

# METABOLIC ASSESSMENT IN CHILDREN WITH GROWTH HORMONE DEFICIENCY

## BEFORE, DURING AND AFTER HUMAN GH REPLACEMENT THERAPY

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- The role of rhGH replacement therapy in children with GHD on lipid profile and glucose homeostasis

**BACKGROUND** – Hypopituitary adults have increased cardiovascular (CV) risk factors which may be attributable to untreated chronic growth hormone (GH) deficiency (GHD). Recombinant human GH therapy (rhGH) in adults can reverse many of the individual adverse CV risk factors associated with the GHD. The existing evidence indicates that atherosclerotic CV disease (CVD) begins in childhood. In childhood few longitudinal studies have investigated the effect of GHD and rhGH therapy on metabolic parameters that may increase the risk of CVD.

**AIM OF THE STUDY** – The objective of this longitudinally study was to evaluate the change of body mass index (BMI), fasting glucose–insulin homeostasis, fasting lipid profile, and CVD risk in children and adolescents with GHD before, during, and after rhGH therapy.

### POPULATION AND METHODS

We determined

<b>What?</b>	<ul style="list-style-type: none"> <li>▪ auxological data (height SDS, BMI SDS)</li> <li>▪ insulin-like growth factor 1 (IGF-1) levels, glucose metabolism [glycemia (G), insulin (I)], and lipid profile [total cholesterol (TC), low-density lipoprotein (LDL), high-density lipoprotein (HDL), triglycerides (TG)]</li> <li>▪ insulin resistance: fasting glucose-to-insulin ratio (FGIR) and HOMA-IR</li> <li>▪ atherogenic index (AI): TC to HDL ratio</li> </ul>
<b>Who?</b>	Forty-six subjects (25 boys; 11.3±2.28 years old) with GHD were enrolled in the study (13 total GHD and 33 partial GHD) We excluded children with multiple pituitary hormone deficiency in order to avoid other possible influences on glucose and lipid metabolism. The patients enrolled had never received any kind of hormonal replacement therapy or drug
<b>When?</b>	All data were evaluated: at diagnosis (T0); during rhGH therapy (1-year, T1; 2-year, T2; stop-therapy, T3), and at 1-year off-therapy (T4)

### RESULTS

#### 1 AUXOLOGICAL DATA AND IGF-1

	Age (yrs.)	rhGH (mg/kg/day)	Ht (SDS)	BMI z-score	IGF-1 (ng/ml)
T0	11.3±2.28	--	-2.15±0.45	-0.01±0.98	162.1±77.6
T1	12.3±2.29	0.034±0.003	-1.77±0.55	-0.09±0.91	384.1±151.8
T2	13.3±2.28	0.030±0.003	-1.52±0.54	0.04±0.80	401.2±178.8
T3	14.9±1.42	0.028±0.004	-1.28±0.61	0.01±1.06	526.2±199.4
T4	16.1±1.41	--	-1.16±0.82	-0.07±1.03	395.1±149.1
χ <sup>2</sup>	87.3	--	43.1	5.89	30.6
p	<0.0001	--	<0.0001	0.2072	<0.0001

- ▶ Patients were not obese
- ▶ The mean daily dose of rhGH was titrated to clinical response and to maintain serum IGF-1 levels within the normal range for sex and chronological age

#### 2 LIPID PROFILE

	Age (yrs.)	TC (mg/dl)	LDL (mg/dl)	HDL (mg/dl)	TG (mg/dl)	AI
T0	11.3±2.28	164.9±28.7	89.9±17.6	61.6±15.3	61.5±27.9	2.77±0.52
T1	12.3±2.29	163.5±30.1	89.5±20.1	62.1±15.2	68.3±20.9	2.73±0.48
T2	13.3±2.28	169.5±19.9	90.0±16.1	65.2±10.1	74.3±27.4	2.69±0.43
T3	14.9±1.42	154.3±25.2	87.4±18.6	56.0±17.7	75.1±25.5	3.00±0.78
T4	16.1±1.41	153.9±30.7	93.0±21.7	52.8±16.6	56.0±18.9	3.12±0.74
χ <sup>2</sup>	87.3	9.38	1.71	13.3	13.5	4.69
p	<0.0001	0.0522	0.7895	0.0100	0.0092	0.3208

- ▶ None of the patients included in the study was on lipid modifying treatment
- ▶ HDL values increased during rhGH treatment; they were lower 1-year after rhGH was stopped but always in the normal range
- ▶ No change of AI was found

#### 3 GLUCOSE METABOLISM

	Age (yrs.)	Glycemia (mg/dl)	Insulin (μU/ml)	FGIR	HOMA-IR
T0	11.3±2.28	87.6±10.4	6.65±4.17	18.1±10.7	1.41±0.88
T1	12.3±2.29	88.5±7.18	13.4±5.19	7.27±2.44	2.91±1.27
T2	13.3±2.28	88.6±6.35	10.2±2.55	9.40±3.88	2.20±0.61
T3	14.9±1.42	89.8±9.06	16.1±6.76	6.50±2.92	3.65±1.88
T4	16.1±1.41	85.9±9.06	9.07±4.05	11.9±7.31	1.91±0.91
χ <sup>2</sup>	87.3	1.78	36.8	34.4	34.0
p	<0.0001	0.7757	<0.0001	<0.0001	<0.0001

- ▶ Insulin sensitivity was influenced by rhGH therapy with an increase in HOMA-IR, related to increased insulin levels without any change in glycemia
- ▶ No patients developed diabetes mellitus during and at the end of the study

### CONCLUSIONS

- The dose of rhGH did not result in supra-physiological IGF-1 levels
- HDL values increased during rhGH treatment while the other parameters of lipid profile were not influenced by rhGH therapy
- All levels were always in the normal range and the high prevalence of partial GHD may explain these results
- During rhGH treatment we demonstrated a significant worsening of insulin-resistance indexes that returned within normal range 1-year after the off-therapy
- It is interesting to note that in subjects who discontinue rhGH therapy at completion of linear growth, there were not unfavorable effects on BMI and lipid profiles

**In our subjects GHD and rhGH therapy don't impair CV risk factors**