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Roflumilast is safe and effective in improving symptoms and lung function in severe COPD

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ABSTRACT: ***Roflumilast is safe and effective in improving symptoms and lung function in severe COPD. M. Bonini, P. Palange.***

The case of a 66-year-old man with severe chronic obstructive pulmonary disease (COPD) is presented. Diagnosis was based on baseline pulmonary function tests (PFTs) and clinical examination. Therapy with tiotropium 18 µg (once daily) and salmeterol/fluticasone 50/500 µg (twice daily) failed to achieve optimal disease control. Roflumilast (Daxas) 500 µg once daily was therefore added and a progressive improvement in the patient's condition was observed during the 1-year follow-up. In this patient with severe COPD, roflumilast represented a safe and effective therapeutic strategy for managing clinical symptoms and for significantly improving lung function parameters.
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Keywords: Roflumilast, COPD, Case report, Lung function.

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Case Report

A 66-year-old man presented in our Department having suffered, in the last five years, from the onset and progressive worsening of exertional dyspnoea.

The patient had accessed the emergency room in the previous month due to high fever and productive cough, which resolved after antibiotic therapy. Clinical history revealed no familiarity of systemic, allergic and respiratory diseases. The patient was a former heavy smoker (30 pack-years), worked as a painter and was a moderate alcohol consumer. No relevant pathological conditions were reported, apart from sporadic episodes of extrasystolia.

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The patient was not following any pharmacological therapy at the time of the first visit. At clinical evaluation, the patient was eupneic and apyretic; blood pressure was 120/80 mmHg and heart rate was 68 beats/min; height was 160 cm, weight was 57 Kg and BMI was 22.3. Chest physical examination showed a significant reduction in physiological lung sounds with bilateral diffuse expiratory wheezing. Baseline pulmonary function tests (PFTs) showed a very severe bronchial obstruction: forced expiratory volume in the first second (FEV_1) was 0.62 L (25% of predicted), FEV_1/FVC (forced vital capacity) was 59%; FEV_1 recorded after the bronchial reversibility test (salbutamol 400 mg) increased by 23% (30% of predicted). Oxygen saturation was 99%. Chest X-rays showed an increased bronchovascular marking in the absence of pleuroparenchymal lesions.

The patient was therefore prescribed the following drugs as inhalers: tiotropium 18 µg once daily and salmeterol/fluticasone 50/500 µg twice daily. Furthermore, the patient was advised to undergo a cardiovascular screening (echocardiography, Holter and stress electrocardiogram) and a follow-up visit was scheduled after 3 months.

At the new clinical evaluation, the patient referred the persistence of exertional dyspnoea and the occurrence of a second acute disease exacerbation with high fever and productive cough, treated with oral antibiotics. PFT showed only a slight improvement of lung function: FVC 1.33 L (42% of predicted), FEV_1 0.73 L (29% of predicted), FEV_1/FVC 54%; post-bronchodilator FEV_1 increased by 19% (34.1% predicted). Oxygen saturation was 97%. Chest physical examination did not change compared to the previous one, a part from the presence at rest of sporadic isolated monomorphic ventricular premature beats in the presence of a normal echocardiography.

The persistence of symptoms and wheezing, as well as evidence of recurring exacerbations showed an unsatisfactory disease control. Moreover, the high increase in post-bronchodilator FEV_1 (+23% and +19%) suggested a status of ongoing bronchosphasm

Table 1. - Main functional and clinical parameters recorded before roflumilast treatment and during the 1-year follow-up

Parameters	Visit 1 (-3 months)	Visit 2 (Time 0) Start of roflumilast	Visit 3 (6 months)	Visit 4 (12 months)
FVC	32%	42%	60%	64%
FEV_1	25%	29%	41%	49%
FEV_1/FVC	59%	54%	54%	59%
FEV_1 post BD	+23%	+19%	na	na
Sat. O_2	99%	97%	98%	98%
Exacerbations per year	1	2	0	0

FVC, forced vital capacity; **FEV_1**, forced expiratory volume in the first second; **BD**, bronchodilator test; **Sat. O_2**, oxygen saturation; **na**, not available.

associated with bronchial inflammation. On the basis of the available clinical and functional parameters and in accordance with "Global Obstructive Lung Disease (GOLD) guidelines" [1], a diagnosis of very severe (stage D) chronic obstructive pulmonary disease (COPD) was made.

It was therefore decided to add roflumilast 500 µg once daily to the previously prescribed treatment [2]. The patient, in fact, completely fulfilled both clinical and functional criteria requested to be administered roflumilast: severe COPD phenotype (FEV_1 post-bronchodilator <50%), symptoms not under control and history of frequent exacerbations (>2/year). The patient was therefore listed in the Italian Drug Agency monitoring register [3].

On subsequent clinical evaluations, the patient showed a significant improvement in respiratory symptoms with a consistent reduction of exertional dyspnoea and no significant side effects. No weight loss was recorded, although a more frequent alvus was reported. In view of the above clinical benefits and of the lack of serious adverse events, it was decided to continue roflumilast 500 µg once daily as add-on therapy. After three months of treatment with roflumilast the therapeutic plan was renewed in accordance with requirements set by the Italian Drug Agency [3].

After six months of roflumilast therapy, respiratory symptoms were progressively improving and no exacerbations occurred. At the chest physical examination no adjunct pathological sounds were present any more. Pulmonary function tests were further improved: FVC 1.88 L (60% of predicted), FEV_1 1.02 L (41% of predicted).

Twelve months after his first clinical evaluation the patient was re-evaluated. Respiratory symptoms appeared to be completely under control and no exacerbations occurred since the previous visit. Body weight was still stable and alvus frequency was now regular. Chest physical examination revealed no pathological sounds. Oxygen saturation was 98%. PFT showed a further improvement in lung function (FVC 64%, FEV_1 49%).

Discussion

Interestingly, on top of the widely reported positive effects on respiratory symptoms [4], our patient showed a progressive significant improvement in lung function during the roflumilast treatment period. Baseline FEV_1 almost doubled over a 12-month treatment period, from 25% to 49%. Similarly, FVC increased up to 64%. A further important outcome was represented by the complete absence of exacerbations, since beginning of roflumilast therapy [5]. Moreover, except for a transient change in the alvus frequency, no adverse events were experienced [4, 6].

In conclusion, this one-year follow-up case report shows that roflumilast represents a safe and effective therapeutic strategy in severe COPD patients, not only for managing clinical symptoms and exacerbation rates, as already consistently reported, but also for significantly improving lung function parameters.

Riassunto

Viene di seguito presentato il caso di un uomo di 66 anni con broncopneumopatia cronica ostruttiva (BPCO). La diagnosi veniva posta sulla base dei test di funzionalità polmonare in condizioni di base e l'esame clinico. Il trattamento con tiotropio 18 µg (una volta al giorno) e salmeterolo/fluticasone 50/500 µg (due volte al giorno) non consentiva un controllo ottimale della malattia. Roflumilast (Daxas) 500 µg una volta al giorno veniva quindi aggiunto alla terapia. Da allora, è stato osservato un progressivo miglioramento delle condizioni del paziente durante un anno di follow-up. In questo paziente con BPCO di grado grave, la terapia

con roflumilast si è dimostrata una strategia sicura ed efficace, in grado di migliorare sia i sintomi clinici che i parametri di funzionalità respiratoria.

Parole chiave: Roflumilast, BPCO, Caso clinico, Funzionalità polmonare.

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