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The effect of bronchodilators administered via aerochamber or a nebulizer on inspiratory lung function parameters

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Summary
Background: In chronic obstructive pulmonary disease (COPD) the clinical efficacy of bronchodilator therapy delivered via a nebulizer versus an aerochamber on FEV_1 is controversial. No studies comparing changes in inspiratory pulmonary function parameters (ILPs) using these inhaler devices are currently available. This information might be of interest because due to dynamic bronchial compression, the relationship between the ILPs and dyspnea is more reliable than that between FEV_1 and dyspnea. Therefore, our study aimed to investigate whether changes in ILPs after use of these inhaler devices were similar to the changes in FEV_1 and correlate with VAS (Visual Analogue Scale).
Methods: Forty-one stable COPD patients participated in a crossover trial. Spirometry was performed before and after two puffs Combivent (200 mcg salbutamol and 20 mcg ipratropium per puff) using an aerochamber or 2 mL of Combivent (2.5 mg salbutamol and 250 mcg ipratropium per mL) using a nebulizer. Differences in lung function parameters and changes in VAS were measured.
Results: ILP values improved significantly from baseline after Combivent administration using both devices ($p \leq 0.004$). With both devices, the mean percent changes were significantly greater for FEV_1 than the ILPs ($p \leq 0.003$), except for IC ($p = 0.19$). The mean VAS score did not differ significantly between the devices ($p = 0.33$), but significant correlations were found between the VAS and forced inspiratory flow at 50% of the vital capacity (FIF_{50}) and peak inspiratory flow (PIF) when a nebulizer was used. With an aerochamber, no significant

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correlations between lung function parameters and VAS were found.
Conclusions: The present study demonstrates that ILPs improved significantly after using either device. Although significant correlations were found between the VAS and FIF_{50} and PIF for the nebulizer, in stable COPD patients, the pMDI plus spacer is a better route of administration than a nebulizer.

Introduction

In chronic obstructive pulmonary disease (COPD), bronchodilator therapy using a dry powder inhaler (DPI) or a metered-dose inhaler (pMDI) is more convenient and cost effective than nebulizer therapy.[1] The DPI is breath-activated by inspiration and does not require hand-lung coordination. However, the pMDI, the most commonly used device, is technique dependent because the pMDI requires proper hand-lung coordination. Nebulizers are used for acute therapy in emergency departments and hospitals but are also available for home use. For nebulizers, no special timing or coordination is needed, and they require minimal patient effort. Many studies on bronchodilator therapy using a DPI, pMDI with a spacer and nebulizers for treating COPD have concluded that these delivery devices are equally effective, as measured by changes in the forced expiratory volume in 1 s (FEV_1).[2–7] In contrast, some studies have shown that nebulizers are superior to pMDIs based on improvements in spirometric values and symptoms.[8,9] In two studies, COPD patients were found to benefit from home nebulizer therapy.[10,11]

The relationship between dyspnea scores and FEV_1 appears to be poor.[12,13] Because dynamic compression of the airways during forced expiration may mask the effects of bronchodilators on FEV_1, we are interested in measuring inspiratory lung function parameters (ILPs) when dynamic compression of the bronchi is absent.[14–17] We hypothesized that because of dynamic bronchial compression, the relationship between the ILPs and dyspnea is more reliable than the relationship between FEV_1 and dyspnea. Our interest in changes in the ILPs, as measured by changes in the forced inspiratory volume in 1 s (FIV_1), inspiratory capacity (IC), forced inspiratory flow at 50% of the vital capacity (FIF_{50}) and peak inspiratory flow (PIF), increased when Taube et al. determined a more significant correlation between FIV_1 changes and dyspnea using the visual analogue scale (VAS) ($r = 0.730$, $p < 0.001$) than between the change in FEV_1 and VAS ($r = 0.389$, $p < 0.01$) after administration of the bronchodilator salbutamol to patients with severe to very severe COPD.[14] Other studies have shown changes in dyspnea symptoms and in forced inspiratory volumes following bronchodilator therapy at rest and changes in IC during exercise.[18–24] In our previous study, in subjects with COPD, we found that the ILPs, FEV_1 and VAS score significantly improved after bronchodilator inhalation.[25] However, no studies investigating changes in ILPs and dyspnea upon bronchodilator administration using different inhaler delivery devices are currently available. Therefore, our study aimed to investigate whether ILPs show equal changes in FEV_1 after administering bronchodilators using a pMDI and an aerochamber or a nebulizer and whether any improvement in lung function parameters correlated significantly with changes in dyspnea symptoms as measured by the VAS.

Methods

Patients

From January 2007 to August 2007, 41 stable COPD patients (23 males and 18 females) from our outpatient clinic were recruited. The subjects had either severe or very severe COPD ($FEV_1 < 50\%$ predicted) according to the Global Initiative for Chronic Obstructive Lung Disease (GOLD) guidelines.[26] The inclusion criteria were stable COPD, age of 40–80 years, current or former smoker with more than a 10 pack-year history, and reversibility of $FEV_1 < 12\%$ of the predicted normal value and <200 mL.[27,28] Stable COPD was defined as the absence of exacerbations within 2 months prior to the study, no changes in COPD medications in the last 8 weeks, no use of oral corticosteroids in the last 2 months and no use of antibiotics in the last month. Patients on oxygen and patients with allergic rhinitis, asthma, heart disease, neuromuscular disorders, malignancy or an inability to respond to the questionnaires were excluded. The medical ethical commission of Arnhem–Nijmegen in the Netherlands gave permission for this study, and all the patients provided written informed consent.

Study design

A randomized, crossover trial comparing the two administration methods of inhaled Combivent therapy (i.e., a nebulizer or a pMDI with an aerochamber) was conducted. The sequence order was determined according to a computer-generated randomization list. Each subject participated in the study on two different days within a two-week period. On each study day, inspiratory and expiratory spirometric tests with reversibility testing were performed with Combivent administered using a compressed-air nebulizer (jet nebulizer) or a pMDI.

Pulmonary function testing

All the subjects were asked not to use short-term bronchodilators for at least 6 h prior to the study and long-term bronchodilators for at least 12 h prior to the study. Tiotropium and theophylline were not allowed within 24 h prior to spirometric testing.