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Clinical Trial Paper

Inspiratory muscle training during rehabilitation in successfully weaned hypercapnic patients with COPD

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ABSTRACT

Background: This study is aimed to evaluate the effect of inspiratory muscle training (IMT) added to rehabilitation in patients with chronic obstructive pulmonary disease (COPD) who remain hypercapnic and use non-invasive ventilation after successful weaning.
Methods: Patients received rehabilitation and were randomized to inspiratory muscle or sham training for 4 weeks. The primary outcome was distance walked within 6 min. Secondary outcomes were inspiratory muscle strength, endurance, lung function, and blood gas levels.
Results: Twenty-nine patients participated in this study. Walking distance of the sham group increased from 93 ± 52 m at baseline to 196 ± 85 m at week 4 ($p = 0.019$, 95% CI: 11–196 m). Patients in the IMT group significantly improved their walking distance from 94 ± 32 to 290 ± 75 m ($p < 0.0001$ [107–286 m]; $p = 0.04$ [3–186 m] for between-group comparison). Patients in the IMT group increased their maximal inspiratory pressure from −35 ± 8 to −55 ± 11 cmH_2O ($p = 0.001$; −6 to −33 cmH_2O), while the increase in the sham group failed to reach significance (−29 ± 10 to −37 ± 13 cmH_2O [−22 to 6 cmH_2O]). Inspiratory power increased from 9.6 ± 5.4 to 20.7 ± 9.7 joules/min (2.6–19.5 joules/min, $p = 0.003$) in the IMT group, while no significant change occurred in the sham group (7.6 ± 4.2 joules/min at study entry and 11.1 ± 6.9 joules/min [−5.2–12.3 joules/min] at study end).
Conclusions: Rehabilitation of successfully weaned patients with COPD and persistent hypercapnia significantly improves functional exercise capacity. Additional IMT significantly enhances functional exercise capacity and increases respiratory muscle strength and power.

1. Introduction

Inspiratory muscle training (IMT) in patients with chronic obstructive pulmonary disease (COPD) has been investigated for over 30 years [1]. IMT improves inspiratory muscle strength [2–9], inspiratory muscle endurance [8–12], walking endurance [5,8,9,12], dyspnea [8,9], and quality of life [3,8,9,12]. However too strenuous respiratory muscle exercise overloads the respiratory muscles and damages the muscle structure [13].

Hypercapnia is considered a sign of respiratory muscle overload in patients with COPD [14–16]. However, whether IMT can improve respiratory muscle performance in the presence of muscular overload is unclear. To date, studies on IMT in patients with COPD did not include hypercapnic individuals or did not report CO_2 levels [8]. Recent data on ventilator-dependent patients have suggested that IMT is feasible in this patient group and might improve weaning outcome when used alternating with ventilation [17]. Muscle wasting occurs early in critical illness [18]. Patients who have successfully been weaned from prolonged invasive mechanical ventilation suffer from persistent impaired inspiratory muscle strength and endurance [19].

This study aimed to evaluate the effect of IMT in hypercapnic patients with COPD who remain hypercapnic and require continued non-invasive ventilatory support after being weaned from invasive mechanical ventilation. The primary outcome of this study was endurance of the patients as measured by the 6-minute walking distance (6MWD). Secondary outcomes were respiratory muscle strength, respiratory muscle endurance (work and power), lung function, and blood gas levels.

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Abbreviations list

6MWD	Six minute walking distance
6MWT	Six minute walking test
ABG	Arterial blood gas analysis
BMI	Body mass index
CO2	Carbon dioxide
COPD	Chronic obstructive pulmonary disease
DLCO	Diffusing capacity of the lung for carbon monoxide
ECCS	European Community for Coal and Steel
EPAP	Expiratory positive airway pressure
FeV1	Forced expiratory volume in one second
FeV1% pred.	Percentage of the predicted forced exspiratory volume in one second
FeV1/FVC	Tiffeneau index
FVC % pred.	Percentage of the predicted forced vital capacity
HCT	Hematocrit
IMT	Inspiratory muscle training
IPAP	Inspiratory positive airway pressure
KCO %	Percentage of the predicted diffusion capacity
MV	Mechanical ventilation

2. Method

Patients with persistent hypercapnic respiratory failure who required non-invasive ventilation after prolonged weaning according to the criteria of Boles et al. [20] with the main diagnosis of COPD were eligible to enter the study. Subjects had to be admitted to our in-patient post-weaning rehabilitation unit, had to be ambulatory, cooperative, and physically able to participate in twice-daily physiotherapeutic sessions. Patients had to have confirmed COPD stage 3 or 4 by a lung function test (forced expiratory volume in 1 s [FeV1] < 50%, Fev1/forced vital capacity [FVC] < 70%), and had to be free of exacerbation. All patients received inhalation therapy with a long-acting beta agonist and a long-acting antimuscarinic agent throughout the investigational period. Exclusion criteria included renal impairment (serum creatinine levels $\geq$ 2 mg/dl) and severe cardiac impairment (ejection fraction < 40%).

2.1. Study design

The study was conducted in a randomized, controlled fashion. The treatment group received 4 weeks of IMT and the control group received sham IMT. Regular physiotherapy is the mainstay of rehabilitation after prolonged mechanical ventilation. Therefore, we designed a protocol where IMT and sham IMT were administered in addition to physiotherapy. During a 1-week screening phase prior to randomization, resting lung function, inspiratory muscle strength, inspiratory muscle endurance, 6MWD, and blood gas parameters were measured. After 2 weeks of training and at the end of study (4 weeks) these measurements were repeated. Parameters of non-invasive ventilation (NIV) and NIV compliance were recorded. Patients could use their noninvasive ventilators at night and during daytime resting periods, but not during training sessions. The responsible ethics committee of the medical council Westfalen-Lippe approved our protocol (permission number 2011-321-f-S) and participants provided informed consent prior to randomization. The investigation was registered in the NIH trial database (ClinicalTrials.gov; NCT00291460).

Patients were randomized to IMT or sham training by allocation of sealed envelopes. Training in either group was conducted once daily during weekdays under supervision of a respiratory therapist for 4 weeks. For active IMT training, we used a Respifit S Trainer (Biegler, Mauerbach, Austria). Active IMT training consisted of power and endurance exercises. Power training was adjusted to achieve a load range of 80% of the maximal inspiratory pressure (Pimax), while endurance training had a target range of 60% of Pimax. The Respifit S Trainer is capable of measuring pressure and determines flow based on the preselected resistance. Training with this device is based on Pimax determined by the device itself from a series of six maximal inspiratory maneuvers. For training purposes, we measured Pimax weekly and made adjustments to the training loads for the consecutive week. Power training consisted of 20 successful inspiratory exercises where the patient had to maintain an inspiratory pressure of at least 80% of Pimax for 1 s. During this exercise, the patient received feedback though a dumbbell on the device display, which had to be moved and kept above a target line. Pauses between single attempts were kept at 20–30 s. For the endurance exercise, the patient had to accomplish minute ventilation through a pre-selected resistance at negative inspiratory pressure that represented 60% of Pimax. Display graphics provided visual feedback to the patient in the form of a balloon, which was raised during inspiration and fell during expiration, and had to be maintained within a certain range. Three 1-minute endurance exercises were interrupted by a 3-minute recovery time.

Sham training was conducted using the Threshold IMT device (Threshold IMT; Philips-Respironics, Pittsburgh, PA, USA), which was set to a sub-therapeutic setting (5 cm H_2O). The protocol for the sham training group consisted of eight 1-minute sessions where the patient was instructed to breathe through the device with his or her normal respiratory pattern, while the nostrils were occluded with a nose clip. Every training session (sham and IMT) was supervised by a respiratory therapist.

Parallel to the inspiratory muscle or sham training, all of the patients participated in twice daily, hour-long physiotherapy group sessions in the rehabilitation gym. Physiotherapy sessions included training with arm and leg ergometers, as well as weight training. Additionally, every patient participated in daily ergotherapy group sessions lasting 1 h each to improve fine motor skills. Every training unit was supervised by a physiotherapist who was not informed about the patient group allocation.

Training of subjects, measurement throughout the investigational period, and data collection were performed by different investigators. Blinding of subjects was ensured by private (one to one) training sessions that were directed by a respiratory therapist.

2.2. Measurements

All measurements were performed at study entry (day 0), after 2 weeks (day 14), and after 4 weeks (day 28) of IMT.

Spirometry, body plethysmography, and measurement of the diffusion capacity were performed using a Jaeger Masterscreen (Jaeger/CareFusion, Hoechberg, Germany). Predicted values for static and dynamic lung function parameters were calculated according to the European Community for Coal and Steel (ECCS) [21]. The diffusing capacity of the lung for carbon monoxide (DLCO) was performed according to the American Thoraxic Society (ATS) recommendations [22]. Measurements were corrected for alveolar ventilation (DLCO/VA [KCO]). Arterial blood gas samples were taken from the arterialized earlobe (Finalgon Extra Strong©; Boehringer Ingelheim Austria GmbH, Vienna, Austria) for immediate analysis (MD 300D; Oxigeno Healthcare, D-85098 Grossmehring, Germany).

Inspiratory pressure during the maximal inspiratory maneuver starting from residual volume [23] was measured with the Jaeger Masterscreen pressure module (Jaeger/CareFusion, Hoechberg, Germany).