Changes of Serum AMH and Inhibin B levels in Girls with Central Precocious Puberty before and during Treatment with GnRH Agonists

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Introductions

In females, anti-müllerian hormone (AMH) is glycoprotein expressed by granulosa cells in preantral and small antral ovarian follicles. Circulating AMH levels strongly correlates with antral follicle count in adult women. AMH levels increase slightly from birth onward and plateau during adolescence. AMH levels decreased after GnRH agonist administration independent of gonadotropin levels in healthy women. Inhibin B is glycoprotein hormone secreted from preantral and small antral follicles. It is undetectable in prepubertal girls and rise during puberty. Circulating levels of inhibin B reflect the pituitary-stimulated activity of early developing follicles. It is unclear whether serum AMH levels reflect long-term effects of GnRH agonist therapy on reproductive function in patients with central precocious puberty (CPP).

Objectives

This study was aimed to evaluate

1) whether serum AMH and inhibin B levels are affected in girls with CPP

2) whether gonadotropin suppression by GnRH agonist affects serum AMH and inhibin B levels

Methods

1. Study subjects
   1) CPP group (n=50)
      - 7≤ age < 9 yrs, Korean girls
      - Tanner breast stage: 2-3
   2) Control group
      - before treatment (control group I)
        : 7 ≤ age < 9 yrs, n=35
        age-matched healthy Korean girls
        Tanner breast stage I
      - after 12 months of GnRH agonist treatment (control group II)
        : ≤ age < 10 yrs, n=18
        age-matched healthy girls
        Tanner stage : I

2. Methods

1) The GnRH stimulation test was conducted in CPP group.

2) All subjects were treated with GnRH agonists (GnRHa) every 4 weeks.

3) Anthropometry
   - height, weight, BMI

4) Hormone assays
   - blood sampling: at baseline (0), at 6 and 12 months after treatment
   - serum AMH, inhibin B levels
     : Gen II ELIZA kit

Results

Table 1. Basal characteristics of subjects

	Before treatment			After 12 months of treatment		
	CPP	Control (I)	*P*-value	CPP	Control (II)	*P*-value
Number	50	35		50	18	
Age (yr)	8.4±0.5	8.2±0.5	0.07	9.4±0.4	9.5±0.3	0.27
Bone age (yr)	10.5±0.7	-	-	11.5±0.6	-	-
Height (cm)	134.9±5.1	125.2±4.9	<0.001	141.8±4.8	133.4±4.5	<0.001
Height SDS	1.2±0.9	-0.3±0.7	<0.001	1.3±0.7	-0.1±0.7	<0.001
Weight (kg)	34.4±5.8	25.5±3.5	<0.001	40.2±6.2	29.3±4.8	<0.001
Weight SDS	1.2±0.8	-0.2±0.8	<0.001	1.4±0.7	-0.3±0.8	<0.001
BMI (kg/m²)	18.8±2.4	16.2±1.7	<0.001	19.3±3.2	16.4±2.4	<0.001
Tanner stage	II-III 31 III 19	I	-	II-III 23 III 27	I	-
Basal LH (IU/L)	1.31±0.9	-	-	0.9±0.6	-	-
Peak LH (IU/L)	12.4±8.9	-	-	-	-	-
Basal FSH (IU/L)	3.3±1.8	-	-	1.2±0.7	-	-
Peak FSH (IU/L)	17.4±6.6	-	-	-	-	-

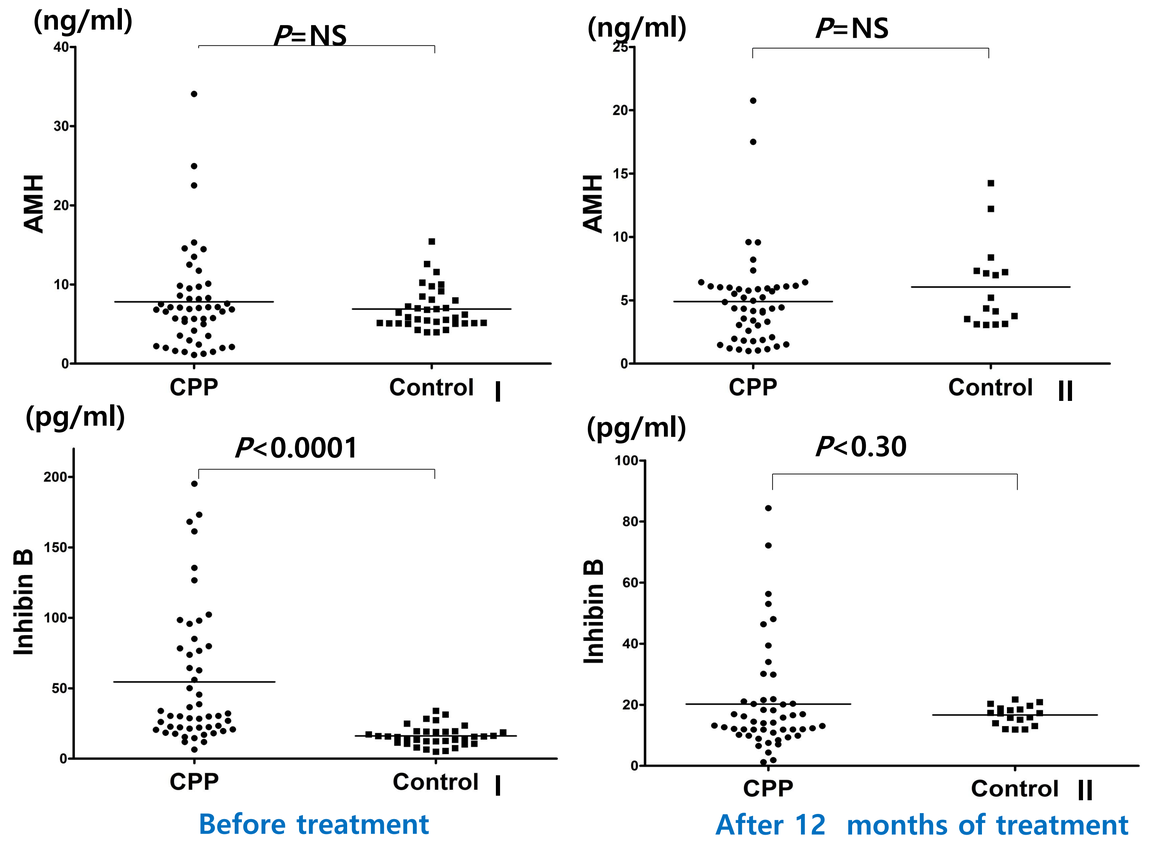

Fig 1. Comparison of serum AMH and inhibin B levels between CPP and control groups before and after treatment

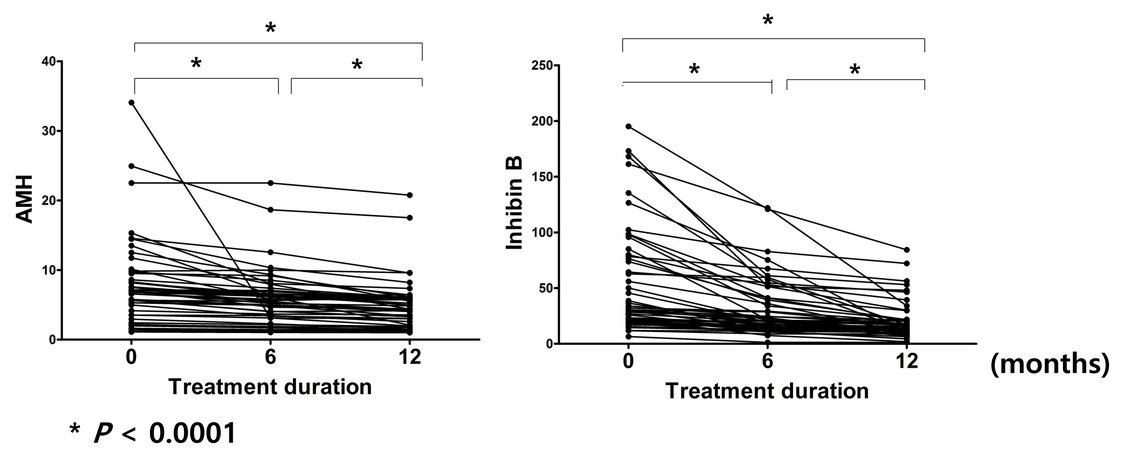

Fig 2. Changes of serum AMH and inhibin B levels before and during GnRHa treatment

Table 2. Correlation between AMH, inhibin B and other variables

	Before treatment				After 6 months of GnRHa treatment			
	AMH		Inhibin B		AMH		Inhibin B	
	r	*P*-value	*r*	*P*-value	*r*	*P*-value	*r*	*P*-value
Basal LH	-0.18	0.21	-0.15	0.29	-0.09	0.51	0.34	0.02
Peak LH	0.05	0.72	0.14	0.31	0.05	0.72	0.20	0.15
Basal FSH	-0.10	0.47	-0.02	0.88	0.05	0.73	0.07	0.58
Peak FSH	-0.25	0.09	0.09	0.53	0.14	0.30	0.28	0.04
E2	0.29	0.06	-0.08	0.57	0.23	0.10	-0.09	0.54

Conclusion

1. The result that a decrease of inhibin B levels was dependent on peak FSH levels during treatment suggests that ovarian inhibin B production is regulated by gonadotropin stimulation.
2. Our result demonstrated that the suppression of serum AMH levels during GnRHa treatment occurred independent of gonadotropin levels. This finding suggests that AMH suppression during treatment is mediated by a direct effect of GnRHa on granulosa cell expression of AMH or an indirect effect of GnRHa on the dynamics of the follicle pool, not by a direct effect of FSH.

Disclosure of conflict of interest

None to declare

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