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Relationship between growth velocity and change of serum insulin-like growth factor-1 (IGF-1), serum IGF binding protein-3 (IGFBP-3) concentrations, and IGFBP-3 promoter polymorphism during gonadotropin-releasing hormone agonist (GnRHa) treatment

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Disclosure Statement

Kyung Hee Yi and Seung Yang have no relevant financial relationships to disclose or conflicts of interest to we solve.

Introductions and Objectives

- Factors affecting the better response to GnRHa treatment and final height outcome
  - –Younger chronological age (CA) at puberty or start of treatment (*Paul D et al. J Clin Endocrinol Metab 1995 Feb;80:546-51*)
  - –Greater height at the initial evaluation and target height (*Allali S et al. Med Sci Monit 2011;17:PH41-8)*
  - –Shorter interval between the onset of the CPP and treatment (*Kauli R et al. Horm Res 1997;47:54-61)*
  - –Advanced bone age (BA) and lower predicted adult height (*Adan L et al. Clin Endocrinol 2002 Mar;56:297-302)*
- Effects of sex steroids on GH–IGF-1 axis
  - –Mean IGF-1 concentration in precocious children with GH deficiency was significantly above than prepubertal GH-deficient children.
  - –Sex steroids increase IGF-1 levels by increasing GH production. (*Cara JF et al. J Pediatr 1989;115:64-8*)
- This study aims to investigate the effect of GnRHa on GH-IGF-1 axis and to evaluate if -202 A/C IGFBP-3 promoter polymorphism affects the growth velocity during treatment on girls with central precocious puberty (CPP).

Methods

Data was collected from 97 girls, diagnosed under 9 year of age and treated by GnRHa for at least 1 year between 2014-2015. Their body height, weight, ∆ Height standard deviation score (SDS), serum IGF-1 and IGFBP-3 concentrations and bone age were measured at the start and after a year of GnRHa treatment. -202 A/C IGFBP-3 promoter polymorphism were analyzed. Possible correlations between the variables were calculated.

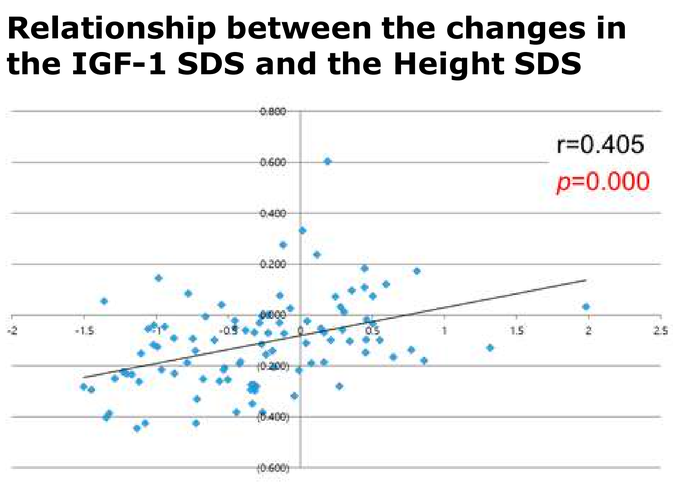
Results

Table 1. Characteristics of the 97 girls treated with GnRH agonist

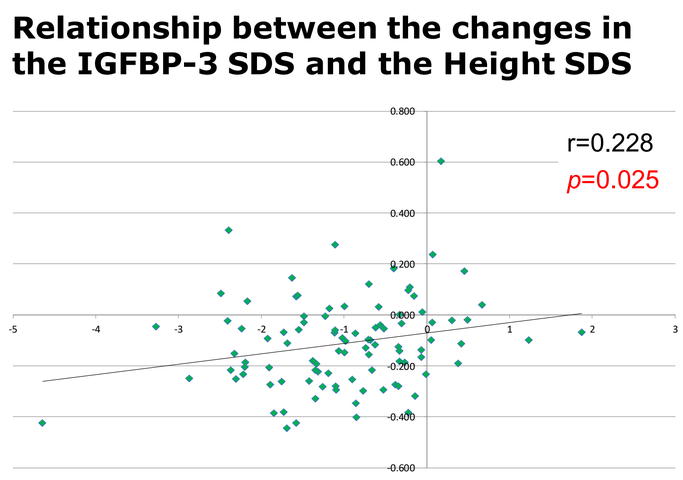
Characteristic	At diagnosis	After a year	*P*-value
CA (yr)	8.5±0.5	9.6±0.5	-
BA (yr)	10.5±0.6	10.9±0.6	-
BA–CA (yr)	2.0±0.6	1.3±0.6	0.000
Height SDS	1.2±0.8	1.1±0.8	0.000
IGF-1 SDS	0.8±1.0	0.5±0.9	0.000
IGFBP-3 SDS	3.3±1.1	2.3±0.9	0.000
IGF-1/IGFBP-3	60.7±16.3	60.5±16.8	0.000
Midparental height (cm)	160.0±3.2	-	-

Values are presented as mean±standard deviation.
GnRH, gonadotropin-releasing hormone; CA, chronological age; BA, bone age; SDS, standard deviation score; IGF-I, insulin like growth factor I; IGFBP-3, insulin-like growth factor binding protein 3.
**P<0.05* compared to before the treatment.

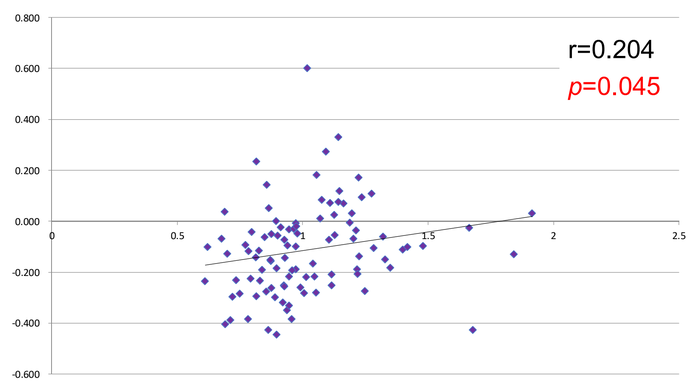
Relationship between the changes in the IGF-1 SDS and the Height SDS



Relationship between the changes in the IGFBP-3 SDS and the Height SDS

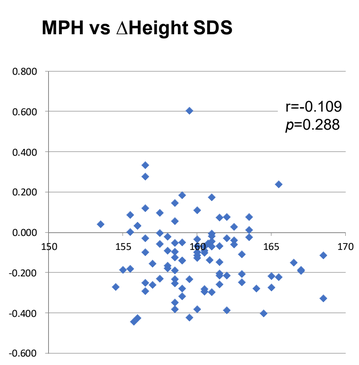


Relationship between the changes in the IGF-1/IGFBP-3 ratio and the Height SDS

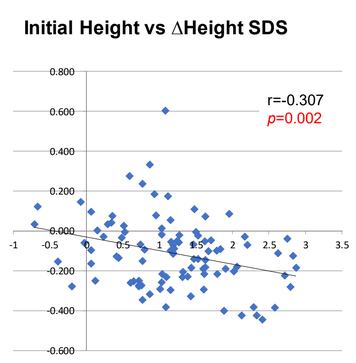


Relationship between MPH, Initial Height and the ∆Height SDS

MPH vs ∆Height SDS



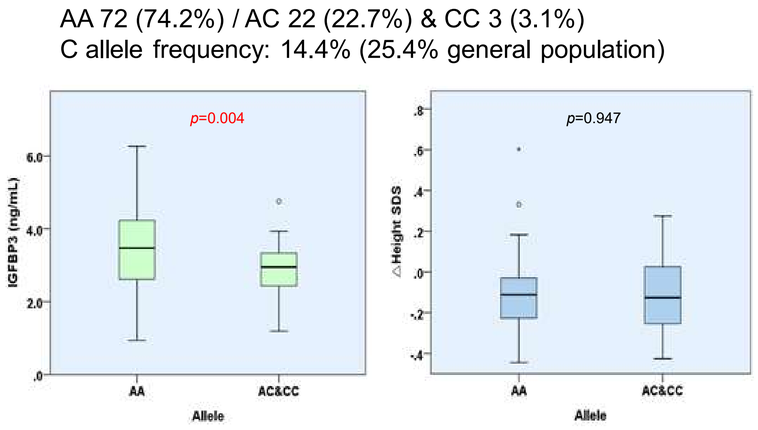
Initial Height vs ∆Height SDS

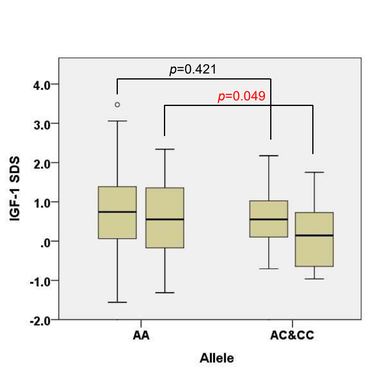


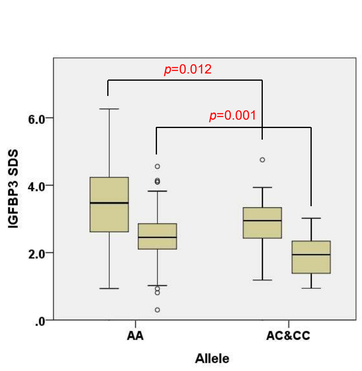
-202 A/C IGFBP-3 Promoter Polymorphism

AA 72 (74.2%) / AC 22 (22.7%) & CC 3 (3.1%)
C allele frequency: 14.4% (25.4% general population)

IGF-1, IGFBP3 level before and after the treatment according to allele







Conclusions

The results suggest that the growth velocity during GnRHa treatment may be related to serum IGF-1 and IGFBP-3 thus GnRHa may affect GH-IGF-1 axis. C allele in -202 A/C IGFBP-3 promoter region showed no statistically significant correlation with the height SDS, but may affect both serum IGF-1 and IGFBP-3 after the treatment.