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Rapid effect of inhaled fluticasone on airway responsiveness to AMP: Research implications

To the Editor:

We read with great interest the recent article by Ketchell et al,¹ in which a marked reduction in airway responsiveness to inhaled AMP was observed in subjects with mild asthma as early as 2 hours after a single inhalation of fluticasone propionate. These findings are somewhat in agreement with the results of our detailed longitudinal assessment of changes in airway response to AMP with inhaled budesonide.² Changes in airway response to AMP promptly detected inflammatory changes of the asthmatic airways as early as the first week of treatment with budesonide (0.8 mg daily), whereas changes in responsiveness to methacholine and in percentages of eosinophil and epithelial cell counts in the sputum could be observed only by the fourth week of treatment.² Taken together, these findings validate the exquisite sensitivity of AMP responsiveness to topical glucocorticosteroids.

Considering the relative insensitivity of AMP in detecting changes in airway hyperresponsiveness after steroid therapy in patients with chronic obstructive pulmonary disease,³ the finding that a single inhalation of fluticasone propionate markedly attenuates airway response to AMP might also be of diagnostic relevance because it indicates an additional way by which adenosine challenge might be useful in discriminating asthma from true chronic obstructive pulmonary disease.

Although monitoring of airway response to AMP might be one of the most accurate guides to monitor inhaled glucocorticosteroid requirements in asthma and to establish the appropriate dose needed to control airway inflammation,^{4,5} the extreme sensitivity of AMP to inhaled fluticasone propionate is seemingly inconvenient. It is therefore imperative to assess whether the early reduction in airway responsiveness to AMP reported by Ketchell et al¹ with fluticasone propionate is also shared by other commonly prescribed topical glucocorticosteroids. In addition, the apparent lack of dose response in this acute study is in stark contrast with the dose-dependent decrease in airway response to AMP observed after chronic administration with 100 and 400 µg of ciclesonide⁶ or 100 and 200 µg of mometasone furoate.⁷

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Reply

To the Editor:

We thank Dr Prosperini and colleagues¹ for their interest in our recent article.² We agree that our findings highlight the exquisite sensitivity of AMP responsiveness to inhaled glucocorticosteroids in contrast to other markers of airway inflammation, as detailed so comprehensively by Dr Prosperini and colleagues in a recent edition of the Journal.³ Their findings that a week of 0.8 mg of inhaled budesonide per day reduced airway responsiveness (AR) to AMP was comparable with results seen after a single inhalation of 100 µg of fluticasone propionate (FP) in our study. Moreover, their findings are similar to those reported by our respective groups in the past.^{4,5} Before our recent study, the most likely explanation for such an exquisite effect of inhaled glucocorticosteroids on AMP challenge was a reduction in airway mast cell numbers. Patently, this cannot explain the effects after a single inhalation.

Dr Prosperini and colleagues raise an interesting point about the possible diagnostic utility of AMP in distinguishing between asthma and chronic obstructive pulmonary disease. Obviously further investigation is required, and this will require careful study design and planning. Our group has no particular experience of AMP challenge in chronic obstructive pulmonary disease.

The acute effect on AMP challenge is not specific to FP. In a study to be presented at the forthcoming American Thoracic Society meeting in Seattle, we have shown similar effects with other inhaled glucocorticosteroids. As we highlighted in our article, these surprising acute effects beg the question of mechanism and indeed of onset of action. We now know from another study of ours, also to be reported at the American Thoracic Society meeting in Seattle, that the acute inhaled glucocorticosteroid effect on AMP is seen as early as 1