

## Pituitary Evaluation and Growth Hormone Treatment in Prader-Willi Syndrome

Angulo et al evaluated the spontaneous growth hormone (GH) secretion and GH responses to clonidine, levodopa, and insulin-induced hypoglycemia in 11 obese and 4 nonobese Prader-Willi syndrome (PWS) patients, 1.5 to 15.5 years of age. Ten patients (3.7 to 15.5 years of age) were treated with GH at 0.1 mg/kg tiw for 6 months.

Integrated concentrations (ICs) of GH using a Cormed-Kowarski constant withdrawal pump, with the specimens being collected over 24 1-hour periods, ranged between 1.0 to 2.1  $\mu\text{g/L}$ , which the authors state was markedly deficient in all.

The responses to insulin, clonidine, and levodopa were variable. Only 1 patient had a serum GH level above 8.0  $\mu\text{g/L}$ , following 150  $\mu\text{g/m}^2$  po of clonidine. Values of serum GH following levodopa were above 8.0  $\mu\text{g/L}$  in 3 patients (12.6, 11.4, and 11.4  $\mu\text{g/L}$ ). The response to insulin (0.1 U/kg IV) was 8  $\mu\text{g/L}$  or above in 8 patients. The authors conclude that GH deficiency probably was present in all patients. The somatomedin-C (Sm-C) determinations were  $<1.0$  U/mL and compatible with GH deficiency in 9 of 15 patients. Bone age (BA) determinations were not less than -2 standard deviations (SD) for chronologic age (CA) in any patients.

GH treatment over 6 months increased the mean growth velocity (GV) from  $2.0 \pm 2.3$  cm/yr to  $5.3 \pm 1.5$  cm/yr. GV doubled in all patients except in a 15.5-year old male with a BA of 14.5 years, a BA at which the average male has only 5% of his ultimate height yet to be gained. The patients gained little weight. Sm-C levels routinely increased to above 1.2 U/mL with a mean of  $1.5 \pm 0.2$  U/mL.

The authors conclude that "short stature associated with obesity, hypotonia, decreased energy expenditure, delayed skeletal maturation and failure to respond to GH stimuli makes PWS children potential candidates for GH therapy. Further studies, however, are necessary to investigate the safety and long-term effects of this form of therapy."

**Editor's comment:** *The authors performed a well-designed study. The data provide both the stimulation and basis for future investigation of GH secretion and response to GH therapy by PWS patients. The data, as presented, support the concept that these patients may have GH deficiency. Responses of GH release secondary to pharmacologic testing with 3 stimulating agents certainly appear to be low. Seven of the patients had no peak of GH  $>8.2$  ng/mL in any of the tests (insulin, clonidine, levodopa). Only 2 patients in the entire group of 15 had a value  $>8.0$  ng/mL in more than 1 of the 3 tests. The IC values of GH were  $<2.1$  ng/mL in all which logically prompts one to suspect GH deficiency. Unfortunately, the authors have not provided data of IC for children of normal size. Their control data are taken from the literature, which is always suspect because of the variability of studied groups and the different assays employed, and from studies they have published for children with delay of growth and pubertal development (J Pediatr Endocrinol 1989;3:225). In that study, the IC of GH for 44 of 49 short patients was  $2.2 \pm 0.6$  ng/mL. Although some investigators have shown that children with similar short stature have normal ICs of GH, as compared with children of normal size, others have not. Therefore, Angulo et al need to publish concerning their study controls of normal size to diagnose GH deficiency in the PWS patients by using the IC of GH. The response to GH treatment by PWS patients is encouraging, although the study of GH treatment was for only 6 months.*

*It must be noted that the dose of GH used (0.1 mg/kg tiw) is a pharmacologic dose, and may be expected, therefore, to often produce an increased GV in both children of normal and short stature. However, the fact that increased growth rate in PWS patients results from pharmacologic doses does not diminish its potential therapeutic application. I use the word "potential," as the effect on final height is the ultimate criterion for GH treatment in these patients. The authors appropriately conclude that further studies are necessary to investigate safety and long-term effects. All of us will follow with interest the subsequent periods of treatment.*