EFFECT OF GONADOTROPIN RELEASING HORMONE ANALOGUE TREATMENT ON ADULT HEIGHT IN GIRLS WITH BORDERLINE EARLY PUBERTY OR NORMAL PHYSIOLOGICAL PUBERTY DEPEND ON BONE AGE ADVANCEMENT AND PREDICTED HEIGHT : A RETROSPECTIVE STUDY

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Background: Borderline early puberty or normal puberty can pace at a slow or fast tempo. In those with a fast tempo bone age (BA) advancement may result in a decrease in predicted adult height (PAH). Gonadotropin releasing hormone analogue (GnRHa) treatment is not indicated routinely in these children however evaluation on an individual basis may be necessary.

Objective: To study the effectiveness of GnRHa treatment in improving adult height (AH) in girls with advanced BA and decreased PAH in borderline early or normal physiological puberty.

Patient Groups: One hundred thirty-five girls whose puberty started between 6. 8 and 9.7 years (8.0±0.8years) were divided into two groups according to BA advancement and decreased PAH after 7.3±8.9 (0-34) months of follow up after the onset of puberty: Group I (n=63) with low PAH at follow up was treated with 3.75 mg triptorelin or leuprolide IM every 4 weeks for 2.2±0.9 years, Group II (n=72) with normal PAH at follow up was followed without treatment. All girls had a BA of at least 14 years at last visit.

Methods: The clinical and laboratory (hormonal and pelvic US) data at onset and at follow up were recruited from the files. Cases with organic causes, hypothyrodism, congenital adrenal hyperplasia and other pathologies were excluded. All measurements were done by an auxologist. Target height (TH) was calculated as mother's height+father's height-13/2. BA age was evaluated by Greulich Pyle method and PAH by Bayley-Pinneau method by average BA. All measurements and body mass index (BMI) (kg/m^2) were expressed as SDS according to national references. Ethical approval was obtained.

Results

- Values between the groups were compared at presentation and at the onset of therapy in group I and at respective time in group II. The results are shown in Table 1. AH and TH values are shown in Table 2.

- There was no difference in PAH-TH between the Groups at presentation however at follow up PAH-TH decreased significantly in Group I. ΔBA/ΔCA was significantly higher in Group I. This was the basis for initiating therapy.

- There was no difference between AH and AH-TH SDS between Group I and Group II.

- In Group I, 87.3% and in Group II 86.5% of the girls reached an AH within TH±1 SD (6 cm). Stepwise linear multiple regression analysis showed that AH within TH ± 1SD was mainly affected by PAH at follow up and BA in both Groups. In Group I basal LH level also was a contributing factor.

- Comparison of girls with an AH < TH-1 SD with those with an AH in the TH range showed that PAH-TH SDS was significantly lower in girls with short stature in both Groups (p= 0.000 and 0.044 in Group I and II respectively).

- Menarcheal age was 12.3±1.1 years in Group I and 11.3±1.1 years in Group II (p=0.000).

- BMI SDS was not different between the groups at any time at follow up.

- Pelvic US findings were not different between the groups at presentation and at onset of therapy.

Table 1. Comparison of anthropometric and hormonal parameters between Group I at onset of therapy and Group II at respective time and at presentation.

		Group I (n=63)		Group II (n=72)		p value	
		At Presentation	At onset of therapy	At Presentation	At respective time at follow up	Comparison between Group I and II at presentation	Comparison between Group I at onset of therapy and Group II at respective time at follow up
Age (years)		8.5±0.9	9.1±0.9	9.0±1.0	9.6±0.9	0.002	0.007
Interval after presentation for intervention (months)		7.3±8.9		7.2±2.8		0.912	
Height SDS		0.7±1.3	0.9±1.3	0.5±1.2	0.6±1.1	0.551	0.240
Weight SDS		0.9±1.2	1.0±1.2	0.8±1.1	0.9±1.0	0.654	0.480
BMI SDS		0.8±1.1	0.8±1.1	0.8±1.0	0.8±1.0	0.846	0.840
BA (years)		10.1±1.5	11.1±1.1	9.9±1.9	10.3±1.8	0.564	0.003
ΔBA/ΔCA		2.0±1.3		1.1±1.3		0.003	
PAH SDS		-1.0±1.2	-1.1±1.3	-0.5±1.1	-0.4±1.0	0.015	0.002
PAH SDS-TH SDS		0.1±1.1	-0.0±1.1	0.4±1.0	0.5±1.0	0.081	0.025
Pubertal stage	Breast	2.5±0.8	2.9±0.7	2.2±0.8	2.6±0.9	0.017	0.026
	Pubic hair	2.0±0.9	2.4±1.0	2.1±0.9	2.5±0.9	0.425	0.719
LH (mIU/mL)		1.8±2.3	2.3±2.3	0.7±1.0	1.1±1.5	0.000	0.038
Peak LH		14.9 ±17.0		5.9±7.3		0.037	
FSH (mIU/mL)		3.8±2.4	4.1±2.1	2.8±1.5	3.7±2.7	0.005	0.496
Peak FSH		13.9±9.5		12.6±5.5		0.617	
Peak LH/Peak FSH		1.0 ±0.7		0.5±0.4		0.002	
Estradiol (pg/mL)		31.1±28.0	39.3±31.9	21.6±20.8	33.5±40.9	0.042	0.550

Table 2. Comparison of adult height and target height between Group I and Group II.

	Grup I (n=63)	Grup II (n=72)	p value
TH SDS	-1.1±0.9 (-4.1-1.7)	-0.9±0.8 (-2.4 – 1.9)	0.150
AH SDS	-1.1±1.1 (-4.1 – 2.0)	-1.1±1.0 (-3.4 – 1.7)	0.923
AH SDS- TH SDS	0.1±1.0 (-2.6 – 2.1)	-0.2±0.8 (-2.0 – 1.5)	0.131

Conclusion

Slowly progressing puberty cases do not need treatment.
The patients with advanced BA and decreased PAH should be evaluated individually. However the consequences of not treating these children in this age group can not be answered by the results of this study.