Glucagon Stimulation Test for Cortisol & Growth Hormone

Test Name: CHILD GLUCAGON STIMULATION FOR CORTISOL AND GROWTH HORMONE DFT

Principle

This test can be used as an alternative to the insulin-induced hypoglycaemia test in the evaluation of central adrenal insufficiency. Glucagon requires endogenous ACTH to cause cortisol secretion.

Indication

- To identify secondary adrenal insufficiency or combined ACTH/GH deficiency

Precautions

- The test should not be performed on a patient with phaeochromocytoma or insulinoma as it may provoke an attack.
- The test should not be carried out following starvation of >48 hours or in the presence of a glycogen storage disease. The inability to mobilise glycogen may result in hypoglycaemia.
- The test should not be carried out in patients with severe hypocortisolaemia (9 am level <100 nmol/L)
- Thyroid function must be normal as thyroxine deficiency may reduce the GH and cortisol response.

Side Effects

- Nausea and abdominal pain are common (30%) and patients may rarely vomit.

Preparation

- Thyroid function and cortisol must be checked to rule out panhypopituitarism.
- GH should be stopped for at least 2 weeks prior to the test.
- All glucocorticoid therapy (other than dexamethasone or betamethasone) interferes with the assay of cortisol. If the patient is on prednisolone therapy, this must be discontinued for 24 hours prior to the test. If the patient is on a supra-physiological dose of hydrocortisone, this should be reduced to a physiological level (6 micrograms/m^2/day) prior to the test. Omit the dose the night before and on the morning of the test. If the paediatric endocrine consultant is very anxious about the degree of adrenal insufficiency, then omit only the morning hydrocortisone dose. However, the patient should take their usual dose of corticosteroid as soon as the test is completed.
- Patients must fast for 8 hours prior to the test (water only is allowed).
- A small amount of water may be swallowed during the test.
- Sex steroid priming may be necessary, see ***Diagnosis of Growth Hormone Deficiency***

Protocol

Children can become hypoglycaemic after glucagon administration, usually 90 – 120 minutes post dose. Children <8 yrs of age are at particular risk. Check glucose levels (by glucose meter) at the time of every sample. Check that the child is responsive at the time of every sample. If they do not respond, then follow instructions for the emergency management of hypoglycaemia.

1. Insert an indwelling 22 gauge, blue, cannula and wait 30 minutes before taking the baseline (t=0) sample for cortisol and growth hormone.

2. Check glucose level by meter.
   - If glucose < 2.6 mmol/L at the start of the test - DO NOT PROCEED WITH TEST & DO NOT ADMINISTER GLUCAGON. Discuss with endocrine team. It may be necessary to administer 10% glucose 2 ml/kg throughout the test. Take a sample for glucose and growth hormone before administering glucose.
   - If glucose level >2.6 mmol/L then administer ***glucagon:***

Generic	*Route*	*Dose*	*Frequency*
Glucagon	*i.m*	*30 micrograms/kg of body weight up to a maximum dose of 1 mg.*	*Bolus*

3. Take further blood samples for cortisol at 60, 90, 120, 150 and 180 min post glucagon administration.
4. Observe for signs of hypoglycaemia throughout the test and record in patient's notes.
5. Remember to check the child's glucose level by meter and the responsiveness at every sample.
6. A sweet drink and a full meal must be eaten and tolerated after the test and the child should be observed for 1 hour after the test. Blood glucose (by meter) must be >4 mmol/L before discharge.

Time Points:

Time post glucagon (min)	Procedure	Blood Sample
-30	Check blood glucose using meter	Cortisol, Growth Hormone
0	Check blood glucose using meter	Cortisol, Growth Hormone
60	Check blood glucose using meter	Cortisol, Growth Hormone
90	Check blood glucose using meter	Cortisol, Growth Hormone
120	Check blood glucose using meter	Cortisol, Growth Hormone
150	Check blood glucose using meter	Cortisol, Growth Hormone
180	Check blood glucose using meter	Cortisol, Growth Hormone

Samples

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

Growth Hormone 1.2 mL clotted blood (white top)

Interpretation

- A peak plasma cortisol concentration of ≥430 nmol/L is indicative of a normal response and normal adrenal function.
- A peak plasma GH concentration of ≥7 µg/L indicates a normal response to the test and no further investigations are required.
- A peak plasma GH concentration of <5 µg/L is diagnostic of growth hormone deficiency but requires a second GH provocation test to confirm the diagnosis.
- A peak plasma GH concentration of 5–7 µg/L may still be indicative of GH deficiency and requires further investigation.
- In adults, a peak plasma GH concentration of <3 µg/L is diagnostic of growth hormone deficiency.
- Peak GH responses are also highly dependent on both short-term nutritional status and on BMI – higher peak GH levels after short-term fasting and in those with lower BMI.

References

1. Basildon and Thurlow University Hospitals NHS Foundation Trust Clinical Biochemistry Department paediatric department Glucagon Stimulation test Paediatric protocol
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3. Strich D., Terespolsky N. and Gillis D. (2009) Glucagon stimulation test for childhood Growth Hormone deficiency: Timing of the peak is important. *The Journal of Pediatrics* 415 – 419
4. Secco A., di Iorgi N., Napoli F., Calandra E., Ghezzi M., Frassinetti C., Parodi S., Casini M.R., Lorini R., Loche S. and Maghnie M. (2009) The Glucagon Test in the diagnosis of growth hormone deficiency in children with short stature younger than 6 years. *JCEM* **94**(11): 4251-4257