Effects of a gonadotropin-releasing hormone agonist (GnRHa) and etiology in boys with early puberty

Young Suk Shim[a], Hae Sang Lee[b], Hwal Rim Jeong[b], Eun Byul Kwon[b], Jin Soon Hwang[b]

[a]Department of Pediatrics, Hallym University Medical Center, School of Medicine, Hallym University, Seoul, Korea; [b]Department of Pediatrics Ajou University Hospital, School of Medicine, Ajou University, Suwon, Korea

OBJECTIVES

Early puberty (EP) can be defined as the development of secondary sexual characteristics between the age of 9 and 11 years in boys. Gonadotropin-releasing hormone agonist (GnRHa) may be used in boys with early puberty.

We investigated (1) the effects of GnRHa treatment on auxological outcomes in Korean boys with early puberty and (2) the etiology of EP, including the possibility of organic brain lesions, by brain magnetic resonance imaging (MRI).

METHODS

The clinical records of 33 Korean boys with EP who were treated with GnRHa for more than 2 years at Ajou University Hospital in Suwon, Korea, from 2003 to 2013 were reviewed. EP was diagnosed according to the following criteria: (1) objective testicular volume of ≥4 mL between 9.0 and 10.9 years of age, (2) advanced bone age (BA) >1 year above chronological age (CA), and (3) pubertal luteinizing hormone (LH) peak values (cut-off value of ≥5 IU/L) with GnRH stimulation tests performed between 9.0 and 10.9 years of age. The patients were retrospectively divided into two groups: group 1 subjects (*n* = 17) were diagnosed with EP and received GnRHa treatment between 9.0 and 9.9 years of age, and group 2 subjects (*n* = 16) were diagnosed with EP and received GnRHa treatment between 10.0 and 10.9 years of age. Fifteen boys underwent MRI studies of the hypothalamic-pituitary area. The standard treatment regimen was the administration of subcutaneous leuprolide-acetate or triptorelin–acetate at 3.75 mg every 4 weeks. GnRHa was discontinued at a BA of close to 14 years.

Table 1. Effects of therapy with GnRHa and differences in the effects of GnRHa treatment between groups 1 and 2.

	Early puberty Group 1 (n = 17)	Early puberty Group 2 (n = 16)	*P* value
CA (years)			
At the start of treatment	9.82 ± 0.22	10.44 ± 0.30	<0.001
1 year of treatment	10.84 ± 0.23*	11.44 ± 0.32*	<0.001
2 years of treatment	11.90 ± 0.21*, **	12.45 ± 0.30*, **	<0.001
BA (years)			
At the start of treatment	12.43 ± 0.59	12.67 ± 0.45	0.190
1 year of treatment	13.01 ± 0.61*, **	13.27 ± 0.37*,**	0.166
2 years of treatment	13.46 ± 0.49*, **	13.70 ± 0.33*, **	0.090
BA – CA (years)			
At the start of treatment	2.61 ± 0.62	2.24 ± 0.45	0.057
1 year of treatment	2.18 ± 0.64*	1.83 ± 0.38*	0.065
2 years of treatment	1.55 ± 0.52*, **	1.26 ± 0.37*, **	0.124
Height SDS			
At the start of treatment	1.29 ± 0.91	1.04 ± 0.67	0.380
1 year of treatment	1.36 ± 0.88	1.05 ± 0.69	0.262
2 years of treatment	1.08 ± 0.83*, **,	0.72 ± 0.66*, **	0.175
Weight SDS			
At the start of treatment	1.09 ± 0.65	0.84 ± 0.75	0.322
1 year of treatment	1.10 ± 0.68	0.96 ± 0.69	0.585
2 years of treatment	1.03 ± 0.79	0.91 ± 0.71	0.662
BMI SDS			
At the start of treatment	0.76 ± 0.66	0.55 ± 1.02	0.217
1 year of treatment	0.76 ± 0.70	0.71 ± 0.90	0.866
2 years of treatment	0.77 ± 0.75	0.79 ± 0.84	0.961
Testes volume (mL)			
At the start of treatment	5.44 ± 1.59	6.97 ± 1.81	0.015
1 year of treatment	3.94 ± 0.86*	4.72 ± 1.34*	0.055
2 years of treatment	3.88 ± 0.91*	4.44 ± 0.96*	0.099

Figure 1. Comparison of target height standard deviation score (TH SDS) and predicted adult height standard deviation score (PAH SDS) at the start of treatment, PAH SDS at 1 year of treatment and PAH SDS after 2 years of treatment in group 1 (A) and group 2 (B).

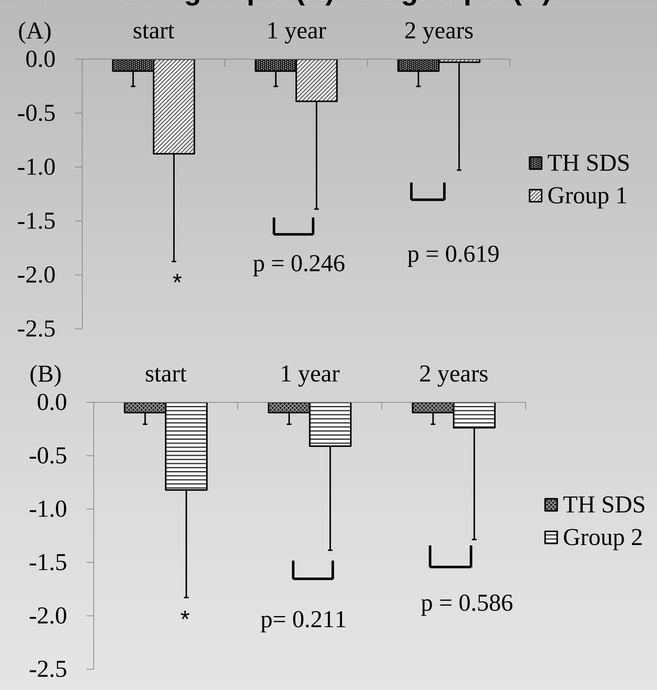

Table 3. Factors influencing predicted adult height standard deviation score (PAH SDS) after 2 years of treatment in 33 GnRHa-treated boys with early puberty (EP) (R^2 =0.825, P <0.001).

Predictive factor	Estimate	Standard error	P value
PAH SDS at the start of treatment	0.964	0.080	<0.001

RESULTS

Effects of GnRHa Treatment

There was a significant increase in PAH SDS after 2 years of treatment in group 1 (p < 0.001) and group 2 (p < 0.001). In group 1, PAH SDS increased from -0.39 ± 1.03 after 1 year of treatment to -0.03 ± 1.06 after 2 years of treatment (p < 0.001). In group 2, PAH SDS increased from -0.41 ± 0.97 after 1 year of treatment to -0.24 ± 1.05 after 2 years of treatment (p < 0.001)

Organic CNS Lesion as Etiology of EP

Sellar MRI was performed in 15 patients in group 1 (Table 1). An MRI abnormality was detected in 1 of 15 (6.7%) boys with EP. The one boy with the MRI abnormality was diagnosed with pituitary hyperplasia at 9.60 years of CA. He had no hormonal abnormalities and received GnRHa alone.

CONCLUSIONS

GnRHa treatment significantly improved the growth potential of boys with EP. PAH after 2 years of treatment was positively correlated with PAH at the start of treatment. Organic CNS lesions were not frequent as an etiology of EP.

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