

Protein loading test for hypoglycaemia

Test Name: CHILD PROTEIN LOADING TEST FOR HYPOGLYCAEMIA DFT

Please discuss with Endocrine Team before carrying out this test. This fast is designed primarily for the use of the Endocrine teams at RMCH.

Management of hypoglycaemia

If at any time during the fast the child becomes hypoglycaemic with bedside finger prick glucometer reading ≤ 2.6 mmol/L (but remember blood glucose [BG] levels are inaccurate at low levels) or if symptomatic, do the following without delay:

- **take blood samples as listed as for the next time point** and
- stop the test immediately after the blood has been taken.
 - If symptomatic, give glucose (3 mL/kg of i.v. 10% glucose) - **INFORM DOCTOR**
 - Give feed if able to tolerate, if not intravenous maintenance fluids, 10% glucose + sodium chloride (e.g., 10% glucose/0.45% sodium chloride)
 - Recheck finger prick BG every 15 min until glucose >4.0 mmol/L
 - If BG remains low, consider further bolus and increase glucose concentration/ fluid rate (INFORM DOCTOR)
 - CONTACT ENDOCRINE CONSULTANT ON CALL IF ANY CONCERNS

Principle

Protein sensitivity is observed in some patients with CHI and is often seen in patients with GLUD1 gain of function mutations (hyperinsulinism/hyperammonaemia HI/HA syndrome). Protein sensitivity is also observed in patients with mutations in *ABCC8* gene encoding the SUR1 protein. **Caution - these patients can become severely hypoglycaemic in response to a protein/leucine load.** This test should only be done after consultation with the consultant looking after the patient. For safety reasons protein is used in the test, not pure leucine. The protein can be administered in the form of a drink (Maxipro/Vitapro) or as steamed fat-free chicken breast.

Indication

Patients suspected of having congenital hyperinsulinism with hyperammonaemia syndrome.

Precautions

- This test should not be performed on patients who are under physical stress e.g., post-surgery, trauma or infection or extreme psychological stress as these may give misleading results.
- This test should not be performed on patients with hypokalaemic periodic paralysis.

Side Effects

Some patients feel nauseated and may have vasovagal symptoms during this test.

Preparation

The patient should be fasted for a period of 3 to 8 h, the time period chosen should be dependent on the patient's age and the patient's usual interval between meals. However, this may not be possible with some patients.

Finger prick blood glucose should be monitored by a ward bedside monitor throughout the duration of the test. If $BG < 3.0$ mmol/L, check again in 15 minutes. If $BG < 2.6$ mmol/L or if the child is symptomatic of hypoglycaemia (feels hot, sweaty, flushed, tachycardia, decreasing consciousness), a venous sample for glucose, insulin and ammonia should be taken immediately and hypoglycaemia treated as above.

Options for protein loading

For a protein drink - Order Maxipro (1.5g/kg)/ Vitapro from the diet kitchen the day before the test.
For a protein meal - 35 g protein per m^2 surface area as steamed fat-free chicken breast to be eaten within 30 min.

Procedure

Remember to take all necessary precautions when carrying out this test. Treat in a similar manner to a diagnostic fast.

1. At t = 0 measure blood glucose using meter and take blood samples for glucose, insulin and ammonia
2. Administer the protein drink/meal. The drink/meal should be consumed within 30 min.
3. At 30 mins measure the bedside blood glucose. If the bedside glucose is <3.0 mmol/L take blood samples for glucose, insulin and ammonia. Record this information in the chart on the next page and write on t = 30 min on all samples.
4. Repeat this at 60 min, 90 min, 120 min, 150 min and 180 min. At 120 min take blood samples for plasma glucose, insulin and ammonia (as normal OGTT protocol). Even if bedside glucose is not <2.6 mmol/L.
5. If the child becomes hypoglycaemic at any stage of the test, stop and treat the hypoglycaemia.

Time Points:

Time (min)	Procedure	Blood Samples
0	Check blood glucose using meter. Take blood samples then administer protein load (Maxipro/Vitapro or steamed fat-free chicken breast).	Plasma glucose, insulin and ammonia
30	Check blood glucose using meter	If bedside glucose is <2.6 mmol/L take the following blood samples: Plasma glucose, insulin and ammonia
60	Check blood glucose using meter	If bedside glucose is <2.6 mmol/L take the following blood samples: Plasma glucose, insulin and ammonia
90	Check blood glucose using meter	If bedside glucose is <2.6 mmol/L take the following blood samples: Plasma glucose, insulin and ammonia
120	Check blood glucose using meter	Plasma glucose, insulin and ammonia (as normal OGTT protocol).
150	Check blood glucose using meter	If bedside glucose is <2.6 mmol/L take the following blood samples: Plasma glucose, insulin and ammonia
180	Check blood glucose using meter	If bedside glucose is <2.6 mmol/L take the following blood samples: Plasma glucose, insulin and ammonia

Samples

Glucose 1.2 mL fluoride oxalate (yellow top)

Insulin 1.2 mL lithium heparin (orange top)

The insulin samples must reach the lab within 4 hours of collection

Ammonia 1.2 mL EDTA (pink top)

Ammonia is unstable – send sample IMMEDIATELY to laboratory on ice for analysis

Interpretation

Detectable insulin and elevated ammonia when blood glucose is <2.5 mmol/L is inappropriate.

The insulin samples will be vetted by the laboratory – only insulin samples that have concurrent laboratory glucose of <3.0 mmol/L will be analysed – except for the baseline and 120 min samples.

References

1. Fournier C, Stanley A, Kelly Protein-sensitive hypoglycemia without leucine sensitivity in hyperinsulinism caused by KATP channel mutations. The Journal of Pediatrics, 2006, Volume 149, Issue 1 , Pages 47 - 52.
2. Kelly A, Ng D, Ferry RJ Jr, Grimberg A, Koo-McCoy S, Thornton PS, Stanley CA. Acute insulin responses to leucine in children with the hyperinsulinism/ hyperammonemia syndrome. J Clin Endocrinol Metab. 2001;86(8):3724–3728.
3. Heslegrave A, Kapoor RR, Eaton S, Chadeaux B, Akcay T, Simsek E, Flanagan SE, Ellard S, Hussain K. Leucine-sensitive hyperinsulinaemic hypoglycaemia in patients with loss of function mutations in 3-Hydroxyacyl-CoA Dehydrogenase. Orphanet J Rare Dis. 2012 May 14;7:25

Protein loading test for hypoglycaemia chart

Name	
DOB	
Hospital no	
Consultant	
Date	

Interval (mins)	Time collected	BM (mmol/L)	Glucose (mmol/L)	Insulin (pmol/L)	Ammonia (µmol/L)

1