

GLUCOSE METABOLISM IN CHILDREN WITH PRADER-WILLI SYNDROME (PWS): THE EFFECT OF GH THERAPY

Grugni G¹, Fintini D², Bocchini S², Convertino A², Cappa M³, Crinò A²

¹Division of Auxology, Italian Auxological Institute, Research Institute, Verbania, Italy; ²Autoimmune Endocrine Diseases Unit, Bambino Gesù Children's Hospital, Research Institute, Palidoro, Rome, Italy; ³Endocrinology and Diabetic Unit, Bambino Gesù Children's Hospital, Research Institute, Rome, Italy

INTRODUCTION AND OBJECTIVES

Low fasting insulin concentrations and lower insulin resistance, compared with BMI-matched controls, have been reported in PWS subjects. Proposed reasons for the increased insulin sensitivity in PWS include relative diffuse as opposed to visceral obesity, lower GH levels, and higher ghrelin levels for the degree of obesity. Nevertheless, other authors have observed that PWS and obese controls had similar insulin levels and were similarly insulin resistant. These discrepancies might be due to the different clinical characteristics of the study groups, including age, degree of weight excess, variable percentage of fat body mass and number of patients undergoing GH therapy (GHT).

Aim of this study was to compare measures of insulin secretion and glucose levels in PWS children with those in BMI-, gender- and age-matched obese controls (OC), highlighting the influence of GHT on glucose metabolism.

METHODS

Three groups of children were studied:

- Group A: 12 PWS (8 males, median age 12.9 yrs and BMI-SDS: 3.37) on GHT (PWS-GHT) from at least 2 years;
 - Group B: 8 PWS (2 males, median age 13.1 yrs and BMI-SDS: 3.25) without GHT (PWS-noGHT);
 - Group C: 40 OC (21 males, median age 13.1 yrs and BMI-SDS: 3.7).
- Cytogenetic analysis was performed in all PWS subjects and 11 of them had a deletion of the paternally derived chromosome 15 (Group A= 6; Group B= 5), while maternal uniparental disomy of chromosome 15 was found in 9 individuals (Group A= 6; Group B= 3).

All subjects underwent a standard OGTT, and the following parameters were evaluated: glucose (GL), insulin (In) ISI, QUICKI, HOMA-IR, insulinogenic index (InsIn), and the area under the curve of In (AUC-In) and GL (AUC-GL). Diagnosis of altered glucose metabolism was defined according to the ADA criteria. The study protocol was approved by the Ethics Committee of all participating Institutions. Written informed consent was obtained from all participants by their parents.

RESULTS

No adverse effects were noticed during or after the test in any of the subjects studied. Altogether, impaired glucose tolerance was detected in 1 PWS-GHT (7%), 2 PWS-noGHT (25%) and 6 OC (15%). IFG or overt T2DM were absent. No significant difference in QUICKI, HOMA-IR, AUC-In, and AUC-GL was seen between the 3 study groups (data not shown). The more relevant findings are reported in the table:

	GI 0'	In 120'	ISI	InsIn
PWS-GHT	76.7±7.9*	64.6±30.8 ⁺	3.81±2.37	2.1±0.91
PWS-noGHT	73.2±8.5*	75.0±45.4	6.05±5.44 [§]	1.17±0.83 [°]
OC	82.1±6.9	141.9±90.8	2.63±2.60	2.63±1.43

* $p < 0.05$ vs OC; ⁺ $p < 0.02$ vs OC; [§] $p < 0.03$ vs OC; [°] $p < 0.02$ vs OC

CONCLUSIONS

Our preliminary data support the relative hypoinsulinemia and greater insulin sensitivity in obese children with PWS compared to OC. To be noted, GHT does not seem to negatively affect glucose and insulin homeostasis in PWS subjects.

Doubts on whether GHT can impair glucose homeostasis in subjects prone to develop T2DM have risen in past years. Moreover, there are some data showing that insulin resistance could be disturbed under GHT. On the contrary, other studies have recently demonstrated that long-term GHT did not adversely affect glucose homeostasis in all ages. Based on our findings, we may speculate that impaired glucose metabolism during substitutive therapy could be mainly due to weight gain rather than to GH administration. The negative influence of weight excess on the individual metabolic risk clustering in the PWS population supports the view that an early intervention to prevent obesity remains the most important goal of any PWS treatment programme.

ESSENTIAL REFERENCES

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