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Efficacy of non-invasive ventilation as a rescue therapy for relieving dyspnea in patients with stable severe COPD☆

Yong-er Ou, PhD [1], Zhi-min Lin, MD [1], Wei-liang Wu, PhD, Qun Luo, MD, PhD, Rong-Chang Chen, MD *

State Key Laboratory of Respiratory Disease, National Clinical Research Center for Respiratory Disease, Guangzhou Institute of Respiratory Disease, First Affiliated Hospital of Guangzhou Medical University, Guangzhou, 510120, China

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ABSTRACT

Exertional Dyspnea is a troublesome symptom in chronic obstructive pulmonary disease (COPD) even after optimal therapy, which is a physiological and perceptional burden to limit their activities. Non-invasive ventilation (NIV) might provide rescue therapy for this population to relieve exertional dyspnea.

This was a randomized crossover study in 18 patients with stable severe COPD. Exertional dyspnea was induced with maximal symptom-limited incremental cycle exercise. Then the patients would randomly receive oxygen or NIV plus oxygen therapy. Patients were crossed to another therapy in the second day. During the whole process, breathing pattern were monitored continuously until complete recovery. At every 30s interval, inspiratory capacity (IC) and Borg scale were assessed. Changes were compared between two interventions.

Compared with oxygen therapy, NIV plus oxygen therapy resulted in increase of tidal volume and minute ventilation, decrease in dyspnea intensity at isotime (reduction of 1.0 ± 2.0 Borg units, $p < 0.05$) and a tendency but not statistically significant shortening in total dyspnea recovery time (326.2 ± 132.0s vs 356.5 ± 156.9s, $p = 0.225$). These improvements were negatively correlated with baseline FEV_1 ($r = -0.617$, $p < 0.01$). Subjects were divided into responders ($n = 9$) with dyspnea recovery time shortening > 30s or non-responders. Responder subgroup had significantly poorer pulmonary function in FEV_1, FEV_1%, IC than non-responder subgroup, indicating that NIV is effective as rescue therapy for exertional dyspnea in stable COPD with poorer pulmonary function.

NIV as rescue therapy could help relieve dyspnea after exercise in patients with stable severe COPD with a poor pulmonary function.

1. Introduction

Chronic obstructive pulmonary disease (COPD) is one of the leading causes of morbidity and mortality throughout the world [1]. Its main symptom is chronic exertional dyspnea which is a physiological and perceptional burden to limit their activities [2,3]. COPD patients often unconsciously adopt a sedentary lifestyle, probably due to distressing exertional dyspnea. The sedentarism results in physical deconditioning and alterations of the peripheral muscles, which leads to a vicious circle and contribute to the debilitation of the patients [4]. Thereby, intervention should be taken to intervene this vicious cycle. It has been reported that non-invasive ventilation (NIV) could help unload the inspiratory muscle [5,6], lessen the airflow limitation, and prolong the expiratory time, which in turn improved lung hyperinflation. NIV was also reported to improve neuro-mechanical coupling [7], oxygenation, dyspnea

Abbreviations: FEV_1, forced expiratory volume in 1s; FRC, functional residual capacity; FVC, forced vital capacity; IC, inspiratory capacity; RV, residual volume; TLC, total lung capacity; MVV, maximal voluntary ventilation; MIP, maximal inspiratory pressure; HR, heart rate; RR, respiratory rate; Vt, tidal volume; VE, minute ventilation; Ti, inspiratory time; Te, expiratory time; Ttot, total time of the respiratory cycle; Ti/Ttot, inspiratory duty cycle; Vt/Ti, mean inspiratory tidal flow; Vt/Te, mean expiratory tidal flow.

☆ Some of the results have been presented as oral presentation in the 2016 Chest World Congress conference.

* Corresponding author. First Affiliated Hospital of Guangzhou Medical University, 151 Yanjiang Road, Guangzhou, Guangdong, China

E-mail addresses: ouyongercandy@126.com (Y.-e. Ou), doctorlin3@126.com (Z.-m. Lin), 781816296@qq.com (W.-l. Wu), luoqunx@163.com (Q. Luo), rcchengird@163.com (R.-C. Chen).

[1] These authors contributed equally to this work and should be considered co-first authors.

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during exercise in COPD patients [8–10]. However, in these reports, NIV was used as add-on therapy during exercise or at resting condition before exertional dyspnea occurred, it is unclear that whether or not NIV can be used at the time of exertional dyspnea occurred as the rescue therapy to relieve dyspnea after exercise in patients with stable severe COPD, which might relieve their physiological and perceptional burden to limit their activities. So, our hypothesis was that NIV plus oxygen therapy as a rescue therapy is more effective than oxygen therapy alone in relieving dyspnea after exercise.

The purpose of this study was therefore to determine the effectiveness and potential respiratory mechanics of NIV plus oxygen as rescue therapy to relieve dyspnea after exercise in patients with stable severe COPD.

2. Methods

2.1. Subjects

Severe COPD patients were recruited from the first affiliated hospital of Guangzhou Medical University from March 2013 to April 2014. The diagnosis of COPD was confirmed by physician's diagnosis and spirometry. The inclusion criteria were as following: 1) $FEV_1 < 50\%$ predicted; 2) In stable condition (no acute exacerbation in the last 4 weeks); 3) long term maintenance medications were kept constant at least for three months; 4) dyspnea as a main symptom that limited daily activities. The exclusion criteria were as following: any contra-indication of NIV; coronary artery disease or cardiac arrhythmias or potential electrocardiographic alterations; uncontrolled hypertension; other respiratory diseases other than COPD; musculoskeletal or neurological disorders; failure to comply with the research protocol. Sixty patients with severe COPD were screened, forty-two patients were excluded from the study, eighteen patients were enrolled in the study (Fig. 1).

2.2. Study design and experimental procedure

This was a prospective randomized cross-over study. The study was approved by institutional Ethics Committee (Approval Acceptance Number: 2013-41). After giving written informed consent, patients completed screening tests to determine eligibility for the study. Before the experimental visits, subjects were asked to keep on taking regular medicines, avoiding caffeine alcohol and heavy meals at least for 4 h and major physical exertion at least for one day. All visits were conducted at the similar time period of day for each subject. 1) an initial visit designed to collect the basic information and familiarize the patients with all tests that would be performed during subsequent intervention visits, including clinical assessment, chronic dyspnea evaluation, pulmonary function tests, maximum inspiratory pressure (MIP) (details on these assessments can be found in the online supplement), a maximal symptom-limited incremental cycle exercise test, a trial use of NIV and Borg scale assessment. 2) The procedure of second and third visits were the same except the interventions after symptom-limited maximal exercise when exertional dyspnea occurred. Maximal Symptom-limited cycle exercise tests were conducted on an electronically braked cycle ergometer (Ergoselect 200K; Cosmed) by use of a cardiopulmonary exercise testing system (Quark CPET; Cosmed) as previous studies described [11] (details of the settings are provided in the online data supplement).

Patients performed a maximal symptom-limited incremental cycle exercise testing with a full face mask in which 5 L/min oxygen

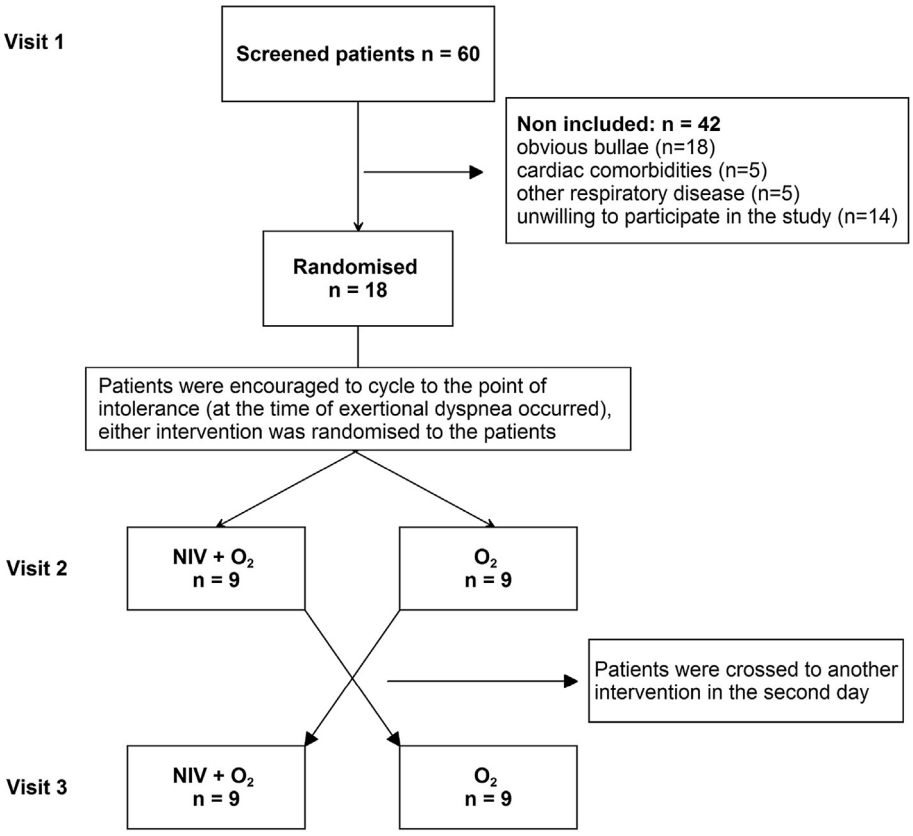

Fig. 1. Study flowchart.