A case-control study of exposure to bisphenol-A and phthalates in girls with early onset of puberty

A. Deodati[1], G. Bottaro[1], S. Tait[2], F. Maranghi[2], L. Busani[2], C. La Rocca[2], R. Tassinari[2], V. Della Latta[3], F.Carli[3]. Buzzigoli[3], A.Gastaldelli[3], S. Cianfarani[1;4]

1. Dipartimento Pediatrico Universitario Ospedaliero, 'Bambino Gesù' Children's Hospital–University of Rome Tor Vergata, Rome, Italy
2. Department of Food Safety, Nutrition, Veterinary Public HealthIstituto Superiore di Sanità Rome, Italy
3. Institute of Clinical Physiology, CNR, Pisa,Italy
4. Department of Women's and Children's Health, Karolinska Institutet, Stoccolma, Svezia

INTRODUCTION

Over the past several decades, the age of pubertal onset in girls has shifted downward worldwide. A number of factors including genetic predisposition, psychosocial and socio-economic conditions, diet and ethnicity may have contributed to this phenomenon. The widespread presence of endocrine disrupting chemicals (EDCs), in particular estrogen-like EDCs during critical windows of development, may play role in this trend. Epidemiological and animal studies have shown that the exposure to bisphenol-A (BPA) and phthalates (DEHP) may be associated with early onset of puberty in girls.

OBJECTIVE

To investigate the association between the exposure to BPA, DEHP's metabolites with alterations of puberty in girls with idiopathic premature thelarche (IPT) or idiopathic central precocious puberty (ICPP).

METHODS

A case-control study was conducted in 97 girls, subdivided into 3 groups: 31 girls with ICPP (mean age 7.3±0.07), 39 with IPT (mean age 6.56 ± 1.6) and 27 controls (mean age 6.67± 2.3).

Urine BPA and DEHP metabolites were measured by gas chromatography and high-performance liquid chromatography, coupled with mass spectrometer (LC–MS/MS). Metabolic and hormone levels were assessed. Individual environmental exposure was evaluated through "ad hoc" questionnaires providing data on life styles, diet and other potential determinants of exposure.

RESULTS

- Our findings showed the presence of measurable concentrations of the EDCs in all girls, including the control group. These data demonstrate the widespread exposure to these compounds

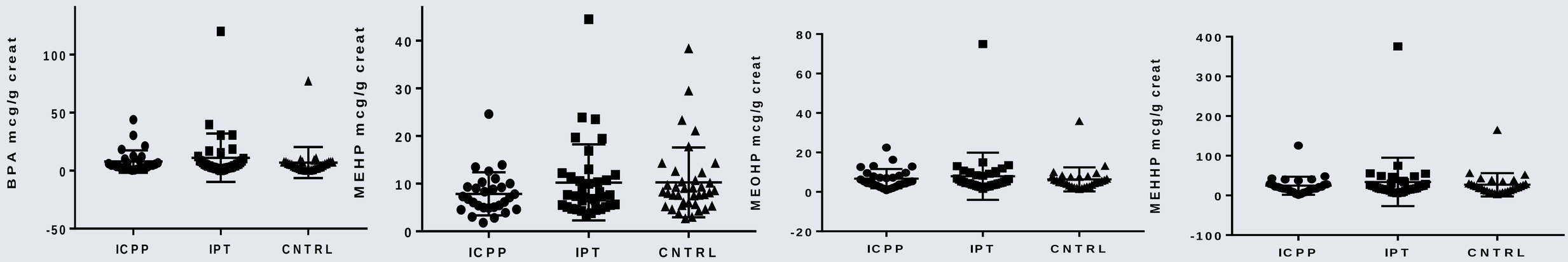
- ICPP and IPT girls showed no significantly difference in EDCs levels neither compared to controls nor compared to each other

- In IPT group, a significant positive correlation between DEHP metabolite levels and FSH peak response to GnRH stimulation test was found, suggesting that phthalates could potentially cause self-limited breast development without progression to true precocious puberty ($p<0.05$). Furthermore, in IPT group significant negative correlations were found between DEHP metabolites and KISS serum levels and Anti-mullerian hormone ($r= -0.4$, $p= 0.01$; $r= -0.37$, $p= 0.02$, respectively).

- Higher levels of phthalates in children were associated with: i) use of disposable plastic (plates, glasses, etc.); ii) use of plastic containers in microwave; iii) playing many hours a day with plastic toys including electronic toys. The use of disposable plastic (plates, glasses, etc.) was also associated with higher levels of BPA.

	ICPP n=31 *(mean ±SD)*	IPT n=39 *(mean ±SD)*	CNTRL n=27 *(mean ±SD)*	p
Peak LH (mUI/ml)	14.8±10.6	2.35±0.96	-	<0.001**
Peak FSH (mUI/ml)	16.24±4.71	16.0.4±6.32	-	NS
LH peak/FSH peak ratio	0.95±0.66	0.15±0.05	-	<0.001**
17-β estradiol (pg/ml)	23.7±11.7	17±6.25	-	<0.05**
Anti-Mullerian Hormone (AMH) ng/mL	0.53 (0.18-0.87)	0.95 (0.58-1.32)	2.39 (1.71-15.39)	<0.05**,***
Kisspeptin (pg/mL)	39 (39-934.29)	316.07 (39-837.24)	39 (39-687.5)	<0.001**, ***
Urinary BPA (mcg/g creat)	6.99 (2.9-17.54)	6.52 (3.27-13.87)	5.38 (3.11-864)	NS
Σ Phthalates (mcg/g creat)	30.01 (22.94-45.76)	31.94 (23.96-53.58)	33.33 (20.34-50.1)	NS

▪P<0.05 was considered significant; - = Not done; NS = Not Significant
▪ *ICPP vs PT and CNTRL; **ICPP vs PT;***IPT vs CNTRL



CONCLUSIONS

Our findings suggest that concentrations of urine BPA and DEHP's metabolites are measurable in all girls. The use of plastic exposes girls to a higher contamination from both BPA and DEHP. These results warrant further experimental and prospective clinical investigations to clarify the potential role of EDCs in modulating the timing of puberty in girls.

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Annalisa Deodati
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