

Hypothalamic-pituitary-adrenal axis suppression associated with the use of inhaled fluticasone propionate

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Inhaled glucocorticosteroids (GCS) are effective antiinflammatory medications used for long-term control of persistent asthma. Side effects are uncommon, and the potential for systemic adverse effects, such as growth suppression in children, osteoporosis, and adrenal suppression, remains controversial. Hypothalamic-pituitary-adrenal axis suppression with inhaled GCS has been reported.¹ We report 4 patients treated with fluticasone propionate (FP) who experienced clinical and/or laboratory evidence of adrenal suppression.

CASE REPORTS

Case 1

A 12-year-old boy with mild asthma experienced an exacerbation requiring increased use of inhaled albuterol. No improvement resulted after 2 weeks of inhaled cromolyn sodium. He began receiving inhaled triamcinolone acetonide (400 µg twice daily) and oral prednisolone (22.5 mg twice daily for 5 days). Six weeks later, inhaled GCS was changed to FP (660 µg twice daily) by means of a spacer. After 4 months of treatment with FP, the patient had symptoms of increased thirst, acne, facial swelling, and a 7-lb weight gain. Fasting morning serum cortisol was undetectable (normal range, 4 to 22 µg/dL [110 to 607 nmol/L]). Urinalysis was normal.

Case 2

A 54-year-old woman with severe, poorly controlled asthma while using inhaled triamcinolone began taking FP (660 µg twice daily) by means of a spacer. She improved significantly. Three months later, fasting morning serum cortisol was 1 µg/dL (27.59 nmol/L).

Case 3

A 16-year-old girl with severe asthma failed to improve with high-dose inhaled beclomethasone dipropionate and flunisolide. She was treated with inhaled FP (880 µg twice daily) by means of a spacer and a 10-day course of oral prednisone. Two months after discontinuation of prednisone, fasting cortisol was 11 µg/dL (303.5 nmol/L). After 8.5 months of treatment with FP (and 8 months after discontinuation of prednisone), the patient presented with fatigue and Cushingoid facies. At this time, fasting morning cortisol was undetectable.

Abbreviations used

FP: Fluticasone propionate
GCS: Glucocorticosteroids

Case 4

An 11-year-old girl with HIV infection and asthma was treated with inhaled beclomethasone (84 µg four times daily). After an exacerbation, her treatment was changed to oral prednisolone (25 mg/day) and flunisolide (500 µg twice daily). Three weeks later, flunisolide was replaced by FP (220 µg twice daily). After 4 months of prednisolone therapy, the dosage had been weaned to 5 mg every other day. During the ensuing 2 months the prednisolone was discontinued entirely. On follow-up, a 7-lb weight gain and a Cushingoid appearance were noted. Serum cortisol level was not performed.

DISCUSSION

Inhaled corticosteroids have previously been reported to cause Cushing syndrome in rare cases.¹ Inhaled FP is considered to be a safe and effective medication with negligible side effects owing to its first pass metabolism by the liver, high topical potency, high affinity for the glucocorticoid receptor, and a long elimination half-life.² In one clinical study in adults, fasting morning cortisol levels remained within the normal range during treatment with inhaled fluticasone at a dose of 2000 µg/day.³ Recently, studies have shown that despite only 1% bioavailability after oral FP, a significant amount (15%) may be absorbed from the lung after treatment with inhaled FP.² In another study 1000 µg of inhaled FP had a systemic effect equivalent to 10 mg of oral prednisolone as measured by suppression of 8 AM plasma cortisol levels.⁴ Inhaled FP has also been associated with suppression of growth and adrenal function in children.⁵ The patients presented herein provide further clinical support to these prior studies, indicating that FP may have significant systemic side effects in some patients.

The previous use of oral and/or inhaled GCS in these patients are confounding variables. However, in patient 1 the clinical manifestations and low cortisol level were noted 5 months after completion of a short course of prednisolone. In patient 2 the low cortisol level was obtained 3 months after changing the inhaled GCS to FP. In patient 3 the morning serum cortisol level was initially normal 2 months after completion of oral prednisone therapy. The clinical manifestations and undetectable cortisol level were noted 8 months after discontinuation

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of prednisone (during which time the patient continued using inhaled FP). In patient 4 because weight gain and Cushingoid appearance were noted 1 to 2 months after discontinuation of prednisolone, we think it likely that the clinical manifestations were at least in part due to inhaled FP therapy.

Although the vast majority of patients using inhaled GCS experience no clinical side effects, multiple case reports indicate the potential for systemic effects in a small number of patients. As emphasized by this report, clinicians should be aware of this potential, especially with FP given in high doses or after oral GCS therapy.

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