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# Final adult height after human growth hormone treatment in patients with Turner syndrome

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## Introduction

Turner syndrome (TS) is a chromosomal disorder caused by complete or partial monosomy of the X chromosome in a phenotypic female, which is associated with a short stature and primary ovarian failure. Short stature is the most common clinical feature of TS. Prenatal growth failure, followed by impaired childhood growth and the absence of a pubertal growth spurt in patients with TS result in a final height that is approximately 20 cm shorter than that of normal female population.The guidelines of the Turner Syndrome Study Group recommend that GH should be administered at the US Food and Drug Administration (FDA)-approved dose of 0.375 mg/kg/week; this dose can be adapted according to the growth response and IGF-1 levels. It is also recommended that GH treatment should be considered as soon as growth failure is evident, possibly after the age of 2 years. Estrogen therapy to induce pubertal development should be started at 12 years of age. In this retrospective study, we assessed the effect of GH replacement therapy on final adult height by comparing the final adult height in TS patients undergoing GH therapy with those in TS patients without GH treatment and height standard deviation score (SDS) gain after treatment.

In addition, we analyzed contributing factors determining the effect of GH treatment on final adult height.

## Subjects and Methods

We enrolled 73 patients with TS who underwent GH treatment and reached adult height and 14 patients who did not undergo treatment. To assess the effectiveness of GH therapy, we evaluated final adult height (AH), height gain over the predicted AH, and height gain over the projected AH.

In addition, to analyze the factors affecting final AH, we studied correlations between final AH (or height SDS, height gain) and treatment variables.

## Results

Table 1

Baseline characteristics and final adult height in patients with Turner syndrome with and without GH treatment

| | Treated group (n = 73) | Untreated control group (n = 14) |
|---|---|---|
| At first visit | | |
| Chronological age (y) | 8.87 ± 3.73 | 17.32 ± 2.8 |
| Bone age (y) | 8.06 ± 3.48 | 14.00 ± 1.46 |
| Height (cm) | 114.41 ± 21.3 | 137.8 ± 5.89 |
| Mid-parental height (cm) | 158.50 ± 3.41 | 158.17 ± 5.80 |
| Height SDS (general population) | -2.71 ± 1.03 | -4.48 ± 1.04 |
| Height SDS (age-specific Turner) | 0.33 ± 1.03 | 0.10 ± 1.04 |
| Predicted adult height (cm) | 144.3 9 ± 7.81 | 141.30 ± 5.34 |
| Projected adult height (cm) | 139.82 ± 0.63 | 139.67 ± 0.67 |
| 45, X karyotype (%) | 26/73 (35) | 0/14 (0) |
| At completion of adult height | | |
| Chronological age (yr) | 15.40 ± 1.46 | 20.31 ± 2.23 |
| Bone age (yr) | 14.78 ± 0.55 | 15.78 ± 0.43 |
| Height (cm) | 152.03 ± 4.66 | 143.57 ± 4.06 |
| Height SDS (general population) | -1.93 ± 1.03 | -3.87 ± 0.98 |
| Height SDS (age-specific Turner) | 1.60 ± 0.59 | 0.51 ± 0.52 |
| Treatment duration (yr) | 6.47 ± 3.02 | |
| Height SDS gain (general population) | 0.79 ± 1.05 | 0.60 ± 0.59 |
| Height SDS gain (age-specific Turner) | 1.27 ± 0.84 | 0.41 ± 0.91 |
| Height gain from predicted adult height (cm) | 7.6 ± 6.44 | 2.26 ± 3.85 |
| Height gain from projected adult height (cm) | 12.21 ± 4.33 | 3.89 ± 3.80 |

Table 2
Correlation between growth outcome and clinical characteristics in GH treated group

| | Adult height (cm) | | Ht SDS (general) | | Ht SDS (Turner) | | Gain over Projected AH (cm) | |
|---|---|---|---|---|---|---|---|---|
| | R2 | p-value | R2 | p-value | R2 | p-value | R2 | p-value |
| Chronological age at start (yr) | 0.202 | 0.364 | 0.198 | 0.375 | 0.206 | 0.354 | -0.4 | 0.078 |
| Height SDS at start | 0.504 | 0.036 | 0.481 | 0.046 | 0.511 | 0.036 | 0.204 | 0.349 |
| MPH SDS | 0.192 | 0.084 | 0.201 | 0.073 | 0.192 | 0.085 | -0.121 | 0.344 |
| Treatment duration (yr) | 0.029 | 0.890 | 0.028 | 0.897 | 0.030 | 0.887 | -0.429 | 0.061 |
| Age at initiation of estrogen (yr) | -0.094 | 0.389 | -0.099 | 0.389 | 0.094 | 0.388 | -0.211 | 0.158 |

Table 3.
Clinical characteristics between the groups attained to normal range or not after GH treatment

| | Group attained to normal (n=35) | Group not attained to normal (n=38) | p-value |
|---|---|---|---|
| Chronological age at start (yr) | 8.80±3.30 | 8.86±4.13 | 0.874 |
| Height at start (cm) | 118.39±15.23 | 110.75±25.32 | 0.127 |
| Height SDS at start (general) | -2.3±1.0 | -3.09±0.92 | 0.001 |
| Height SDS at start (Turner) | 0.77±0.97 | -0.07±0.92 | 0.000 |
| MPH SDS | -0.28±1.0 | -1.0±0.9 | 0.002 |
| BA-CA | -0.97±1.01 | -0.67±1.60 | 0.328 |
| Treatment durarion (yr) | 6.28±2.66 | 6.65±3.35 | 0.616 |
| Age at initiation of estrogen (yr) | 14.7±1.17 | 15.48±1.43 | 0.017 |
| 45, X Karyotype (%) | 56.7 | 51.2 | 0.416 |
| Adult height (cm) | 155.72±2.77 | 148.6±3.24 | 0.000 |
| Adult height SDS (general) | -1.11±0.58 | -2.68±0.75 | 0.000 |
| Adult height SDS (Turner) | 2.07±0.35 | 1.17±0.42 | 0.000 |
| Height SDS gain (general) | 1.19±0.83 | 0.41±1.1 | 0.001 |
| Height SDS gain (Turner) | 1.30±0.83 | 1.23±0.86 | 0.741 |
| Height gain over predicted adult height (cm) | 7.18±6.58 | 8.0±0.64 | 0.631 |
| Height gain over projected adult height (cm) | 15.62±2.5 | 9.06±3.09 | 0.000 |

## Conclusion

In conclusion, our study shows that GH treatment initiated at an early age increases the final AH and height gain in patients with TS. The data also shows near half of the patients attain an AH in the normal range of height for normal population after GH treatment. In our study, attaining a normal height after treatment depends on height SDS at the start of treatment, genetically determined growth potential (MPH SDS), and earlier replacement of estrogen.