THE INCREASE IN ADIPOSE TISSUE DURING GH TREATMENT INDUCES INSULIN RESISTANCE

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1 Background

Patients with congenital IGhD or MPHD develop adiposity already "in utero". The effects of growth hormone (GH) treatment on adipose tissue are controversial, some claiming that GH reduces body fat (1). Others reports that long-term GH treatment causes increase in the adipose tissue mass (2,3) ,glucose intolerance, insulin resistance, followed in some instances even by diabetes (4).

2 Objective

To determine whether long-term hGH treatment (33µg/kg/day s.c.) of children with congenital isolated growth hormone deficiency (cIGHD) or congenital multiple pituitary hormone deficiency (cMPHD) causes insulin resistance.

3 Subjects

Forty patients with cIGHD (22M, 18F) due to hGH gene deletion (n=33) or GHRH – receptor mutations (n=7) and 46 patients with cMPHD (28M, 18F) were included in the study. The mean age at start of hGH was 7 and 10 yrs respectively. The mean duration of treatment was 8.5 yrs.

4 Methods

Fasting glucose and insulin levels, data on weight, subscapular skinfold thickness (SF), were collected from Medical Records of our clinic. HOMA as a measure of insulin resistance was calculated using the formula HOMA-IR = Glucose x Insulin ÷ 22.5. As BMI is an unreliable measure of adiposity in GH deficiency with an underdeveloped muscular and bone mass we determined subscapular skinfold thickness as an index of body fat using a Harpenden caliper. Statistical analysis was by ANOVA.

5 Results

Parallel data on weight, BMI, subscapular skinfold thickness (SF), blood glucose and insulin concentration were found in 35 patients with cIGHD, and in 37 patients with cMPHD.

Table 1: presents the weight, subscapular skin folds, BMI-SDS and HOMA-IR in the two groups studied.

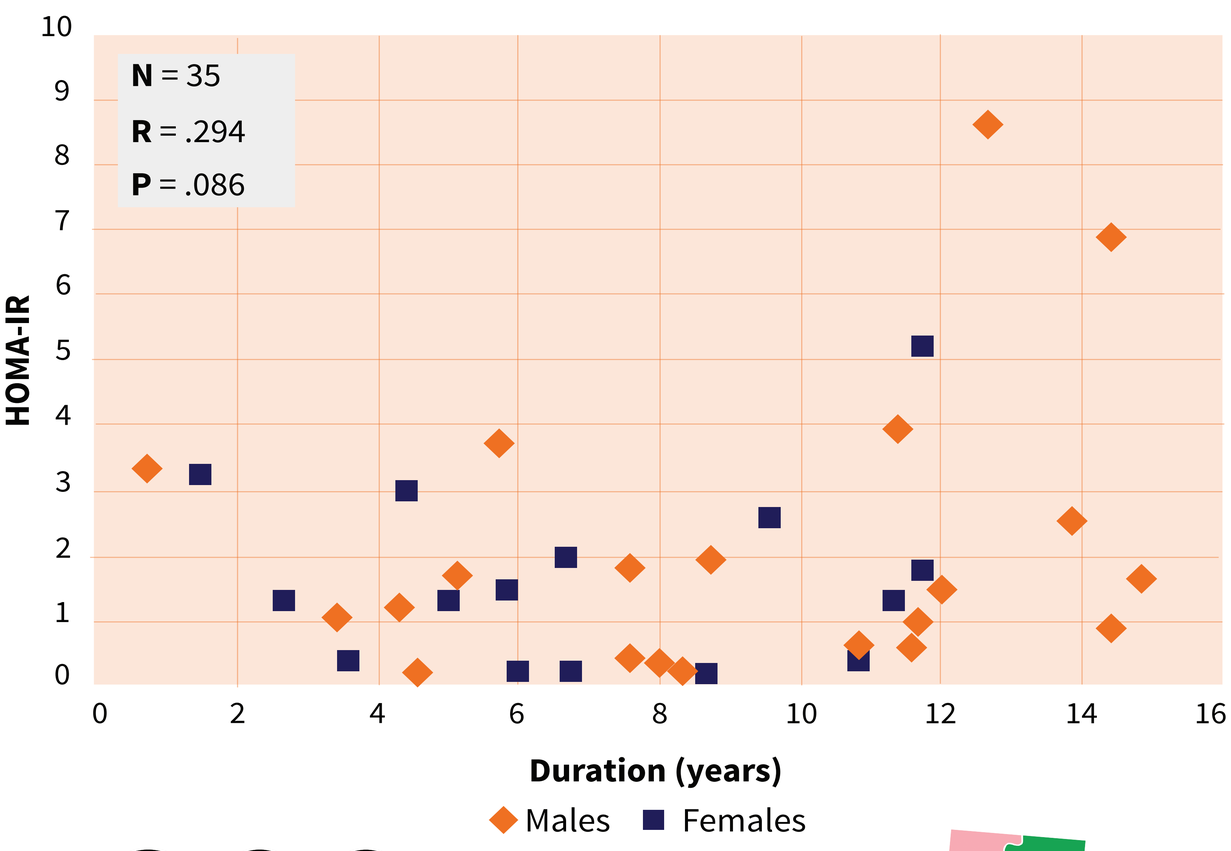
	cIGHD			cMPHD		
	Start	**End**	**P**	**Start**	**End**	**P**
Weight	15.6 ± 9.3	49.2 ± 16.6	<0.001	22.7 ± 9.4	38.9 ± 11.8	<0.001
SF (mm)	10.2 ± 6.1	15.2 ± 7.3	<0.001	11.7 ± 5.9	16.2 ± 7.5	0.001
BMI SDS	-0.4 + 0.7	0.1 + 0.8	0.18	-0.4 ± 0.7	-0.5 + 0.6	0.023
HOMA IR	3.4 ± 3	1.6 ± 2.4	0.31	1.7 ± 1	1.3 ± 1.4	0.32

It is seen that in both groups of patients, weight and subscapular skinfold thickness increased significantly during GH treatment. BMI and HOMA-IR did not show a difference, nor did HOMA-IR correlate with duration of hGH treatment (Fig1). However, when correlating HOMA-IR with subscapular skinfold thickness the difference was close to significance (R=0.427), more so, in the cMPHD patients alone (R=0.708).
HOMA-IR was slightly elevate at the start of treatment in both groups and did not change significantly during treatment (norm:<2). The BMI measurements were not contributory. Two patients developed diabetes between ages 39-50.

6 Conclusions

The increase in HOMA-IR during low-dose long term GH treatment correlated with the increase in body adiposity.

Fig 1: Correlation between HOMA IR and duration of hGH treatment in patients with cIGHD and cMPHD



7 References

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