Low Dose Dexamethasone Test – Full Clinical Guideline

Reference No: CHISCG7

Low dose Dexamethasone Test for the Confirmation of Cushing's Syndrome

THIS TEST IS ONLY TO BE PERFORMED FOLLOWING DISCUSSION WITH A CONSULTANT BIOCHEMIST OR ENDOCRINOLOGIST

1. Introduction

Dexamethasone is a synthetic steroid with 25 times the glucocorticoid activity of cortisol. It does not interfere with cortisol measurement.
Cortisol secretion in normal subjects will suppress following low dose dexamethasone.
The low dose dexamethasone suppression test may be performed following failure of suppression of cortisol in the overnight test, but is not indicated following normal suppression in the overnight test.

2. Guideline

INDICATIONS

As a diagnostic test for Cushing's Syndrome (and initial determination of differential diagnosis).

CONTRAINDICATIONS

Severe stressful illness/infection
Active peptic ulceration

SIDE EFFECTS

- Possibility of slightly raised blood sugars in Diabetic patients
- Patients with depression may experience a slight mood alteration

PRECAUTIONS

Care in patients with:
1. Diabetes Mellitus
2. Psychiatric symptoms in Cushing's syndrome which may worsen

A number of conditions may cause non-suppression with low-dose dexamethasone in the absence of Cushing's syndrome and therefore consideration should be given to whether the test is appropriate:
1. *Severe endogenous depression:* Patients may have an abnormal circadian rhythm.
2. *Alcoholism (alcoholic pseudo-Cushing's):* The mechanism is ill-understood; rapidly reverses on stopping drinking.
3. *Hepatic enzyme-inducing drugs:* e.g. Phenytoin, Phenobarbitone, Rifampicin etc. These cause more rapid metabolism of dexamethasone to levels which fail to suppress the normal pituitary-adrenal axis. A circadian rhythm study, 24h urine cortisol collection or CRH test may help resolve the problem.
4. *Glucocorticoid resistance syndrome:* A rare familial disorder in which basal glucocorticoid levels are high and only partially suppress with dexamethasone. The patients are not cushingoid and the disorder is due to receptor mutation.

5. *Failure to take dexamethasone correctly:* Check with patient.
6. *Oestrogen therapy:* Patients on the oral contraceptive will have high basal cortisol due to an increased cortisol binding globulin. Suppression will occur, but may not be completely normal.

PREPARATION

Planning: This test can be done as an inpatient procedure, or as an outpatient procedure provided the patient fully understands the importance of the dose and sample collection times and can attend the hospital for the blood tests. A patient information leaflet exists for this test and should be sent to the patient ahead of the procedure.

Patient: No special patient preparation is required.

Equipment:

- Dexamethasone, 0.5 mg tablets x 8
- One purple top (EDTA) tubes for ACTH sample
- Two yellow top (SST) tubes for cortisol samples (and final dexamethasone level)

PROCEDURE

The request form must state clearly that samples are part of a dexamethasone suppression test and should state date, day of test, and time of sample, and for urines dates and times of collection period. All medication should be noted on the request form. It is important that dexamethasone tablets are taken **strictly 6-hourly** for this test. The timings shown below may need to be adjusted if the basal sample is not collected at exactly 09:00.

Sample Requirements:

- Serum cortisol and final check dexamethasone level (Yellow top sample). Note that the sample will only be sent for dexamethasone level if the final cortisol is not suppressed to <50 nmol/L.
- Plasma ACTH (Purple top, EDTA sample). This assay will only be done if cortisol results indicate the need

Day & Time	Blood sample	Dexamethasone
1 09:00	Take basal sample at 09:00 before giving dexamethasone (Cortisol – Yellow top, ACTH – purple top)	0.5 mg
15:00		0.5 mg
21:00		0.5 mg
2 03:00		0.5 mg
09:00		0.5 mg
15:00		0.5 mg
21:00		0.5 mg
3 03:00		0.5 mg
09:00	48hr sample at 09:00 (Cortisol and dexamethasone level – Yellow top)	

INTERPRETATION

Normal response

Serum cortisol is in the normal resting 09:00 range (166 - 507 nmol/L) and suppresses to undetectable (<50 nmol/L) levels at 48 hrs.

At 48h (after the low dose dexamethasone)
A serum cortisol <50 nmol/l at 48h excludes Cushing's syndrome unless clinical suspicion is very high (very rarely patients with Cushing's syndrome may show normal suppression and more frequently the condition may be cyclical).

When dexamethasone is >3.3 nmol/L, a cortisol of ≤50 nmol/L is typically observed in patients without Cushing's syndrome. Dexamethasone levels of ≤3.3 nmol/L indicate that insufficient dexamethasone is present in circulation to suppress cortisol and a corresponding cortisol ≥50 nmol/L may be a false positive result. In these circumstances the test may need to be repeated or an alternative investigation for Cushing's syndrome conducted eg 24 hour urine cortisol.

In ACTH dependant Cushing's serum cortisol may suppress to 50% or less of the basal value in Cushing's disease (i.e. ACTH secretion from the pituitary), but not in ectopic ACTH secretion, macronodular hyperplasia or in adrenal tumours. Approximately 10% of patients with Cushing's disease may fail to suppress while the occasional patient with the ectopic ACTH syndrome does. If the 48h cortisol from the low dose dexamethasone suppression test suppresses to 50% of the basal value then there is no additional information gained from conducting the high dose test.

3. References

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4. Documentation Controls

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