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.
TABLE 1. Baseline Data on 2652 NCGS Patients* With TS Naive to Treatment With GH

<table>
<thead>
<tr>
<th>Mean Value</th>
<th>SD</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (y)</td>
<td>10.1</td>
</tr>
<tr>
<td>Height (cm)</td>
<td>118.5</td>
</tr>
<tr>
<td>Height age (y)</td>
<td>6.8</td>
</tr>
<tr>
<td>Height SDS (NCHS)</td>
<td>-3.1</td>
</tr>
<tr>
<td>Bone age (y)</td>
<td>8.7</td>
</tr>
<tr>
<td>Bone age SDS</td>
<td>-2.0</td>
</tr>
<tr>
<td>Midparental height SDS</td>
<td>-0.2</td>
</tr>
<tr>
<td>Growth rate (cm/y)</td>
<td>4.0</td>
</tr>
</tbody>
</table>

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

TABLE 2. Data on Treatment With GH in 2475 NCGS Patients With TS

<table>
<thead>
<tr>
<th>Mean Value</th>
<th>SD</th>
</tr>
</thead>
<tbody>
<tr>
<td>Duration of treatment with GH (y)</td>
<td>3.2</td>
</tr>
<tr>
<td>Change in NCHS height SDS</td>
<td>0.8</td>
</tr>
<tr>
<td>Change in TS-specific height SDS</td>
<td>1.2</td>
</tr>
<tr>
<td>GH dose (mg/kg/wk)</td>
<td>0.33</td>
</tr>
<tr>
<td>Number of injections/wk</td>
<td>6.0</td>
</tr>
<tr>
<td>Pretreatment (n = 1617)</td>
<td>4.0</td>
</tr>
<tr>
<td>Year 1 (n = 1738)</td>
<td>7.5</td>
</tr>
<tr>
<td>Year 2 (n = 1205)</td>
<td>6.1</td>
</tr>
<tr>
<td>Year 3 (n = 870)</td>
<td>5.3</td>
</tr>
<tr>
<td>Year 4 (n = 563)</td>
<td>4.8</td>
</tr>
</tbody>
</table>

Table 2 shows the cumulative change in TS-specific height SDS as a function of duration of treatment with GH.

A number of variables were evaluated to determine predictors of the cumulative change in TS-specific height SDS in patients treated with GH. The variables that had a significant positive association with the change in TS-specific height SDS were the duration of treatment (P < .0001), average number of injections of GH per week (P = .0005), onset of puberty (either spontaneously or after estrogen replacement) during treatment (P = .010), midparental height (P = .0005), and BA delay (n = 457; P = .008). Variables with a significant negative (ie, inverse) association with the change in TS-specific height SDS were the percentage of injections of GH missed (P = .0005), baseline TS-specific height SDS (P = .0001), and baseline CA (P < .0001) (ie, girls who were younger when they began treatment with GH had greater increases in height SDS). Factors that were not significant predictors were the GH dosage, body mass index, maximum stimulated level of GH, and pretreatment growth rate. Duration of treatment was the strongest predictor.

Data on adult height were available for 622 subjects. Their data before, during, and after GH treatment are shown in Table 3. As a subgroup, these subjects were older (12.9 ± 2.5 years) than the rest of this TS group. Their height SDS (NCHS, −3.3 ± 0.9; TS, 0.3 ± 0.9) and midparental stature (−0.2 ± 0.9) were similar to those for the TS group as a whole. Before treatment with GH, their projected adult height was 141.9 ± 6.2 cm. In contrast, their last measured (hence, adult) height was 148.3 ± 5.6 cm. Thus, the average gain in adult height over pretreatment projected height in this subgroup of 622 subjects was 6.4 ± 4.9 cm.

Figure 2 shows the frequency distribution of the gain in adult height in this subgroup. In 60% of these patients, adult height was at least 5 cm greater than the pretreatment projected adult height. Forty percent showed a gain in adult height of at least 7.5 cm.

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-
A frequency distribution of the gain in adult height over pretreatment projected height, using the Lyon projection method.

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-
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*Pediatrics* 1998;102;479

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