



# Long term effects of GnRH agonist therapy on BMI in girls with idiopathic central precocious puberty

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## INTRODUCTION AND OBJECTIVE

Overweight/obesity is a predisposing factor for precocious puberty in girls. Although treatment with GnRH analog (GnRHa) may increase BMI during treatment, it is not well known whether pre-treatment BMI may have effect on that. The aim of this study is to investigate the effects of GnRHa treatment on weight status and to determine the factors which may effect the changes in BMI.

## SUBJECT AND METHODS

Medical files of 138 girls who completed GnRHa (leuprolide acetate) for idiopathic central precocious puberty (CPP) were evaluated retrospectively. The patients were grouped based on their pre-treatment BMI as normal weight (NW), overweight (OW) and obese (OB). Auxological and hormonal data of the patients in the three BMI groups prior to GnRHa treatment were compared to each other. OB and OW groups were combined for further longitudinal analysis of the changes in BMI-SDS and height-SDS during and two years after GnRHa treatment.

## RESULTS

- The auxological and hormonal data of the patients at the beginning of the treatment is shown in table 1.
- At the beginning of treatment, 82 (59.4%) had NW, 42 (30.4%) were OW, and 14 (10.2%) were OB (Table 1).
- The mean pre-treatment BMI increased significantly during treatment and returned to baseline levels following two years after treatment (Table 2,  $p < 0.001$ ).
- In the NW group BMI-SDS increased significantly during treatment ( $0.42 \pm 0.54$  vs  $0.87 \pm 0.33$ ) whereas there was no significant change in BMI-SDS in OW/OB patients ( $1.66 \pm 0.48$  vs  $1.69 \pm 0.53$ ) (Table 2).
- BMI-SDSs of both groups returned to baseline levels two years after completion of treatment (Table 2).
- Overall, mean height SDS decreased significantly during GnRHa treatment (Table 2).
- $\Delta$  Height-SDS during treatment differed between NW and OW/OB patients ( $-0.14 \pm 0.47$  vs  $-0.01 \pm 0.40$ ,  $< 0.001$ ).
- Mean height-SDS returned to baseline in both groups two years after completion of GnRHa treatment (Table 2).
- Two factors affecting  $\Delta$ BMI-SDS in multiple linear regression analyses were baseline BMI-SDS and  $\Delta$ height-SDS, both correlated negatively with  $\Delta$ BMI-SDS ( $p < 0.001$  and  $p < 0.001$  respectively).

Table 1. Auxological and hormonal data of the patients prior to GnRHa treatment

	Total (n=138)	NW (n=82)	OW(n=42)	OB(n=14)	p value*
Age at diagnosis (years)	8.5±1.0	8.6±0.9	8.4±0.6	8.3±0.5	0.150
Bone age (BA) (years)	10.7±0.9	10.7±0.9	10.6±0.8	10.6±0.8	0.422
BMI-SDS	0.92±0.74	0.42±0.54 <sup>a,c</sup>	1.33±0.32 <sup>a,b</sup>	2.15±0.10 <sup>b,c</sup>	<0.001**
Height-SDS	1.29±0.70	1.13±0.60	1.50±0.58	1.55±0.61	0.991
Duration of treatment (months)	29.9±9.2	28.8±10.8	31.2±7.2	32.4±6.0	0.234
Peak LH in GnRH test (IU/L)	12.7± 6.0	11.6±5.2 <sup>a,c</sup>	13.5±6.5 <sup>a,b</sup>	16.6±9.2 <sup>b,c</sup>	<0.001**

\* One-way Anova test

\*\* Multiple comparisons with post Hoc Tukey; <sup>a</sup> NW vs OW, <sup>b</sup> OW vs OB, <sup>c</sup> NW vs OB,  $p < 0.001$

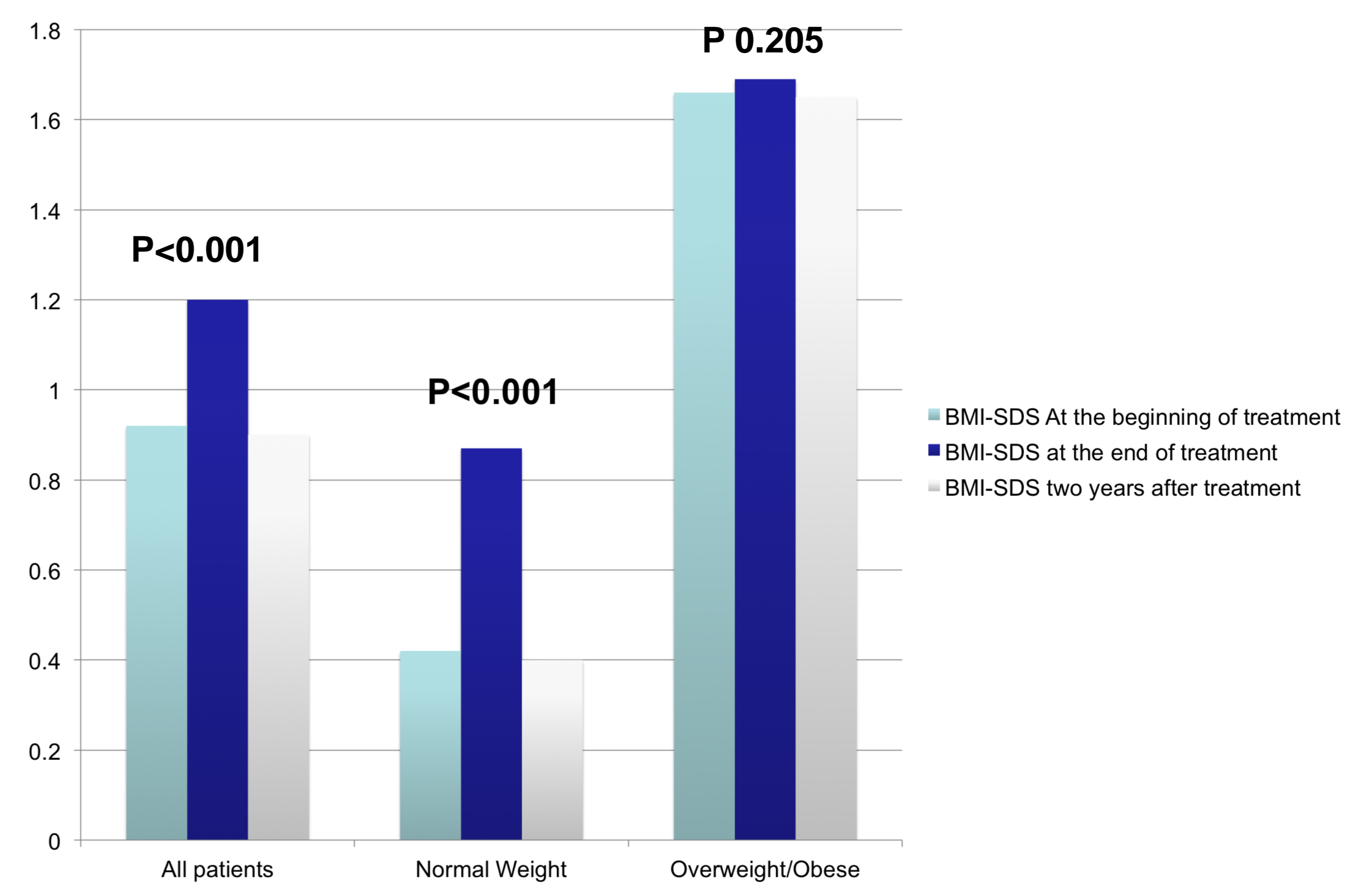
Table 2. Changes in BMI-SDS and height SDS during and in follow up after GnRHa treatment

		At the beginning of treatment	At the end of the treatment	Two years after completion of treatment	P value
All patients (n:111)	BMI-SDS	0.92±0.74 <sup>a</sup>	1.20±0.51 <sup>a,b</sup>	0.90±0.62 <sup>b</sup>	<0.001
	Height-SDS	1.28±0.57 <sup>a</sup>	1.19±0.64 <sup>a,b</sup>	1.27±0.51 <sup>b</sup>	<0.001
Normal Weight (n:66)	BMI-SDS	0.42±0.54 <sup>a</sup>	0.87±0.33 <sup>a,b</sup>	0.40±0.48 <sup>b</sup>	<0.001
	Height-SDS	1.13±0.49 <sup>a</sup>	0.99±0.64 <sup>a,b</sup>	1.10±0.44 <sup>b</sup>	<0.001
Overweight/Obese (n:45)	BMI-SDS	1.66±0.48	1.69±0.53	1.65±0.52	0.205
	Height-SDS	1.49±0.75	1.48±0.63	1.51±0.61	0.098

\*Change in each parameter over time was compared using a repeated measures ANOVA test, (n:111).

\*\* Pairwise comparisons with Bonferroni adjustment ( $p < 0.017$  as statistically significant),  $a < 0.001$ ,  $b < 0.001$

Figure 1. BMI-SDS of the patients according to the pre-treatment BMI during and in follow up of the patients



## CONCLUSION

Normal weight girls with CPP are more likely to increase BMI-SDS during GnRHa treatment however they returned back to normal two years after the completion of treatment. BMI-SDS remained stable during and in follow-up in OW or OB girls. Dietary recommendations should be provided for all girls regardless of their initial BMI-SDS.

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