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Letter to the Editor

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Use of inhaled corticosteroids in bronchiectasis

Uso de corticosteroides inhalados en bronquiectasias

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Dear Editor:

We are writing to you regarding the article entitled «Recommendations for diagnostic approach and treatment of bronchiectasis»[1] recently published in this prestigious journal, in order to address the point of use of inhaled corticosteroids in patients with bronchiectasis.

Bronchiectasis presents itself as a disease of heterogeneous nature, exhibiting diverse etiologies that converge in a pernicious, persistent, progressive and irreversible cycle.[2] Its complexity is manifested in the variability of the severity of all the elements that make up its pathophysiology, such as mucociliary dysfunction, the microbiology involved and the diverse patterns of inflammation.[2] For this reason, the current and most recent research suggests directing attention to clinical phenotypes, inflammatory endotypes and disease overlap, with the aim of providing personalized and targeted therapies, focusing on treatable features.[2,3] With the goal of preserving lung function, halting disease progression, improving quality of life, preventing hospitalization and decreasing mortality.[2,3]

At present, international guidelines agree on the lack of indication for inhaled corticosteroids as routine treatment in patients with bronchiectasis; however, they recognize that the existing scientific evidence supporting this recommendation is limited and that more than 50% of patients with this disease are treated with inhaled corticosteroids.[3]

In this review, the authors refer to the meta-analysis published by Kapur N, *et al*.[4] The latter covered a set of seven clinical trials, highlighting the presence of improvement in the clinical parameters of dyspnea as well as a reduction in sputum production in the group of patients who received inhaled corticosteroids. These results could translate into an improvement in quality of life. In addition, in the cohort of patients treated with inhaled corticosteroids for a period of six months or less, two studies did not identify a significantly increased risk of *Pseudomona aeruginosa* colonization compared to the placebo group.[4]

Recently, Shoemark A, *et al*.[5] demonstrated that blood eosinophil counts of approximately 300 cells/μL are common in bronchiectasis and are found in a subgroup representing approximately 20% of patients with this condition. It was also established that elevated blood eosinophil counts are a risk factor for exacerbation in patients with bronchiectasis.

This study added to recent data showing clinically significant improvement in quality of life with high-dose inhaled corticosteroid therapy in patients with bronchiectasis who had blood eosinophil counts > 3% or 150 cells/μL. This identifies a specific population of patients who may respond to inhaled corticosteroids.[5]

Finally, Miguel Á. Martínez-García and his team detailed that, in individuals affected by bronchiectasis, the presence of both eosinophilia and eosinopenia is associated with greater severity, presumably due to the dual function of eosinophils, derived from their proinflammatory and bactericidal properties. And only in those patients with eosinophilia was there a significant reduction in the number of exacerbations associated with the use of inhaled corticosteroids.[6]

In conclusion, the decision to use inhaled corticosteroids in the treatment of bronchiectasis should be based on an individualized assessment, not limited only to patients with associated comorbidities such as asthma, chronic obstructive pulmonary disease (COPD) or allergic bronchopulmonary aspergillosis (ABPA).[4] It now also extends to individuals with bronchiectasis who lack additional comorbidities and present elevated peripheral eosinophil counts, which represents about 20% of this population.[5]

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Reply

Respuesta

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We appreciate the valid and substantiated commentary, limiting the frequent recommendation to limit the use of inhaled corticosteroids in bronchiectasis; this position is present in most guidelines, derived in part from the paucity of information on the management of bronchiectasis phenotypes. The largest cohort of patients with bronchiectasis (EMBARC) shows that up to 53% use inhaled corticosteroids, demonstrating frequent use despite recommendations, and this group has lower lung function, older age, high Bronchiectasis Severity Index (BSI) score, frequent exacerbations and more *Pseudomona aeruginosa* colonization.[1]

The use of inhaled corticosteroids in the presence of eosinophils > 400 cells/μL protects against exacerbations (RR = 0.70) and hospitalizations (RR = 0.56)[2] but, on the other hand, general users of inhaled corticosteroids are at higher risk of exacerbations (RR = 1.21) and hospitalizations (RR = 1.14), although with no increase in mortality;[1] showing a clinically simple and known marker,[3] for example, in patients with chronic obstructive pulmonary disease (COPD), that can guide the selection of patients who benefit from inhaled corticosteroids.[4] Hopefully, information will soon be available to select the most effective inhaled corticosteroid with the greatest benefits and lowest risks.

The benefit provided by inhaled corticosteroids may be associated with induction of apoptosis and eosinophil depletion, with reduction of proinflammatory cytokines from lymphocytes, epithelial cells and macrophages, and perhaps because they also deplete mast cells and dendritic cells, and reduce mucous secretion.[3]

In COPD, which shares certain inflammatory features with bronchiectasis, also only patients with eosinophilia (> 300 cells/mL) improve with inhaled corticosteroids.[4] Interestingly, there is a relationship between *Pseudomona aeruginosa* infection and a Th2 (T Helper Lymphocyte) response[5] and leaves the question of whether there is any relationship between this microbe and the benefit of inhaled corticosteroids. Similarly, other Th2 biomarkers such as exhaled fraction of nitric oxide (FeNO) remain to be explored, but when eosinophils and FeNO are measured the Th2 response increases by 20-30% in patients with bronchiectasis.[6] As in other chronic respiratory diseases, we should be cautious with the use of inhaled corticosteroids in bronchiectasis as they have also been associated with increased risk of pneumonia and mycobacterial infections.[7]

The use of inhaled corticosteroids should be reserved for patients who will reasonably derive clear benefits and few adverse effects; it is encouraging that a marker has been identified in eosinophils that provides guidance in this regard, knowledge that will undoubtedly be incorporated into future versions of the Diagnostic and Treatment Guidelines.

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