Urinary bisphenol A and its relation with kisspeptin in girls with idiopathic central puberty precocious and premature thelarche

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Introduction and objective: Endocrine disruptors cause harmful effects to human body through various exposure routes. These chemicals mainly appear to interfere with the endocrine or hormone systems. Bisphenol A (BPA) is known as an endocrine disruptor with an estrogenic effect and it is supposed that it may have a role on development of precocious puberty (PP). Kisspeptin, a hypothalamic peptide, is a neuromodulator of GnRH and it has a big role on regulation of the onset of puberty. In this study we investigated the BPA levels in girls with PP and premature thelarche (PT) and its relation with kisspeptin levels.

Methodes: Twenty-eight girls with CPP (between 6.38-8.40 years of age), twenty-eight girls with PT (between 5.41-8.12 years of age) and twenty-two prepubertal girls (between 6.00-8.80 years of age) as a control group were enrolled to the study. The girls, who had a breast development before the age of 8, underwent a detailed physical and laboratory examination including anthropometric measurements, pubertal staging, direct radiography of left hand and wrist, pelvic ultrasonography, GnRH stimulating test and imaging with magnetic resonance of brain and pituitary gland to reveal any organic pathology. Among them, the girls with accelerated bone age (which was assessed using Greulich and Pyle atlas) more than 1 year than their chronological age and who had a peak LH levels more than 5 IU/ml during intravenous GnRH stimulating test were included in CPP group and the girls who had a close bone age to their chronological age and who had a peak LH levels less than 5 IU/ml during intravenous GnRH stimulating test were included in PT group. In control group, no girls had a breast development or pubic hair. Urinary BPA and serum kisspeptin levels were compared in groups. Bivariate correlations were performed to evaluate the relation of BPA with kisspeptin and estradiol.

Results: The comparison of the clinical and laboratory features of the CPP, PT and control groups were shown in Table 1. The Mann-Whitney U tests revealed that the girls with CPP had higher basal serum LH, FSH, E2 levels and bone age than both PT and control groups. The serum kisspeptin levels were observed highest in CPP groups. The Mann-Whitney demonstrated that, the kisspeptin levels between CPP and control groups were statistically different (p:0.008). However, regarding kisspeptin levels, the differences were statistically significant neither between CPP and PT groups (p:0.179) nor PT and control groups (p:0.172).

The bivariate correlation analyses revealed no relationship of BPA with kisspeptin (r:0.185, p:0.102), basal LH (r:-0.166, p:0.145), basal FSH (r:0.003, p:0.983), peak LH (r:-0.162, p:0.220), peak FSH (r: 0.042, p: 0.753), E2 (r: -0.115, p: 0.331) and age (r:-0.045, p:0.694).

Table 1. Physical and laboratory characteristics of groups

	Group PP (N=28)	Group PT N=28)	Group control (N=22)	p
Age at admission (years)	7,64 (6.38-8.40)	7.13 (5.41-8.12)	7.63 (6.00-8.80)	0.007
Height z-score	0.77 (-0.97-2.75)	0.71 (-1.23-2.01)	-0.42 (-1.22-1.99)	0.002
BMI z-score	0.62 (-0.96-2.27)	1.08 (-1.14-2.03)	0.63 (-1.58-1.74)	0.070
Basal LH	0.330 (0.001-6.040)	0.070 (0.001-0.300)	0.01 (0.001-0.010)	<0.001
Basal FSH	3.89 (0.28-10.26)	1.70 (0.34-4.16)	1.87 (0.19-5.48)	<0.001
Estradiol	21.02 (11.80-68.34)	11.80 (5.27-26.08)	12.1 (5.00-27.90)	<0.001
Bone age (years)	10.0 (6.50-11.0)	8.00 (5.5-9.0)	8.0 (6.0-9.0)	<0.001
BPA (mcg/gr creatinine)	5.3 (0.0-56,0)	4.95 (0.0-0.70)	4.13 (0.70-31.16)	0.471
Kisspeptin (pg/ml)	306.56 (23.69-926.15)	262.18 (37.67-790.59)	157.62 (22.54-650.41)	0.031

PP: Precocious puberty, PT: Premature thelarche, BMI: body mass index, LH: luteinizing hormone, FSH: Follicle stimulating hormone, BPA: Bisphenol A

Conclusion: The BPA levels did not differentiate between groups and it seems that exposed amount of BPA in daily life has no effect on kisspeptin levels in girls with CPP and PT.

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