

# Determinants of the peak GH response of the glucagon stimulation test in slowly growing children.



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## Introduction & Aims

- ✓ Currently, the minimum of the GH peak (pGH) to GH provocative stimuli, including the glucagon stimulation test (GST), has been arbitrary set in children at 7 µg/L, irrespective of gender and age.
- ✓ It is unclear whether decreases blood glucose after initial increase are related to the GH response.
- ✓ Several doses (fixed or per bodyweight) and ways of administration (IM or SC) of glucagon are being used in daily practice.
- ✓ We therefore wanted to explore the influence of gender, age, and adiposity on the pGH after an IM administered maximal dose glucagon stimulation (0.1 mg/kg (max 2 mg) and the relationship between blood glucose (BG) and GH dynamics.

## Patients & Methods

- ✓ Both auxological and hormonal data of 84 (49 male) slowly growing (growth velocity < P25) children and adolescents (age < 18 years), who underwent a standardized GST in 2013-2014 in two Belgian University Hospitals were retrieved.
- ✓ In 26 subjects an insulin tolerance test (ITT) had been performed before and in 3 subjects after the GST.
- ✓ In 11 subjects the GST was performed after priming with sex steroids.
- ✓ Blood glucose, GH and cortisol was measured at baseline and after 90, 120, 150 and 180 minutes during the GST.
- ✓ GH was measured in all samples by the IDS-iSYS assay.
- ✓ Statistical analysis included Mann Whitney U test for comparisons and Spearman Rank test for correlations.

## Results

Table 1: Comparison of major clinical characteristics and observed basal and peak GH values during GST between the two centers

Parameter	Total group Median (range) (N= 84)	UZ Brussel Median (range) (N= 44)	UZ Gent Median (range) (N= 40)	Significance (p-value)
Age (yr)	8.1 (0.8 – 17.5)	5.7 (0.8 – 15.4)	8.9 (1.2 – 17.5)	<b>0.015</b>
Gender ♂/♀ (n)	49/35	28/16	21/19	0.301
Height (SDS)	-2.70 (-6.30 – -0.80)	-2.70 (-4.50 – -0.80)	-2.70 (-6.30 – -0.80)	0.498
BMI (SDS)	-0.70 (-4.10 – 1.90)	-0.82 (-3.20 – 1.60)	-0.58 (-4.10 – 1.90)	0.764
GH basal (µg/l)	1.4 (0.1 – 22.8)	1.8 (0.1 – 22.8)	0.6 (0.1 – 12.2)	0.106
GH peak (µg/l)	9.4 (0.2 – 31.6)	8.2 (1.2 – 31.6)	10.6 (0.2 – 18.4)	0.320
GH peak < 7 µg/L (Yes/No) (n)	28/56	17/27	11/29	0.280

Table 2: GH peak and glucose nadir values during the GST and the ITT in the non-primed subjects

Parameter	GST Median (range) (N=18)	ITT Median (range) (N=18)	Significance (P-value)
GH peak (µg/l)	8.4 (1.2 – 16.3)	4.4 (0.9 – 6.9)	<b>0.001</b>
GH peak < 7/> 7 µg/L (n) (%)	7/11 39% / 61%	18/0 100% / 0%	<b>0.001</b>
Glucose < 50 mg/dl (n) (%)	6/11 33% / 77%	18/0 100% / 0%	<b>0.001</b>

Table 3: Moment of peak GH during the GST in all subjects

Time (minutes)	Number	Percentage (%)	Cumulative percentage (%)
0	9	10.7	10.7
90	21	25.0	35.7
120	36	42.9	78.6
150	15	17.9	96.4
180	3	3.6	100.0

Table 4: Correlation between GH peak during the GST and clinical and biological parameters in non-primed subjects

Parameter	Correlatiecoëfficiënt rs (N=65)	Significantie (p-waarde)
Age (yr)	<b>0.286</b>	<b>0.021</b>
BMI (SDS)	-0.025	0.899
Height SDS	0.189	0.131
Glucose peak (mg/dl)	0.012	0.925
Glucose nadir (mg/dl)	0.201	0.108
Glucose change (mg/dl)	-0.006	0.963
Dose glucagon (mg)	<b>0.327</b>	<b>0.008</b>
Dose glucagon (mg/kg)	-0.150	0.232
IGF-1 (ng/ml)	<b>0.407</b>	<b>0.001</b>

Table 5: Correlation between BG nadir during the GST and clinical and biological parameters in all subjects

Parameter	Correlatiecoëfficiënt rs (N=84)	Significantie (p-waarde)
Age (yr)	<b>0.316</b>	<b>0.003</b>
Body weight (SDS)	<b>0.230</b>	<b>0.034</b>
Dose glucagon (mg)	<b>0.336</b>	<b>0.002</b>
Dose glucagon (mg/kg)	<b>-0.357</b>	<b>0.001</b>
BG basal (mg/dl)	<b>0.475</b>	<b>&lt; 0.001</b>
GH basal (µg/l)	-0.065	0.554
Cortisol basal (µg/dl)	0.005	0.962
Cortisol peak (µg/dl)	0.162	0.142

## Conclusions

The GST, when performed as a second test in a dose of 0.1 mg/kg bodyweight, is more powerful in releasing GH than the ITT. The pGH after GST is dependent on age in a non-primed condition, but independent of gender or weight status. We propose to use the GST as a first line GH test to avoid the need for a second ITT test, given its higher potency, independency of weight status and low risk of hypoglycemia.