Optimizing O2 supplementation to improve dyspnea and exercise tolerance in fibrotic interstitial lung disease: can we do better with nasal high flow O2 therapy ?

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Résumé

Introduction. Hallmarks of fibrotic interstitial lung disease (f-ILD) include severe hypoxemia, dyspnea and exercise limitation. Although ambulatory oxygen (O2) therapy is widely prescribed, standard low-flow O2 systems (nasal prongs) fail to meet patients' inspiratory demand on exertion resulting in incomplete correction of hypoxemia and limited symptomatic relief (1). Nasal high-flow O2 therapy (NHFO2) delivers heated, humidified, and O2-enriched air at high flow rates. It has recently emerged as a promising alternative to overcome the pre-specified limitations: NHFO2 is more effective in correcting hypoxemia and reducing dyspnea *vs* standard O2 therapy and consistently improved exercise capacity in f-ILD (2,3,4). In fact, NHF *per se* may exert independent physiological benefits such as washout of the anatomical dead space and reduced work of breathing (5). However, the respective effect of respiratory support and improved oxygenation on dyspnea and exercise tolerance remain unexplored in f-ILD.

Methods. Sixteen patients (9 men, 69±14y, 6 with idiopathic pulmonary fibrosis, total lung capacity= 71±24% predicted) randomly performed constant work-rate (WR) exercise tests (70% WRpeak) under 4 conditions: air, supplemental O2 (face mask; 9 L/min), NHF (50-70 L/min; inspired fraction of O2 (FiO2)=0.21) and NHFO2 (FiO2=0.5). We compared endurance time, isotime O2 saturation (SpO2), breathing pattern (respiratory inductive plethysmography), dyspnea (Borg CR10) and *quadriceps* muscle oxygenation (near-infrared spectroscopy) across conditions.

Results. Endurance time improved on O2 and NHFO2 vs air and NHF (683 (903), 690 (1338), 346 (247) and 319 (415) s, respectively; $p< 0.001$). Of note, SpO2 was similar on O2 (98 (2)%) and NHFO2 (99 (3)%; $p> 0.05$), improving from air (87 (17)%; $p< 0.001$). Ventilation was lower on O2 and NHFO2 vs air (41±18, 40±20, 55±30 L/min $p< 0.001$), driven by lower respiratory rates (33±8, 35±6, 39±7 br/min; $p< 0.05$). Dyspnea improved on O2 and NHFO2 vs air (4 (3.5), 3.5 (2.5), 7 (3), respectively; $p< 0.001$) and on NHFO2

*Intervenant

vs NHF (6 (1.5); p< 0.05). NHF offered no independent benefits but numerically reduced ventilation *vs* air (_˜8 L·min-1,p=0.103). Supplemental O2 and NHFO2 similarly enhanced peak-exercise *quadriceps* muscle oxy-deoxyhemoglobin difference *vs* air and NHF (0.2±7.4, 1.9±9.6, -7.0±7.6, -6.2±6.3 μmol·s-1 from rest; p< 0.001).

Discussion. This study is the first to disentangle the individual contribution of NHF and supplemental O2 on dyspnea and exercise performance in f-ILD. Our findings show that supplemental O2 (delivered via a non-rebreather face mask) and NHFO2 provide similar improvements in these outcomes at "iso-O2 saturation", but no independent effect of NHF. This indicates that the key driver of dyspnea relief and improved exercise tolerance in f-ILD is enhanced oxygenation leading to reduced ventilatory demand and enhanced O2 delivery to skeletal muscles. While NHF may modestly reduce ventilation, it did not translate into symptomatic or functional improvement unless combined with adequate oxygenation.

Conclusion/perspectives. NHFO2 significantly alleviated dyspnea and enhanced exercise tolerance in f-ILD showing comparable efficacy to O2 supplementation when matched for O2 saturation. Our results underscore the importance of appropriately correcting hypoxemia, lowering ventilatory demand and improving skeletal muscle functioning to optimize functional and perceptual responses to exercise in this patient population. NHFO2 may thus potentiate the effect of rehabilitative exercise training as compared to standard care (typically O2 therapy through nasal prongs), an endeavor currently addressed in our research group.

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