Don’t Forget about Facilitatory Effects of Corticosteroids on b 2-Adrenoceptors in Acute Asthma

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Published in:
American Journal of Respiratory and Critical Care Medicine

DOI:
10.1164/rccm.202007-2837LE

Publication date:
2020

Document Version
Publisher's PDF, also known as Version of record

Reference

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To the Editor:

We read with interest the findings of Moran and colleagues showing equally rapid reductions in blood eosinophils with oral prednisolone and subcutaneous benralizumab (1) in patients with poorly controlled asthma. The authors go on to suggest that benralizuamb might be used as an alternative to corticosteroids for the treatment of acute exacerbations of eosinophilic asthma. Their data was not obtained in the setting of acute severe airflow obstruction, where airway smooth muscle constriction also plays a key role in airflow limitation in addition to endobronchial inflammation. Pointedly, they did not comment on whether the acute fall in eosinophils was accompanied by a commensurate improvement in airway geometry as FEV_1. In this regard, the findings of Moran and colleagues do not take into account the acute facilitatory effect of systemic corticosteroids such as prednisolone on airway smooth muscle in terms of rapid upregulation and resensitization of β_2-adrenoceptors in patients with acute asthma, especially those who have been taking inhaled corticosteroids with long-acting β_2-agonists (2). Moreover, benralizumab exhibits antiinflammatory activity by suppressing eosinophils alone, whereas corticosteroids have more broad-spectrum activity on a variety of inflammatory cells in asthma. Notably, benralizumab is also considerably more expensive than oral prednisolone. Hence, although we would advocate for benralizumab as a suitable long-term treatment for reducing exacerbations in severe eosinophilic asthma, we would not endorse its routine use for treatment in acute asthma. ■

Author disclosures are available with the text of this letter at www.atsjournals.org.

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Reply to Lipworth *et al.*

From the Authors:

We thank Dr. Lipworth and colleagues for their interest in our work published recently in the *Journal* (1). They rightly point out that the biology of asthma attacks is more complex than blood eosinophils alone and that corticosteroids have a wide range of other potentially relevant antiinflammatory effects. However, local treatment with inhaled corticosteroids (ICS) is usually the mainstay of patients with frequent eosinophilic exacerbations, and therefore in the great majority of patients, the key question is what oral corticosteroids (OCS) add to ICS in an acute attack (2) and whether this effect is seen with benralizumab. We suggest that depletion of circulating eosinophils is the only effect OCS are likely to have that are not shared with ICS (3).

Because OCS are known to have severe side effects, and in noneosinophilic exacerbations of chronic obstructive pulmonary disease they are actually harmful (4), it would be a significant advance to determine whether a combination of ICS and rapidly acting anti–IL-5 treatment would cover all the benefits of OCS in acute asthma while mitigating the harms of OCS. With respect to this, we recently published a case report (5) that showed the addition of benralizumab to ICS resulted in a dramatic improvement of peak flow and FEV_1 within 6 hours when given to treat an asthma attack in a patient in whom systemic corticosteroids were contraindicated. We believe that these findings support the idea that systemic targets of benralizumab that express the IL-5 receptor (such as eosinophils and basophils) play a pivotal role in sustaining the nonbronchodilator responsive airflow limitation seen in asthma attacks.

The use of benralizumab in acute asthma may also provide other benefits. Treatment failure is a major issue in

Originally Published in Press as DOI: 10.1164/rccm.202007-2837LE on September 24, 2020

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Originally Published in Press as DOI: 10.1164/rccm.202008-3106LE on September 24, 2020