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Contrasting pressure-support ventilation and helium–oxygen during exercise in severe COPD☆

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Summary
Helium–oxygen mixtures and pressure-support ventilation have been used to unload the respiratory muscles and increase exercise tolerance in COPD. Considering the different characteristics of these techniques, we hypothesized that helium–oxygen would be more effective in reducing exercise-induced dynamic hyperinflation than pressure-support. We also hypothesized that patients would experience greater increases in respiratory rate and minute ventilation with helium–oxygen than with pressure-support. The hypotheses were tested in ten patients with severe COPD ($FEV_1 = 28 \pm 3\%$ predicted [mean ± SE]) during constant-load cycling (80% maximal workrate) while breathing 30% oxygen-alone, helium–oxygen, and pressure-support in randomized order. As hypothesized, helium–oxygen had greater impact on dynamic hyperinflation than did pressure-support (end-exercise; $p = 0.03$). For the most part of exercise, respiratory rate and minute ventilation were greater with helium–oxygen than with pressure-support ($p \leq 0.008$). During the initial phases of exercise, helium–oxygen caused less rib-cage muscle recruitment than did pressure-support ($p < 0.03$), and after the start of exercise it caused greater reduction in inspiratory reserve volume ($p \leq 0.02$). Despite these different responses, helium–oxygen and pressure-support caused similar increases in exercise duration (oxygen-alone: 6.9 ± 0.8 min; helium–oxygen: 10.7 ± 1.4 min; pressure-support: 11.2 ± 1.6 min; $p = 0.003$) and similar decreases in inspiratory effort (esophageal pressure-time product), respiratory drive, pulmonary resistance, dyspnea and leg effort ($p < 0.03$). In conclusion, helium–oxygen reduced exercise-induced dynamic hyperinflation by improving the relationship between hyperinflation and minute ventilation. In contrast, pressure-support reduced hyperinflation solely as a result of lowering ventilation. Helium–oxygen was more effective in reducing

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exercise-induced dynamic hyperinflation in severe COPD, and was associated with greater increases in respiratory rate and minute ventilation than pressure-support.

Introduction

Exercise tolerance is decreased in patients with chronic obstructive pulmonary disease (COPD).[1,2] Decreased exercise tolerance causes significant disability, which, in turn, profoundly affects quality of life. Mechanisms responsible for decreased exercise tolerance include inability to increase oxygen delivery to the peripheral muscles, variable peripheral-muscle dysfunction, pulmonary gas-exchange abnormalities, pulmonary hypertension, and, possibly, psychological factors.[1] In many patients, however, abnormal lung mechanics and functional respiratory muscle weakness secondary to dynamic hyperinflation predominate.[3–5]

Helium–oxygen mixtures[6–9] and pressure-support ventilation[10,11] have been used to unload the respiratory muscles and, thus, decrease inspiratory effort and increase exercise tolerance in COPD. Considering the different technical characteristics of these techniques, we expect the unloading with helium–oxygen and pressure-support to be achieved by different mechanisms. Unique to helium–oxygen is the improvement in airflow that results from a lower density of helium in relation to air.[12] By improving airflow, helium–oxygen can limit exercise-induced dynamic hyperinflation in COPD.

Unique to pressure-support is a slowing of respiratory frequency.[13] This slowing possibly results from vagally-mediated increases in the duration of neural exhalation.[14,15] In addition, pressure-support increases tidal volume (V_T) while unloading the respiratory muscles[13,16] and it may also hinder expiratory flow.[16,17] We speculate that all these effects of pressure-support could have contrasting consequences on exercise-induced dynamic hyperinflation. A lower frequency might decrease exercise-induced dynamic hyperinflation. Alternatively the combination of a higher V_T in the presence of flow-limitation – almost invariable with severe COPD[18] – and an impediment to expiratory flow could worsen dynamic hyperinflation. We, therefore, expect that in severe COPD helium–oxygen and pressure-support will have different effects on exercise-induced dynamic hyperinflation. Specifically, we hypothesize that exercise-induced dynamic hyperinflation will be less with helium–oxygen than with pressure-support. In addition, considering possible vagally-mediated increases in neural exhalation with pressure-support,[14,15] we also hypothesize that during constant workrate exercise, patients with severe COPD will experience more modest increases in respiratory frequency and minute ventilation with pressure-support than with helium–oxygen.

The primary purpose to perform such a head-to-head comparison of helium–oxygen versus pressure-support is to gain insights into the mechanisms of action that are unique to each modality. Without doing a head-to-head comparison it would be impossible to determine which changes are quantitatively unique for a given modality. Confirmation of our primary and secondary hypothesis will shed new light into the mechanisms of action that are distinctive to helium–oxygen or pressure-support.

Methods

Further methodological details are available in the online supplement.

Patients

Thirteen sedentary patients (modified Baecke score <9)[19] with severe COPD ($FEV_1/FVC < 0.7$, $FEV_1 < 50\%$ predicted)[20] were enrolled in the study. Exclusion criteria were significant cardiovascular, neuromuscular, or orthopedic impairments that could have interfered with exercise testing.[21] Appropriate institutional review boards approved the study and written consent was obtained. After randomization, three patients withdrew or were withdrawn. One withdrew because of newly diagnosed prostate cancer requiring radiation therapy. The second patient withdrew because of newly diagnosed peripheral vascular disease, and the third because of knee pain secondary to degenerative joint disease that required surgery. Characteristics of patients who did not complete the study were similar to those who did.

Experimental setup

Flow and pressure measurements

Inspiratory flow was measured with a heated, large-diameter pneumotachometer connected to a differential pressure transducer. Calibration of the pneumotachometer was confirmed with the experimental gas mixture immediately before each exercise trial.[6–9] Volumes were obtained by electronic integration of the flow signal. The pneumotachometer was attached in series to a low-resistance one-way valve and mouthpiece[22] (Fig. 1E-repository).

Esophageal (Pes) and gastric (Pga) pressures were separately measured with two thin-walled, 10 cm long latex balloon-tipped catheters coupled to pressure transducers. A balloon containing 1.0 mL of air was positioned in the midesophagus; a gastric balloon containing 2.0 mL of air was advanced 70 cm from the nares. Proper positioning of the esophageal balloon was ensured with the occlusion technique.[23] Airway pressure was measured at the mouthpiece using a third pressure transducer.

Protocol

Based on symptom-limited, incremental cycle-ergometry testing, three submaximal constant-load exercise tests, equal to 80% of the highest workrate (Watts) achieved, were selected (Fig. 1). During the three submaximal tests, patients breathed 30% oxygen-alone, 30% oxygen plus 70%