Are short children with low GH secretion metabolically different from children of normal height?

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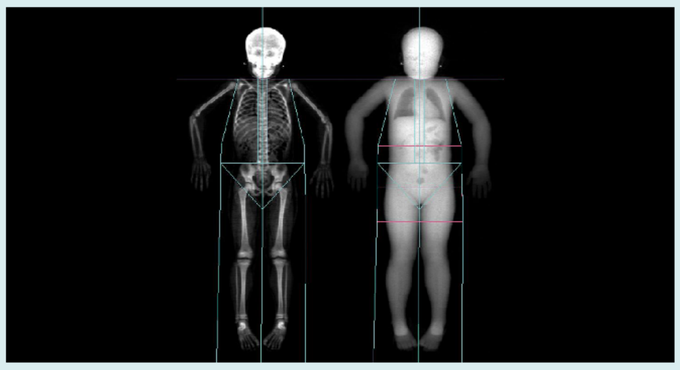
Background

Severe Growth Hormone Deficiency (GHD) leads to several metabolic effects in the body ranging from abnormal body composition with increased abdominal fat and reduced lean body mass to biochemical disturbances such as high insulin sensitivity and hyperlipidemia. However, less is known regarding these parameters in children with a milder deficiency in Growth Hormone (GH) secretion.

Objective

To analyse if short children with a relatively low GH secretion differ metabolically from healthy children of normal height.



Child examined with Dual-Energy X-ray Absorptiometry (DEXA) for measurements of bone and soft tissue composition.

Method

We examined insulin sensitivity index (Si), body composition and fasting levels of glucose, insulin and HbA1c in short children (<-2.5 SDS) between 7-10 years of age (n=35, 22 M/13 F) with GH-peak 7-14 µg/L in Arginine-Insulin Tolerance Test (AITT) and compared the results with an age- and sex-matched control group of normal height (n=12, 8 M/4 F). Si was measured through frequently sampled intravenous glucose tolerance test (FSIVGTT) calculated with MINMOD software (developed by R Bergman) and body composition with DEXA (GE Lunar Prodigy).

We also performed a subgroup analysis comparing these parameters for short children above and below a peak GH secretion level of 10 µg/L during AITT.

Results

The group of short children had a **higher mean Si** compared to the control group (12.9 vs 10.4 $[mu/l]^{-1}$ x min^{-1}, fig.1) but the difference was non-significant unadjusted (p=0.079) and only borderline significant when adjusted for sex (p=0.059).

The comparison of body composition showed that the short children had a **lower percentage of abdominal fat** (AF, 13.3 % vs 16.6 %, fig. 2) and **higher percentage of lean body mass** (LBM, 80.6 % vs 77.5 %, fig. 3) compared to the controls. These differences were significant when adjusted for sex (p=0.05 and p=0.04 respectively). No significant difference of fasting glucose or HbA1c was detected between the groups but **fasting insulin was significantly lower** in the short children (22.4 vs 32.0 pmol/L, fig. 4) when adjusted for sex (p=0.05).

When comparing short children above and below GH-peak level of 10 µg/L, the children with lower GH secretion were shown to have a significantly **lower fasting insulin level** (16.8 vs 27.8 pmol/L, p=0.05, fig. 5) and the other comparisons showed tendencies towards higher Si, lower AF and higher LBM, but these results were non-significant.

Conclusion

Short children with mildly impaired GH secretion are very heterogeneous in terms of their metabolic profile compared with healthy children of normal height.

They show **higher Si** and **lower fasting insulin** levels than the healthy children of normal height but in contrast to the phenotype of GHD the short children have **lower AF** and **higher LBM**, which might have contributed to the differences in insulin sensitivity.

Further analysis

We are currently analysing microdialysis data as well as data from investigations with isotope marked glucose and glycerol to further understand the metabolic differences between the groups.

In the second part of the study the short patients were randomized for GH treatment in 3 different doses (low, normal and high) with an extensive follow-up for 2 years of which the data soon will be presented.

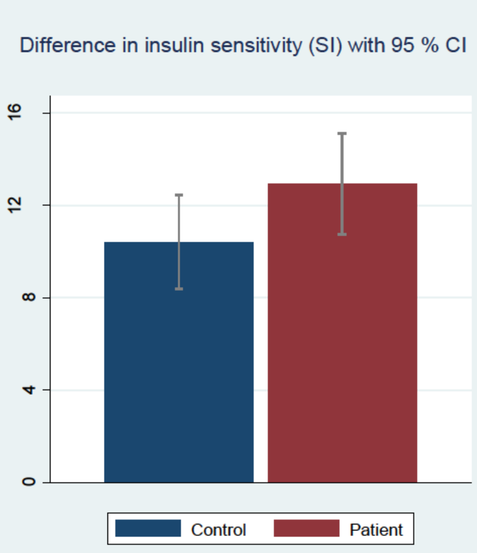


Figure 1

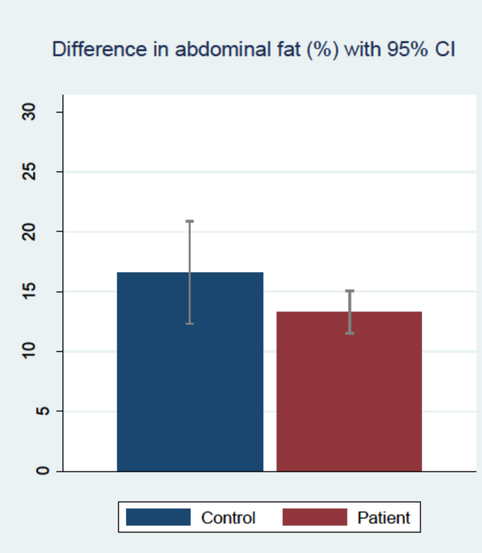


Figure 2

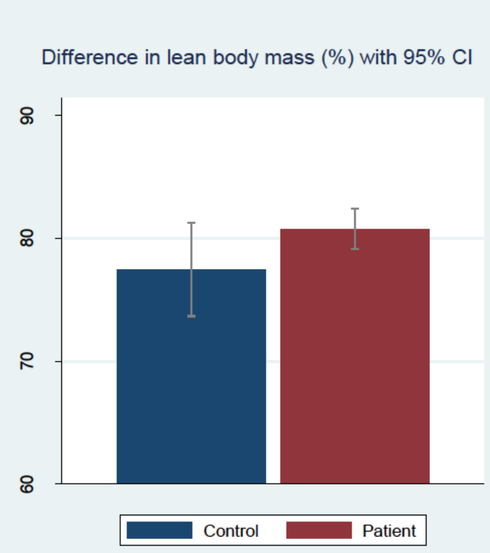


Figure 3

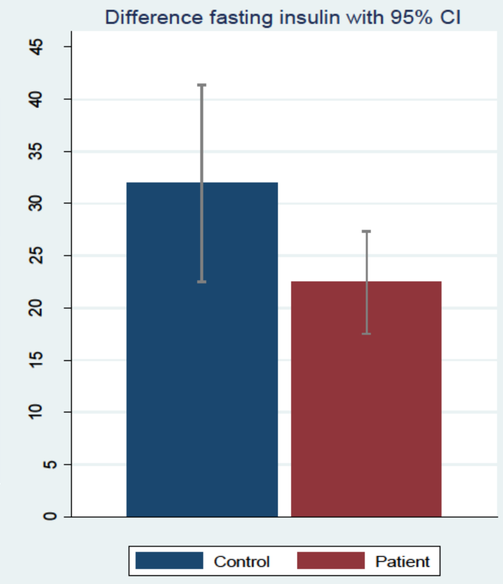


Figure 4

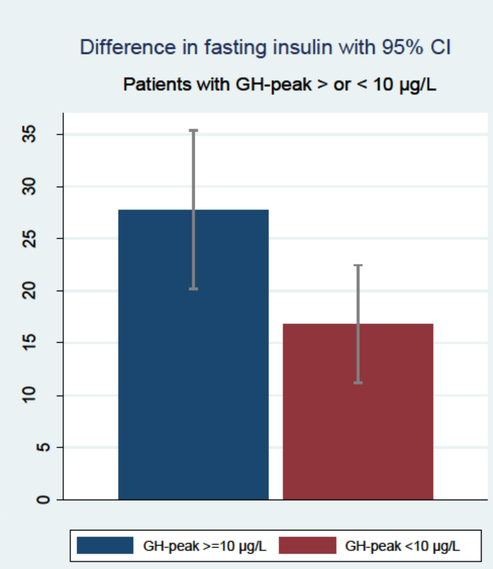


Figure 5

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