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Bronchodilator treatment for COPD in primary care of four Latin America countries: The multinational, cross-sectional, non-interventional PUMA study

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ABSTRACT

Background and objective: Bronchodilators (BDs) are the cornerstone of COPD treatment. However, their underuse has been reported in real-life studies. PUMA is a primary-care study from Argentina, Colombia, Venezuela and Uruguay that could help understand the BD use in terms of frequency for long-acting (LA-BD) and short-acting (SA-BD) BDs alone or associated with corticosteroids (CS), and the use as-needed or on regular basis.

Methods: This is a multicentre, multinational, cross-sectional, non-interventional study including no randomised primary-care centres from each country (total 57 centres) without connection with respiratory specialists. Subjects attending routine visits, at-risk for COPD (≥40 years, current or former smokers or exposed to biomass) completed a questionnaire and performed spirometry. COPD was defined as post-BD $FEV_1/FVC < 0.70$ and by the lower limit of normal (LLN). Prior physician diagnosis of emphysema, chronic bronchitis or COPD was also determined.

Results: 1743 patients were interviewed, 1540 completed spirometry, 309 had COPD by post-BD $FEV_1/FVC < 0.70$, 226 by LLN, and 102 had prior medical diagnosis. A total of 77/309 COPD patients by spirometry (24.9%) used BD (3.6% LA-BDs), 15.2% used BD + CS (13.6% LA-BD + CS). Among these patients, SA-BDs (monotherapy) were the most commonly used medication both as-needed (4.5%) and on a regular basis (17.5%). Similar findings were observed using the LLN criteria. In those with prior medical diagnosis, 66/102 (64.7%) used BDs (9.8% LA-BD), and 25.6% used BD + CS (13.6% LA-BD + CS); among them SA-BDs were the most commonly medication used as-needed (9%) and on a regular basis (48.1%). Having health insurance with medication coverage increased the use of BDs.

Conclusions: Up to 60% of COPD patients by spirometry and 10% of those with prior medical diagnosis attending a primary care sample of four Latin American countries did not use BDs. LA-BDs are widely underused on a regular-basis (2.6% and 8.3% of patients with spirometric and medical-diagnosis,

Abbreviations: BD, bronchodilator; CS, corticosteroid; FEV_1, forced expiratory volume in 1 s; FVC, forced vital capacity; LABA, long-acting β-agonist; LA-BD, long-acting bronchodilator; LAMA, long-acting muscarinic antagonist; LLN, lower limit of normal; PUMA, "**P**revalencia y práctica habit**U**al (diagnóstico y trata**M**iento) en población de riesgo de EPOC en atención primaria en **A**mérica Latina" [Spanish], Prevalence Study and Regular Practice, Diagnosis and Treatment, Among General Practitioners in Populations at Risk of COPD in Latin America [English]; SA-BD, short-acting bronchodilator.

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respectively) This represents a considerable gap between guideline recommendations and BD prescribing pattern in these centres.

1. Introduction

In general, all current COPD guidelines for the management of the disease are driven by the need to reduce symptoms, prevent exacerbations, reduce disease severity, improve health status and exercise tolerance [1–4]. Bronchodilators (BD) are central to this therapeutic approach, especially with regards to symptom management. The main BD used in the treatment of COPD are β_2-agonists and anticholinergics. The choice among these medications depends on a number of factors, including the individual's response in terms of symptom relief and side effects, availability and cost.

The guidelines also recommend that bronchodilators are prescribed on as-needed or a regular basis to prevent or reduce symptoms [1–4]. Inhaled short-acting BDs (SA-BD) are recommended in mild COPD patients on as-needed basis for symptom relief, whereas long-acting BDs (LA-BD) are recommended on regular (maintenance) basis in patients whose symptoms are not controlled with as-needed SA-BD or in those who have more severe airway obstruction and/or frequent exacerbations. It is well known that in these patients LA-BDs are more effective at producing maintained symptom relief than SA-BDs [5–7].

Although clinical practice guidelines have been developed for COPD, their influence on primary-care practice is currently unclear and there is a considerable gap between the guidelines' recommendations for the use of bronchodilators in COPD and the prescribing pattern in real-life [8–12].

In a large, commercial, Medicare COPD population, Make et al. [12] found that long-term maintenance medication was not prescribed in the majority of patients and that a LA-BD was prescribed in less than one-third of patients. Similar findings have been reported in the Copenhagen General Population Study involving COPD patients with $FEV_1 < 60\%$ [13].

The under-management of COPD with LA-BD therapy has also been reported in a survey of primary-care physicians, which found that only 35% of physicians chose a LA-BD if use with a SA-BD agent had failed to manage a patient's symptoms [14]. Furthermore, data from the UK primary-care setting showed that in the total UK COPD population a small proportion of patients in all GOLD subgroups were only using LA-BD monotherapy [9].

No information exists regarding BD medication use in COPD patients from the Latin American primary-care setting. Therefore, the aims of this study were to assess the frequency of use of SA-BD and LA-BD therapies, both as needed (rescue) and on a regular basis (maintenance), in patients with COPD attending primary-care settings in four Latin American countries.

2. Methods

PUMA study, acronym after study original Spanish name "**P**revalencia y práctica habit**U**al (diagnóstico y trata**M**iento) en población de riesgo de EPOC en atención primaria en **A**mérica Latina" or in English "The Prevalence and Regular Practice, Diagnosis and Treatment, Among General Practitioners in Populations at Risk of COPD in Latin America" was conducted in the primary-care setting in four countries: Argentina, Colombia, Venezuela and Uruguay. Details of the methodology have been published previously [15]. Briefly; the PUMA study is a multicentre, multinational, cross-sectional, non-interventional study performed in 2012. The larger countries of South America were invited to participate in the study. However, the countries that finally participated were those that accepted the invitation and had availability of local resources to conduct the study. Participating sites were selected according to local feasibility from previous local available database of potential principal investigators (not randomised) and included primary care centres (family doctors, general practitioners etc.), including social security centres with no direct connection with respiratory medicine specialists, These sites were selected trying to reflect national primary care practice in terms of geographical distribution (urban and rural) and healthcare sector (public and private). Subjects were enrolled during routine spontaneous or scheduled visits unrelated to the study objectives (with or without respiratory symptoms). Participants were all subjects at risk for COPD attending the selected primary care centres during the study period. The ethics committees for each site approved the protocol and all subjects enrolled provided written informed consent.

All subjects at-risk for COPD were included in the study; key inclusion criteria were: ≥40 years of age, current or ex-smokers (≥10 pack-years, ≥50 pipes/year or ≥50 cigars/year) and/or exposure to biomass smoke (wood or coal, for cooking and heating; exposure ≥100 h/year).

The participants completed a modified version of the Proyecto Latinoamericano de Investigación en Obstrucción Pulmonar (PLATINO) study [16] questionnaire for information on factors potentially associated with COPD; these included demographics, smoking habits, education, employment, respiratory symptoms, use of respiratory medication, prior spirometry testing, and data on the medical coverage and lung medication payment by health insurance. Information on prior medical diagnosis of asthma, chronic bronchitis, emphysema or COPD, were also obtained. Spirometry was performed using the portable, battery-operated ultrasound Easy One spirometer (ndd Medical Technologies, Zurich, Switzerland). Spirometry tests were performed at baseline and 15 min after inhalation of 400 μg salbutamol, according to the American Thoracic Society (ATS) criteria of acceptability and reproducibility.

2.1. COPD definitions

1. A ratio of post-BD $FEV_1/FVC < 0.70$ (fixed ratio).
2. A ratio of post-BD FEV_1/FVC less than the LLN; defined as the lower 5th percentile for predicted post-BD FEV_1/FVC.

Severity of COPD airway obstruction was stratified using the GOLD criteria [1]. Additionally, a prior diagnostic label of COPD was determined using a patient self-reported physician diagnosis of emphysema, chronic bronchitis or COPD. This definition of COPD was also assessed in order to have a better understanding of the bronchodilator prescription pattern in this real-life study, since up to 77% of the COPD subjects diagnosed by post-BD $FEV_1/FVC < 0.70$ criteria in PUMA did not have previous diagnosis [17].