High Dose Dexamethasone Suppression Test

Test Name: CHILD HIGH DOSE DEXAMETHASONE SUPPRESSION TEST

Principle

This test is used in patients who have Cushing's syndrome established by screening, but with requirement for the aetiology to be further identified. The test works on the basis that in most situations the corticotroph tumour cells in Cushing's disease retain some responsiveness to the negative feedback of glucocorticoids, whilst tumours ectopically secreting ACTH will not. However, the HDDST maybe abnormal in healthy people and normal in patients with Cushing's syndrome and therefore may not be helpful in establishing the diagnosis. Indeed, for adults the pre-test probability of ACTH-dependent Cushing's syndrome being secondary to pituitary dependent Cushing's disease is 85-90%. The HDDST correctly identifies 69% of adult patients as having Cushing's disease. Since the diagnostic accuracy of this test in identifying Cushing's disease is less than the pre-test probability of making this diagnosis, this test is now rarely used. As ectopic causes of Cushing's syndrome are extremely rare in children, there is a very limited evidence base concerning the use of this test, although one group advocate the use of the low dose dexamethasone suppression test as an adequate alternative (with suppression of >30% being suggestive of Cushing's disease).

Indication

- To differentiate pituitary-dependent and ectopic causes of Cushing's syndrome.

Precautions

- False positive results may be obtained following the use of drugs that accelerate dexamethasone metabolism including phenobarbital, phenytoin, carbamazepine, rifampin, rifapentine, ethosuximide, diltiazem or cimetidine. If possible, these should be stopped a few weeks prior to the test.
- Drugs that increase cortisol binding globulin (CBG) may also falsely elevate cortisol results including oestrogens.
- Dexamethasone clearance maybe reduced in patients with liver and/ or renal failure.
- Dexamethasone should be used cautiously in a child with diabetes mellitus with meticulous measurements of blood glucose during the period of the test.
- The child should not be on exogenous glucocorticoids during the test including steroid creams, inhalers and eye drops.

Side Effects

- No significant side effects.

Preparation

- This test may be performed sequentially following the LDDST.

Protocol

ACTH samples should be sent IMMEDIATELY to laboratory on ice for centrifugation and freezing

1. **Day 1 -** Take blood samples for cortisol and plasma ACTH at 0900h and 2400h
2. **Days 2 and 3 -** Starting at 0900h administer dexamethasone every 6 hours (i.e. 1500, 2100, 0300h) as follows:

    a. ***If the patient weighs more than 40 kg use a dose of 2 mg dexamethasone***
    b. ***If the patient weighs less than 40 kg use a dose of 120 micrograms/kg/day (divided into 4 daily doses)***

    All doses must be adhered to for the test to be valid.
3. **Day 4 -** Take blood sample for serum cortisol and plasma ACTH at 0900h, 6 hr after the last dose of dexamethasone.

Time Points:

Day	Time (h)	Procedure	Sample
1	0900	-	Blood for Cortisol/ ACTH
	2400	-	Blood for Cortisol/ ACTH
2	0900	Oral Dexamethasone	-
	1500	Oral Dexamethasone	-
	2100	Oral Dexamethasone	-
3	0300	Oral Dexamethasone	-
	0900	Oral Dexamethasone	-
	1500	Oral Dexamethasone	-
	2100	Oral Dexamethasone	-
4	0300	Oral Dexamethasone	-
	0900	-	Blood for Cortisol/ ACTH

Samples

ACTH 1.8 mL EDTA tube (pink top)
Send IMMEDIATELY to laboratory on ice for centrifugation and freezing

Cortisol 1.2 mL lithium heparin (orange top) or clotted blood (white top)

Interpretation

- Patients with pituitary-dependent hypercortisolism (Cushing's disease) will usually show suppression of plasma cortisol to at least 50% of basal values. Those with ectopic ACTH secretion will not show any suppression of Cortisol. Please note that approximately 10% of patients with Cushing's disease fail to suppress and approximately 10% of those with ectopic ACTH secretion will suppress.

References

1. Nieman L.K., Beverly M.K.B., Findling J.W., Newell-Price J., Savage M.O., Stewart P.M. and Montori V.M. (2008) The Diagnosis of Cushing's Syndrome: An endocrine society clinical practice guideline. *JCEM* **93**:1526-1540