

Pubertal Height Gain in Females with Isolated Growth Hormone Deficiency Treated with rhGH alone or in combination with GnRHan

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Background knowledge

A significant component of the total linear growth is height gain achieved after the initiation of puberty (i.e., Pubertal Height Gain). Children with Isolated Growth Hormone Deficiency (IGHD) frequently come for evaluation around the peripubertal stage. Therefore, increasing pubertal height gain in IGHD children **entering puberty with a relatively low height** is important. Researchers have tried to assess effectiveness of various interventions using key measurements and a variety of end-points. Specifically, the possible superiority of combining rhGH and GnRHan vs rhGH or GnRHan alone has been studied in children with idiopathic short stature, Small for Gestational Age and those with early puberty on GnRHan and declining Growth Velocity. Results are equivocal.

Defining criteria for such interventions is very important in order to avoid unnecessary or incomplete therapies.

Objective and hypothesis

The aim of our study was to examine whether pubertal growth can be increased in girls with IGHD **entering puberty with low height**, by adding GnRHan to the therapeutic regime of rhGH. In order to compare the effect of rhGH with or without the use of a GnRHan we calculated the height gained from puberty initiation (Tanner Breast II) to final height in girls with IGHD.

Patients and Methods

We retrospectively analysed pertinent data of females with IGHD receiving either rhGH alone (n=15) or rhGH and GnRH (n=15). 22 females with Hashimoto thyroiditis, always euthyroid and, normal growth served as “controls” (n=22). None of the participants had health problems (other than IGHD for patients) that could affect growth potentials. Kruskal-Wallis test used for statistical comparison. Criteria for inclusion: Available data on height at Tanner B2, Target and Final height and normal birth weight.

Results and Discussion

The **Age at Puberty Initiation** (Tanner B2) in the rhGH, rhGH+GnRHan and “control” group was 10.87±0.55, 10.23±0.72 and 10.4±0.63, respectively (**Figure 1A**). Age at puberty initiation differs between the rhGH and the rhGH+GnRH group (p=0.015). The **Height at Puberty Initiation** (Tanner B2) in the rhGH, rhGH+GnRHan and “control” group was 132.5±3.3, 126.8±3.3 and 139.8±5.1, respectively (**Figure 1B**). Height at puberty initiation differs between the rhGH and the rhGH+GnRH group (p=0.015).

Pubertal Height gain in girls who received rhGH alone did not differ from controls (22.6±2.7cm versus 20.1±3.15cm, p=0.21) whereas Pubertal Height gain of girls who received both rhGH and GnRHan (27.67±4.16cm) was significantly higher than both controls and girls receiving rhGH alone (p<0.001 for both, **Figure 2**). Differences in Pubertal Height gain between the rhGH and rhGH+GnRH groups remain significant even after adjusting for differences in age of puberty initiation (p=0.004).

Target and Final Height in the rhGH, rhGH+GnRHan and “control” group are depicted in **Figure 3**. Target and Final Height do not differ between the rhGH and rhGH+GnRHan groups (p=0.11 and 0.61, respectively).

BMI z-scores do not differ between the GH, rhGH+GnRHan and “control” group.

rhGH therapy duration for the rhGH and the rhGH+GnRHan groups were 4.24±1.3 and 4.1±1.12 years, respectively.

GnRHan treatment duration was 1.89±0.5 years.

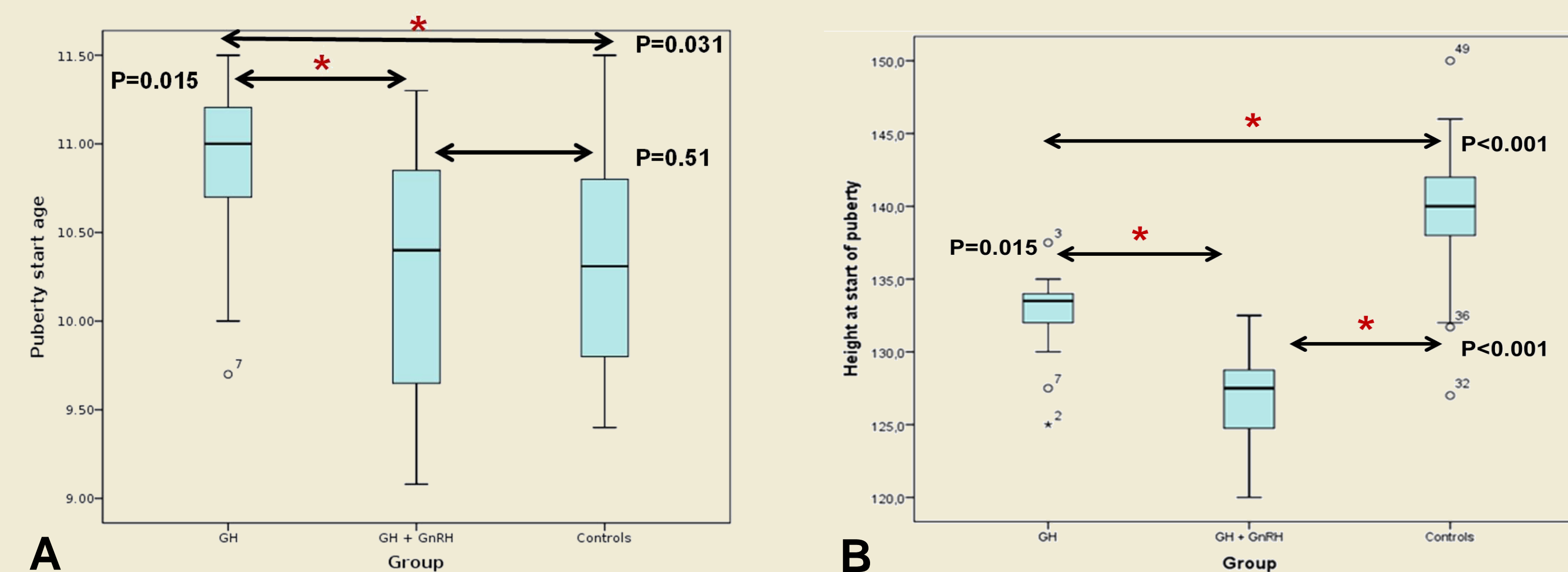


Figure 1: (A) Age and (B) Height at Puberty Initiation (Tanner B2) in the rhGH, rhGH+GnRHan and “control” group.

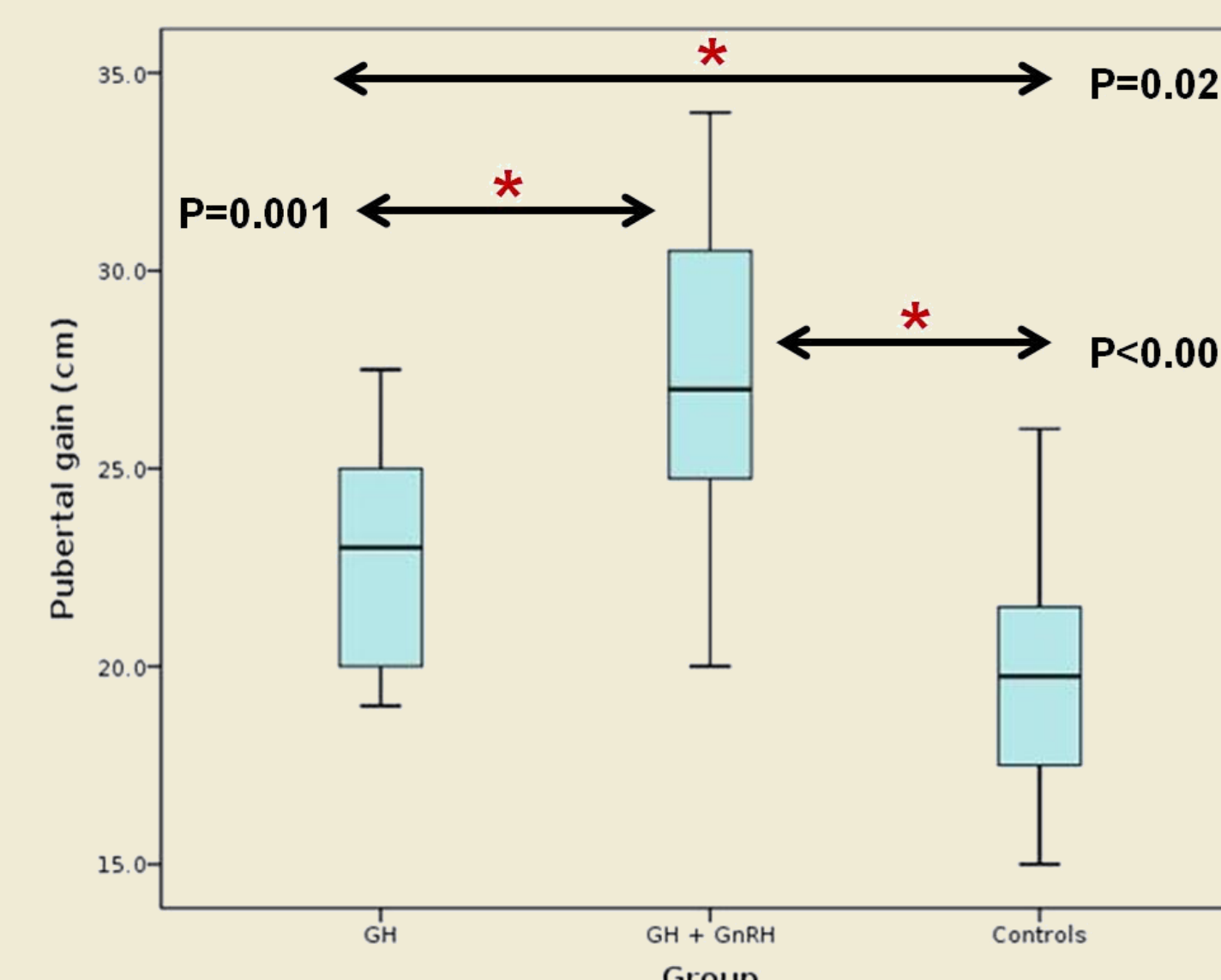


Figure 2: Pubertal Height gain in the rhGH, rhGH+GnRHan and “control” group. Difference in Pubertal Height gain between the rhGH and rhGH+GnRHan group remain significant even after adjusting for age at puberty initiation (p=0.004)

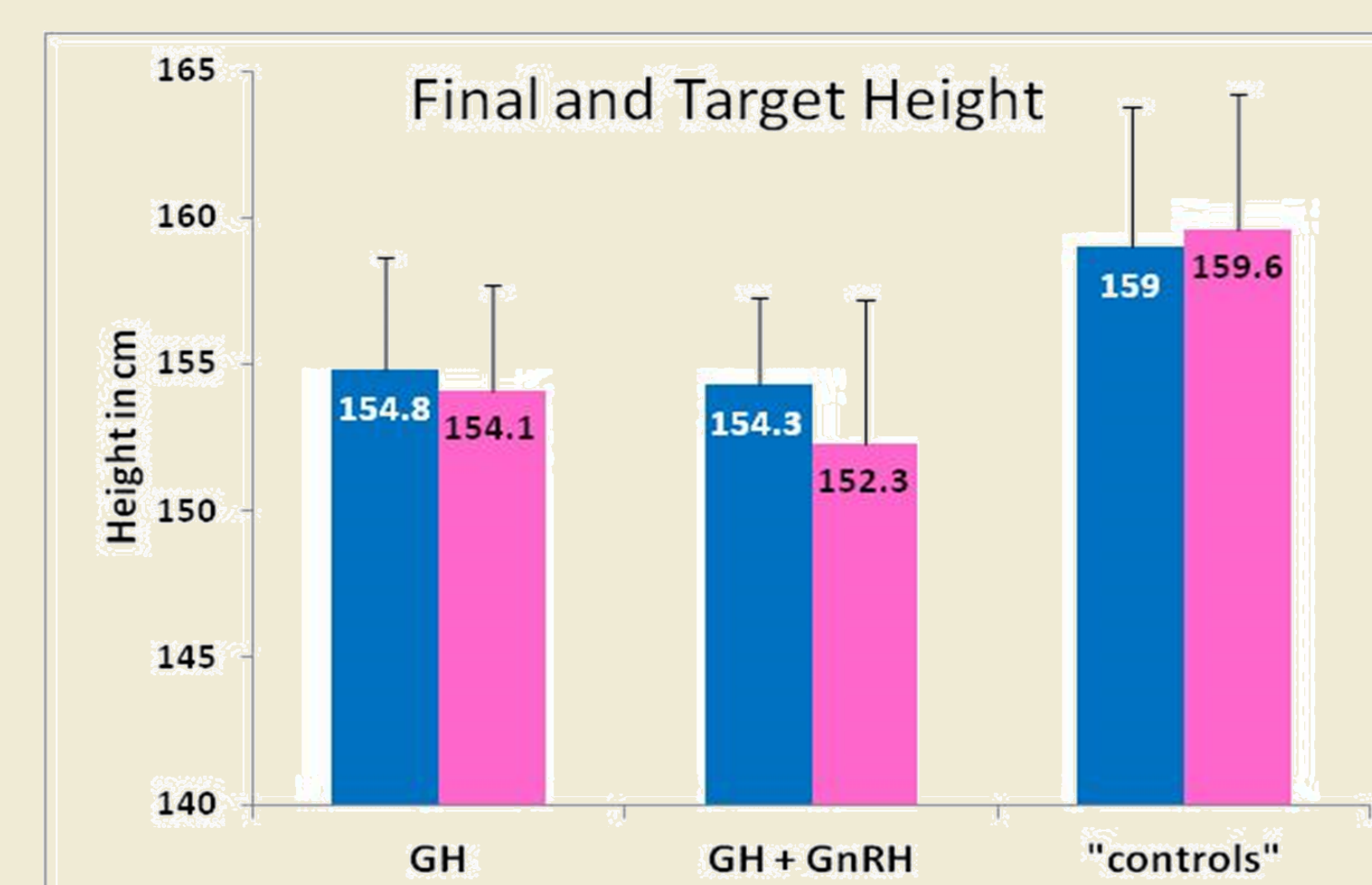


Figure 3: Final (blue columns) and Target (pink columns) Height in the rhGH, rhGH+GnRHan and “control” group. Target and Final Height do not differ between the rhGH and rhGH+GnRHan groups.

Conclusions

It seems that with rhGH treatment, pubertal gain expected for children with normal growth is achieved. Combined rhGH and GnRHan treatment seems to significantly increase pubertal gain compared to either non-GH deficient girls or IGHD girls treated only with rhGH children. Although girls receiving both rhGH and GnRH started puberty with low height, their Final Height achieved is comparable to Target Height.

Defining criteria for such interventions is very important in order to avoid unnecessary or insufficient therapies. Obviously, more studies are needed in order to respond to existing questions.