Growth Hormone Treatment of Girls With Turner Syndrome: The National Cooperative Growth Study Experience

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ABSTRACT. Objective. To evaluate growth rate and adult height with recombinant growth hormone (GH) treatment in girls with Turner syndrome (TS) and predictors of their growth response.

Methods. Data on girls with TS who were treated with GH in the National Cooperative Growth Study (NCGS) were evaluated. As of January 1997, there were 2798 girls with TS in the NCGS database, 2652 of whom had not previously received GH. Follow-up data on growth were available for 2475 subjects, and data on adult height were available for 622.

Results. The average age of girls with TS at enrollment in the NCGS was 10.1 ± 3.6 years. These patients had severely short stature compared with that of unaffected American girls (height, 118.5 ± 16.5 cm; height standard deviation score [SDS], −3.1 ± 0.9), but their heights were typical of those of American girls with TS (TS-specific height SDS, 0.01 ± 0.9). Treatment with GH for an average duration of 3.2 ± 2.0 years resulted in an increase in height SDS of 0.8 ± 0.7 compared with unaffected girls and of 1.2 ± 0.8 compared with TS standards. Growth rates increased from 4.0 ± 2.3 cm/year before treatment to 7.5 ± 2.0 cm/year after 1 year of treatment. Duration of treatment with GH was the strongest predictor of change in height SDS. After 6 to 7 years of treatment with GH, there was a cumulative change of 2.0 in mean height SDS.

The 622 girls who reached adult height were older when they began taking GH. Their mean height gain over pre-GH projected height was 6.4 ± 4.9 cm after 3.7 ± 1.9 years of treatment. Their adult height was 148.3 ± 5.6 cm.

Conclusions. Although the response to treatment with GH varied, it was associated with highly significant gains in growth and adult height in girls with TS. Duration of treatment with GH was the most important variable predicting adult height. Pediatrics 1998;102: 479–481; Turner syndrome, growth hormone, growth.

ABBREVIATIONS. TS, Turner syndrome; GH, growth hormone; NCGS, National Cooperative Growth Study; SDS, standard deviation score(s); NCHS, National Center for Health Statistics; CA, chronologic age; BA, bone age.

Turner syndrome (TS) is a chromosomal disorder that affects about 1 of every 2000 to 2500 live-born girls. More than 95% of girls with TS have short stature. The average difference between adult height of women with TS and that of unaffected women is 20 cm. Gonadal failure (>90%) and infertility (>99%) are other frequent findings. However, as many as 10% to 20% of girls with TS will develop breasts spontaneously, and a small minority (2% to 5%) will have spontaneous menstrual cycles.

Biosynthetic growth hormone (GH) recently was approved in the United States for use in augmenting height in patients with TS. This study examines the outcomes from a large national database of girls with TS who were treated with GH.

METHODS

The National Cooperative Growth Study (NCGS) began its follow-up of patients treated with Genentech’s GH products in 1985. Methods of enrolling subjects and collecting data have been described previously. As of January 1997, there were 2798 girls with TS enrolled in the NCGS. Of these, 2652 were naive to treatment with GH at enrollment. Follow-up data on growth were available for 2475 enrollees, and data on adult height were available for 622 enrollees. Data on height are presented as height standard deviation score(s) (SDS) relative to unaffected American girls (National Center for Health Statistics [NCHS]) and to girls with TS. The dosage of GH used is reported as the mean in milligrams per kilogram of body weight per week. Cumulative growth during GH treatment is reported as TS-specific height SDS.

Adult height was considered to have been attained if the chronologic age (CA) and bone age (BA) were older than 14 years at the time of the last reported measurement of height, or if the CA was at least 18 years. If the BA was not available when the height was last measured and the CA was between 14 and 18 years, an extrapolated BA was calculated by using a BA that had been recorded in the previous 3 years. If this BA was at least 14 years, the last height measured was considered the adult height.

The Lyon projection method, which assumes that the adult height SDS of girls with TS will equal their height SDS when first seen, was used to predict what the subjects’ heights would have been had they not been given GH. This method has been validated in the United States for patients with TS.

Frequency data are reported as percentages. Variables are presented as means ± SD.

RESULTS

Baseline data on girls with TS who had not been treated previously with GH are shown in Table 1. These girls were extremely short by NCHS standards (height SDS, −3.1 ± 0.9), but their TS-specific height SDS was 0.01 ± 0.9.

Table 2 shows data on treatment with GH in the 2475 girls for whom follow-up data on growth were available. The average duration of treatment was...
With TS Data on Treatment With GH in 2475 NCGS Patients

Table 2. * At baseline, 88.9% prepubertal; 11.1% pubertal.

Table 3. Data on the 622 NCGS Patients With TS Who Attained Adult Height

Discussion

In general, the girls with TS in the NCGS database are typical of girls with TS in the general population, as indicated by the fact that their mean TS-specific height SDS is nearly 0.0, with an SD of 0.9. Factors that can affect the apparent benefit of GH in TS are the patient’s age at the start of treatment, height deficit at the start of treatment, duration of the treat-
Turner Syndrome and Osteoporosis: Mechanisms and Prognosis

Karen Rubin, MD

ABSTRACT. Despite only limited reports of a greater number of fractures during childhood or adulthood, osteoporosis historically has been described as a feature in Turner syndrome, because of the frequent observation of radiographic osteopenia and the coarse trabecular pattern of the carpal bones on radiographs. The pathogenesis of the skeletal demineralization remains unclear, but the data support the concept of an intrinsic bone defect that is then exacerbated by a number of hormonal factors, including the growth-regulating hormones, the gonadal steroids, and possibly the calcium-regulating hormones. The advent of more refined methods, such as single- and
discussion with GH, use of estrogen replacement, parameters used to define adult height, and method used to predict what the adult height would have been without treatment with GH.

Although the cumulative change in TS-specific height SDS shows much variability, the increase in height SDS observed with increasing duration of GH treatment, overall, is highly significant. The importance of the duration of treatment should be kept in mind in evaluating published reports of the effect of GH on adult height in patients with TS. Other variables that affect outcomes favorably are younger CA and BA at the start of treatment and more frequent injections of GH. The lack of a statistically significant effect of the size of the doses of GH on the change in height SDS probably reflects the narrow range of doses used, because other studies have shown a logarithmic relation between the rate of growth and the size of the doses of GH.12

The definition of adult height used for analyzing data also may affect the perceived benefit of treatment with GH. The criteria of CA and BA as described previously would likely underestimate (not overestimate) adult height and therefore would yield relatively conservative data on the effect of treatment with GH.

The method used to estimate what the adult height would have been without treatment with GH will affect the observed gain in height. Attie and associates11 compared five methods of predicting adult height in patients with TS, using data from patients with TS in the United States who had not been given growth-promoting drugs. They found that the Lyon projection method, used in our study, was one of the most reliable means of predicting adult height, with a mean overprediction of only 0.3 cm.

Because the age of the patients in this analysis was greater than the average age of girls with TS who were enrolled in the NCGS, we may expect that outcomes will improve as data from patients who began taking GH at younger ages and who have been taking GH for longer periods of time become available. Nevertheless, even though the patients with TS whom we have described began taking GH at a relatively older age and took it for a relatively short period, 60% still showed clinically meaningful gains in adult height compared with their pretreatment projected height.

REFERENCES

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*Pediatrics* 1998;102;479

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