



BODY COMPOSITION AND GH RESPONSE TO GHRH+ARGININE IN ADULT PATIENTS WITH PRADER-WILLI SYNDROME

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INTRODUCTION: The complications associated with obesity seem to be the main risk factors for death in the older subjects with Prader-Willi syndrome (PWS). On the other hand, an awareness is rising that poor health outcomes of PWS subjects may not be entirely caused by obesity alone. It is currently unclear whether risks of critical illnesses of PWS are influenced by GH deficiency (GHD). However, a GH/IGF-I-mediated control of cardiac risk in PWS has been recently found (Marzullo et al., J Clin Endocrinol Metab 2005). In this context, we have recently reported a reduced GH secretion in PWS adults when compared with a control group with similar BMI (Grugni et al., Clin Endocrinol 2006). Nevertheless, BMI is not an exact measure of adiposity in PWS as it underestimates % of body fat (Goldstone et al., Am J Clin Nutr 2002; Kennedy et al., Int J Obes 2006). In fact, PWS harbour a higher fat mass than simple obesity, under the same degree of weight excess, both in children and in adults (Brambilla et al., Am J Clin Nutr 1997; Theodoro et al., Obesity 2006). The aim of this study was to examine the role of body composition in the blunted GH secretion in PWS adults.

PATIENTS AND METHODS: 8 patients with PWS (2M/6F, 6 del15/2 UPD15, age 28.0±2.2 yrs, BMI= 44.1±2 kg/m²; mean±SEM) were included in the study. Dual-energy x-ray absorptiometry (GE-Lunar, Madison, WI) was used for measurements of fat mass (FM%= 54.5±1.5). A control group of 8 obese subjects (SO) (1M/7F, age 29.5±2.7 yrs, BMI= 42.7±0.43 kg/m²) with comparable body composition (FM%= 52.2±1; p=0.2) was enrolled. In all patients the pituitary GH secretion was analyzed by dynamic testing with GHRH+arginine. GH responses were evaluated either as mean peak values (ng/ml), or as the area under the curve (AUC, ng/ml/h) and the net incremental area under the curve (nAUC, ng/ml/h). In addition, the baseline IGF-I levels were determined.

RESULTS: Both GH responses to GHRH+arginine test and IGF-I levels were significantly lower in PWS subjects, in comparison to SO patients (table 1). According to the literature (Corneli et al., Eur J Endocrinol 2005), 3 PWS individuals (37.5%) could be defined as severe GHD, as well as one SO (GH peak ≤4.2 ng/ml). Seven PWS and 3 SO had subnormal IGF-I levels (normal values: 182-782 ng/ml).

Table 1	GH peak (ng/ml)	GH AUC (ng/ml/h)	GH nAUC (ng/ml/h)	IGF-I (ng/ml)
PWS	7.0±1.3	405±75	367±75	104±18
SO	21.9±4.7	1325±315	1294±313	256±37
p=	0.009	0.013	0.012	0.003

CONCLUSIONS: Our findings seem to demonstrate that the differences in stimulated GH levels between our PWS and SO are not related to body FM%. These data suggest that GHD in PWS is not merely secondary to altered body composition.