Cardiovascular risk factors and metabolic parameters in Growth Hormone deficient patients

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Introduction

Growth hormone deficiency (GHD) in adulthood is associated with increased cardiovascular risk, which is attributed to unfavorable changes in body composition and in metabolic parameters.

We evaluated haemodynamic, metabolic, inflammatory and coagulation indices that may contribute to the increased cardiovascular risk in adult GH deficient subjects.

Methods

Twenty-four patients diagnosed with GHD (13 male), with a mean (SD) age of 54.3(2.7), were compared to 15 age, sex and body mass index (BMI) matched, controls.

Diagnosis of GHD had been made with an insulin tolerance test (peak GH<3ng/ml), unless the patient had been diagnosed with at least another two pituitary hormone deficiencies and had known structural pituitary pathology.

Anthropometric characteristics: BMI and waist-to-hip ratio (WHR)

Haemodynamic parameters: Blood pressure

Metabolic parameters: After an overnight fast
plasma glucose, insulin, haemoglobulin A1c (HbA1c),
lipid levels [T-Chol, Trigs, HDL-Chol, Lp(a)], lipoproteins ApoA1 and ApoB

Surrogate measures of insulin resistance/sensitivity and beta-cell function:
HOMA-IR, HOMA-β, QUICKI model and **Matsouda ISI** (the latter in 10 subjects who had undergone an oral glucose tolerance test)

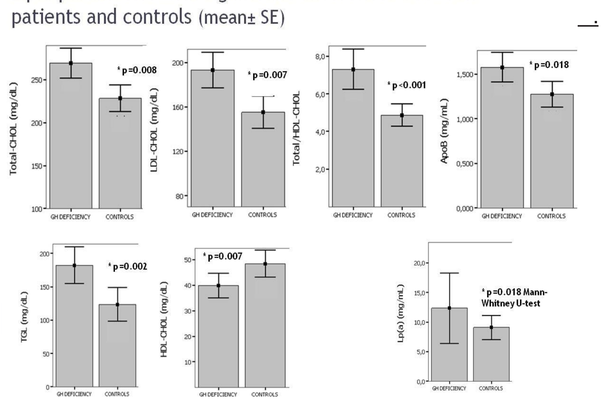
Inflammatory and coangulation indices:
High sensitivity-CRP (hs-CRP) fibrinogen, PAI-1, t-PA and circulating thrombomodulin levels

Graphs and tables

Variables	GHD	controls	P-value
Demographic and clinical characteristics			
Age (years)	54,3± 2,7	52,9± 3,4	NS
Age at diagnosis (years)	44,9± 3,4		
Disease duration (years)	12,8± 1,6		
Height (m)	1,7± 0,02	1,7± 0,02	NS
Weight (Kg)	79,7± 2,9	75,3± 2,9	NS
BMI (Kg/m^2)	28,7± 0,7	26,8± 0,9	NS
Waist circumference (cm)	98,9± 2,2	92,2± 3,2	NS
Hip circumference (cm)	105,3±1,5	103,9± 1,8	NS
WHR (Waist-to-Hip Ratio)	0,94± 0,02	0,88± 0,02	P=0,052
SBP (mm Hg)	132,1± 3,1	132,7± 3,7	NS
DBP (mm Hg)	80,4± 1,8	82,3± 1,9	NS
Glucose homeostasis and surrogate markers of insulin resistance			
HbA_{1c} (%)	6,5±0,17	6,2±0,15	NS
Fasting Glu (mg/dL)	97,8±8,6	98,5±4,8	NS
Fasting Ins (mIU/L)	10,7±1,1	7,4±1,0	0,042
HoMA-IR	2,05 (1,37-3,03)	1,37 (1,09-2,43)	NS
HoMA-B	191,1±32,4	96,2±15,7	0,034
QUICKI	0,341±0,006	0,359±0,009	NS
GIR	8,5 (6,7-13,6)	16,2 (8,8-18,9)	0,008
ISI [Matsuda]	4,03±1,07	6,91±0,7	0,046
Lipid, coangulation and inflammatory factors			
Total-Chol (mg/dL)	269,4± 8,5	228,3± 7,2	0,002
Triglycerides (mg/dL)	182,2± 13,3	123,5± 11,7	0,004
HDL-Chol (mg/dL)	39,9± 2,3	48,4± 2,5	0,02
LDL-Chol (mg/dL)	193,1± 7,7	155,1± 6,8	0,002
T-Chol/HDL-Chol	7,3± 0,5	4,9± 0,3	0,001
$ApoA_1$ (mg/mL)	1,6± 0,07	1,6± 0,08	NS
ApoB (mg/mL)	1,58± 0,08	1,28± 0,07	0,016
Lp(a) (mg/dL)**	9,0 (6,6-10,3)	8,0 (6,7-10,8)	NS
Fibrinogen (mg/dL)	335,9± 13,9	296,2± 14,5	NS
PAI-1 (ng/mL)	10,18± 1,2	6,93± 1,48	NS
Thrombomodulin (ng/mL)	9,5± 0,8	8,8± 0,7	NS
t-PA (ng/mL)	4,5± 0,9	2,6± 0,2	0,051
hs-CRP (mg/L)	0,61± 0,14	0,40± 0,12	NS

Values are expressed as mean±SE, or as median (IQR) for variables with skewed distribution

Lipid parameters with significant differences between patients and controls (mean± SE)



Glucose homeostasis and surrogate measures of insulin resistance (mean, SD, SE)

Results

- Patients with GHD exhibited a marginally increased WHR.
- Total-Chol, LDL-Chol ,triglyceride and ApoB levels were higher and HDL-Chol levels lower, in patients with GHD , compared to controls.
- GH deficient patients had significantly higher fasting insulin levels and lower fasting glucose-to-insulin ratio. Insulin resistance as reflected by HOMA-IR was comparable in the two groups, however, GHD patients were less insulin sensitive than controls by HOMA-B and Matsuda-ISI.
- Fibrinogen levels and PAI-1 levels did not differ significantly, and t-PA was only marginally increased compared to controls. Thrombomodulin levels were not affected.

Conclusions

A considerable number of cardiovascular risk factors including lipid and lipoprotein levels and insulin sensitivity, irrespective of BMI, are affected in GH deficient adults. Studies addressing whether GH substitution results in decreased CVD morbidity and mortality are needed so therapy could be more vigorously implemented in such patients.

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Pituitary clinical
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DOI: 10.3252/pso.eu.17ece.2015
Poster presented at: ECE2015 16-20 May 2015 DUBLIN, IRELAND 17th EUROPEAN CONGRESS OF ENDOCRINOLOGY