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Letter to the Editor

Re: Self TH, Patterson SJ, Headley AS, *et al.* Action plans to reduce hospitalizations for chronic obstructive pulmonary disease exacerbations: focus on oral corticosteroids. Curr Med Res Opin 2014;30(12):2607-15

Dear Editor,

It is with great interest that I have reviewed an article titled 'Action plans to reduce hospitalizations for COPD exacerbations: focus on oral corticosteroids' by Self *et al*. This informative review underscores the importance of early identification and treatment of patients at heightened risk for readmission. Repeated exacerbations lead to irreversible decline in lung function and efforts should therefore be made to reduce exacerbations and their severity, to recognize and treat exacerbations. However, no valid tools exist today for evaluating prognosis in the short and medium term after hospital discharge for COPD patients. The majority of patients with COPD are readmitted to the hospital for the same diagnosis or a closely related condition, suggesting that better management of the patient's condition could prevent both the initial hospitalization as well as readmissions. However, patients often present late in the time course of the exacerbation and evidence suggest that delayed treatment of exacerbation leads to longer exacerbations and hospital admission[1]. Trials have investigated pulmonary rehabilitation, education, and self-management, but the results have been contradictory.

Clearly, systemic corticosteroids (SCSs) have been proven to be an effective initial treatment for COPD exacerbations, regardless of its severity and SCSs remain a cornerstone of the pharmacologic management of acute COPD exacerbations. However, COPD is also a highly heterogeneous condition with many different factors contributing to its pathophysiology. The relative contribution of these factors varies from patient to patient, although this is rarely taken into account in studies of exacerbations, which are heterogeneous in their own right. For this and other reasons, conclusions regarding the etiology as well as inflammatory processes involved and their effects remain unresolved[2].

The term COPD principally encompasses two conditions – chronic bronchitis and emphysema. Chronic bronchitis is characterized by airway obstruction resulting from inflammation and remodeling of the larger airways, with edema, increased mucus production and impaired mucus clearance[3]. The principal symptoms of impaired mucus clearance are cough and dyspnea. Dyspnea is caused when mucus obstructs airflow by occupying the lumen of numerous airways[4]. Exacerbations involve increased airway inflammation and worsening airway obstruction, in variable contributions. Patients with diagnosis of chronic bronchitis have been reported to have almost twice the risk for exacerbations.

Small-airway mucus obstruction is characteristic of COPD, even in patients who do not expectorate mucus. Conversely, patients with COPD who have copious expectoration may have little airflow obstruction, probably because the mucus from large airways and causes minimal obstruction[5]. As has been noted by the authors, current evidence indicate that antibiotics may not be particularly useful in the majority of patients with COPD exacerbation presenting without sputum purulence, suggesting that factors other than infection may play a key role in COPD exacerbation. Moreover, the effectiveness of various non-steroidal treatment modalities in reducing the severity and frequency of exacerbations (bronchodilator drugs)[6] and the differential effect of bronchodilators and corticosteroids on exacerbations[7] suggest that exacerbations can involve worsening airway obstruction in the absence of airway inflammation, assuming that these bronchodilators do not exert anti-inflammatory effects in patients with COPD in vivo[8].

It is important to recognize the role of mucus in clinical presentation. It is necessary to clear mucus from the airway lumen in order to resolve symptoms and allow effective delivery of aerosol therapies[5]. This author's own data indicate that a failure to clear excessive mucus plugs from the patient's small airways is largely responsible for failure to achieve improvement with SCS treatment alone, regardless of the dose and duration of SCS treatment. This in turn places patients with persistent COPD exacerbation at risk for readmissions in the first 30 days after discharge[9].

The defining feature of chronic obstructive pulmonary disease (COPD) is progressive airflow limitation that causes air trapping and hyperinflation. Hyperinflation increases acutely under conditions such as exercise or exacerbations[8]. COPD exacerbations that are not responsive to SCSs are characterized by excessive airway plugging with non-resolving hyperinflation. Mucus clearance has been studied extensively in mucocillary clearance and cough clearance. In diseases like asthma and COPD, large amounts of mucous plugs are observed in airways[10], which contribute to morbidity and mortality. Thus, removing mucus from the lung is essential to reduce morbidity and mortality associated with COPD exacerbation and to reduce hyperinflation and dyspnea as well as the high readmission rate associated with COPD exacerbation, particularly in patients with symptoms of persistent chronic bronchitis. In clinical practice that means early consultation with an expert pulmonologist with consideration for early bronchoscopy.

Data from six single studies that specifically targeted COPD did not provide evidence for significant short-term benefit from non-bronchoscopic airway clearance modalities[11]. Early recognition of COPD exacerbations and initiation of oral steroid (OS) treatment is important and can have a positive impact on the duration, severity and hospitalization rate for COPD exacerbation. Nevertheless patients with COPD exacerbation requiring hospital readmissions within 30 days post-discharge appear to have a different pathophysiology of exacerbation with less inflammation and more persistent mucous small airways plugging.

Recent insights into the formation of pathologic mucus in disease have led to the introduction of tailored therapies such as hydration by means of aerosolized hypertonic solutions or the reduction of mucus viscosity by aerosolized dornase alfa[5]. Targeted treatment of pathologic airway mucus, which often in clinical practice means therapeutic bronchoscopy, not only improves symptoms of cough and dyspnea but also decreases the frequency of disease-related exacerbations and slows disease progression. As a recent editorial published in the Lancet[12] noted: "Preventing readmissions is in everyone's interest and promoting reimbursement centered on quality of care – not the number of admissions or procedures – seems sound. The challenge lies in assessing quality and making an individualized but scalable framework that health-care systems can be evaluated against."

Sincerely,

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