Low dose (1 microgram) Synacthen test for suspected adrenal insufficiency

http://www.pathology.leedsth.nhs.uk/dnn_bilm/Investigationprotocols/Synacthen tests short long/LowDose1µgShortSynacthenTest.aspx

Indication

This is performed for the investigation of adrenal insufficiency. The standard Synacthen test utilising 250 µg Synacthen has been used successfully for many years but it is now clear that 250 µg represents approximately 500 fold greater dose than is required for maximal adrenal response. The cortisol response to 250 µg shows a steady increase for several hours, whereas the low dose which utilises 1 microgram demonstrates a rise and fall within 60 min. The Synacthen test gives unreliable results within 2 weeks of pituitary surgery.

Principle

Adrenal glucocorticoid secretion is controlled by adrenocorticotropic hormone (ACTH) released by the anterior pituitary. This test evaluates the ability of the adrenal cortex to produce cortisol after stimulation by synthetic ACTH (tetraicosactide: Synacthen ®). It does not test the whole pituitary-adrenal axis. The short test assesses the ability of the adrenal gland to respond to ACTH but is not reliable within 2 weeks of pituitary surgery.

Side effects

There are rare reports of hypersensitivity reactions to ‘Synacthen’ particularly in children with history of allergic disorders. See position statement from the Society for Endocrinology about the Use of Synacthen in Patients with a History of Asthma.

Preparation

There are no dietary restrictions for this test. The test is often performed in the morning as the cortisol responses between the morning and late afternoon may vary. In practice this test may also be performed in the afternoon.

Hydrocortisone should be omitted on the morning of the test. Prednisolone should be stopped 24 hours before the Synacthen test and recommenced after (unless instructed to the contrary).

Requirements

Preparation of 1 microgram Synacthen

- Synacthen (Tetraicosactide) - 250microgram / 1ml vial
- 500 mL 0.9% Sodium Chloride
- Procedure: dissolve 125microgram Synacthen in 500 mL saline and mix well
- 1 microgram of Synacthen is 4 mL of solution
- 3 plain and 1 EDTA tube are required for blood collection. ACTH is sent in an EDTA on ice.

Procedure

<table>
<thead>
<tr>
<th>Time</th>
<th>Action</th>
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</thead>
<tbody>
<tr>
<td>0900</td>
<td>Take 2 mL blood for cortisol and 1ml for ACTH inject Synacthen IV</td>
</tr>
<tr>
<td>0920</td>
<td>Take 2ml blood for cortisol</td>
</tr>
<tr>
<td>0930</td>
<td>Take 2ml blood for cortisol</td>
</tr>
</tbody>
</table>

Interpretation

1. Adrenal insufficiency is excluded by an incremental rise in cortisol of > 200nmol/L and a peak value > 600 nmol/L at either 20 or 30 min.
2. The above definition only defines adrenal insufficiency. The definition of normality is problematic since there is considerable variation in healthy individuals and a significant overlap with patients who have adrenal insufficiency.

3. In ACTH deficiency the response to the short test may be normal or reduced.

4. The response to Synacthen is not affected by obesity.

5. There is no difference in cortisol response between IV & IM administration.

6. Baseline and incremental cortisol values do NOT apply to women taking oral contraceptives because oestrogens increase cortisol binding globulin.

**Sensitivity and Specificity**

It should be noted that there are significant differences between cortisol measurements introduced by the assay used in your laboratory (Clark et al 1998, Klose et al 2007)

In children, and depending on the clinical context, a lower peak cortisol level (500 to 550 nmol/L) is occasionally acceptable. Please discuss any suboptimal results with the paediatric endocrinology department.

**References**


