Overnight Dexamethasone Suppression Test

Indications

This is one of the first line screening tests for Cushing's syndrome.
Cushing's syndrome is a collective name for a number of endocrine conditions associated with the overproduction of cortisol by the adrenal gland. Cortisol production is controlled by the secretion of adrenocorticotrophic hormone (ACTH) from the pituitary and is under negative feedback control from cortisol. Excess cortisol production can be secondary to an ACTH secreting pituitary tumour (Cushing's disease, 70% of cases), ectopic secretion of ACTH (12% of cases) or an adrenal adenoma/carcinoma (18% of cases).

Dexamethasone is a synthetic glucocorticoid, more potent than cortisol and can act to suppress ACTH and hence cortisol production in healthy individuals but not in Cushing's syndrome.

Preparation

The test can be done on an outpatient basis with the patient taking the dexamethasone between 2300 and 2400, presenting for a blood test the following day.

Procedure

1. Patient takes 1mg of Dexamethasone orally between 23:00 and mid-night.

2. The next day at 09:00 collect blood (serum/gold top) for "Post Dexamethasone Cortisol"

NB. Dexamethasone causes adrenal suppression; therefore other hormones should not be measured at the same time.

Interpretation

Suppression of cortisol to less than 50nmol/L excludes Cushing's syndrome. Sensitivity 95% and specificity 80% (although specificity is increased to 95% if a cut off 140nmol/l is used). If levels are not suppressed please contact the laboratory to discuss further investigation

Confounding factors

1. Morbid obesity can cause false positives.
2. Weight loss: recent weight loss, including anorexia nervosa, may result in a false lack of suppression in 25% of patients

3. Stress & depression: Psychological or physical stress and depression override normal cortisol feedback in 30-50 % of cases giving false results. Findings can mimic Cushing's. It is recommended to avoid testing during intercurrent illness.
4. Alcohol: Chronic alcohol abuse can produce a clinical and biochemical Cushing's syndrome which resolves after as little as one week abstention. Clinical interpretation will need to take account of possible clandestine alcohol consumption.
5. Therapeutic drugs (table 1): Drugs which induce hepatic enzymes, e.g. phenytoin, carbamazepine, phenobarbitone and rifampicin, may enhance clearance of dexamethasone resulting in false lack of suppression. Oestrogens, oral contraceptives and tamoxifen increase cortisol binding globulin resulting in a false lack of suppression in up to 50 % of subjects.
   Renal failure and haemodialysis: CKD patients and those on haemodialysis may show false positive results, due to diminished cortisol and dexamethasone clearance, respectively.

Drugs that accelerate dexamethasone metabolism by induction of CYP 3A4 (false positive results)	**Drugs that impair dexamethasone metabolism by inhibition of CYP 3A4 (false negative results)**	**Drugs that increase CBG and may falsely elevate cortisol results (false positive results)**
Phenobarbital	Aprepitant/fosaprepitant	Oestrogens
Phenytoin	Itraconazole	Mitotane
Carbamazepine	Ritonavir	Tamoxifen
Primidone	Fluoxetine	
Rifampin	Diltiazem	
Rifapentine	Cimetidine	
Ethosuximide		
Pioglitazone		

Table 1 – drugs affecting cortisol results, adapted from Nieman et al., 2008

References

Wood, Barth, Freedman, Perry and Sheridan. Evidence for the low dose dexamethasone suppression test to screen for Cushing's syndrome – recommendations for a protocol for biochemistry laboratories. Ann Clin Biochem 1997; 34: 222-29.

Nieman, LK., Biller, BMK., Findling JW., Newell-Price J., Savage, MO., Stewart, PM., Montori, VM. The Diagnosis of Cushing's Syndrome: An Endocrine Society Clinical Practice Guideline. J Clin Endocrinol Metab 2008; 93 (5): 1526-1540