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Systemic effects of inhaled fluticasone propionate

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To the Editor:

We read with interest the 4 case reports of hypothalamic-pituitary-adrenal (HPA) axis suppression associated with the use of inhaled fluticasone propionate described by

Duplantier et al¹ in the October issue of The Journal. The patients in these reports appeared to have moderate-to-severe asthma, with 3 patients who had documented HPA axis suppression being treated with 1320 to 1760 µg/day inhaled fluticasone propionate. The fourth patient, an 11-year-old child with HIV, had successfully been weaned off of chronic systemic corticosteroids during treatment with 440 µg/day inhaled fluticasone propionate. She was observed to have weight gain and Cushingoid appearance 1 to 2 months after discontinuation of systemic corticosteroids but did not have an assessment of HPA axis function. The findings in the 3 patients with documented HPA axis suppression are consistent with the clinical data presented in the product information for Flovent Inhalation Aerosol, which states "Ten percent (10%) to 16% of patients treated with fluticasone propionate at doses of 440 mcg or more twice daily had an abnormal response as compared to 29% of patients treated with prednisone."²

Although it is important for physicians to be aware of the potential for inhaled corticosteroids to cause systemic effects, it is equally important to maintain a proper perspective regarding

these risks. For all treatments, concerns about safety risks need to be considered in the context of the benefits that the treatment provides. The availability and use of high doses of inhaled fluticasone propionate has substantially improved the management of patients with severe asthma, many of whom had required systemic corticosteroids for control of their asthma. Data from Noonan et al³ showed that 69% to 88% of patients previously unable to discontinue approximately 10 mg of oral prednisone on average were able to do so by using 1320 to 1760 µg/day fluticasone propionate. This change in treatment from oral to inhaled corticosteroid therapy was also associated with an objective improvement in lung function (FEV₁, 180 to 520 mL > baseline), as well as other measures of asthma control with evidence of improvement in HPA axis function. Thus the benefit-to-risk ratio associated with the use of high-dose fluticasone propionate in patients with severe asthma favors its use. Subsequent to this study, numerous well-designed, well-controlled, clinical trials have demonstrated that considerably lower dosages of fluticasone propionate can provide comparable or greater clinical benefits with equal or less risk of HPA axis suppression than triamcinolone, beclomethasone, or budesonide.^{4,7}

Because the risks associated with the use of inhaled corticosteroids are dose related, it is imperative to titrate therapy to the lowest effective dose for control of asthma, as recommended by the National Asthma Education and Prevention Program Expert Panel Report 2.⁸ If this approach had been used in these patients, the clinical data available to date indicate that considerably lower doses of fluticasone propionate could have been administered to achieve the desired clinical outcome. Additionally, with all inhaled corticosteroids, titrating therapy to the lowest effective dose will ensure that the benefit-to-risk ratio for an individual patient will be optimized. If, on the other hand, these patients needed to be maintained on high doses of fluticasone propionate because of asthma severity, then clinical evidence indicates that this approach would have a better benefit-to-risk ratio compared with use of systemic corticosteroids.

Duplantier et al were shown this letter and declined to respond.

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