

EDITORIAL

Critical Issues of Inhaled Corticosteroids (ICS) use in Chronic Obstructive Pulmonary Disease (COPD) Patients

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ABSTRACT

Chronic obstructive pulmonary disease (COPD) is a chronic inflammatory disorder of lungs associated with progressive disability leading to increased morbidity and mortality. Guidelines recommend spirometry examination as key test for the diagnosis of COPD, and bronchodilators as main pharmacological treatment. The choice of pharmacological therapy depends on COPD stage (A-D) that is based on the spirometry-measured degree of airflow reduction, risk of exacerbations, and symptoms evaluated using standard scales i.e. (Cat Test or mMRC). Specifically, in the first stage of the disease only short-acting inhaled bronchodilators, as needed, are indicated, while in the following stages long-acting inhaled bronchodilators, should be prescribed, and only, in the advanced stages, in combination with inhaled corticosteroids (ICS). However, critical issues in the correct diagnosis and treatment (i.e. spirometry not commonly used to confirm COPD diagnosis in routine care, use of inhaled corticosteroids (ICS) in early stage of COPD) have been documented worldwide. In light of these reasons, specific educational programs as well as clinical audit should be encouraged among primary care, physicians, and specialists, to promote the appropriate management of COPD, particularly to optimize the use of ICS in COPD therapy

Key words: COPD; Appropriate treatment; Inhaled corticosteroids (ICSs) therapy

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EDITORIAL

Chronic obstructive pulmonary disease (COPD) is an irreversible chronic inflammatory disorder of lungs caused by exposure to noxious agents, such as tobacco smoke^[1].

COPD is characterized by progressive pulmonary airflow reduction associated with progressive disability leading to increased morbidity and mortality, if not treated promptly and thoroughly^[2]. According to the latest World Health Organisation (WHO) estimates, 65 million people around the world have currently COPD that will become the third leading cause of death worldwide by 2030^[3]. In Italy a prevalence of COPD equal to 3% has been estimated in 2013^[4].

Spirometry examination is essential for diagnosis and staging of COPD. A forced expiratory volume in 1 second (FEV1)/ forced vital capacity (FVC) ratio of value < 0.70 when measured post-bronchodilator confirms the presence of persistent airflow limitation that is typical of COPD^[5]. Each pharmacological treatment should be tailored to each patient depending upon COPD stage. Staging of COPD (A-D) is defined on the basis of the severity of symptoms, airflow limitation degree, and frequency/severity of exacerbations, as reported in the international guidelines "Global Initiative For Chronic Obstructive Lung Disease" (GOLD 2015)^[5]. These guidelines recommend in the first stage of the disease (A) only short-acting inhaled bronchodilators (SABA or SAMA), as needed, while in the following stages (B-C-D) long-acting inhaled bronchodilators, including long-acting β_2 -agonists (LABA) and long-acting antimuscarinic agents (LAMA), should be always prescribed. The use of inhaled corticosteroids (ICSs) improves symptoms, lung

function, and quality of life, and mostly reduces the frequency of exacerbations in COPD patients with predicted FEV1 < 60%^[5-7]. For this reason, ICSs are recommended only for patients in advanced COPD stage (C-D: severe to very severe airflow limitation, with more than 2 exacerbations per year, and/or ≥ 1 with hospitalization for exacerbation) but should be always used in association with bronchodilators. Despite these recommendations, ICSs are widely used in COPD patients, including those at low risk of exacerbations, thus unnecessarily exposing the patients to the risks associated to ICS^[8]. Several epidemiological studies warned about risks of potentially inappropriate use of ICS in COPD patients, as a result of poor adherence to treatment guidelines among primary-care physicians^[9-10]. Challenging differential diagnosis of COPD and other chronic respiratory diseases such as asthma and pulmonary fibrosis adults presenting with airways disease plays an important role in the inappropriate use of ICS^[10]. The CADRE (COPD and asthma diagnostic/ management reassessment) study among UK primary-care practices found a high rate of misdiagnosis among adults with airways disease, with a tendency to overdiagnose asthma and underdiagnose COPD^[11]. The underutilization of spirometry testing is strongly associated with an increased risk of misdiagnosis of respiratory disease. Han MK *et al*^[12] found that approximately 32% of patients with a new diagnosis of COPD had undergone spirometry in the specified interval. Furthermore, spirometry frequency was lower in older patients, particularly in those ≥ 75 years old^[12]. Therefore, the lack of diagnosis accuracy may lead to inadequate treatment and overuse of ICS^[13-14], mainly for patients with COPD (e.g. used as monotherapy or in early stage of COPD)^[10-15].

Notably, the National Report on Medicines use in Italy, which traces all drugs dispensed and reimbursed by the National Healthcare System (NHS), in 2014 reported that 38.2% of COPD patients were inappropriately treated with ICS as monotherapy^[4].

Moreover, a recent drug utilization study from UK general practice reported that over 37% of COPD patients were over-treated, with ICSs accounting for most of the reasons for overtreatment^[16].

Use of ICS has been associated with well-known local and systemic side effects, as skin thinning and easy bruising, oral fungus candida infection, pneumonia, osteoporosis, early onset diabetes, cataracts, and tuberculosis^[17,21].

With reference to pneumonia, in particular, long-term use of ICS (at least 24 weeks, has been associated with an increased risk of pneumonia in patients with COPD, according to the results of a meta-analysis of randomised trials^[22], showing up to 70% increase in the pneumonia risk with ICS use alone or in combination with a long-acting β agonist; especially with high dose treatments^[22-23].

Indeed, the 3-year TORCH and 2-year INSPIRE trials reported increases in pneumonia risk with fluticasone (1,000 μ g per day) in 64% and 94% respectively^[24-25], while Kardos P. *et al* found a threefold increase in the risk using the same daily dosage^[26].

However, uncertainties still remain whether all the ICS carry a similar increased risk of pneumonia and whether the effect is dose related^[21].

In May 2015, European Medicines Agency (EMA) has started a review of safety of inhaled corticosteroid-containing medicines in the treatment of COPD^[27].

To improve COPD care, several strategies have been adopted worldwide. Data from Denmark, Swiss and Spain suggest that training programs for GPs and practice assistants could be useful to improve the management of COPD^[28-30]. Soler N. *et al* showed that training GPs in performing spirometry test can improve the rate of correct COPD diagnosis from 56% to 89%^[30].

As an alternative approach, auditing the diagnostic and prescribing practice of the primary care physicians as well as specialists has been shown to be successful intervention for the management of a wide range of diseases including respiratory ones^[28].

The auditing cycle emphasises the need to establish the best practice, to set standards, to measure practice against standards, and then to change practice to meet those standards with the active involvement of the prescribers.

Taking into consideration heterogeneous factors influencing the management of COPD at national and loco-regional level, implementation of specific educational programs as well as clinical audit should be encouraged among primary care physicians and specialists to promote appropriate diagnostic work-up and pharmacological and non-pharmacological management of COPD which may also optimize the use of ICS in COPD therapy.

This intervention might result ultimately in reduction of risks and costs associated with inappropriate use and overtreatment of ICS thus improving quality care of COPD patients.

CONFLICT OF INTERESTS

The authors declare that they do not have conflict of interests.

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