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Lesson of the week

Raised cortisol excretion rate in urine and contamination by topical steroids

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Beware of contamination of urine samples with topical cortisol during screening for Cushing's syndrome

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The clinical features of type 2 diabetes (obesity, hypertension, and glycosuria) often overlap with those of Cushing's syndrome, and as impaired glucose tolerance occurs in up to 20% of patients with Cushing's syndrome, its incidence in people with diabetes is higher than among people without diabetes.[1] Diagnosis relies on clinical suspicion and abnormal results of biochemical tests. Measurement of the excretion rate of free cortisol in the urine forms the basis of the initial outpatient investigations and should reflect the overall cortisol secretion provided it is measured accurately. We present two cases from diabetic clinics in which patients had raised urinary free cortisol excretion rates as a result of urinary contamination by vaginal cream containing hydrocortisone.

Case reports

Case 1—A 49 year old woman with type 2 diabetes mellitus, hypertension, and depression was referred for investigation of possible Cushing's syndrome. The history was of deteriorating control of glycaemia and blood pressure. Outpatient measurement of overnight urinary cortisol:creatinine ratios showed grossly raised values (mean 255 µmol cortisol/mol creatinine; range 15-1191; normal <25 µmol/mol creatinine). She was admitted and underwent a series of complex tests to define her Cushing's syndrome, all of which yielded normal results. Despite this, the urinary free cortisol excretion rate remained high (4365 nmol/24 hour; normal rate <250 nmol/24 hour). This pattern strongly suggested the presence of a factor interfering in the measurement of urinary free cortisol, which we confirmed using gas chromatography. This showed excipients consistent with the use of topical steroid cream. Further questioning of the patient revealed that she had been using an antifungal cream containing hydrocortisone (Canesten HC, Baypharm, Bayer, Berks) for vaginal candidiasis. Once this was stopped, urinary free cortisol excretion rates returned to normal (120 nmol/24 hour).

Case 2—A 38 year old woman with type 2 diabetes, gross obesity, and facial plethora also underwent investigations for Cushing's syndrome. Overnight urinary cortisol:creatinine ratios were again moderately raised over a two month period (range 14 to 137 µmol/mol creatinine; normal <25 µmol/mol creatinine), but serum cortisol concentrations were within reference limits with a normal diurnal variation and a normal result of an overnight dexamethasone suppression test. Because of the similarity with case 1, the patient was interviewed and also admitted using Canesten HC cream on perineal and vaginal areas to treat candidiasis. After she discontinued this treatment, urinary cortisol:creatinine ratios returned to normal on all three occasions tested (5, 11, and 11 µmol/mol creatinine).

Discussion

In both patients contamination of their urine with Canesten HC during collection was responsible for the increased urinary cortisol values. This cream contains 1% hydrocortisone and a normal application is about 0.5 g. Direct contamination with as little as 0.035 mg of cream (0.007% of that applied) would raise urinary free cortisol concentration to above the normal range. Urinary free cortisol measurements are often used as an initial inexpensive screening test for patients with clinical symptoms of Cushing's syndrome. The pitfalls of the test are many and include incomplete 24 hour collection, solutes interfering with the competitive binding assay, and the presence in the urine of administered steroids.[2 3] Steroids are administered by numerous routes, and the above cases show that before investigations are conducted patients should be asked if they are using any topical preparation, as drugs given topically are often not considered a medication by the patient and consequently not mentioned.

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