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Case Report

Early COPD diagnosis and treatment: A case report

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ABSTRACT

Chronic obstructive pulmonary disease (COPD) refers to a group of widely diffuse diseases that cause airflow blockage characterized by persistent respiratory symptoms such as dyspnea, chronic cough, recurrent wheezing, chronic sputum production, and progressive restricted airflow associated with exacerbations. COPD is the third leading cause of death worldwide and can only be treated not cured.

Pulmonary function tests do not permit the identification of initial obstructive airways disease. Forced expiratory flow (FEF_{25-75}), which calculates obstruction severity at small and medium bronchial airways levels, allows an early COPD diagnosis.

We report a 72-year-old ex-smoker male not exposed to occupational risk with symptoms suggesting early COPD. Baseline pulmonary function tests were normal, except FEF_{25-75}. The patient did not respond to the first 6 months of treatment with long-acting muscarinic antagonist (LAMA), whereas he showed a clear clinical and FEF_{25-75} response to 1-year treatment with LAMA associated with long-acting β2 agonist (LABA).

This clinical case report highlights the usefulness of FEF_{25-75} evaluation in early COPD diagnosis and monitoring and confirms the efficacy of LAMA–LABA association for small airways obstruction treatment.

1. Introduction

Chronic obstructive pulmonary disease (COPD) refers to a group of widely diffuse diseases, including emphysema and chronic bronchitis, that cause airflow blockage. It is characterized by persistent respiratory symptoms such as dyspnea, chronic cough, chronic production of sputum, recurrent wheezing, and restricted airflow [1]. COPD is characterized by airflow limitation that is not fully reversible. Airflow limitation is progressive and associated with abnormal inflammatory response of the lungs, particularly caused by cigarette smoking [2].

COPD is the third leading cause of death worldwide because of associated comorbidities such as smoking, environmental pollution, and occupational risk [3]. Despite accurate studies and clinical trials analyzing COPD etiology and phenotypes, currently it can only be treated not cured.

Although COPD affects the lungs, it causes systemic damages with heart involvement developing pulmonary hypertension and cor pulmonale [4].

The importance of exacerbations is closely related to COPD clinical course, and their reduction increases the outcome and improves the quality of life (QOL). Exacerbations are events requiring therapy with antibiotics, systemic steroids, or both. The severity

Abbreviations: COPD, chronic obstructive pulmonary disease; LAMA, long acting muscarinic antagonist; LABA, long acting β2-receptor agonist; FEF 25-75, forced expiratory flow 25-75%.

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of exacerbations is defined by the location of care such as home and emergency room or hospital. Mild exacerbations involve upper airways and are treated with adjustments in bronchodilator or inhaled corticosteroid therapy, and moderate exacerbations involve lower respiratory tracts and are treated with antibiotics and systemic corticosteroids. Based on the Global Initiative for Chronic Obstructive Lung Disease (GOLD) guidelines [1], the COPD classification of airflow limitation severity is defined as follows: (i) mild forced expiratory volume in 1 second (FEV_1) ≥ 80% predicted; (ii) moderate 50% ≤ FEV_1 < 80% predicted; (iii) severe 30% ≤ FEV_1 < 50% predicted; and (iv) very severe FEV_1 < 30% predicted. An additional sensitive parameter to evaluate early airflow obstruction in peripheral airways is forced expiratory flow (FEF) rate between 25% and 75% of forced vital capacity (FVC). The normal value of $FEF_{25–75\%}$ depends on age and height, and the results of $FEF_{25–75\%}$ are little effort-dependent and representative of air movement through small airways [5,6].

The aim of this clinical case is to highlight the usefulness of pulmonary function tests and particularly $FEF_{25–75\%}$ in early COPD diagnosis to improve therapeutic approach, reduce acute exacerbations, QOL, and disease outcome.

2. Case report

A 72-year-old ex-smoker male, 5 pack-years, was admitted with exertional dyspnea lasting 6 months and productive cough lasting 3 months suggesting early COPD. The patient was not exposed to occupational risk and was neither affected by allergy nor other relevant comorbidities. Physical chest examination showed fine rhonchi without wheezing and crackling sounds. Cyanosis was absent, and pulse oximetry was 96% in room air. No signs of cardiovascular failure were detected.

Pulmonary function tests at baseline, including FEV_1 and FEV_1/FVC ratio, were in the normal range and did not suggest an initial obstructive airways disease. Note that the FEF_{25-75} values were suggestive of moderate small airways obstruction (Table 1). The patient was first treated with long-acting muscarinic antagonist (LAMA – umeclidinium bromide 65 mcg/daily). However, dyspnea and cough did not ameliorate, and the patient suffered from exacerbation responsive to antibiotics. Spirometry after 6 months of LAMA therapy showed a decrease of FEF_{25-75}, especially of FEF_{25} from 59% to 50%. Then, the treatment was modified using the association of LAMA with long-acting β2 agonist (LABA – vilanterol 22 mcg/daily) according to GOLD guidelines. Patient evaluation after 12 months of LAMA–LABA therapy revealed excellent response with decreased dyspnea and cough and absence of exacerbations. Spirometry showed clear regression of small airways obstructive parameters. Notably FEF_{25} increased from 50% to 62% (Table 1 and Fig. 1).

3. Discussion

In the reported case, the patient's symptoms such as productive cough associated with dyspnea under exertion worsened and were poorly controlled, particularly in the course of an exacerbation occurring during 6-month LAMA therapy. The persistent symptoms required more effective treatment and led, according to GOLD guidelines, to a therapeutic change replacing LAMA alone with LAMA–LABA association [7] (Fig. 2).

Table 1
FEF_{25-75} values before and after treatment.

	Baseline	After 6 months of LAMA therapy	After 1 year of LAMA–LABA therapy
FEF_{25}	59	50	62
FEF_{50}	42	41	42
FEF_{75}	43	43	47

FEF: forced expiratory flow; LAMA: long-acting muscarinic antagonist; LABA: long-acting β2 agonist.

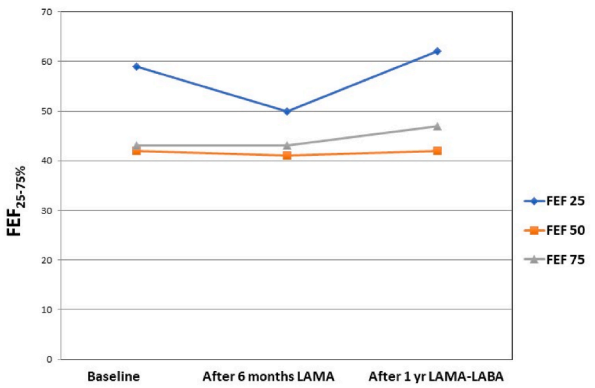

Fig. 1. FEF_{25-75} behavior during LAMA and LAMA–LABA treatment.

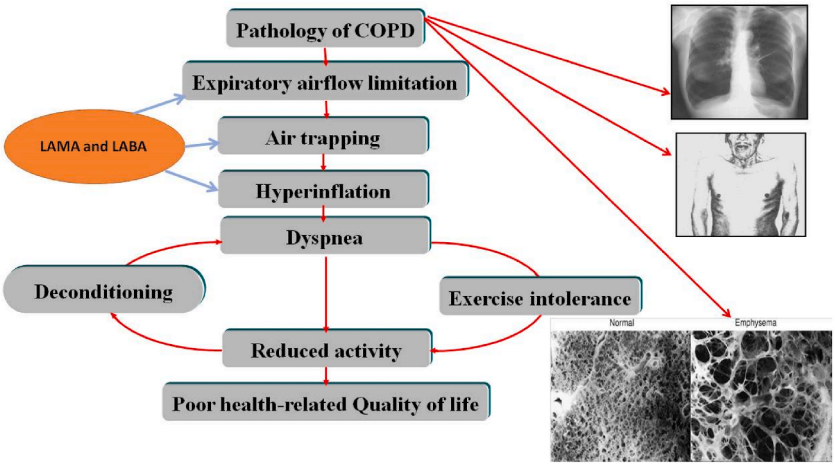

Fig. 2. Efficacy of LAMA–LABA therapy in COPD.

The efficacy of umeclidinium plus vilanterol led to an evident reduction in symptoms avoiding COPD exacerbations at 6, 12, and 18 months of follow-up. The therapeutic benefit was confirmed by spirometry, particularly by FEF_{25-75} increase. These findings confirm the usefulness of the association of antimuscarinic agent with LABA in COPD treatment [1].

Finding normal parameters in pulmonary function tests does not permit, as in this case, to identify an initial obstructive airways disease. Only $FEF_{25-75,}$ which calculates obstruction severity at several small and medium bronchial airways levels, allows an early COPD diagnosis.

Recently, Kwon Sun et al. [5] confirmed that FEF_{25-75} is reduced in early COPD and associated with small airway disease**.** Interestingly, the previously performed Boston early-onset COPD study identified FEF_{25-75} as a potential indicator of genetic susceptibility to develop COPD. However, the same authors suggested that this measure does not provide information beyond FEV_1/FVC for demonstrating small airways disease [8]**.**

Note that many clinical trials assessing COPD diagnosis and treatment used only FVC and FEV_1 to evaluate the severity of airways obstruction and therapeutic response [3,9–14].

The hallmarks of the present case are that it (i) underlines that FEF_{25-75} decrease is the earliest and sensitive pulmonary function test parameter suggesting COPD diagnosis; (ii) FEF_{25-75} decrease reflects the loss of elastic recoil and air trapping from emphysema and COPD small airways; and (iii) highlights that lower FEF_{25-75} is closely associated with an increase in COPD severity, providing new knowledge of pathophysiological and anatomical mechanisms that lead to clinical outcomes in COPD [6].

Authors' contributions

RGC and GB: conceptualization and investigation. FP: reviewing and editing.

Ethics approval

Not applicable.

Consent to publication

Not applicable.

Availability of data and material

Not applicable.

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Declaration of competing interest

The Authors do not have any conflict of interest.

Abbreviations

COPD	chronic obstructive pulmonary disease
FEF	forced expiratory flow
FEV_1	forced expiratory volume in 1 second
FVC	forced vital capacity
GOLD	Global Initiative for Chronic Obstructive Lung Disease
LABA	long-acting β2 agonist
LAMA	long-acting muscarinic antagonist
QOL:	quality of life

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