

Partial GH Deficiency in Short Prepubertal Children with Intra-uterine Growth Retardation

Three European groups of pediatric endocrinologists have recently emphasized the frequency with which a low or abnormal secretion of growth hormone (GH) is found in children with intrauterine growth retardation (IUGR), with or without Silver-Russell syndrome (SR).

Albertsson-Wikland reports data on 16 IUGR children with lengths 3 SD below normal at birth. These children were studied between 2 to 6 years of age, when their heights were 2.7 to 5.5 SD below normal. (In addition, 6 children had features of SR.) Their mean GH response to an arginine-insulin test was 15.7 ± 7.2 ng/mL; five of these had peak responses below 10 ng/mL. A 24-hour GH profile (withdrawals every 30 min) in 3 of the 6 SR patients and in 2 of the 10 other IUGR children showed low spontaneous secretion. Most of the other children showed minor disturbances in their circadian rhythm of GH secretion. All were treated with GH, 0.1 IU/kg/day, resulting in an average increase in growth velocity of 3.7 cm and 3.0 cm in the SR and the other IUGR children, respectively, during the first year of treatment. The gain in height was negatively correlated with the 24-hour GH secretion, evaluated by the area under curve ($r = -0.56$, $P < 0.05$), but not with the peak result of the arginine-insulin stimulation test.

Rochiccioli et al studied 24 prepubertal IUGR children born with lengths below the 10th percentile for gestational age. At the time of the study their mean age was 5.5 years and their mean height -3.3 SD. One or two GH stimulation tests (glucagon-betaxolol, clonidine-betaxolol, or arginine-insulin) and a 24-hour (20-30 min sampling) profile of serum GH were performed in each patient. Of the 24, 7 had both a 24-hour integrated concentration of GH below 1.5 ng/mL and GH peaks not exceeding 5

ng/mL at the two stimulation tests. Another 9 had low integrated circadian concentrations, with either normal ($n = 4$) or low ($n = 5$) peak responses to stimulation. Only 8 had both normal responses to the stimulation tests and normal spontaneous GH secretory profiles. Of the 24, 9 (unclear which children) were treated with GH, 0.4 IU/kg/week, and had an increase in growth velocity from 3.5 ± 0.8 cm/year before GH to 7.0 ± 0.9 cm/year during the first year of treatment.

Stanhope and associates report data on 31 IUGR prepubertal children with mean age 6.0 years, mean height -2.84 SD, mean birth weight -2.82 SD, and mean growth velocity -0.76 SD, during the year preceding the study. Seventeen had signs of SR. GH secretion (15 min sampling) was determined overnight (8 P.M. to 8 A.M.): 4 of 31 had no spontaneous GH peak above 10 ng/mL and thus were considered to be GH deficient. Nine (8 with SR) had a single nocturnal pulse of GH. A therapeutic trial of GH was performed in 23 patients, with randomization to two clinically similar groups receiving either 15 IU/m²/week or 30 IU/m²/week of GH, by daily SC injections (approximately 0.45 and 0.90 IU/kg/week). Short-term mean results were: in the low-dose group, an increase of height velocity from -0.61 to +1.09 SD for 0.82 year; in the high-dose group, an increase from -0.61 to +3.48 SD for 0.92 year. The authors conclude 1) that GH deficiency—mainly abnormal rhythm of nocturnal GH secretion—is apparently common in growth retarded children with IUGR; 2) that the short-term effect of GH in these patients is positive and dose dependent; 3) that these initial results cannot determine whether GH treatment may improve the final height of IUGR patients, some of whom may have an accelerated skeletal mat-

uration and an early onset of puberty.

Albertsson-Wikland K. *Acta Paediatr Scand (Suppl)* 1989; 349:35-41.

Rochiccioli P, Tauber M, Moisan V, Pienkowski C. *Acta Paediatr Scand (Suppl)* 1989;349:42-46.

Stanhope R, Ackland F, Hamill G, et al. *Acta Paediatr Scand (Suppl)* 1989;349:47-52.

Editor's comment—*Although these three studies differ in terms of protocol, their results are similar. They clearly show that some degree of abnormality in the secretion of GH is found, more often than previously reported, in very short children born small-for-date, irrespective of whether they have the features of Silver-Russell syndrome. In these children frequent circadian or nocturnal measurement of the serum GH levels is perhaps a better way to evaluate GH secretion than the usual stimulation tests. However, nothing is known at present about the long-term usefulness of GH therapy in non-GH-deficient IUGR children. A dose dependency may exist during the first year of treatment, but beyond this time data do not exist. We can conclude that studies such as these in IUGR children are extremely useful, but that they must be developed and conducted in long-term, controlled protocols. We cannot at present extend the data from these trials to conclude that the use of GH in endocrinologically normal children with short stature of prenatal onset is efficacious.*

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