CORTICOTROPHIN RELEASING HORMONE TEST

INTRODUCTION

This test is useful to differentiate between patients with pituitary Cushing's (Cushing's disease) and those with an ectopic source of ACTH. In the majority of patients with Cushing's disease, the intravenous administration of CRH causes an excessive rise in plasma ACTH and cortisol, while in patients with ectopic ACTH secretion such an effect is seen only very rarely.

CONTRAINDICATIONS AND SIDE EFFECTS

Allergic reactions, flushing dyspnoea and hypotension have been described after ovine CRH and so the test must only be performed with full medical support present, although human CRH is now in wide usage.

PATIENT PREPARATION

Oestrogen containing medications, including the contraceptive pill and hormone replacement therapy, should be stopped for six weeks prior to the test. This is because oestrogen induces cortisol binding globulin and leads to elevations in measured serum total cortisol. Any steroid containing medications should also be avoided, as they may interfere with the hypothalamo-pituitary-adrenal axis, or cross react with the cortisol assay.

PROTOCOL

Please use the separate pro-forma to record samples taken and timing.

1. After overnight fast (only water allowed), insert indwelling intravenous cannula.
2. Ensure patient lies supine for **at least 30 minutes prior to starting the test** and remains so throughout the test.
3. Label 8 EDTA (pink/purple) and 8 serum (SST gold-top) tubes with patient details and sample timings.
4. **Inject CRH intravenously (see box below)**

CRH Dosage:

- 1 microgram/kg of ovine CRF **or**
- Total of 100 micrograms

5. Plasma ACTH and cortisol samples are taken as per pro-forma at –15, 0, 15, 30, 45, 60, 90 & 120 minutes. The EDTA samples (pink/purple topped tubes) for ACTH must be **placed on ice** and after collection of the first five samples they must be transported quickly on ice to the laboratory, then the last three samples may follow together in the same way. Failure to transport samples to the laboratory within 1 hour of collection will result in a delay in processing and potentially unreliable results.

INTERPRETATION

A rise in **cortisol** from basal to peak of > 20 % suggests a pituitary source.

A rise of **ACTH** from basal to peak of > 50 % suggests a pituitary source.

Also, a rise by 35 % in ACTH at + 15 and +30 min (mean) in comparison to basal values also suggests a pituitary source.

These responses may be lower if human CRH is used instead of ovine CRH due to lower stimulatory action.

Ectopic ACTH and Adrenal tumours usually show a flat response.

SENSITIVITY AND SPECIFICITY OF TEST

With ovine CRH, when criteria is used for ACTH responses, sensitivity is 86% and specificity is 90%.

With human CRH, cortisol response criteria give better sensitivity for Cushing's disease.

10% of patients with Cushing's disease do not respond to CRH but they usually show suppression to the HDDST.

10 % of ectopic ACTH syndrome may respond to CRH but these patients usually fail to suppress with dexamethasone.

Thus high dose dexamethasone suppression test and CRH test used in combination allows correct differentiation between pituitary and ectopic ACTH secretion in most cases.

NOTE

Patients with depression may show a normal cortisol but reduced ACTH response and patients who are grossly obese may show a blunted or reduced cortisol response.

CONTACTS

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REFERENCES

Imperial endocrinology handbook. http://imperialendo.co.uk/Bible2018.pdf. (accessed 18/5/2020)
Uptodate.com: CRH stimulation test (accessed 18/5/2020)