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A 6MWT index to predict O_2 flow correcting exercise induced SpO_2 desaturation in ILD

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Summary
Introduction: Ambulatory oxygen (O_2) is prescribed to interstitial lung disease (ILD) patients with mild hypoxemia, breathlessness and dyspnea on exertion. Oxygen titration is generally done with the 6 minute walk test (6MWT) to determine the O_2 flow preventing **oxygen saturation by pulse oximetry (SpO_2)** from falling below 88%. His study was designed to generate a 6MWT index predicting the O_2 flow allowing completion of the 6MWT without oxygen desaturation.
Methods: Oxygen titration data from a group of 66 ILD patients and 30 controls, were used to generate the algorithm determining an index (O_2-GAP) predicting oxygen flow required to complete a 6MWT without desaturation below 88%. This index was validated in a group of 93 ILD patients.
Results: The O_2-GAP index, as obtained from the derivation population, ($r^2 = 0.97$, $p < 0.001$) was shown to correctly predict the oxygen flow required to complete the 6MWT without SpO_2 falling below 88% validated in the validation population ($r^2 = 0.842$; $p < 0.001$).

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Conclusions: The O_2-GAP index appears to be a useful tool to titrate ambulatory O_2 with a single 6MWT on room air in ILD patients with breathlessness and dyspnea on exertion.

Introduction

The use of long-term oxygen therapy (LTOT) effectively improves disease symptoms and prolongs survival in chronic obstructive pulmonary disease (COPD) patients with severe hypoxemia (resting PaO_2 on room air $<$ 55 mmHg) [1—3]. However, oxygen is also administered to individuals with moderate hypoxemia at rest for relief of breathlessness, either as short-burst oxygen therapy or as ambulatory oxygen therapy given during activities of daily living or exercise. Although its efficacy in ameliorating both breathlessness and exercise endurance is supported by a number of studies, there are no data showing that it prolongs survival [4—7].

In patients with interstitial lung diseases (ILDs), a large group of pulmonary disorders classified together because of similar clinical, roentgenographic and physiologic features, gas exchange worsening with exercise is recognized as a central feature in disease pathophysiology [8,9]. The Royal College of Physicians guidelines recommend LTOT in ILD patients with PaO_2 below 60 mmHg and also advise to prescribe oxygen to those patients who experience oxygen saturation by pulse oximetry below 90% during a walk test on room air [10]. Oxygen therapy has also been recently recommended by the American Thoracic Society (ATS)/European Respiratory Society (ERS)/Japanese Respiratory Society (JRS)/Latin America Thoracic Association (ALAT) idiopathic pulmonary fibrosis (IPF) guidelines for diagnosis and management, based upon physiological reasons, extrapolation from data in COPD and ethical concern over withholding oxygen therapy [9].

In this regard, ambulatory oxygen therapy has in fact been shown to improve exercise capacity in the 6 minute walk test (6MWT) in IPF patients [11] and a recent retrospective study on ILD patients including a majority of patients with IPF, showed that ambulatory oxygen improves patient performance in the 6MWT and ameliorates breathlessness [12].

A number of exercise tests have been used to evaluate the efficacy of ambulatory and short-burst oxygen supplementation, including the treadmill, cycle ergometry and the 6MWT, with a variety of oxygen supplementation devices [13]. Overall, these studies have shown that the use of ambulatory oxygen reduces exercise induced breathlessness, may speed up recovery from breathlessness and improves exercise capacity [7]. Generally, the amount of supplemental oxygen needed to compensate for exertional hypoxemia is determined by repeating the 6MWT at different oxygen flow rates in order to identify the lowest oxygen flow rate needed to maintain oxygen saturation by pulse oximetry above 88% [5,9,14,15]. Oxygen titration though, a time consuming procedure, is taxing for the dyspneic patient. The aim of this study was to develop and validate a 6MWT index, obtained from a single test performed on room air, capable of predicting the flow of ambulatory oxygen needed to complete the test while maintaining oxygen saturation by pulse oximetry (SpO_2) equal or above 88%, without the need of repeated testing using increasing oxygen flow rates.

Material and methods

Design of the study

The study was designed to generate an algorithm to predict the flow of supplemental oxygen [in liters per minute (l/min) to be administered through a nasal cannula] required to maintain oxygen saturation by pulse oximetry equal or above 88% during the 6MWT in ILD patients, as monitored by pulse oximetry. To this end, a group of 66 individuals with ILD and from 30 subjects without cardiopulmonary disease, were evaluated at the pulmonary function testing laboratory (PFT lab) of the Respiratory Diseases Unit of the Tor Vergata University Hospital, Rome. The algorithm hitherto derived was prospectively validated in a group of 93 ILD-affected individuals.

The oxygen supplementation estimated by the algorithm was defined as "O_2-GAP index" so that when the 6MWT is carried out on room air, the "O_2-GAP index" indicated the flow of supplemental oxygen required to maintain oxygen saturation by pulse oximetry equal to or above 88%. When the 6MWT was performed by patients already on supplemental oxygen, the "O_2-GAP index" indicated the extra flow of oxygen required to complete the test.

The study was approved by the Independent Ethics Committee of the Tor Vergata University Hospital (Rome, IT) and was conducted in accordance with the Declaration of Helsinki (number: 156/12).

Derivation population

A population of 96 subjects was evaluated between October 1, 2008 and December 31, 2009. It was comprised of 66 ILD-affected individuals, referred for dyspnea on exertion, and 30 non ILD-affected subjects as the control group, with pulmonary function tests within normal range and no apparent clinico-radiological signs of cardiopulmonary disease, who were referred for perceived breathlessness that resulted imputable to deconditioning, metabolic causes (obesity) or anxiety. The ILD patient group was comprised of 30 individuals with IPF, nine with non specific interstitial pneumonia (NSIP), nine with sarcoidosis, four with cryptogenic organizing pneumonia (COP), three with hypersensitivity pneumonitis (HP), one with berylliosis, two with undifferentiated connective tissue disease, one with rheumatoid arthritis (RA), one with histiocytosis-X (HX), one with lymphangioleiomyomatosis (LAM), one with neurofibromatosis, and two with scleroderma. All subjects underwent pulmonary function testing and the 6MWT. Individuals whose oxygen saturation by pulse oximetry fell below 88% during the test underwent oxygen titration, as described in the 6MWT Section. The demographic, biological, pulmonary function and echocardiographic characteristics of the derivation population are shown in Table 1.