

The Effects of Delaying Puberty with Gonadotropin-Releasing Hormone Agonists (GnRHa) in Patients with Idiopathic Growth Hormone Deficiency (IGHD)

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Background

Treating central precocious puberty with GnRHa to increase height gain is well-established. Although not recommended, GnRHa have also been used in patients with IGHD at onset of puberty yet there are few data on its efficacy.

Hypothesis

Growth prediction models derived from KIGS (Pfizer International Growth Database) may provide an opportunity to estimate additional height gain produced by pubertal blockade.

Methods

Growth data from all IGHD patients in KIGS treated with GH and GnRHa (with start and end dates) were analyzed. From total pubertal growth (TPG) prediction models, we know the estimates for the effect of age at start of puberty; boys = -4.0 cm and girls = -3.7 cm for each year of delayed puberty⁽¹⁾. Therefore, we can estimate the effect of GnRHa by adjusting the model effect accordingly. By replacing the model effect with the actual cm in height, while on GnRHa, an estimated height gain can be calculated.

SAS[®] version 9 for Sun Solarix (SAS Institute, Cary, North Carolina) was used for all statistical analyses.

Results

All results are summarized in Table 1: Pubertal growth in a cohort of IGHD patients treated with GH and GnRHa. Of the patients on GH and GnRHa, 90 % had a positive estimated delta height, cm (adjusted per the KIGS model). The estimated gain in adult height after 1.5 years on GnRHa treatment is ~3 cm, which results an estimated height gain of 2 cm per year. The smaller group of patients that have reached near adult height (NAH) confirms the results.

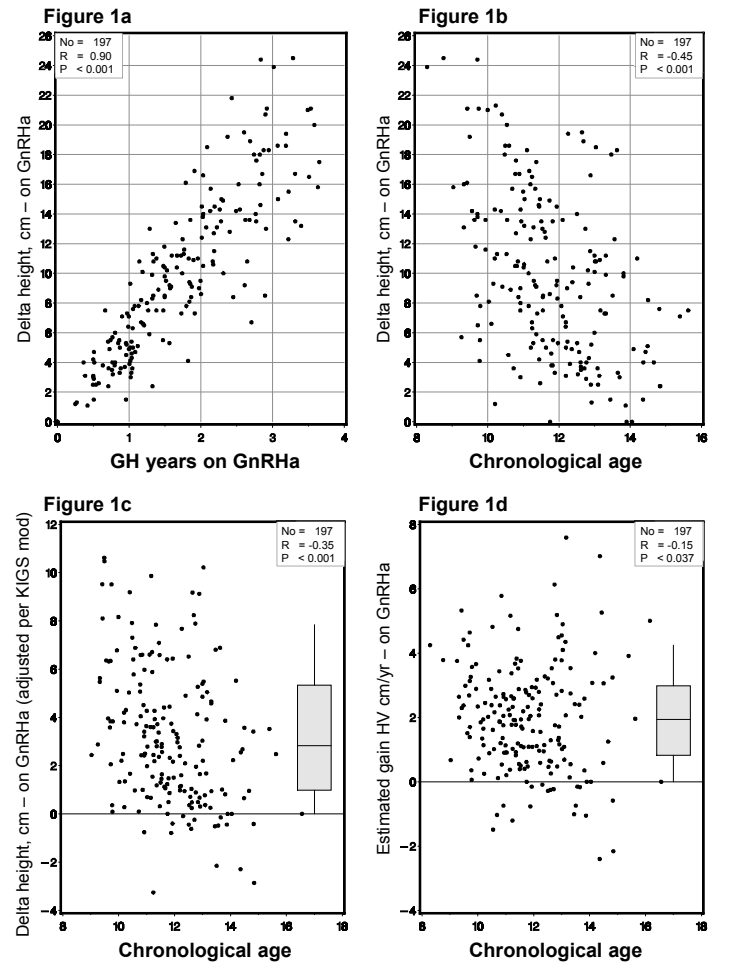
Table 1: IGHD patients treated with GH and GnRHa

	Boys* (N=84)		Girls* (N=113)		NAH* (N=12: Girls=8))	
	Median	10/90 Centiles	Median	10/90 Centiles	Median	10/90 Centiles
Start of GH						
Age (yrs)	9.7	4.5/14.4	9.5	3.6/11.9	7.9	6.5/9.2
ht SDS	-2.9	-4.2/-2.0	-3.3	-5.2/-2.1	-3.1	-4.4/2.2
Age at start of puberty ¹	11.4	10.1/13.3	10.1	8.8/12.6	10.9	8.8/13.3
Start of GnRHa						
Age (yrs)	12.3	10.8/14.7	11.2	9.5/13.0	11.3	9.3/13.6
Height SDS	-1.8	-2.9/-0.4	-2.1	-3.3/-1.0	-1.6	-2.3/-0.3
End of GnRHa						
Delta Height (cm)	9.3	3.0/18.5	9.3	3.7/16.9	8.7	3.8/13.1
Delta Height (cm) adjusted per KIGS model	2.7	-0.1/7.9	3.0	0.0/7.7	2.5	-1.6/7.8
Estimated cm/yr	1.8	-0.1/4.1	2.2	0.1/4.2	1.4	-1.8/3.8
Duration of GnRHa (yrs)	1.6	0.5/2.9	1.7	0.7/3.3	1.3	0.7/2.8

¹(girls B2, boys testicular volume > 3 mL); *All are median values

Delta height in cm from start of GnRHa to end of GnRHa is very dependent on years of GnRHa, $r=0.9$ (Figure 1a) as well as on age at start of GnRHa, $r=-0.45$, (Figure 1b).

Delta height in cm from start of GnRHa to end of GnRHa adjusted for the expected cm using KIGS puberty models is still dependent on start age of GnRHa, $r=-0.35$ (Figure 1c), but less than without adjustment. Delta height in cm from start of GnRHa to end of GnRHa adjusted for the expected cm using KIGS puberty models and corrected for time on GnRHa (as cm/yr) is almost independent on start age of GnRHa, $r=-0.15$ (Figure 1d).



Conclusion

With addition of GnRHa to treat relatively early puberty in GH-treated children with IGHD, the estimated additional median gain in adult height is 2 cm/year on GnRHa (boys=1.8 cm/year and girls=2.2 cm/year).

Our data show that this therapeutic concept may not achieve the desired benefit in height according to the TPG model.

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