 0.3 (4 L/min of 100% oxygen) and is maximal at an FIO2 of 0.5 (6 L/min of 100% oxygen),4,10,13,16,18 indicating that the increase in PAO2 is the driving force rather than the increase in SaO2. In about half of COPD patients, a plateau in leg O2 uptake, O2 extraction, and blood flow occurs during normoxic exercise despite the increases in workload and total O2 uptake.24 The metabolic capacity of the lower limb muscles appears not to be exhausted at peak normoxic exercise in patients with COPD.21 The most consistent responses that have been observed in COPD patients during hyperoxic exercise are decreases in dyspnea, respiratory rate, and minute ventilation. PACO2 often increases with an accompanying fall in blood pH. Blood lactate level is usually minimally affected but may increase. Dyspnea is decreased mainly due to a decrease in respiratory frequency and dynamic hyperinflation (decreased end-expiratory and end-inspiratory lung volumes) during exercise. The decrease in respiratory frequency and tidal volume...
likely relate to a decrease in respiratory drive, primarily because of a decrease in stimulus from the aortic and carotid bodies, which is in turn due to the hyperoxia-induced increase in \( \text{PaO}_2 \). All patients do not have the same degree of relief from hyperoxia and some have none. Since the main factors causing increased performance during hyperoxic exercise in COPD patients are related to muscle function and the alleviation of hypoxic ventilatory drive, it is hardly surprising that the results of forced expiratory spirometry, lung volume measurements, resting \( \text{SaO}_2 \) levels, or diffusing capacity measurements are not predictive of enhanced hyperoxic exercise performance.

**Suggested Action Plan**

It is estimated that in the United States there are currently about 16 million persons with COPD. There were 107,000 deaths due to COPD in 1998, and, extrapolating from the 1998 data, in the current year there will be about 115,000 deaths due to COPD. Assuming that on the average, persons have severe COPD for 10 years before they die, it follows that of the 16 million persons with severe COPD currently alive in the United States, at least 1.2 million (7.5%) have severe disease. A conservative estimate of the number of persons receiving LTOT in the United States is 750,000, and the average cost per patient for LTOT is \$3,600 per year. Authorizing reimbursement for oxygen therapy during exercise for severely obstructed, mildly hypoxemic COPD patients could add a sizeable amount to the cost of LTOT in the United States. However, patients with end-stage COPD carry an enormous burden of suffering and, surely, the pulmonary community has a responsibility to do the research to determine whether or not hyperoxic exercise has a place in the management of severely obstructed, minimally hypoxemic COPD patients. Hyperoxic exercise should be considered as a means of improving exercise performance in severely impaired persons. In my view, the question of whether hyperoxic exercise prolongs life is not pertinent. The goal is palliation, and that goal is worthwhile whether or not life is prolonged.

**The Research Questions**

1. What is the prevalence of COPD patients, who are not receiving LTOT and who have severe airflow limitation (ie, \( \text{FEV}_1 < 1.0 \text{ L} \) or 35% of predicted values) and mild hypoxemia (ie, resting \( \text{SpO}_2 \geq 90\% \))?

2. What proportion of severely obstructed, mildly hypoxemic COPD patients will improve their exercise endurance in a brief test?

3. Is improved performance during a brief hyperoxic exercise test translated into a meaningful increase in the activities of daily living?

It is apparent that, apart from a full elucidation of the physiologic effects of hyperoxia, many other research questions arise from the issues considered in this essay. For example, in COPD patients who are hypoxemic at rest or during mild exercise, does the simple correction of hypoxemia by oxygen therapy result in optimal improvement in exercise performance, or is hyperoxia required? Will \( \text{CO}_2 \) retention, and perhaps oxygen toxicity, be deleterious to condition of COPD patients who are hyperoxic during exercise for several hours each day?

**The Next Step**

It is beyond the scope of this essay to spell out the precise procedures for answering these questions. However, I have some suggestions for consideration by experts in the rehabilitation of persons with COPD.

**Hyperoxia Endurance Test**

Since pulmonary function tests do not predict who will benefit from oxygen treatment, an exercise endurance hyperoxia test should be developed that will indicate which patients might benefit from supplemental oxygen therapy during exercise. Almost 10 years ago, Leach et al pointed out that training runs were needed for both an endurance walk and a 6-min walk, but that fewer runs were needed for the endurance walk. More importantly, these authors showed that the endurance walk was more sensitive to hyperoxia than was the 6-min walk. A possible protocol for a hyperoxic exercise endurance test, done in a \( \geq 100\)-foot corridor with measurements marked at 20-foot intervals, might be performed as follows.

1. Perform a training endurance walk in which the patient is connected to a pulse oximeter and walks as far as possible breathing ambient air. Record the distance walked, the endurance time, and the resting and minimum exercise \( \text{SpO}_2 \).

2. Repeat the endurance walk for the record.

3. Repeat the endurance walk but with the patient breathing 100% \( \text{O}_2 \) at 4 L/min via nasal cannula from a source that is carried or wheeled by the patient.

4. Repeat the endurance walk but with the patient breathing 100% \( \text{O}_2 \) at 6 L/min via nasal cannula from a source that is carried or wheeled by the patient.
5. If exercise endurance fails to increase during endurance walks carried out with $O_2$ flows of 4 and 6 L/min, the patient is not suitable for the prescription of hyperoxic therapy during exercise.

6. If exercise endurance is increased by hyperoxic therapy, repeat the endurance walk using a DODS set at the flow rate that gave the greater increase in endurance. The particular DODS tested should fully correct hypoxemia during exercise and should be prescribed only if the exercise endurance while using the DODS is comparable to that during continuous-flow oxygen therapy.

**HYPEROXIC EXERCISE PERFORMANCE**

If preliminary studies warrant, a randomized, clinical, interventional trial should be organized to determine whether exercise hyperoxia has a therapeutic role in the segment of the population of COPD patients with high-grade airflow obstruction but limited hypoxemia. The end points of the study should be enhanced exercise performance, decreased dyspnea during exercise, enhanced performance of activities of daily living, and increased well-being.

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