Coexisting Heart Failure and Chronic Obstructive Pulmonary Disease: Report of Two Cases Treated with Indacaterol/Glycopyrronium

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Abstract

Chronic obstructive pulmonary disease (COPD) is a major cause of morbidity and mortality worldwide, and it is associated with a high economic burden. Heart failure shares some general symptoms with COPD; thus, diagnosing COPD is difficult in subjects with a history of heart failure, and spirometry is mandatory for confirmation. Moreover, COPD is a highly prevalent comorbidity negatively impacting the outcome of heart failure patients. We document here the treatment with indacaterol/glycopyrronium in 2 patients with concomitant COPD and heart failure. Overall, the combination of indacaterol and glycopyrronium resulted in a reciprocal potentiation with a maximal bronchodilatory effect.

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Introduction

Chronic obstructive pulmonary disease (COPD) is a major cause of morbidity and mortality worldwide, and it is associated with a high economic burden. In 2014, ap-

proximately 15 million Americans were diagnosed with COPD [1]. Its prevalence increases with age, ranging from 2.6% in adults aged 18–34 years to 12.3% in 75-year-old subjects [1]. It has been reported that >50% of adults with some degrees of pulmonary dysfunction ignore their disease; thus, COPD prevalence might even be higher than estimated [2]. COPD is associated with a reduction in the working abilities of the individuals due to functional limitations [3].

Of note, COPD shares some general symptoms with heart failure, and thus diagnosing COPD becomes even more challenging in patients with a history of heart disease. In turn, COPD may be associated with a worsening of heart failure outcomes [4].

We report here the cases of 2 patients with concomitant COPD and heart failure, successfully treated with indacaterol/glycopyrronium for their respiratory disease.

Case Descriptions

Case 1

We present the case of a 67-year-old man with multiple cardiovascular risk factors (active smoker, arterial hypertension, diabetes mellitus, chronic atrial fibrillation, and hypothyroidism secondary to chronic thyroiditis currently treated with hormonal therapy). In 2014, he was hospitalized for acute respiratory failure, and he received a diagnosis of heart failure. At that time, echocardiography

Table 1. Respiratory parameters in patient 1

	Baseline	6 months
FEV ₁ , %	61	89
FEV ₁ /FVC, %	55	95
CAT score	16	8

FEV₁, forced expiratory volume in the first second; FVC, forced vital capacity; FEV₁/FVC, Tiffeneau index; CAT, COPD Assessment Test.

Table 3. Respiratory parameters in patient 2

	Baseline	6 months
FEV ₁ , %	66	80
FEV ₁ /FVC, %	60	70
CAT score	25	14

FEV₁, forced expiratory volume in the first second; FVC, forced vital capacity; FEV₁/FVC, Tiffeneau index; CAT, COPD Assessment Test

revealed the presence of concentric left ventricular hypertrophy with a preserved ejection fraction of 52%, with relevant valvulopathies affecting both the mitral valve (mild steno-insufficiency) and the aortic valve (mild-to-moderate aortic regurgitation), highly suspicious of rheumatic origin. Another finding was moderate biatrial enlargement. On spirometry, forced expiratory volume in the first second (FEV₁) was 61% of the predicted value, with a FEV₁/forced vital capacity (FVC) ratio of 55%; the COPD Assessment Test (CAT) was performed and the final score was 18. The patient was discharged on the following medications: ramipril 10 mg/day, bisoprolol 5 mg/day, digoxin 0.125 mg/day, furosemide 50 mg/day, warfarin 5 mg/day, tiotropium bromide 18 µg/day, and levothyroxine 75 mcg/day. The patient was re-hospitalized twice in 2015 and 2016 for pneumonia, and initial signs of heart failure were noted, secondary to the progression of the valvular diseases. In particular, the patient presented New York Heart Association (NYHA) functional class III symptoms in 2017 (marked limitation of physical activity, with less than ordinary activity causing fatigue, palpitation, or dyspnea), with a worsened left ventricular function.

The patient was excluded from valve replacement surgery due to anesthesiological risk. Spirometry was unchanged, with a CAT score of 16.

We decided to add the bronchodilator combination indacaterol/glycopyrronium (85/43 µg/day) to the patient's therapy, and after 6 months with this therapy, his FEV₁ improved to 89% of the predicted value with a FEV₁/FVC ratio of 75% and a CAT score of 8. Additionally, the sinus rhythm was restored with a heart rate of 62 bpm, and echocardiography improved.

Tables 1 and 2 depict the results of the main tests performed in our patient at baseline (start of indacaterol/glycopyrronium) and

Table 2. Clinical and laboratory parameters in patient 1

	Baseline	6 months
Systolic BP, mm Hg	131	128
Diastolic BP, mm Hg	76	74
Heart rate, bpm	68	69
EF, %	52	58
BNP, pg/mL	150	100

BP, blood pressure; EF, ejection fraction.

after 6 months of treatment; all parameters were confirmed after further 6 months of follow-up.

Case 2

An 80-year-old woman, who was an active smoker with a history of coronary artery disease, had been treated in 2001 with a coronary angioplasty on the left main coronary artery for moderate stenosis, conditioning angina on exertion.

In 2006 during regular follow-up, she was diagnosed with COPD. Spirometry revealed a FEV₁ of 68% of the predicted value, and she was immediately advised to start a therapeutic regimen combining fluticasone and salmeterol, with clinical benefit. However, in 2014, she experienced several bronchitis exacerbations, needing oral steroid cycles. In 2015, the patient was re-hospitalized for concomitant heart failure, secondary to atrial fibrillation, and pneumonia. Echocardiography revealed hypertensive heart disease with moderate diastolic dysfunction, biatrial enlargement, moderate tricuspid regurgitation with an estimated systolic pulmonary artery pressure of 45 mm Hg (normal range <35 mm Hg); ejection fraction was preserved (54%). BNP was markedly increased (1,500 pg/mL). After all appropriate treatments, the patient was discharged home with NYHA III with the following therapies: pantoprazole 20 mg/day, amlodipine 5 mg/day, atorvastatin 20 mg/day, allopurinol 300 mg/day, doxazosin 2 mg/day, bisoprolol 5 mg/day, furosemide 125 mg/day, irbesartan 300 mg/day, acetylsalicylic acid 100 mg/day, 14 units of slow insulin, apixaban 5 mg b.i.d., and the association indacaterol/glycopyrronium at the dose of 85/43 µg/day.

Importantly, FEV₁ at 30 days was 66% of the predicted value with a Tiffeneau index (FEV₁/FVC) of 60% (normal value >80%). The CAT score was 25. At the 6-month follow-up, we registered some clinical improvements with all the assessed parameters demonstrating a favorable trend (systolic pulmonary artery pressure 30 mm Hg with only mild tricuspid regurgitation, FEV₁ 80% of the predicted value, Tiffeneau index 70%, and CAT score 14; Table 3), with a persistent NYHA II class. The combination therapy with indacaterol/glycopyrronium was overall well tolerated.

Discussion

COPD induces several cardiovascular comorbidities and exerts a negative prognostic effect on the outcomes of heart failure patients [4]. We presented 2 cases of pa-

tients with concomitant COPD and heart failure treated with indacaterol/glycopyrronium for their respiratory disease. The combination of indacaterol and glycopyrronium results in reciprocal potentiation with a maximal bronchodilatory effect [5], by several possible mechanisms.

As already demonstrated in the FLAME and CRYSTAL studies, the combination indacaterol/glycopyrronium is superior to other treatments in improving dyspnea rapidly [6–8]. This quality was also evident in our patients in whom dyspnea was significantly retrieved when the combination was added to the patients' therapies, as expressed by the reduction of the CAT score.

Moreover, several concerns exist about the use of the long-acting beta-agonist (LABA) and long-acting muscarinic antagonist (LAMA) combination in patients with

any type of cardiac abnormalities (arrhythmias, heart failure, coronary disease). Caution is recommended in these cases. However, in this report we showed that their use is feasible in patients with cardiac disorders.

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Financial Disclosure and Conflicts of Interest

The authors have no conflict of interest directly relevant to this paper.

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