Glucagon stimulation test

Recent studies suggest using lower GH cut-points for the glucagon stimulation test (GST) in diagnosing adult GH deficiency (GHD), especially in obese patients. There are limited data on evaluating GH and hypothalamic-pituitary-adrenal (HPA) axes using weight-based dosing for the GST.

To define GH and cortisol cut-points to diagnose adult GHD and secondary adrenal insufficiency (SAI) using the GST, and to compare fixed-dose (FD: 1 or 1.5 mg in patients >90 kg) with weight-based dosing (WB: 0.03 mg/kg). Response to the insulin tolerance test (ITT) was considered the gold standard, using GH and cortisol cut-points of ≥3 ng/ml and ≥18 µg/dL, respectively.

28 Patients with hypothalamic-pituitary disease and 1-2 (n = 14) or ≥3 (n = 14) pituitary hormone deficiencies, and 14 control subjects matched for age, sex, estrogen status and body mass index (BMI) underwent the ITT, FD- and WB-GST in random order.

Age, sex ratio and BMI were comparable between the three groups. The best GH cut-point for diagnosis of GHD was 1.0 (92 % sensitivity, 100 % specificity) and 2.0 ng/mL (96 % sensitivity and 100 % specificity) for FD- and WB-GST, respectively. Age negatively correlated with peak GH during FD-GST (r = -0.32, P = 0.04), but not WB-GST. The best cortisol cut-point for diagnosis of SAI was 8.8 µg/dL (92 % sensitivity, 100 % specificity) and 11.2 µg/dL (92 % sensitivity and 100 % specificity) for FD-GST and WB-GST, respectively. Nausea was the most common side effect, and one patient had a seizure during the FD-GST.

The GST correctly classified GHD using GH cut-points of 1 ng/ml for FD-GST and 2 ng/ml for WB-GST, hence using 3 ng/ml as the GH cut-point will misclassify some GH-sufficient adults. The GST may also be an acceptable alternative to the ITT for evaluating the HPA axis utilizing cortisol cut-points of 9 µg/dL for FD-GST and 11 µg/dL for WB-GST [1].

Until a potent, safe and reliable test becomes available, the GST should remain as the alternative to the insulin tolerance test (ITT) in the United States. In order to reduce over-diagnosing adult GHD in overweight/obese patients with the GST, Yuen et al propose utilizing a lower GH cut-point of 1 µg/L in these subjects. However, this lower GH cut-point still needs further evaluation for diagnostic accuracy in larger patient populations with varying BMIs and degrees of glucose tolerance [2].

1)
Hamrahian AH, Yuen KC, Gordon MB, Pulaski-Liebert KJ, Bena J, Biller BM. Revised GH and cortisol cut-points for the glucagon stimulation test in the evaluation of GH and hypothalamic-pituitary-adrenal axes in adults: results from a prospective randomized multicenter study. Pituitary. 2016 Feb 20. [Epub ahead of print] PubMed PMID: 26897383.
2)
Yuen KC, Tritos NA, Samson SL, Hoffman AR, Katznelson L. AMERICAN ASSOCIATION OF CLINICAL ENDOCRINOLOGISTS, AMERICAN COLLEGE OF ENDOCRINOLOGY DISEASE STATE CLINICAL REVIEW: UPDATE ON GROWTH HORMONE STIMULATION TESTING AND PROPOSED REVISED CUT-POINT FOR THE GLUCAGON STIMULATION TEST IN THE DIAGNOSIS OF ADULT GROWTH HORMONE DEFICIENCY. Endocr Pract. 2016 Jul 13. [Epub ahead of print] PubMed PMID: 27409821.

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Last update: **2024/06/07 02:57**