Probable Adrenal Suppression from Intranasal Beclomethasone

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Although adrenal suppression has been known to occur with intranasal dexamethasone (Decadron Phosphate Turbinaire), this side effect has not been reported for the less-potent beclomethasone dipropionate (Beconase, Vancenase) or flunisolide (Nasalide). The following case, however, strongly suggests adrenal suppression from the administration of intranasal beclomethasone and flunisolide.

CASE REPORT

J.H.G., a 27-year-old married man, was first seen in November 1983 when he presented with fatigue. He denied fever, night sweats, or symptoms of depression. Review of systems was negative; family history was noncontributory.

Past medical history was significant for longstanding nasal obstruction, frontal headaches, and postnasal discharge. He had undergone a septoplasty, bilateral intranasal antrostomy, and partial inferior turbinectomy in 1980, and a left Caldwell Luc procedure in 1981. Following these procedures, his symptoms had improved somewhat, although he had multiple episodes of acute purulent sinusitis requiring antibiotics, and had frequent bifrontal headaches.

The patient had no prior use of parenteral or oral steroids.

By the end of April 1983 he was placed on beclomethasone nasal spray (one inhalation in each nostril four times per day). This treatment was switched in mid-May 1983 to flunisolide (Nasalide) 0.025 percent (two sprays in each nostril twice per day), which did not help so much as the beclomethasone.

In September 1983 he was returned to the beclomethasone nasal spray, which again significantly helped his nasal symptoms and which he was still taking when seen in November for the fatigue. A nasal cautery was also done in November 1983 to improve the nasal airway. Pharmacy records confirm the patient was not exceeding his prescribed doses.

On examination the patient was a normally developed, underweight pale man, appearing quite tired. Significant findings consisted of orthostatic blood pressure drops on several occasions. No thyromegaly was noted. Examination was otherwise normal with normal pigmentation. A psychiatric consultant did not find the patient to be depressed.

Laboratory tests, including complete blood count, urinalysis, chemistry profile, tuberculosis skin test, Monospot, serologic test for syphilis, thyroid-stimulating hormone, and thyroxine, were normal or negative, as was a chest roentgenogram.

A baseline midafternoon serum cortisol level was 11.7 μg/100 mL (10 to 15 μg/100 mL expected range), rising only to 12.1 μg/100 mL after a synthetic adrenocorticotropic hormone (Cortrosyn) injection. (The protocols used for testing adrenal function are those of the *Scientific American Medicine* textbook.)[1] In light of the results of this screening test indicating adrenal suppression, the eight-hour adrenocorticotropic hormone infusion test was performed. The results are presented in Table 1 and are consistent with the protocol criteria for adrenal suppression.

The patient was started in late December 1983 on replacement oral steroids (oral cortisone acetate, 20 mg every morning upon arising and 10 mg in the late afternoon, and oral fludrocortisone, 0.05 mg every day). Gradually, over a three-week period, he became less tired, and three and one-half weeks later the orthostatic blood pressure drop was gone. Because there was not a dramatic, immediate improvement and because there had never been any hyperpigmentation, the diagnosis was considered to be mild adrenal suppression secondary to the use of nasal steroids rather than Addison's disease.

The replacement oral steroids were tapered off in February 1984 (nasal steroids had been stopped in December 1983). Two weeks after stopping oral steroids,

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TABLE 1. URINE STEROID LEVELS

	Baseline (mg/d)	Day 1 (mg/d)	Day 2 (mg/d)
17-Corticosteroids	0.92 (3-10 normal)	3.23	5
17-Ketosteroids	3.50 (9-22 normal)	8.08	12

repeat testing showed normal morning and afternoon cortisol levels (19.6 μg/100 mL and 8.1 μg/100 mL, respectively). Repeat screening of the synthetic adrenocorticotropic hormone (Cortrosyn) test two weeks later showed a healthy response (5.8 μg/100 mL going to 24.2 μg/100 mL).

DISCUSSION

Intranasal dexamethasone (Decadron Phosphate Turbinaire) has been shown to cause adrenal suppression.[2] Nasal aerosol administration of beclomethasone dipropionate (Beconase, Vancenase), however, given in recommended doses of up to 400 μg daily, has not been reported to cause adrenal suppression after up to 12 weeks of use.[3,4] Even after several times the recommended dose, up to 1,600 μg/d intranasally, systemic absorption and adrenal suppression have not been reported. A dose of 8,000 μg daily intranasally (equivalent to 190 bursts) did produce a clear reduction in morning plasma cortisol levels, and lesser daily quantities of intranasal combined with inhaled beclomethasone have produced disturbances of cortisol secretion.[5] Intranasal flunisolide has been reported to cause adrenal suppression only in doses greatly exceeding the recommended ranges.[6]

Inhaled beclomethasone dipropionate may produce a degree of adrenal suppression approximately twice that of an equivalent dose of intranasal aerosol. In adults, a dose of 1,600 μg/d of inhaled beclomethasone causes a significant decrease in morning cortisol levels not seen at a lower dose.[7] A number of authors have argued whether normal therapeutic doses of beclomethasone can cause significant adrenal suppression in children, but no consensus has been reached. A trend toward suppression of the hypothalamic-pituitary-adrenal axis has been reported with inhaled flunisolide when used to treat chronic asthma.[8]

In summary, the literature suggests intranasal beclomethasone dipropionate, except in inordinately high doses, should not cause adrenal suppression, and it has never been shown to cause clinical signs of suppression. This report, however, describes a case where nasal steroids were probably responsible for secondary adrenal suppression. It should be noted that the patient is unusual in having severe sinus disease with multiple related surgeries. Perhaps his mucosal lining absorbed more than the average person with asthma or allergic rhinitis who has been reported in the literature.

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