

## Three-Year Results of a Randomized Prospective Trial of Methionyl GH and Oxandrolone in Turner Syndrome

Seventy girls with Turner syndrome were divided into four groups to receive growth hormone (GH) (0.125 mg/kg, 3 times/week), oxandrolone (either 0.125 mg or 0.062 mg/kg daily), or a combination of both agents. Sixty-five subjects were evaluated after three years of therapy.

GH given alone over three years increased the growth velocity (GV) from  $-0.1$  standard deviations (SDs) on the Turner growth charts to  $+3.1$ ,  $+2.0$ , and  $+1.4$  SDs for the first, second, and third years, respectively. By the end of three years the mean height was  $+0.7$  SD, and five of 17 patients (29%) had heights above the 90th percentile. The increment in bone age over three years was  $2.73 \pm 0.72$  years. The  $\Delta$  Turner height age/ $\Delta$  bone age was 1.6 at the end of three years, and the  $\Delta$  predicted height was  $+4.5 \pm 0.9$  cm. After three years, four of 16 girls receiving GH alone achieved their projected adult height according to the Turner growth curves. All 16 were still growing at the end of the evaluation period. GV fell from a mean of 6.6 cm the first year of treatment to 5.4 and 4.6 cm during the second and third years, respectively. This compares to a value of 4.5 cm/year before therapy. The decrease in GV occurred although the insulin-like growth factor-I (IGF-I) values increased progressively over four years from 0.55 to 2.46 U/mL, indicating that the GV did not correlate over a long period of time with the IGF-I concentrations.

Combination therapy proved more effective than GH therapy alone. This was without apparent adverse effect on the rate of bone maturation or predicted adult height. The GV in this group increased from  $-0.1$  SD on the Turner growth charts to  $+6.6$ ,  $+4.3$ , and  $+1.4$  SDs for the first, second, and third years of treatment, respectively. By the end of

three years the mean height was  $+2.0$  SDs, and 11 of 16 patients (69%) had heights above the 90th percentile on the Turner growth curves. The increment in bone age over three years was  $4.0 \pm 1.2$  years. A  $\Delta$  Turner height age/ $\Delta$  bone age was 1.6 at the end of three years and the  $\Delta$  predicted height was  $+8.2 \pm 1.4$  cm for this group. After three years, ten of 16 girls receiving the combination therapy achieved their projected adult height according to the Turner growth curves, and all were still growing. GV fell from a mean of 9.8 cm during the first year of treatment to 7.4 and 6.1 cm for the second and third years, respectively. These compared to a pre-therapy value of 4.3 cm/year. As in the group on GH therapy, the IGF-I values increased with therapy but did not correlate with GV.

Oxandrolone was used alone in 17 patients and for only one year. The mean GV increased from 4.1 to 7.6 cm/year. Since these patients then received combination therapy, the prolonged effect of oxandrolone could not be evaluated, but previously published data indicate that GV in such patients return to the pretreatment rate during the third year of treatment. Oxandrolone used alone resulted in no significant increase in IGF-I values.

The GV data from the patients receiving GH alone compare favorably with those reported in three other studies. The effect of therapy on adult height is more

difficult to assess, but all 65 subjects who completed the study continue to grow. However, the median  $\Delta$  height age/ $\Delta$  bone age values suggest a permanent increase in predicted adult height since 65% of those receiving combination therapy have already equalled or exceeded their projected adult heights.

Appropriately, the authors point out that GH and oxandrolone are potent anabolic agents and are capable of causing insulin resistance, virilization, and the clinical stigmata of acromegaly. Also, patients with Turner syndrome do not respond to GH as well as GH-deficient patients, and the expectations of the patient, family, and physician for increased growth must be realistic. The authors also point out that it still remains to be seen whether such treatment will permit a significant number of these girls to attain a "normal" adult height of  $>150$  cm.

Rosenfeld RG, Hintz RL, Johanson AJ, et al. *J Pediatr* 1988;113:393.

**Editor's comment**—*This editor has avoided treating patients with Turner syndrome with GH, but the current evidence suggests that we may eventually see an increase in ultimate height. If patients with Turner syndrome are to be treated, I certainly agree with the authors' comments that the expectations of the patients and parents for increased growth must be realistic.*

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