THE SIGNIFICANCE OF GONADOTROPIN RELEASING HORMONE STIMULATION TEST, LEPTIN, AND PELVIC ULTRASOUND FINDINGS FOR DIFFERENTIATING IDIOPATHIC CENTRAL PRECOCIOUS PUBERTY FROM PREMATURE TELARCHE

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Aims

We aimed to investigate the differences of serum leptin,and gonadotropin hormone levels on gonadotropin releasing hormone (GnRH) stimulation test, and pelvic ultrasound (US) findings between girls with idiopathic central precocious puberty (ICPP) and premature thelarche (PT). Additionally, we aimed to determine correlations between leptin levels and other parameters.

Subjects and methods

Thirty nine girls who had breast budding before the age of 8 years and 19 healthy age-matched girls without breast development constituted the prepubertal group. Subjects with any additional conditions that might affect puberty onset (hypothyroidism, growth hormone deficiency, and congenital adrenal hyperplasia) were excluded from the analysis. Clinical features of McCune-Albright syndrome were not present in any of the patients. Additionally, none of the patients had known exposure to exogenous androgens or estrogens.

In all subjects, anthropometric measurements, left hand and wrist radiography for bone age, and pelvic ultrasonography were performed, as well as basal plasma levels of luteinizing hormone (LH), follicle stimulating hormone (FSH), and estradiol measurements. After clinical, laboratory and hormonal evaluations, subjects were divided into the following 3 groups: 1) prepubertal group (n=19), 2) ICPP group (n=17), and 3) PT group (n=22).

A GnRH stimulation test was performed for diagnosis of ICPP in girls with breast budding. All participants underwent anthropometric and bone age assessment and pelvic ultrasound. Basal gonadotropin and leptin levels were evaluated in all participants.ICPP was defined as the onset of breast development before the age of 8 years in girls and a pubertal response to exogenous GnRH (intravenous injection of 100 µg gonadorelin) with a peak LH level above 5 IU/L (16). PT was defined as isolated breast development before the age of 8 years and a prepubertal response to exogenous GnRH (intravenous injection of 100 µg gonadorelin) with a peak LH level below 5 IU/L. Since girls with breast development who were 8 to 8.5 years of age were included in the ICPP and PT groups, age-matched girls were selected for the prepubertal group.Body mass index (BMI) was calculated by dividing the weight in kilograms (kg) by the height in meters squared (m^2). Standard deviation scores (SDS) for height, weight, and BMI were calculated according to local standards.The Kruskal-Wallis test, Mann-Whitney *U* test, and/ or Pearson's or Spearman's correlation analysis were used for statistical evaluations.

Results

Age, anthropometric characteristics, basal levels of gonadotropins and estradiol, and bone age of the ICPP, PT, and prepubertal groups are presented in Table 1. Significantly higher weight SDS of the ICPP group was found than those of PT and prepubertal groups (p=0.022, 0.007 and p=0.05, 0.032, respectively). Basal levels of FSH and LH and bone age in the ICPP group were also significantly higher than those in the PT and prepubertal groups (p<0.05).

No significant difference was found in leptin levels among girls with ICPP, PT and prepubertal healthy peers (p>0.05). Although significant greater ovarian volumes in girls with ICPP and PT were found compared to prepubertal girls, there was no significant difference in ovarian volumes between girls with ICPP and PT. Girls with ICCP revealed a significantly greater endometrial thickness than other groups (0.001).

Significantly higher LH levels at 30 and 60 min in the GnRH test were found in girls with ICPP compared to girls with PT (p=0.001). There was no difference in baseline levels of LH in the GnRH test between girls with ICCP and PT (p=0.08). There was positive correlation between leptin levels and body weight in all subjects. Leptin was strongly correlated with estradiol in girls with ICCP (r:0.725, p<0.01).

Table 1. Age, anthropometric characteristics, and basal levels of gonadotropins and estradiol in the study groups

	Groups			
Parameters	**ICPP (n=17)**	**PT (n=22)**	**Pre-pubertal (n=19)**	**P**
Age (years)	7.8±0.6	7.03±1.14	7.13±1.8	0.09
Height SDS	0.62±1.0	0.24±0.95	-0.18±1.3	0.109
Weight SDS	0.60±1.0	-0.03±1.0	-0.42±1.2	0.028*
BMI SDS	1.19±1.3	0.47±1.0	0.38±1.6	0.097
LH levels (mIU/mL)	0.65±0.7	0.31±0.3	0.24±0.6	0.029*
FSH levels (mIU/mL)	3.54±2.0	2.28±1.32	1.7±0.8	0.006*
Estradiol levels (pg/mL)	28.29±12.5	23.0±6.8	22.3±5.2	0.44

*p≤0.05 was considered statistically significant. SDS: standard deviation scores, BMI: body mass index; LH: luteinizing hormone; FSH: follicle stimulating hormone.

Table 2. Bone age, findings of pelvic USG and leptin levels in the study groups.

	Groups			
Parameters	**ICPP (n=17)**	**PT (n=22)**	**Pre-pubertal (n=19)**	**P**
Bone age (years)	9.4±1.75	7.02±1.64	7.76±1.68	0.01*
Right ovarium volume (cc)	1.47±0.79	1.26±1.03	0.72±0.61	0.03*
Left ovarium volume (cc)	1.57±1.16	1.11±0.85	0.65±0.36	0.01*
Endometrium thickness (cm)	1.26±0.62	0.13±0.35	0.05±0.22	0.001*
Leptin levels (ng/ml)	4.05±4.77	3.11±6.0	3.92±6.62	0.511

Conclusion

Our results indicate that leptin level does not change in girls at the same age according to onset of puberty. This result suggests that leptin doesn't act as the critical metabolic signal initiating puberty. In pubertal girls, leptin is positively correlated with estradiol level and body weight. Increase in leptin levels closely paralleled increase in body weight and estradiol levels in early puberty. These results indicate that leptin might have a direct effect on the gonads in early puberty.

A blood sample obtained at 30 min in the GnRH stimulation test may be adequate for the differentiating between ICPP and PT. An ovarian volume assessment is a useful examination. However, it seems not to differentiate ICPP from PT. Endometrial thickness may be a useful parameter for the diagnosis of central precocious puberty.