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Adrenal suppression with intranasal betamethasone drops

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Abstract
Intranasal betamethasone sodium phosphate drops (Betnesol) are frequently used to relieve nasal congestion due to polyposis. We report a case of significant hypothalamic-pituitary-adrenal suppression secondary to the long-term use of intranasal betamethasone drops. This case emphasizes that the topical application of potent corticosteroids may produce systemic effects.

Introduction

The absorption of potent corticosteroids through mucosal surfaces may result in significant systemic effects. Suppression of the hypothalamic-pituitary-adrenal axis is a recognized complication of high dose inhaled corticosteroids used in the treatment of bronchial asthma (Smith and Hodson, 1983) but is thought to be uncommon with the use of topical intranasal corticosteroids. We report for the first time a case of secondary adrenal suppression related to treatment with intranasal betamethasone sodium phosphate drops 0.1 per cent (Betnesol).

Case report

A 75-year-old man was admitted as an emergency with a history of recurrent syncope. He had postural hypotension with a standing blood pressure of 80/0 mmHg compared with a supine measurement of 110/80 mmHg. His symptoms could not be attributed to dehydration, autonomic failure or cardiac dysrhythmia and his clinical presentation was thought to be due to hypoadrenalism. He had a history of bronchial asthma and of nasal polyposis treated with surgery 7, 13, 17 and 25 years earlier. He had been using betamethasone 0.1 per cent nasal drops (Betnesol) continuously for a minimum of three years in a prescribed dosage of one drop to each nostril, four times daily. On direct questioning he had been more liberal in his application frequently squirting it into his nostrils. He also used a 'Ventide' inhaler (salbutamol combined with beclomethasone) administering a maximum of one puff twice daily (maximum dose of beclomethasone 100 micrograms daily).

Adrenal insufficiency was confirmed by the measurement of a 9.00 am basal serum cortisol of only 47 nmol/l (normal >150 nmol/l), rising to only 271 nmol/l (normal >550 nmol/l), one hour after the administration of 250 micrograms of intravenous tetracosactrin (Synacthen) (Clayton, 1989). There was no evidence of hypopituitarism and primary adrenal insufficiency (Addison's disease) was excluded by an absence of pigmentation, negative adrenal antibodies and normal plasma renin activity. Plasma adrenocorticotrophic hormone (ACTH) was only 15 ng/l in contrast to values >200 ng/l which would be expected in primary adrenal failure (Clayton, 1989). Adrenal stimulation with an intramuscular injection of 1 mg of tetracosactrin (Synacthen Depot), confirmed secondary adrenal suppression with a baseline serum cortisol of 20 nmol/l rising to only 228 nmol/l at four hours but rising to 664 nmol/l by 24 hours (serum cortisol remains <280 nmol/l in primary hypoadrenalism).

He was treated with intravenous hydrocortisone and subsequently with hydrocortisone 20 mg in the morning and 10 mg in the evening. His nasal polyps were treated by surgery and his topical nasal corticosteroids discontinued. Oral corticosteroids replacement was continued for 14 months until there was evidence of the return of normal function of his hypothalamic-pituitary-adrenal axis when his 9.00 am cortisol achieved the normal range after temporary corticosteroid withdrawal.

Discussion

Betamethasone is a potent corticosteroid which, when administered as nasal drops, has been demonstrated in a double blind placebo controlled trial to be effective in controlling symptoms of nasal polyps (Chalton *et al.*, 1985).

Adrenal suppression is reported with the intranasal application of dexamethasone (Normal *et al.*, 1967) and with beclomethasone in a case with previous multiple surgery and recurrent sinusitis (Sorkin and Warren, 1986).

There are no specific formal studies of betamethasone absorption but nasal corticosteroids absorption may be facilitated by an engorged nasal mucosa and an increase in mucosal surface area due to nasal polyps. Nasally administered corticosteroids may also be swallowed and betamethasone is freely absorbed from the gastrointestinal tract (Reynolds, 1989) without being destroyed in theliver. The potential for systemic absorption of betamethasone is illustrated by a reported case of iatrogenic Cushing's syndrome related to abuse of betamethasone nasal drops (Stevens, 1988).

A regular dose of oral prednisolone in excess of 7.5 mg will result in adrenal suppression. The total prescribed dose of intranasal betamethasone in this case is estimated as 200 micrograms/day (Chalton *et al.*, 1985), which is equivalent to less than 3 mg of prednisolone. It is probable that our patient exceeded the prescribed dosage of intranasal betamethasone on an intermittent basis, for a prolonged period of time. Adrenal suppression resulted from both increased nasal and intestinal absorption. His presentation with adrenal insufficiency may reflect an inadvertent reduction in his betamethasone administration or a minor intercurrent illness precipitating adrenal crisis. Betamethasone has little mineralocorticoid activity (Reynolds, 1989) which may have contributed to the presentation with postural hypotension and syncope. A period of 9–12 months before the recovery of adrenal function is to be expected (Dixon and Christy, 1980).

Inhaled beclomethasone (as Ventide inhaler) is unlikely to have contributed significantly to adrenal suppression in this case

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as inhaled doses of 1600 micrograms daily are required to produce detectable adrenal suppression (Sherman *et al.*, 1982) and doses of 8000 micrograms if administered intranasally (Harris *et al.*, 1974).

Adrenal suppression as described here is a gross end product of the systemic absorption of topical corticosteroids. It is important to be aware of more subtle effects such as are being reported with inhaled corticosteroids which include impaired glucose and lipid metabolism (Krusynska *et al.*, 1987) and impaired bone metabolism which may predispose to osteoporosis (Ali *et al.*, 1991). Unsuspected adrenal suppression may also put the patient at risk during intercurrent illness and in the peri-operative period if consideration is not given to appropriate temporary glucocorticoid replacement.

This case supports the recent recommendation to limit the use of intranasal corticosteroids to a one month course used not more than six times a year (Drug and Therapeutics Bulletin, 1989) and emphasizes that topical steroids should be prescribed with care. Consideration should be given to the use of metered dosages and the use of other corticosteroids such as Budesonide which may have less systemic absorption and have less systemic bioavailability due to more rapid degraduation and higher first pass clearance (Ryrfeldt *et al.*, 1982, Pedersen and Fugslang, 1988).

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