tery for low resource settings, including further research on developing simple, acceptable, and low cost approaches for sterilisation and reuse of cautery tips.

The experts also discussed programmatic research, including prospective evaluations of different techniques, studies to determine the feasibility of implementing and training providers on various techniques, and research to identify practical differences between the techniques and perhaps to make recommendations for providers depending on the number of vasectomies done in a particular clinical setting. Future research should clarify the appropriate use of cautery and fascial interposition in low resource settings.

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Lesson of the week

Carbamazepine and false positive dexamethasone suppression tests for Cushing's syndrome

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The clinical features of Cushing's syndrome may be subtle to begin with, and they resemble those of patients with metabolic syndrome. The key to diagnosing Cushing's syndrome is a high index of suspicion and the use of screening tests. The 1 mg overnight dexamethasone suppression test is commonly used. Subsequent biochemical evaluation often uses higher doses of dexamethasone. The overnight dexamethasone suppression test is also increasingly used in the functional evaluation of incidental adrenal masses.

We describe two patients, both of whom were suspected of having Cushing's syndrome based on abnormal results from overnight dexamethasone suppression tests. Subsequent evaluation excluded Cushing's syndrome in both patients. The false positive

suppression tests were because of accelerated metabolism of dexamethasone caused by carbamazepine. Awareness of this potential pitfall in the diagnosis of Cushing's syndrome is important to avoid unnecessary investigations and anxiety.

Case reports

Case 1

A 24 year old woman was referred to the clinic for investigation of her weight gain. She had noticed progressive weight gain in recent years. She had a known history of depression, for which she has been prescribed alprazolam, sertraline, and propranolol. She had no history of steroid use. She was a non-smoker and was teetotal. On examination, she was

Drugs that induce metabolism of dexamethasone can lead to misdiagnosis of Cushing's syndrome

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obese with a round face and moderate facial acne. She was normotensive. Serum electrolytes were normal.

We suspected her as possibly having Cushing's syndrome and arranged a 1 mg overnight dexamethasone suppression test. This showed failure of suppression with a cortisol concentration of 256 nmol/l (normal < 50 nmol/l) after the dexamethasone. She was subsequently admitted to hospital for further investigations, and we did a low dose dexamethasone suppression test. This showed failure of suppression on low dose dexamethasone (baseline serum cortisol 269 nmol/l, cortisol 204 nmol/l after dexamethasone 0.5 mg every six hours for 48 hours). Baseline adrenocorticotrophic hormone was low (< 2.2 ng/l).

We made a provisional diagnosis of Cushing's syndrome and arranged imaging studies. Computed tomography of her abdomen showed normal adrenal glands. We later found out that she had been taking, for temporal lobe epilepsy, 400 mg carbamazepine three times a day, which may have interfered with her biochemical tests. A 24 hour collection of urine for free cortisol, measured by radioimmunoassay, was normal. Further investigations showed normal daily variation in cortisol concentration, with a low midnight cortisol concentration of 7 nmol/l (normal < 50 nmol/l) and 503 nmol/l in the morning. We decided that she did not have any clinical evidence of Cushing's syndrome and that her failed dexamethasone suppression tests were due to the effect of carbamazepine inducing the metabolism of dexamethasone. She was last seen in May 2004 and was well with stable body weight.

Case 2

A 52 year old woman with a history of type 2 diabetes and hypertension was referred to the clinic for management of her diabetes. She did not smoke and did not drink alcohol regularly. She was overweight, and we arranged an overnight dexamethasone suppression test. This showed failure of suppression with a cortisol concentration of 149 nmol/l (normal < 50 nmol/l) after giving 1 mg dexamethasone. We initially suspected that she had Cushing's syndrome. Further questioning found that she had trigeminal neuralgia, for which she has been taking carbamazepine 400 mg three times a day for a year. After discussion with her neurologist, we took her off carbamazepine and switched her to amitriptyline. An overnight dexamethasone suppression test repeated three weeks later was normal, with a cortisol concentration of 19 nmol/l after suppression.

Discussion

Cushing's syndrome arises from excess production of cortisol and has a high mortality if left untreated. The overnight 1 mg dexamethasone suppression test is widely used as a screening test for Cushing's syndrome, but it is not specific for this syndrome. The test has a false positive rate of 2-12%,^{1,2} which could be due to stress, weight loss,³ alcohol withdrawal,⁴ failure of ingestion of dexamethasone, or altered metabolism of the drug. Consequently, a positive overnight dexamethasone suppression test is usually followed by further endocrine testing, which usually includes low dose and high dose dexamethasone suppression. The dexamethasone suppression test is designed to assess the

ability of exogenous dexamethasone to suppress endogenous corticotrophin and hence cortisol production. Dexamethasone is primarily metabolised by the cytochrome P450 system, by hepatic CYP3A4, an enzyme complex responsible for the metabolism of many xenobiotics.⁵ Considerable increases in cytochrome P450 enzymes can be seen in regular smokers and people who drink alcohol regularly.⁶ Several drugs such as phenobarbital, primidone, ethosuximide, carbamazepine, and rifampicin induce the activity of CYP3A4, and can lead to false positive dexamethasone suppression tests.⁷⁻⁹

Conversely, patients with adrenal insufficiency and taking steroid replacement may need increased doses of steroids if also taking these enzyme inducers.¹⁰ During endocrine testing, patients should ideally stop taking these interacting drugs. If this is not feasible, alternative strategies for evaluation include use of midnight cortisol,^{11,12} late night salivary cortisol,¹³ or hydrocortisone suppression tests.¹⁴ Measurement of urinary free cortisol may be helpful, although carbamazepine has also been reported to interfere with urinary cortisol measurements by high performance liquid chromatography.¹⁵ In screening patients for Cushing's syndrome, be aware of potential drug interactions with dexamethasone, which may lead to false positive results. Appropriate investigations and interpretation of results is necessary to avoid misdiagnosing Cushing's syndrome.

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