



# Prescription is not enough: the importance of adherence to pharmacological treatment of COPD

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COPD is a chronic and progressive disease characterized by persistent respiratory symptoms and reduction in airflow, secondary to an abnormal inflammatory response of the lungs to the inhalation of noxious particles or toxic gases, and influenced by host factors including abnormal lung development and genetic susceptibility. In addition to affecting the lungs, COPD is also accompanied by systemic manifestations that have a serious impact on the quality of life and survival of patients.<sup>(1)</sup>

Data on COPD prevalence vary widely due to differences in survey methods and diagnostic criteria. Despite the complexities, data are emerging that enable more accurate estimates of COPD prevalence. The Latin American Project for the Investigation of Obstructive Lung Disease (PLATINO)<sup>(2)</sup> investigated the prevalence of post-bronchodilator airflow limitation among individuals > 40 years of age living in five Latin American countries. The prevalences ranged from 7.8% in Mexico City (Mexico) to 19.7% in Montevideo (Uruguay).<sup>(2)</sup>

According to the WHO,<sup>(3)</sup> COPD is the third leading cause of death in the world, and 80% of these deaths occur in low- and middle-income countries. COPD represents a considerable human burden due to its high prevalence, morbidity, and mortality, creating a formidable challenge for health care systems.<sup>(3,4)</sup>

Patients with COPD usually present with respiratory symptoms, comorbidities, decline in lung function, and episodes of acute exacerbation. The severity and frequency of exacerbations are strongly correlated with patient prognosis. Patients with a higher frequency of exacerbations have an accelerated decline in lung function, poor health-related quality of life, and increased mortality. The management of the disease requires early diagnosis, removal of risk factors, as well as pharmacological and nonpharmacological treatments.<sup>(1,4)</sup>

Pharmacological therapy for stable COPD includes inhaled long-acting bronchodilators (long-acting muscarinic antagonists and long-acting  $\beta_2$  agonists) that can be used individually or in combination with inhaled corticosteroids as dual or triple therapy. Increasing evidence from randomized controlled trials suggests that pharmacological treatments may have meaningful benefits on a range of endpoints including dyspnea, health-related quality of life, frequency of exacerbations, and mortality.<sup>(5-7)</sup>

In this issue of the Brazilian Journal of Pulmonology, Moreira et al.<sup>(8)</sup> have reported an association between nonadherence to pharmacological treatment and overall mortality among patients with COPD monitored at a public disease management program from the Brazilian public health care system. They observed, among

moderate-to-severe COPD patients, an overall adherence rate of 87.2%. Using an adjusted Cox regression model, the investigators observed that the chance of mortality was almost two times greater in nonadherent patients.

The authors recognize that they used an indirect method to assess treatment adherence. However, it is important to note that there is no gold standard method to assess adherence to inhaled medications.<sup>(9)</sup> One of the most accurate method is directly observed administration, but this is largely impractical in the setting of clinical practice and research protocols.

The increasing advances in medicine result in benefits for human health, although the costs are also increasing and often reach an economically unsustainable point. Therefore, it is important that resources are used efficiently to benefit as many patients as possible.

Guidelines for the treatment of COPD and other diseases are primarily based on evidence gathered from randomized controlled trials that assess the efficacy of drugs.<sup>(1)</sup> However, evidence gathered from real-life observational studies that assess effectiveness is also important. Nonadherence is pointed out as an important contributor to reduce effectiveness.

Nonadherence to COPD treatment can be primary, when the patient does not follow the prescription, or secondary, when the medication is not used in the recommended dose or the inhalation device is used incorrectly. Both primary and secondary types of nonadherence contribute to reducing the effectiveness of treatment.<sup>(9,10)</sup>

Several factors are identified as modifiers of the level of adherence, including those related to the drugs and those related to the patient. The quality of communication between prescribers and patients influences the level of adherence to treatment. Good quality communication with information about the disease, drugs, and device use techniques can improve primary and secondary adherence.<sup>(9,10)</sup>

The route of administration can also influence adherence. Overall, oral drugs have higher adherence rates than do inhaled drugs of the same class. This is particularly a problem for patients with asthma or COPD, since the use of inhaled medications is desirable because of the lower incidence of side effects. Errors in the inhalation technique are common and interfere with the proper administration of the drug.<sup>(9,10)</sup>

The Brazilian public health care system provides access to inhaled medications, free of charge, for COPD patients in order to reduce the heavy social and economic burden of the disease.

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We consider that the results in the study by Moreira et al.<sup>(8)</sup> are highly important to alert physicians and health care managers to the need of assessing the level of primary and secondary adherence and to implement actions aimed at increasing the effectiveness of treatment and efficiency of health care.

## AUTHOR CONTRIBUTIONS

The authors equally contributed to this work.

## CONFLICT OF INTEREST

None declared.

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