Absorption of High-Dose Inhaled Corticosteroids

To the Editor:

The appropriate and safe use of inhaled corticosteroids (ICS) is an important issue in managing asthma, and we read with interest the article by Wals et al (June 1999).1 This is now the seventh report showing increased adrenal suppression with very high doses of fluticasone propionate (FP) compared to budesonide (BUD) in volunteers.2–7 However, normal subjects do not generally receive these doses of ICS, and it is difficult to see the relevance of these studies to clinical practice.

Absorption of fluticasone is largely via the lung, and this is substantially reduced in asthmatics. We have recently compared plasma FP and cortisol levels after steady-state dosing with 1,000 μg FP (hydrofluorocarbon metered-dose inhaler via Volumatic Spacer; Glaxo Wellcome; Greenford, UK) in normal subjects and patients with moderately severe asthma (mean FEV1, 54% predicted). The area under curve (AUC) plasma FP was reduced by 62% and AUC plasma cortisol was significantly higher in the asthmatic subjects. This reduced systemic bioavailability in asthma would lend support to extensive clinical studies that show similar levels of adrenal suppression for FP and BUD at equal microgram dose in patients with asthma (summarized in Barnes et al)ab).

We would conclude that pharmocokinetic studies comparing drugs with different absorption pathways should be carried out in the patient group for which their use is intended, and not in normal volunteers where results can be misleading and open to misinterpretation. ICS remain the cornerstone of asthma management. However, irrespective of which specific ICS patients are taking, it is incumbent on health care professionals to treat asthmatics with the minimum dose compatible with good disease control. Patients must be “stepped down,” and not left indefinitely on high-dose ICS, especially as lung function normalizes.

Martin Brutsche-Carlen, MD
Ingrid Carlen-Brutsche, PhD
Ashley Woodcock, MD
Wythenshawe Hospital
Manchester, England

Correspondence to: Ashley A. Woodcock, MD, Respiratory Physiology, Wythenshawe Hospital, South Moor Road, Manchester M23 9LT, England; e-mail: ashley@nchng.u-net.com

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Corticosteroids in the Emergency Treatment of Acute Severe Asthma

To the Editor:

I read with interest the review by Drs. Rodrigo and Rodrigo (August 1999)1 on the role of corticosteroids in the emergency treatment of acute asthma. In a meta-analysis, they found no evidence for either rapid (<6 h) improvement of pulmonary function or reduction in hospital admission rates. From the pooled results of six studies, they calculated a 32% reduction in admission rates in patients treated with IV corticosteroids, and they estimated that the average number of patients treated to avoid one hospitalization would be 12.5 (95% confidence interval [CI], 7.1 to 50). However, their survey did not include the randomized controlled study by Lin et al,2 who administered IV methylprednisolone (125 mg) to adult asthmatics who had predicted peak expiratory flow rates of <50% after initial albuterol aerosol treatment. Lin et al2 reported significant improvement in pulmonary function 60 min and 120 min following IV treatment with corticosteroids. This improvement was in addition to the effect of inhaled ipratropium and albuterol, which was administered to all subjects. They also noted a nonsignificant reduction in the admission rate of 31%. In an accompanying editorial, Gallagher3 incorporated the results of the study by Lin et al2 in another meta-analysis, and estimated that the number of patients needed to be treated with IV corticosteroids to avoid one admission was seven (95% CI, 4 to 16).

At our institution, the average cost of hospitalization is $1,000 (for an adult patient with an average stay of 3.8 days).4 By contrast, the cost of IV methylprednisolone, 125 mg, is $19. On average, then, 53 second-line treatments with methylprednisolone in the emergency department are comparable in cost to a single admission for asthma. This ratio is higher than the break points estimated by both Rodrigo and Rodrigo (50:1).5 and Gallagher (16:1).3 A similar comparison may be made with inhaled corticosteroids, which are the second-line agents actually recommended by Rodrigo and Rodrigo.1 This is based on their own study, which showed the efficacy of inhaled flunisolide as primary treatment in acute severe asthma.6 Inhaled flunisolide is not available to us in Singapore, but 6 mg of inhaled fluticasone (which has higher potency than flunisolide) would cost $13. While the physiologic improvement seems better and the reduction in admission rates...