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Evaluation of the effect of growth hormone treatment on insulin resistance and cardiovascular tissue

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Introduction: Growth hormone (GH), major hormone of linear growth during childhood, takes part in various metabolic pathways . GH treatment may impair glucose metabolism. Monitoring of glucose levels during GH treatment has been recommended in GH deficiency (GHD) especially in those with high risk factors for diabetes. It is well known that insulin resistance (IR), is associated with metabolic syndrome and co-morbidities.

Objective and hypotheses: The aim of our study was to evaluate GH deficiency (GHD) patients on GH treatment for hyperlipidemia, IR and carotid intima media thickness (CIMT) and left ventricular global longitudinal strain (GLS) and assess cardiovascular tissue level effects of insulin sensitivity.

Methods: 71 isolated idiopathic GHD patients on GH treatment (54M, 17F) and 43 (25M,17F)healthy subjects, matched for sex and age as the control group, were recruited in this study. The patients were recruited from those followed in the Pediatric Endocrinology Unit and Well Child Clinic. All subjects underwent anthropometric measurements and physical examination. SDS values for body-mass index (BMI) [weight (kg) / height (m^2)], weight and height and waist circumference were calculated according to national standards. We performed Oral glucose tolerance test (OGTT) in all GHD patients. IR was evaluated with HOMA-IR and Matsuda index, derived from OGTT in GHD subjects, HOMA-IR was used in healthy subjects. Atherogenic index(AI) and serum lipid levels were evaluated. CIMT and GLS were measured by Doppler and two-dimensional ultrasound techniques. The study was approved by the local ethical committee. Informed consent was taken from all parents. Statistical analyses were done using SPSS 15.0. Parametric and nonparametric tests were utilized. $p<0.05$ was accepted as statistically significant.

Results: Clinical features of GHD subjects are shown in Table 1. As weight and height increased on GH treatment, BMI-SDS values decreased in GHD subjects. Althought mean age was similar in GHD and control groups, bone age/age ratio was lower in GHD patients. There was no difference in BMI SDS between the groups (Table 2).

Based on HOMA-IR, there was no difference in percentage of subjects with IR between GHD and Control groups (18 % and 13 % , respectively). However OGTT results showed IR with higher percentage in GHD subjects(n=31, 45%). Non of GHD subjects showed type 2 Diabetes or impaired glucose tolerance (Table 2). Lipid levels and AI showed no statistical differences either.

CIMT and CIMT-SDS values were higher in GHD group ($p = 0.01$; $p=0.03$) but there were no differences in GLS -SDS (Table 3).

As Table 4 shows, GHD subjects were divided into two groups with respect to the presence of IR . Groups with or without IR showed no difference in weight-SDS, BMI-SDS, waist circumference SDS, AI, GLS-SDS and CIMT-SDS value.

GLS-SDS and CIMT-SDS values showed no correlation with Matsuda index and HOMA-IR.

Table 1. Clinical features of GHD patients (Mean± SD)

Age(year)		13.7 ±2.6
Sex n (%)	Female Male	17 (52.6) 54 (47.4)
Age of diagnosis (year)		11.2 ±2.3
Treatment duration (year)		2.5±1.4
GH peak value (ng/dl) 1st test		3.2±2.4
GH peak value (ng/dl) 2nd test		4.3±2.3

Table 2. Evaluation of GHD patients before and under GH treatment, and comparison with control group

	Before treatment (BT) (n=71)	Under treatment (UT) (n=71)	Control (C) (n=43)	P1 (BT-UT)	P2 (UT-C)
Age(year)	11.2 ±2.3	13.7 ±2.6	13.3±2.9	-	0.45
Heigth SDS	-2.6 ± 1.0	-1.7 ± 0.9	-0.1 ± 0.9	**<0.001**	**<0.001**
Weight SDS	-1.3 ± 0.9	-1.0 ± 1.3	-0.4 ± 0.8	**<0.001**	**0.01**
BMI SDS	-0.3 ± 0.9	-0.5 ± 1.0	-0.4 ± 0.8	**<0.001**	0.62
Waist Circumference SDS	-	0.5 ± 1.2	0.5 ± 0.8	-	0.895
Bone age/age	0.8 ± 0.1	0.9 ± 0.1	1.0 ± 0.1	**<0.001**	**<0.001**
HOMA-IR	-	2.6±1.5	2.1±1.6	-	0.49
IR as to HOMA-IR n(%)	-	12(18)	4(13)	-	0.65
IR as to OGTT n(%)	-	30(45)	-	-	-

Table 3. Cardiac measurement results in GHD and control subjects

	GHD (n=71)	Control (n=43)	P
Atherogenic index	0.13±0.28	0.12±0.24	0.91
GLS-SDS	1.35±0.481	1.42±0.5	0.66
CIMT	0.47±0.12	0.41±0.09	**0.01**
CIMT-SDS	0.018±0.051	-0.003±0.06	**0.03**

Table 4. Anthropometric and cardiac parameters in GHD subjects

	IR (+) (n=30)	IR (-) (n=36)	p
WeightSDS	-1.1±0.7	-1.2±1.0	0.58
BMI SDS	-0.6±0.8	-0.5±1.0	0.66
Waist circumference SDS	0.5±1.0	0.4±1.2	0.71
Atherogenic index	0.1±0.3	0.1±0.3	0.65
GLS-SDS	-0.9±2.0	-2.2±2.4	0.50
CIMT-SDS	0.018±0.051	-0.003±0.06	0.88

Conclusions:

- GH treatment in GHD children leads to insulin resistance, which may be overlooked by evaluating only HOMA-IR.
- CIMT and CIMT-SDS values were higher under GH treatment in comparison to control group. IR in GHD subjects showed no effect on CIMT. Alterations of CIMT may be caused by direct effects of GH.
- CIMT and GLS as feasible techniques may serve as descriptors of possible effects of GH on cardiovascular tissue.

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GH and IGF Treatment

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