Impairment of GH responsiveness to combined GH-releasing hormone and arginine administration in adult patients with Prader-Willi syndrome

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Objective: it is unclear if poor health outcomes of adult patients with Prader-Willi syndrome (PWS) are influenced by GH deficiency (GHD). Few studies have been focused on PWS adults, but further information on the concomitant role of obesity on GH/IGF-I axis function is needed. The aim of our study was to investigate the prevalence of GHD in a large group of adult subjects with genetically confirmed PWS.

Design and subjects**:** we studied the GH response to a combined administration of GHRH (1 µg/kg i.v. at 0 minutes) and arginine (ARG) (30 g i.v., infused from 0 to 30 minutes) as well as the baseline IGF-I levels, in a group of 44 PWS adults (18 males, 26 females) aged 18-41·1 years. The same protocol was carried out in a control group of 17 obese subjects (7 males, 10 females) aged 21·8-45·8 years.

Measurements**:** blood samples were taken at -15 and 0 minutes and then 30, 45, 60, 90 and 120 minutes after GHRH administration. Serum GH and total IGF-I concentrations were measured by chemioluminescence. Statistical analysis was performed by Student's *t*-test for unpaired data, and using analysis of variance for parametric and nonparametric (Mann-Whitney test) data, where appropriate. The relationship between pairs of variables was assessed by Pearson's correlation. Independent variables influencing GH secretion were tested by multiple linear regression analysis.

Results**:** the GH response to GHRH+ARG was significantly lower in PWS patients (GH peak (mean±SE) 8·4±1·2 µg/l; AUC: 471·4±77·8 µg/l/h) than obese subjects (GH peak 15·7±2·9 µg/l, $P<0·02$; AUC 956±182·9 µg/l/h, $P<0·005$). When considered individually, 17 of 44 PWS individuals (38·6%) were severely GHD, according to the cut-off limit of 4·1 µg/l for obese individuals, and low IGF-I-values were present in 33 PWS patients. Moreover, impaired GH response was combined with subnormal IGF-I levels in all PWS patients with GHD.

Conclusions**:** adult subjects with PWS had a reduced responsiveness to GHRH+ARG administration associated with reduced IGF-I levels. In addition, a severe GHD for age was demonstrated in a significant percentage of PWS subjects. These findings are in agreement with the hypothesis that a complex derangement of hypothalamus-pituitary axis occurred in PWS, and suggested that impaired GH secretion is not an artefact of obesity.